



Hilton Waikoloa  
Village



Waikoloa, HI



March 3-8, 2018

*North American  
Neuro-Ophthalmology Society*

1975-2018



# SCHEDULE-AT-A-GLANCE

## SATURDAY, MARCH 3

		LOCATION
8:00 am - 12:00 pm	NANOS Board Meeting .....	Kona 1
2:00 pm - 7:30 pm	Registration/Help Desk .....	Grand Promenade
3:00 pm - 6:00 pm	Botulinum Course .....	Grand Ballroom
6:00 pm - 7:30 pm	Opening Reception (All are welcome!) .....	Lanai

## SUNDAY, MARCH 4

6:00 am - 6:45 am	Yoga Class (pre-registration required, SOLD OUT) .....	Ocean View Terrace
6:30 am - 7:30 am	Breakfast .....	Grand Promenade
6:30 am - 5:30 pm	Registration/Help Desk .....	Grand Promenade
6:30 am - 3:00 pm	Exhibits .....	Grand Promenade
7:30 am - 5:30 pm	FRANK B. WALSH SESSION .....	Grand Ballroom
9:30 am - 10:00 am	Coffee Break .....	Grand Promenade
12:00 pm - 12:30 pm	Fellowship Director's Meeting .....	Kona 1
12:30 pm - 1:00 pm	Fellowship Committee Meeting .....	Kona 1
12:05 pm - 1:00 pm	Lunch (provided) .....	Grand Promenade
1:00 pm - 3:00 pm	Poster Session I: Clinical Highlights in Neuro-Ophthalmology .....	Kohala Ballroom
3:00 pm - 3:30 pm	Business Meeting .....	Grand Ballroom
5:45 pm - 6:15 pm	Frank B. Walsh Committee Meeting .....	Kona 1
6:00 pm - 7:00 pm	Members-in-Training Reception .....	Lanai
Evening	Dinner on your own	

## MONDAY, MARCH 5

6:00 am - 6:45 am	Yoga Class (pre-registration required, SOLD OUT) .....	Ocean View Terrace
6:30 am - 7:30 am	Breakfast .....	Grand Promenade
6:30 am - 5:30 pm	Registration/Help Desk .....	Grand Promenade
6:30 am - 2:30 pm	Exhibits .....	Grand Promenade
6:30 am - 7:30 am	NOVEL Editorial Board/Curriculum Committee Meeting .....	Kona 1
7:30 am - 9:30 am	Literature Review .....	Grand Ballroom
9:30 am - 10:00 am	Coffee Break Supported by EMD Serono .....	Grand Promenade
10:00 am - 11:00 am	Hot Topics: What's New in the Orbit? .....	Grand Ballroom
11:00 am - 12:00 pm	Hot Topics: What's New in the Optic Nerve? .....	Grand Ballroom
12:00 pm - 12:15 pm	JNO Update .....	Grand Ballroom
12:15 pm - 12:20 pm	NOVEL Update .....	Grand Ballroom
12:20 pm - 12:30 pm	Additional Meeting Announcements .....	Grand Ballroom
12:30 pm - 12:50 pm	Impact and Advantages of the New Specialty Designation .....	Grand Ballroom
12:30 pm - 1:00 pm	International Relations Committee Meeting .....	Kona 1
12:50 pm - 2:00 pm	Lunch Break (on your own)	
2:00 pm - 4:00 pm	Forum for New and Future Neuro-Ophthalmologists .....	Kona 4-5
2:00 pm - 4:00 pm	Neurodegenerative Diseases and Neuro-Ophthalmology .....	Grand Ballroom
4:00 pm - 5:00 pm	Free Hour	
5:00 pm - 7:00 pm	SCIENTIFIC PLATFORM PRESENTATIONS: SESSION I .....	Grand Ballroom

## TUESDAY, MARCH 6

6:00 am - 6:45 am	Yoga Class (pre-registration required, SOLD OUT) .....	Ocean View Terrace
6:30 am - 7:30 am	Breakfast .....	Grand Promenade
6:30 am - 7:30 am	JNO Editorial Board Meeting .....	Kona 1
6:30 am - 12:00 pm	Registration/Help Desk .....	Grand Promenade
6:30 am - 10:30 am	Exhibits .....	Grand Promenade
7:30 am - 9:30 am	SCIENTIFIC PLATFORM PRESENTATIONS: SESSION II .....	Grand Ballroom
9:30 am - 10:00 am	Coffee Break .....	Grand Promenade
10:00 am - 12:00 pm	SCIENTIFIC PLATFORM PRESENTATIONS: SESSION III .....	Grand Ballroom
12:00 pm - 6:00 pm	Free Afternoon	
12:30 pm - 4:30 pm	Optional Excursions (prior registration required) .....	Varied
6:00 pm - 9:30 pm	Poster Session II: Scientific Advancements in Neuro-Ophthalmology .....	Kohala Ballroom
9:00 pm - 10:00 pm	Abstract Committee Meeting .....	Kona 1

## WEDNESDAY, MARCH 7

6:30 am - 7:30 am	Breakfast .....	Grand Promenade
6:30 am - 7:30 am	CME Committee Meeting .....	Kona 1
6:30 am - 5:30 pm	Registration/Help Desk .....	Grand Promenade
7:30 am - 9:30 am	VZV in Neuro-Ophthalmology .....	Grand Ballroom
9:30 am - 10:00 am	Coffee Break .....	Grand Promenade
10:00 am - 11:15 am	Is IIH Idiopathic? .....	Grand Ballroom
11:20 am - 12:00 pm	Jacobson Lecture .....	Grand Ballroom
12:00 pm - 1:30 pm	Lunch (on your own)	
12:15 pm - 1:30 pm	Research Committee Meeting Luncheon .....	Kona 1
1:30 pm - 2:30 pm	We Are WIN .....	Kona 4-5
2:30 pm - 4:00 pm	International Infections: What Lies Beyond the Eye .....	Grand Ballroom
4:00 pm - 4:15 pm	Short Transition Break .....	Grand Promenade
4:15 pm - 5:45 pm	Generation Next: Genetic Testing for Inherited Neuro-Ophthalmic Diseases .....	Grand Ballroom
6:30 pm - 12:00 am	Annual NANOS Reception and Banquet .....	Lanai/Grand Promenade/Kohala

## THURSDAY, MARCH 8

6:30 am - 7:30 am	Breakfast .....	Grand Promenade
6:30 am - 12:00 pm	Registration/Help Desk .....	Grand Promenade
7:30 am - 9:30 am	Unexplained Visual Loss: You have some nerve sending me that patient! .....	Grand Ballroom
9:30 am - 10:00 am	Coffee Break .....	Grand Promenade
10:00 am - 12:00 pm	Eye Movement: Diagnostic & Treatment Pearls for the Daily Clinic .....	Grand Ballroom



North American Neuro-Ophthalmology Society

# 44th Annual Meeting

March 3– March 8, 2018

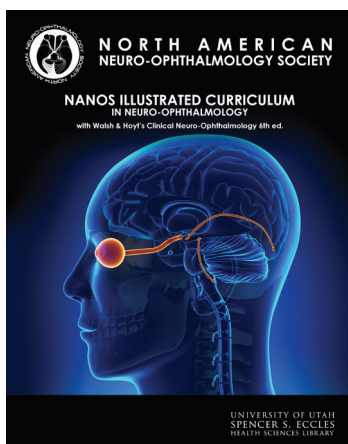
The Hilton Waikoloa Village • The Big Island of Hawaii

## TABLE OF CONTENTS

I.	General Information.....	1
II.	NANOS Donors.....	3
III.	Supporters and Exhibitors.....	4
IV.	Speaker and Moderator List.....	5
V.	Speaker and Planner Disclosure Information.....	7
VI.	Lectures and Abstracts.....	9
	Walsh Cases.....	11
	Poster Session I: Clinical Highlights in Neuro-Ophthalmology.....	45
	Literature Review.....	195
	Hot Topics.....	235
	a. What’s New in the Orbit? .....	235
	b. What’s New in the Optic Nerve? .....	252
	Scientific Platform: Session I.....	257
	Scientific Platform: Session II.....	267
	Scientific Platform: Session III.....	276
	Poster Session II: Scientific Advancements in Neuro-Ophthalmology.....	285
	VZV in Neuro-Ophthalmology.....	433
	Is IIH Idiopathic? .....	450
	Unexplained Visual Loss: You have some nerve sending me that patient! .....	459
	Eye Movement: Diagnostic and Treatment Pearls for the Daily Clinic.....	475
VII.	Tours / Social Events.....	482

Please note that the following resources no longer appear in the NANOS syllabus and are available on the NANOS website: Committee listing, historical Board information, past faculty and meeting archives, award recognition, bylaws, and the membership directory.

# NANOS' Illustrated Curriculum for Neuro-Ophthalmology



This resource is exclusive to STAT!Ref, combining two elements: *NANOS' Illustrated Curriculum* and *Walsh & Hoyt's Clinical Neuro-Ophthalmology*. *NANOS' Illustrated Curriculum* is a collection of resources used to supplement learning by residents, fellows, educators, researchers and clinicians. *Walsh & Hoyt's* is the foundational text. Please see below for more details.

## NANOS Illustrated Curriculum

The NANOS Illustrated Curriculum (IC) was produced by the Neuro-ophthalmology Virtual Education Library (NOVEL) team at the Spencer S. Eccles Health Sciences Library at the University of Utah in collaboration with the North American Neuro-ophthalmology Society (NANOS). Materials added to the IC have been peer-reviewed.

This outline is based on the NANOS Curriculum which was developed by the NANOS Curriculum Committee, approved by the NANOS Executive Board, and published in the *Journal of Neuro-Ophthalmology*. Valerie Biousse, MD, was Chair of the Curriculum Committee during the development and publication of this Curriculum.

The content was licensed for STAT!Ref to support residencies and fellowships, fill curriculum gaps, and increase the availability of resources in neuro-ophthalmology and related disciplines.

## Walsh & Hoyt's Clinical Neuro-Ophthalmology

*Walsh & Hoyt's Clinical Neuro-Ophthalmology* is the most comprehensive reference on diagnosis and treatment of neuro-ophthalmologic diseases. Coverage includes major updates on genetics of diseases, new diagnostic techniques, and the newest treatment options.

- Volume 1 covers the visual sensory system, the autonomic nervous system, the ocular motor system, the eyelid, facial pain and headache, and nonorganic disease.
- Volume 2 covers tumors, the phacomatoses, and vascular disease.
- Volume 3 covers degenerative, metabolic, infectious, inflammatory, and demyelinating diseases.

*Walsh & Hoyt's Clinical Neuro-Ophthalmology* is a Doody's Core title.

**Ask your librarian about adding this valuable resource.**



North American Neuro-Ophthalmology Society

# 44th Annual Meeting

March 3– March 8, 2018

The Hilton Waikoloa Village • The Big Island of Hawaii

## MISSION STATEMENT

The North American Neuro-Ophthalmology Society (NANOS) is dedicated to the achievement of excellence in patient care through the support and promotion of education, communication, research, and the practice of neuro-ophthalmology.

## TARGET AUDIENCE

Neurologists, Ophthalmologists, Neuro-Ophthalmologists, physicians and other health care professionals who have a special interest in Neuro-Ophthalmology, or have fellowship training in Neuro-Ophthalmology and are members of the North American Neuro-Ophthalmology Society.

## POLICY ON COMMERCIAL SUPPORT AND FACULTY DISCLOSURE

The North American Neuro-Ophthalmology Society maintains a policy on the use of commercial support which ensures that all educational activities sponsored by NANOS provide in-depth presentations that are fair, independent, and scientifically rigorous. To this end, all speakers and planners are required to complete a "Disclosure Form". This information is included in this syllabus and/or may be supplemented by announcements by moderators.

## DISCLOSURE OF UNLABELED/UNAPPROVED USES

This educational program may include references to the use of products for indications not approved by the FDA. Areas of unapproved uses will be disclosed at each presentation. Opinions expressed with regard to unapproved uses of products are solely those of the faculty and are not endorsed by the North American Neuro-Ophthalmology Society or any other manufacturers of pharmaceuticals.

## ACCREDITATION

The North American Neuro-Ophthalmology Society is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

## CREDIT DESIGNATION

NANOS designates this live activity for a maximum of 32 AMA PR Category 1 Credits. Physicians should claim only the credit commensurate with the extent of their participation.



North American Neuro-Ophthalmology Society

# 44th Annual Meeting

March 3– March 8, 2018

The Hilton Waikoloa Village • The Big Island of Hawaii

## NANOS CME MISSION STATEMENT

The North American Neuro-Ophthalmology Society (NANOS) is dedicated to achieving excellence in care of patients with neuro-ophthalmic diseases by the support and promotion of education, research, and the practice of Neuro-Ophthalmology.

The Society's main CME activity is its annual scientific meeting. The educational meeting includes seminars, workshops, hands-on training, platform presentations, and discussion of cases and best practices in neuro-ophthalmic research, basic science, and patient care.

The CME goal of the meeting is to improve the attendees' knowledge of Neuro-Ophthalmology basic science and practice. More specifically, the goals of the meeting are:

1) To achieve competence in neuro-ophthalmic diagnosis, treatment, and teaching; 2) To improve performance as physicians, teachers, and researchers by using information presented at the meeting to change clinical practice and instruction; and 3) To review research projects to investigate questions raised by the meeting's scientific sessions.

The expected results of our CME program, and of our annual meeting as its main CME activity, is that our members will increase their knowledge of Neuro-Ophthalmology and improve their skill in its practice, so that they can apply that knowledge and skill to enhance their performance and competence as clinical Neuro-Ophthalmologists, research Neuro-Ophthalmologists, and teachers of Neuro-Ophthalmology.

NANOS uses multiple data sources to measure the impact of its educational activities on learners and on the discipline of Neuro-Ophthalmology. These sources translate professionals' need into current practices to improve competence in knowledge, diagnosis, performance, and treatment of neuro-ophthalmic diseases.

*Approved by the NANOS CME Subcommittee and NANOS Board of Directors as of 2018*



North American Neuro-Ophthalmology Society

## 44th Annual Meeting

March 3– March 8, 2018

The Hilton Waikoloa Village • The Big Island of Hawaii

### **NANOS would like to thank the following individuals for their generous donations: (February 17, 2017-January 18, 2018)**

#### **Silver \$10,000 - \$19,999**

Preston C. Calvert, MD

#### **Glaser Society \$5,000 - \$9,999**

John B. Selhorst, MD

#### **Wirschafter Club \$1,000 - \$2,499**

Valerie Biousse, MD

Thomas Carlow, MD

Sophia Chung, MD

Robert B. Daroff, MD

Kathleen Digre, MD

Edmond J. FitzGibbon, MD

Deborah Friedman, MD

Leah Levi, MD

Patricia McNussen, MD

Nancy Newman, MD

Peter Quiros, MD

Prem Subramanian, MD, PhD

Sharon Tow, MD

Alan Weingarden, MD

#### **Averbuch-Heller Guild \$500 - \$999**

John Keltner, MD

Melissa Ko, MD

Andrew Lee, MD

Valerie Purvin, MD

William Shults, MD

Seema Sundaram, MD

Thomas R. Wolf, MD

#### **Hedges Club \$250 - \$499**

David Bellows, MD

Julie Falardeau, MD

Larry Frohman, MD

Lynn Gordon, MD, PhD

Steven Hamilton, MD

Nick Hogan, MD

Ruth and Robert Lesser

Mark Malton, MD

Thomas Mizen, MD

Mark Moster, MD

Vivian Rismondo-Stankovich, MD

Richard Selbst, MD

Barry Skarf, MD

Floyd A. Warren, MD

#### **Zaret Society \$100 - \$249**

Rachid Aouchiche, MD

Dan Boghen, MD

John Chen, MD

Ivy Dreizin, MD

Thomas Hedges, MD

David Katz, MD

Jacqueline Leavitt, MD

Collin McClelland, MD

Fayçal Mokhtari, MD

Kimberly Wings, MD

#### **Contributors \$1- \$99**

Steven Grosser, MD

Richard Sogg, MD



North American Neuro-Ophthalmology Society

## 44th Annual Meeting

March 3– March 8, 2018

The Hilton Waikoloa Village • The Big Island of Hawaii

**NANOS would like to thank the following Supporters and Exhibitors for their financial support of these activities.**

### **2018 Supporters:**

Quark Pharmaceuticals, Inc - \$10,000

EMD Serono- \$10,000

Biogen - \$5,000

Merz - \$5,000

### **2018 Exhibitors:**

Benign Essential Blepharospasm Research Foundation, Inc.

Biogen

Diagnosys LLC

Fresnel Prism and Lens Co.

Genentech

Good-Lite Company

Heidelberg Engineering

Konan Medical USA

LHON Project at UMDF

Mayo Medical Laboratories

Merz

Novartis Pharmaceuticals

Quark Pharmaceuticals, Inc.

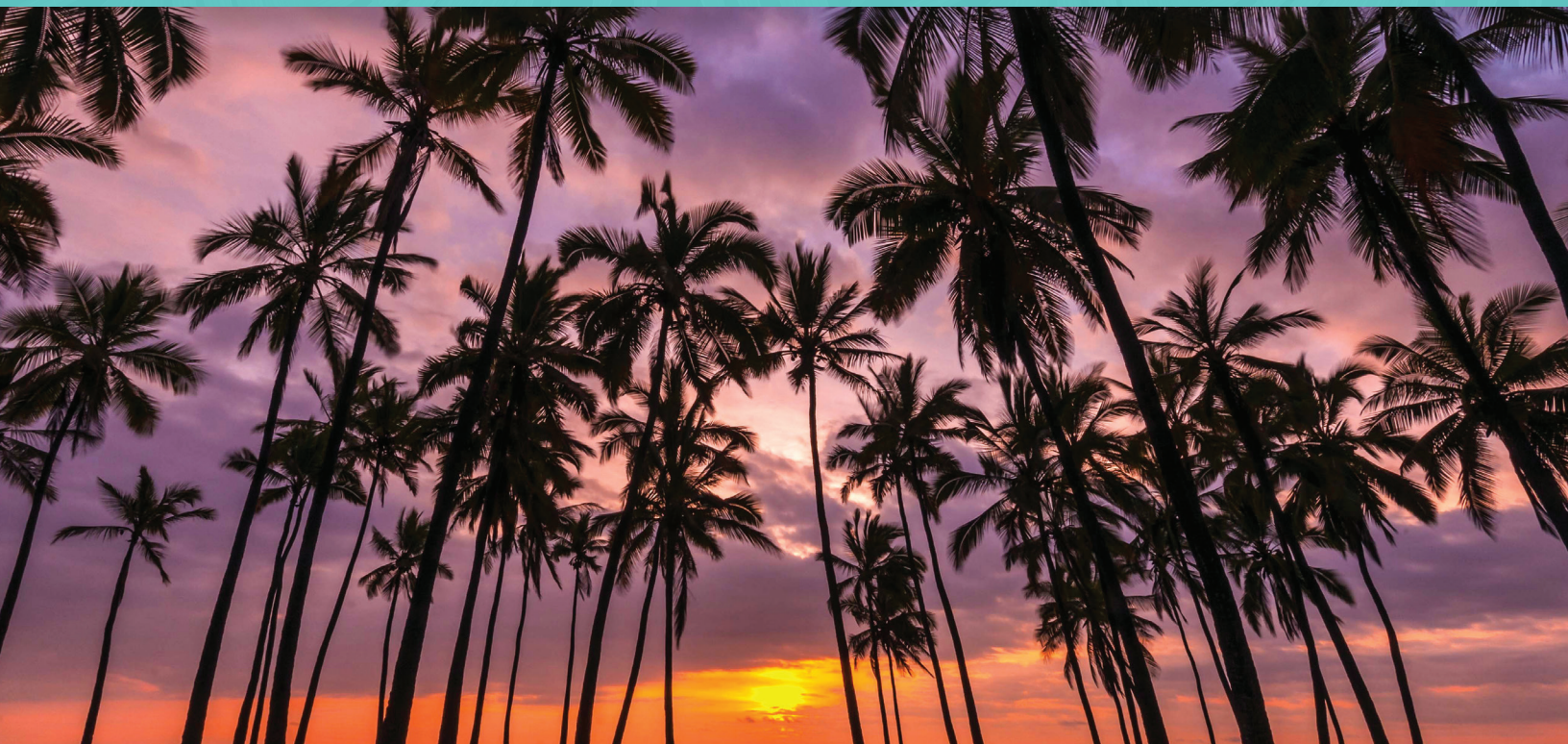
Sanofi-Genzyme

TS Medical USA

Wolters Kluwer



# NANOS 2018 SPEAKERS AND MODERATORS



**Marie D. Acierno, MD**

Mayo Clinic  
Scottsdale, AZ

**Geoffrey Aguirre, MD, PhD**

University of Pennsylvania  
Philadelphia, PA

**Laura Balcer, MD, MSCE**

NYU School of Medicine  
New York, NY

**Susan Benes, MD**

The Eye Center of Columbus and Buena  
Vista, Colorado  
Buena Vista, CO

**Jeffrey Bennett, MD, PhD**

University of Colorado School of Medicine  
Aurora, CO

**Joseph Berger, MD, FACP, FAAN, FANA**

University of Pennsylvania  
Philadelphia, PA

**M. Tariq Bhatti, MD**

Duke Eye Center and Duke University  
Medical Center  
Durham, NC

**Valérie Biousse, MD**

Emory University School of Medicine  
Emory Eye Center  
Atlanta, GA

**Mark Borchert, MD**

Children's Hospital Los Angeles  
Los Angeles, CA

**François-Xavier Borruat, MD**

University of Lausanne, Jules-Gonin Eye  
Hospital  
Lausanne, Switzerland

**Swarupsinh Chavda, MD**

University Hospital Birmingham  
Halesowen, United Kingdom

**John Chen, MD, PhD**

Mayo Clinic  
Rochester, MN

**Wayne T. Cornblath, MD**

University of Michigan  
Ann Arbor, MI

**Helen Danesh-Meyer, MD, PhD**

University of Auckland  
Auckland, New Zealand

**Joseph Demer, MD, PhD**

Stein Eye Institute, UCLA  
Los Angeles, CA

**Marc Dinkin, MD**

Weill Cornell Medical College, NY  
Presbyterian Hospital  
New York, NY

**Charles Eberhart, MD, PhD**

Johns Hopkins University  
Baltimore, MD

**Julie Falardeau, MD**

Casey Eye Institute, Oregon Health and  
Science University  
Portland, OR

**Steven Feldon, MD, MBA**

University of Rochester School of Medicine  
& Dentistry, Flaum Eye Institute  
Rochester, NY

**Edmond FitzGibbon, MD**

National Eye Institute, NIH  
Bethesda, MD

**Courtney Francis, MD**

University of Washington  
Seattle, WA

**Clare Fraser, MBBS, FRANZCO**

University of Sydney  
Sydney, Australia

**Benjamin Frishberg, MD**

The Neurology Center  
Carlsbad, CA

**James Garrity, MD**

Mayo Clinic  
Rochester, MN

**Dan Gold, DO**

Johns Hopkins University  
Baltimore, MD

**Nitza Goldenberg-Cohen, MD**

Bnai Zion Medical Center,  
Israel Institute of Technology  
Haifa, Israel

**Lynn Gordon, MD, PhD**

Stein Eye Institute, UCLA  
Los Angeles, CA

**Jonathan C. Horton, MD, PhD**

Program in Neuroscience, UCSF  
San Francisco, CA

**Hong Jiang, MD, PhD**

Bascom Palmer Eye Institute  
Miami, FL

**Sachin Kedar, MBBS, MD**

University of Nebraska Medical Center  
Omaha, NE

**Greg Kosmorsky, DO**

Cleveland Clinic  
Cleveland, OH

**Howard Krauss, MD**

Pacific Neuroscience Institute  
Santa Monica, CA

**Kaushal Kulkarni, MD**

Sharp Rees-Stealy Medical Group  
San Diego, CA

**Kevin Lai, MD**

Circle City Neuro-Ophthalmology  
Indianapolis, IN

**Leonard Levin, MD, PhD, FRCSC**

McGill University  
Montreal, Canada

**Y. Joyce Liao, MD, PhD**

Stanford University  
Stanford, CA

**Grant Liu, MD**

Perelman School of Medicine at the  
University of Pennsylvania  
Philadelphia, PA

**Tim Matthews, FRCS, FRCOphth**

Birmingham Neuro-ophthalmology,  
University Hospital Birmingham  
Birmingham, United Kingdom

**Dan Milea, MD, PhD**

Singapore National Eye Centre  
Singapore

**Neil Miller, MD, FACS**

Johns Hopkins University  
Baltimore, MD

**Ellen Mitchell, MD**

University of Pittsburgh Medical Center  
Pittsburgh, PA

**Susan Mollan, MBChB, FRCOphth**

Institute of Metabolism and Systems  
Research, University of Birmingham;  
Queen Elizabeth Hospital  
Birmingham, United Kingdom

**Heather Moss, MD, PhD**

Stanford University  
Stanford, CA

**Cameron Parsa, MD**

Quinze-Vingts National Eye Hospital/  
Université Libre de Bruxelles  
Paris, France

**Victoria S. Pelak, MD**

University of Colorado School of Medicine/  
Rocky Mountain Lions Eye Institute  
Aurora, CO

**John Pula, MD**

NorthShore University Health System  
Glenview, IL

**Michael Repka, MD**

Johns Hopkins University  
Baltimore, MD

**Joseph Rizzo, MD**

Massachusetts Eye and Ear/Harvard  
Medical School  
Boston, MA

**Janet Rucker, MD**

New York University School of Medicine  
New York, NY

**Alfredo Sadun MD, PhD**

Doheny Eye Institute/UCLA  
Los Angeles, CA

**Veeral Shah MD, PhD**

Texas Children's Hospital/Baylor College of  
Medicine  
Houston, TX

**Alexandra Sinclair, MBChB, MRCP, PhD**

University of Birmingham  
Birmingham, United Kingdom

**Steven F. Stasheff, MD, PhD**

Children's National Health System &  
National Eye Institute  
Washington, DC

**Prem S. Subramanian MD, PhD**

University of Colorado School of Medicine  
Aurora, CO

**Jody Tanabe, MD**

University of Colorado  
Denver, CO

**Matthew Thurtell, MBBS, MSc, FRACP**

University of Iowa  
Iowa City, IA

**Caroline Tilikete, MD, PhD**

Hospices Civils de Lyon,  
University Lyon I, Centre de Recherche  
en Neurosciences de Lyon  
Bron, France

**Jonathan Trobe, MD**

University of Michigan  
Ann Arbor, MI

**Roger Turbin, MD, FACS**

Rutgers New Jersey Medical School  
Newark, NJ

**Gregory Van Stavern, MD**

Washington University in St. Louis  
St. Louis, MO

**Michael Wall, MD**

University of Iowa  
Iowa City, IA

**Billi Wallace, MD**

Harry S. Truman Veterans Memorial Hospital  
Smithville, MO

**Judith Warner, MD**

University of Utah  
Salt Lake City, UT

**David Zee, MD**

Johns Hopkins Hospital  
Baltimore, MD



North American Neuro-Ophthalmology Society

# 44th Annual Meeting

March 3– March 8, 2018

The Hilton Waikoloa Village • The Big Island of Hawaii

## CME ACTIVITIES FACULTY AND PLANNER DISCLOSURE STATEMENTS

*It is the policy of the North American Neuro-Ophthalmology Society (NANOS) in accordance with the Accreditation Council for Continuing Medical Education (ACCME) to ensure independence, balanced view of therapeutic options, objectivity, scientific rigor, and integrity in all of its continuing education activities.*

*Anyone engaged in content development, planning, or presenting must disclose any relevant financial relationships. The ACCME defines relevant financial relationships as those in which an individual (including the individual's spouse/partner) in the last 12 months: 1) has had a personal financial relationship in any amount with a commercial interest. A commercial interest is any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients; and who 2) also has the opportunity to affect the content of CME activity about the products or services of that commercial interest.*

*Disclosure information is reviewed by the NANOS Scientific Program Committee and CME Committee in advance in order to manage and resolve any possible conflicts of interest prior to the activity. Conflict resolution must be resolved through any of the following options: Peer review for evidence-based content by experts, provide faculty with alternate topic, independent review to ensure evidence supports recommendations, and/or attestation to non-commercial content. If a conflict cannot be resolved, the individual is not allowed to participate in any aspect of the program or planning.*

*Below is the list of relevant financial disclosures for the faculty and planners. Please note that platform presenter disclosure information is listed in the syllabus at the end of each abstract.*

First Name	Last Name	Designations	Commercial Interest	What was received	For what Role
Jeffrey	Bennett (F)	MD, PhD	MedImmune	Consulting Fees	Consulting, Clinical trial Steering Committee
			Novartis	Research funding	Independent Researcher
			Clene Neuroscience	Consulting fees	Consulting, Advisory Panel
			EMD Serono	Consulting fees	Advisory Panel
			Genzyme	Consulting fees	Advisory Panel
Valerie	Biousse (F)	MD	Gensight Biologics	Honorarium	Consultant
Marc	Dinkin (F)	MD	Serenity Medical	Consulting Fees	Consultant
			American Austrian Foundation	Travel Reimbursement	Teacher
			Goldman Ismail and Baum, LLP	Consulting Fees	Expert Testimony
Sachin	Kedar (F)	MBBS, MD	QUARK pharmaceuticals	Research support	Site PI
Leonard	Levin (F)	MD, PhD, FRCSC	Aerie	Consulting fees	Consulting
			Inotek	Consulting fees	Consulting
			Quark	Consulting fees	Consulting
			GSK	Consulting fees	Consulting
			Teva	Consulting fees	Consulting
Tim	Matthews (F)	FRCS FRCOphth	Novartis	Honorarium	Teacher/Speaker
Nancy J.	Newman (F)	MD	GenSight Biologics	Consulting fees	Consultant
			Santhera Pharmaceuticals	Consulting fees	Consultant
			Quark Pharmaceuticals	Consulting fees	Member Data Safety and Monitoring Board
			Bayer	Consulting fees	Consultant
Victoria	Pelak (F)	MD	UpToDate, Inc	Royalties for written work	Author

Caroline	Tilikete (F)	MD, PhD	Novartis	Consulting Fees	Animation of neuro-ophthalmology training
			Teva	Travelship for meetings and consulting fees	Speaker/Consultant
			Santhera	Travelship for meetings	Attend European Neuro-ophthalmology Society
Roger	Turbin (F)	MD FACS	Biogen	Stock Holder	
			Merck	Stock Holder	
			Quark	Site Fee	Site Co-investigator
			Titan	Stock Holder	
Laura	Balcer (P)	MD, MSCE	Biogen	Consulting Fees	Designer
Byron	Lam (P)	MD	Spark	Advisory Board	Consultant
			Quark	Research Funding	Clinical Trial Site PI
			AGTC	Research Funding	Clinical Trial Site PI
			NightstaRx	Research Funding	Clinical Trial Site PI
Mark	Moster (P)	MD	Gensight	Research Support	Investigator
Beau	Bruce (P)	MD, PhD	MedImmune	Consulting Fees	DSMB
			Bayer	Consulting Fees	Expert Testimony/Consultant
			Various Law Firms	Fees	Medicolegal
Prem	Subramanian (P)	MD, PhD	Quark Pharmaceuticals	Honorarium, grant funds	Speaker, Research Support
			Santhera Inc.	Study Support	Research
Larry	Frohman (P)	MD	site PI Quark NAION study	Clinical Study Grant	PI at Site

Key: P = Planner; F = Faculty

All other faculty and planners have declared that they have no relevant financial disclosures.

# PROGRAM

## SATURDAY, MARCH 3

8:00 am - 12:00 pm	<b>NANOS Board Meeting</b> .....	<b>Kona 1</b>
2:00 pm - 7:30 pm	<b>Registration/Help Desk</b> .....	<b>Grand Promenade</b>
3:00 pm - 6:00 pm	<b>Botulinum Course</b> .....	<b>Grand Ballroom</b>

*Chairs: Cameron Parsa, MD, Benjamin Frishberg, MD*

Botulinum toxins are now integral to the clinical care of patients in the Neuro-Ophthalmology Clinic. In this 2 hour course we will compare and contrast the currently available agents namely; Xeomin (incobotulinum toxin), Botox (onabotulinum toxin), Myobloc (rimabotulinum toxin) and Dysport (abobotulinum toxin). We will discuss the relevant on and off label use of neurotoxins for treatment of blepharospasm, hemifacial spasm, chronic migraine and strabismus. There will be further discussion about off label uses that may be helpful for neuro-ophthalmologists. There will be demonstrations of proper dilution techniques as well as injection techniques. We will also discuss reimbursement issues.

Upon completion of this course, participants should be able to: 1) recognize the four available toxins and their current FDA approved uses 2) define the safety and tolerability of the botulinum toxins 3) identify basic techniques for the treatment of chronic migraine, hemifacial spasm and blepharospasm 4) define the use of botulinum toxin in the treatment of chronic migraine, trigeminal neuralgia and other uncommon headache disorders.

6:00 pm - 7:30 pm	<b>Opening Reception (All are welcome!)</b> .....	<b>Lanai</b>
-------------------	---	--------------

## SUNDAY, MARCH 4

6:00 am - 6:45 am	<b>Yoga Class (Pre-registration required, SOLD OUT)</b> .....	<b>Ocean View Terrace</b>
6:30 am - 7:30 am	<b>Breakfast</b> .....	<b>Grand Promenade</b>
6:30 am - 5:30 pm	<b>Registration/Help Desk</b> .....	<b>Grand Promenade</b>
6:30 am - 3:00 pm	<b>Exhibits</b> .....	<b>Grand Promenade</b>
7:30 am - 5:20 pm	<b>FRANK B. WALSH SESSION</b> .....	<b>Grand Ballroom</b>

*Chair: Prem S. Subramanian, MD, PhD*  
*Walsh Committee: Jeffrey Bennett, MD, PhD, Victoria Pelak, MD*  
*Neuroradiologist: Jody Tanabe, MD*  
*Neuropathologist: Charles Eberhart, MD, PhD*

This symposium is designed to present a wide variety of neuro-ophthalmic cases to an audience of physicians with varying neuroscience backgrounds who have a common intellectual interest in the broad range of conditions that impact the human visual pathways and ocular motor systems.

The format is a clinicopathologic conference. Clinical cases will be presented by neuro-ophthalmologists with comments by a neuroradiologist, neuropathologist and other selected experts. Autopsy, surgical and laboratory pathology, and neuroimaging will help illustrate clinical points. Cases will be discussed from clinical, anatomic, radiologic and pathologic aspects with emphasis on diagnosis, pathophysiology and management. Audience participation is encouraged.

Upon completion of this course, participants should be able to: 1) recognize the varied presentations of neuro-ophthalmic disease; 2) correlate the anatomic localization and histopathologic appearance with the clinical presentations 3) effectively use radiologic procedures in diagnosis; 4) recognize both the value and limitations of neuropathology; and 5) discuss newly described diseases and their connection to neuro-ophthalmology.

7:30 am - 9:30 am	<b>Frank B. Walsh Session I</b> .....	<b>Grand Ballroom</b>
-------------------	---------------------------------------	-----------------------

*Moderators: Grant Liu, MD, Courtney Francis, MD*

7:30 am - 7:45 am	<b>Welcome &amp; Introduction to App</b>
7:45 am - 8:05 am	<b>Whipping Up a New Flavor, Meagan Seay, DO</b>
8:05 am - 8:25 am	<b>Lumps and Bumps, Wayne Tie, MD</b>
8:25 am - 8:45 am	<b>Gee...What's Causing that Pap? Susan Mollan, MBChB, FRCOphth</b>
8:45 am - 9:05 am	<b>A Tough Nut to Crack! Lauren Maloley, MD</b>
9:05 am - 9:25 am	<b>What Don't You See? James O'Brien, MD</b>
9:25 am - 9:30 am	<b>Morning Wrap Up</b>

# PROGRAM

## SUNDAY, MARCH 4 *(Continued)*

<b>9:30 am - 10:00 am</b>	<b>Coffee Break</b> .....	<b>Grand Promenade</b>
<b>10:00 am - 12:05 pm</b>	<b>Frank B. Walsh Session II</b> .....	<b>Grand Ballroom</b>
	<i>Moderators: Janet Rucker, MD, Laura Balcer, MD, MSCE</i>	
10:00 am - 10:20 am	<b>One Peak is Worth Twenty Finesses</b> , <i>Steven Newman, MD</i>	
10:20 am - 10:40 am	<b>Testing the Hypophysis</b> , <i>Alberto Distefano, MD</i>	
10:40 am - 11:00 am	<b>A Sad Story</b> , <i>Jason Peragallo, MD</i>	
11:00 am - 11:20 am	<b>A Giant (Cell) Mistake</b> , <i>Behzad Mansouri, MD, PhD, FRCPC</i>	
11:20 am - 11:40 am	<b>When the Problem Becomes the Solution</b> , <i>Ari Shemesh, MD</i>	
11:40 am - 12:00 pm	<b>Triple Take</b> , <i>Johanna Beebe, MD</i>	
12:00 pm - 12:05 pm	<b>Afternoon Wrap Up</b>	
<b>12:05 pm - 1:00 pm</b>	<b>Lunch (Provided by NANOS)</b> .....	<b>Grand Promenade</b>
<b>12:00 pm - 12:30 pm</b>	<b>Fellowship Directors Meeting</b> .....	<b>Kona 1</b>
<b>12:30 pm - 1:00 pm</b>	<b>Fellowship Committee Meeting</b> .....	<b>Kona 1</b>
<b>1:00 pm - 3:00 pm</b>	<b>Poster Session I: Clinical Highlights in Neuro-Ophthalmology</b> .....	<b>Kohala Ballroom</b>
	<b>Authors will be standing by their posters during the following times:</b>	
	<b>Odd-Numbered Posters:</b> 1:15 pm - 2:00 pm	
	<b>Even-Numbered Posters:</b> 2:00 pm - 2:45 pm	
<b>3:00 pm - 3:30 pm</b>	<b>Business Meeting</b> .....	<b>Grand Ballroom</b>
<b>3:30 pm - 5:20 pm</b>	<b>Frank B. Walsh Session III</b> .....	<b>Grand Ballroom</b>
	<i>Moderators: Susan Benes, MD, Wayne Cornblath, MD</i>	
3:30 pm - 3:50 pm	<b>Coming to a Rapid Conclusion</b> , <i>Leanne Stunkel, MD</i>	
3:50 pm - 4:10 pm	<b>It's Always Been Like That</b> , <i>Eric D. Gaier, MD, PhD</i>	
4:10 pm - 4:30 pm	<b>Light at the End of the Tunnel</b> , <i>Noel Chan, MD, FRCSEd</i>	
4:30 pm - 4:50 pm	<b>A Can of Worms</b> , <i>Ali G. Hamedani, MD, MHS</i>	
4:50 pm - 5:10 pm	<b>Cold Fever</b> , <i>Shannon Beres, MD</i>	
5:10 pm - 5:20 pm	<b>Closing Remarks</b>	
<b>5:45 pm - 6:15 pm</b>	<b>Frank B. Walsh Committee Meeting</b> .....	<b>Kona 1</b>
<b>6:00 pm - 7:00 pm</b>	<b>Members-in-Training Reception</b> .....	<b>Lanai</b>
	<i>(All students, residents and fellows-in-training are encouraged to attend.)</i>	
<b>Evening</b>	<b>Dinner on your own</b>	

**Frank B. Walsh Session I**  
**Moderators: Courtney Francis, MD & Grant Liu, MD**

		<u>Page</u>
7:45 AM – 8:05 AM	<b>Whipping Up a New Flavor</b> Meagan Seay, DO	<b>13</b>
8:05 AM – 8:25 AM	<b>Lumps and Bumps</b> Wayne Tie, MD	<b>15</b>
8:25 AM – 8:45 AM	<b>Gee...What's causing that pap?</b> Susan P. Mollan, MBChB, FRCOphth	<b>17</b>
8:45 AM – 9:05 AM	<b>A Tough Nut to Crack!</b> Lauren Maloley, MD	<b>19</b>
9:05 AM – 9:25 AM	<b>What Don't You See?</b> James C. O'Brien, MD	<b>21</b>

**Frank B. Walsh Session II**  
**Moderators: Laura Balcer, MD, MSCE & Janet Rucker, MD**

10:00 AM – 10:20 AM	<b>One Peak is Worth Twenty Finesses</b> Steven A. Newman, MD	<b>23</b>
10:20 AM – 10:40 AM	<b>Testing the Hypophysis</b> Alberto G. Distefano, MD	<b>25</b>
10:40 AM – 11:00 AM	<b>A Sad Story</b> Jason H. Peragallo, MD	<b>27</b>
11:00 AM – 11:20 AM	<b>A Giant (Cell) Mistake</b> Behzad Mansouri, MD, PhD, FRCPC	<b>29</b>
11:20 AM – 11:40 AM	<b>When The Problem Becomes The Solution</b> Ari Shemesh, MD	<b>31</b>
11:40 AM – 12:00 PM	<b>Triple Take</b> Johanna D. Beebe, MD	<b>33</b>

**Frank B. Walsh Session III**  
**Moderators: Susan Benes, MD & Wayne T. Cornblath, MD**

		<u>Page</u>
3:30 PM – 3:50 PM	<b>Coming to a Rapid Conclusion</b> Leanne Stunkel, MD	<b>35</b>
3:50 PM – 4:10 PM	<b>It's Always Been Like That</b> Eric D. Gaier, MD PhD	<b>37</b>
4:10 PM – 4:30 PM	<b>Light at the End of the Tunnel?</b> Noel Chan, MD, FRCSEd	<b>39</b>
4:30 PM – 4:50 PM	<b>A Can of Worms</b> Ali G. Hamedani, MD, MHS	<b>41</b>
4:50 PM – 5:10 PM	<b>Cold Fever</b> Shannon J. Beres, MD	<b>43</b>



## **“Whipping Up a New Flavor”**

Meagan Seay<sup>1</sup>, Tory Johnson<sup>2</sup>, Benjamin Larman<sup>2</sup>, Avindra Nath<sup>3</sup>, Myoung-Hwa Lee<sup>3</sup>, Janet Rucker<sup>1</sup>, Jonathan Howard<sup>1</sup>, Ilya Kister<sup>1</sup>, Matija Snuderl<sup>1</sup>, Laura Balcer<sup>1</sup>, Steven Galetta<sup>1</sup>, **Steven Galetta**

<sup>1</sup>*New York University School of Medicine, New York, New York, USA*, <sup>2</sup>*Johns Hopkins University, Baltimore, USA*, <sup>3</sup>*National Institute of Neurological Disorders and Stroke, Bethesda, USA*,

### **History & Exam**

A 43-year old Indian man presented with two years of progressive gait imbalance, dysarthria, and cognitive decline. Neurological exam revealed supranuclear gaze palsy with impaired downgaze and loss of OKN quick phases, impaired horizontal pursuit, ideomotor apraxia, facial and arm dystonia, foot and toe chorea, hyperreflexia, retropulsion, and gait ataxia. Neuropsychological testing suggested subcortical dementia. Brain MRI revealed multiple nonenhancing, confluent, periventricular and juxtacortical T2 hyperintensities and severe atrophy with a hummingbird sign. A paraneoplastic panel, GAD antibodies, and NMDA antibodies were negative. CSF revealed normal white blood cell count, elevated protein (81), markedly elevated IgG index and synthesis, 15 oligoclonal bands, negative paraneoplastic panel, negative Whipple’s DNA PCR, and negative CJD testing (negative tau quantity and ambiguous 14-3-3, not supporting the diagnosis of CJD). Body PET-CT and EEG were normal. Treatment with high dose steroids, IVIG, and plasmapheresis were ineffective. Brain biopsy showed a hypercellular cortex and white matter with spongiosis, gliosis, and diffuse inflammatory parenchymal and meningeal infiltrate. The cortex contained numerous inflammatory nodules with neuronophagia. Overall the features were nonspecific and most suggestive of an inflammatory meningoencephalitis, such as a viral infection, autoimmune disease, or paraneoplastic process. The patient continued to deteriorate and died from sepsis six years after disease onset. An autopsy was performed.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## “Whipping Up a New Flavor”

*Answer*

### **Final Diagnosis**

Chronic Dengue Encephalitis

### **Summary of Case**

The patient’s specimens were submitted for further research investigation. He was found to have autoantibodies in the CSF to microtubule associated proteins, which were likely not disease mediating, and to Dengue virus. Dengue virus was present throughout the brain as identified by quantitative PCR, RNAscope, immunohistochemistry, and sequencing. Sequencing identified the virus to be from a strain that was in circulation at least three years prior to the autopsy, during the time the patient visited India. A diagnosis of chronic Dengue encephalitis was made. This is a novel finding, as there are no reported cases of chronic Dengue encephalitis in the literature, to our knowledge. Dengue is a single-stranded RNA virus of the flavivirus genus, endemic to southern and southeast Asia. Classically, encephalopathy in Dengue infections was thought to be secondary to metabolic derangements, resulting from liver failure, shock, and coagulopathy. However, Dengue virus has been shown to directly infect the CNS in acute presentations. Though there is no report of chronic CNS infection from Dengue, other flaviviruses, including WNV, have been found to persist in the brain months after infection.

### **Struggle/Dilemma of the Clinical Presentation Description**

1. The patient presented with clinical and radiographic features characteristic of progressive supranuclear palsy, though his age, rapidity of progression, and white matter changes made this unlikely; 2. The presentation mimicked CNS Whipple’s disease; 3. He had very high inflammatory markers in the CNS, though extensive testing for antibodies was negative; 4. The initial biopsy indicated viral infection, however, chronic viral encephalitis is rare and no specific etiology was identified until autopsy.

**Keywords:** Progressive supranuclear palsy, infection, Whipple’s disease, Neuro-degenerative disease

### **References**

Kutiyal A, Malik C, Hyanki G. Dengue Haemorrhagic Encephalitis: Rare Case Report with Review of Literature. *Journal of Clinical and Diagnostic Research*. 11(7):10-12, 2017  
Varatharaj A. Encephalitis in the clinical spectrum of Dengue infection. *Neurology India*. 58(4):585-591, 2010  
Solomon R, Dung N, Vaughn D, et al. Neurological manifestations of Dengue infection. *Lancet*. 355(9209):1053-1059, 2000  
Penn R, Guarner J, Sejvar J, et al. Persistent neuroinvasive West Nile virus infection in an immunocompromised patient. *Clinical Infectious Diseases*. 42(5):680-683, 2006

## **“Lumps and Bumps”**

Wayne Tie<sup>1</sup>, Martha Schatz<sup>2</sup>, Martha P. Schatz, MD

<sup>1</sup>University of Texas Health Science Center San Antonio, San Antonio, Texas, USA, <sup>2</sup>UTHSCSA, San Antonio, Texas, USA

### **History & Exam**

History and Exam A 37 year-old man with no PMH presented with bilateral painful red eyes and progressive proptosis for several months. He noted the increasing protrusion of both eyes, but only complained of recent onset of pain in both eyes over the last four days. He also developed worsening blurry vision in both eyes with the left eye worse than right. Patient had no personal or family history of cancer. His initial examination showed right eye VA of 20/50 and left eye 20/100 at near and massive proptosis and lagophthalmos of both eyes with near complete corneal exposure bilaterally. On his external exam, the patient also had bilaterally enlarged lacrimal glands and submandibular lymph nodes as well as diffusely restricted extraocular movements. He presented with IOPs of 24 OD and 39 OS, reactive pupils, and a 1+ RAPD OS. Patient's ophthalmic exam showed diffusely dry corneal epithelium of both eyes and an inferior corneal ulcer of the left eye. Fundus exam was otherwise unremarkable. Initial CBC and CMP on presentation were only remarkable for mildly elevated WBC. CT orbit w/o contrast demonstrated massive enlargement of the bilateral lateral rectus, inferior oblique, and medial rectus muscles along with severe proptosis and straightening of the optic nerve. Patient was admitted to the hospital for inpatient evaluation.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## **“Lumps and Bumps”**

*Answer*

### **Final Diagnosis**

IgG4 associated infiltrative disease

### **Summary of Case**

Case Summary with References: Due to his exam findings, patient underwent lateral canthotomies and suture tarsorrhaphies of both eyes. He was started on broad spectrum topical antibiotic coverage for his left corneal ulcer secondary to exposure keratopathy. Given concern for systemic malignancy, patient underwent additional CT head, chest, and abdomen/pelvis, which showed additional mass lesions of the submandibular glands, parotid glands, adenoids, pterygopalatine fossa, foramen rotundum and cavernous sinus. His body CTs reported pulmonary nodules in the lung parenchyma, hilar lymphadenopathy, retroperitoneal fibrosis, and soft tissue thickening about the ureters with hydronephrosis. Differential diagnosis included lymphoma, sarcoidosis, thyroid orbitopathy, orbital pseudotumor, and IgG4 disease. Patient had normal TSH, normal ACE level, but significantly elevated serum IgG4 levels. Initial needle biopsy and flow cytometry of submandibular gland cells were inconclusive. Due to high suspicion for IgG4 disease, patient subsequently underwent surgical biopsy of his submandibular gland, which demonstrated “dense storiform fibrosis with lymphoplasmacytic infiltrate.” Immunohistochemical stain of the tissue block showed an increase in IgG4 positive plasma cells. Patient was started on intravenous methylprednisolone 125mg q6hours for 3 days for his optic neuropathy and empiric treatment for IgG4 disease and later transitioned to 125mg daily. Due to the extent of his systemic involvement, IV steroids were chosen in place of oral prednisone. His left eye corneal scraping revealed infiltrate of *Moraxella catarrhalis*, which was successfully treated with moxifloxacin and tobramycin. His IOP stabilized after the canthotomy procedures and was controlled by dorzolamide/timolol. After 7 days, patient had significantly improved proptosis and regression of his EOM and glandular enlargement. His VA improved to 20/30 OD 20/40 OS, pupils without RAPD, and EOMs full. Patient was discharged on prednisone 100mg PO daily and plan for transition to rituximab.

### **Struggle/Dilemma of the Clinical Presentation Description**

There was a broad differential diagnosis on initial presentation: lymphoma, sarcoidosis, thyroid orbitopathy, orbital pseudo tumor, and IgG4 disease. The clinical appearance was dramatic with multi system involvement. However, tissue diagnosis was definitive.

**Keywords:** Myopathy

### **References**

None.

## **“Gee...What's Causing that Pap?”**

Susan Mollan<sup>1</sup>, Daniel White<sup>2</sup>, Santhosh Nagaraju<sup>2</sup>, Swarupsinh Chavda<sup>2</sup>, Tom Hayton<sup>2</sup>, Saiju Jacob<sup>2</sup>

<sup>1</sup>*Birmingham Neuro-Ophthalmology, Queen Elizabeth Hospital, Birmingham, United Kingdom,* <sup>2</sup>*University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom*

### **History & Exam**

A 36 year old woman presented with history of Myasthenia Gravis (MG) since the age of 18. She was known to have dry eyes and hypothyroidism. Past surgical history included a thymectomy (age 23 years). The MG had been difficult to control with past medications including corticosteroids, azathioprine, methotrexate and mycophenolate. Eighteen months prior to this presentation she was enrolled in a double blind placebo controlled trial with Eculizumab, a terminal complement inhibitor. She had required intravenous immunoglobulin (IV IG) as rescue therapy initially and went on to open label Eculizumab 9 months prior to this admission. She had subsequently developed Alopecia areata (no family history), followed by nummular dermatitis, and then Alopecia totalis. The decision was made to have a drug holiday. This precipitated a worsening of the MG requiring IV IG. She restarted Eculizumab and 3 weeks later developed swinging fevers, nausea and vomiting and generalised polyarthralgia. On admission her vision (6/5 OU) and colour vision were normal. She had longstanding symptomatic left limitation of abduction, with normal saccades. She had no relative afferent pupillary defect and enlarged blind spots on Humphrey visual field testing. Dilated examination showed bilateral papilloedema. There was no other cranial neuropathy. Blood tests on admission were normal, including inflammatory markers and three sets of blood cultures with no growth. Inflammatory antibody tests were normal, as was HIV and testing for Tuberculosis. Lumbar puncture opening pressure was 23 cm CSF, with raised protein (0.93g/dl), low CSF glucose compared to serum, a mononuclear pattern, oligoclonal bands in the CSF only and PCR for viral and bacterial factors were negative. Initial MRI imaging was normal. CT thorax, abdomen and pelvis was normal. FDG-PET imaging showed increased uptake along the spinal cord. Bone marrow biopsy was normal. A brain biopsy and one further diagnostic test was performed.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## “Gee...What's Causing that Pap?”

*Answer*

### **Final Diagnosis**

Autoimmune Glial Fibrillary Acidic Protein (GFAP) Astrocytopathy

### **Summary of Case**

Investigation and initial treatment was aimed at the differential diagnosis of an infectious aetiology, an inflammatory or aseptic meningitis and lymphoma. Brain biopsy showed a non-specific meningo-encephalitis. She was treated subsequently with corticosteroids, cyclophosphamide, mycophenolate, IV IG, plasma exchange, and rituximab. Initially she improved, but this was followed by progressive decline with quadriplegia and bilateral blindness; ventilator dependency and she succumbed to her illness. Her CSF was positive for an antibody directed against Glial Fibrillary Acidic Protein (GFAP) with a titre of 1:512 (normal range <1:2). This is a novel astrocytic autoantibody identified as a biomarker of a relapsing autoimmune meningoencephalomyelitis Co-Authors[1]. Transient serum antibodies have been described in traumatic brain injury, brain tumours, autism, lead exposed workers and diabetes mellitus. Autoimmune GFAP astrocytopathy has been characterized by the Mayo clinic series Co-Authors[2] with similar findings to our patient, who was young and female with a prodromal flu-like illness with co-existing autoimmune disorder of MG. Another small series has also expressed treatment difficult with poor response to immunosuppression Co-Authors[3], as experienced in this case.

### **Struggle/Dilemma of the Clinical Presentation Description**

The past medical history and history of immunosuppression this made it difficult to frame a short differential diagnosis. Her health fluctuated during the admission which in the absence of clear initial neuro-imaging and subsequent histopathology findings, made it challenging to reach the diagnosis.

**Keywords:** Papilledema, Meningo-encephalitis, Vision loss

### **References**

- 1 Fang B, McKeon A, Hinson SR, Kryzer TJ, Pittock SJ, et al. Autoimmune Glial Fibrillary Acidic Protein Astrocytopathy: A Novel Meningoencephalomyelitis JAMA Neurol, 73,1297-1307, 2016
- 2 Flanagan EP, Hinson SR, Lennon VA, Fang B, Aksamit AJ, et al. Glial Fibrillary Acidic Protein Immunoglobulin G as Biomarker of Autoimmune Astrocytopathy: Analysis of 102 Patients. Ann Neurol, 81, 298-309, 2017
- 3 Yang X, Liang J, Huang Q, Xu H, Gao C, et al. Treatment of Autoimmune Glial Fibrillary Acidic Protein Astrocytopathy: Follow-Up in 7 Cases. Neuroimmunomodulation, 24, 113-119, 2017

## **“A Tough Nut to Crack!”**

Lauren Maloley<sup>1</sup>, Sachin Kedar<sup>1</sup>, Deepta Ghate<sup>1</sup>, Dominick DiMaio<sup>1</sup>, Jason Helvey<sup>1</sup>, **Sachin Kedar**

<sup>1</sup>*University of Nebraska Medical Center, Omaha, Nebraska, USA*

### **History & Exam**

A 47-year-old previously healthy female was transferred to our facility when she developed left abducens nerve palsy during treatment of intractable sinusitis. Two weeks prior to presentation, she developed headache and sinus congestion. She was treated with amoxicillin-clavulanic acid and prednisone for acute sinusitis at a local urgent care facility. Her symptoms worsened and she was referred to an otolaryngologist who noted bloody material on nasal endoscopy and prescribed clindamycin and dexamethasone. The headache worsened and a week later, she developed blurred vision in the left eye. She was admitted to an outside facility and treated with intravenous levaquin and methylprednisolone. A maxillofacial and head CT was reported to show “complete opacification of bilateral sphenoid and right maxillary sinuses with mucosal thickening in the posterior ethmoid sinus and no intracranial abnormalities”. Nasal endoscopy demonstrated edematous turbinates and mucosanguineous drainage from the right sphenoid ostium; no nasopharyngeal masses were seen. Baseline labs were unremarkable except mild elevation of white cell count ( $13.3 \times 10^9$  cells/L) and C-reactive protein (20.6 mg/L). At transfer, neuro-ophthalmic examination included a visual acuity of 20/25 OU, left Horner’s syndrome and left esotropia with bilateral abduction deficits (worse left eye). Visual fields showed non-specific scatter. Fundus examination was normal. Corneal and facial sensations were intact. MRI brain and orbits showed a contrast enhancing sellar mass with extension superiorly to the hypothalamus, laterally into bilateral cavernous sinuses, anteriorly into the sphenoid sinus and inferiorly into the clivus. Treatment with broad-spectrum antibiotics—vancomycin, ceftriaxone and metronidazole was started. Extensive studies for autoimmune and infectious conditions (including fungal) were unremarkable. She underwent bilateral sphenoidotomy and right maxillary anastomy. Pathology showed nonspecific reactive changes and necrotic debris with negative cultures. A procedure was performed.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## “A Tough Nut to Crack!”

Answer

### Final Diagnosis

Nuclear protein of the testis (NUT) carcinoma

### Summary of Case

An excisional biopsy was performed using transnasal transphenoidal approach. Histopathology showed sheets of atypical epitheloid-appearing cells with extensive areas of necrosis and absence of glandular or squamous differentiation. The tumor cells had a high nuclear to cytoplasm ratio and small nucleoli. An extensive battery of immunohistochemistry staining was inconclusive and contradictory. Multiple epithelial and lymphoma immunostains were negative. A preliminary diagnosis of melanoma was suggested based on diffuse positive staining for SOX10. However, lack of staining for additional melanocytic markers including S100, HMB45, Melan A and MITF argued against that diagnosis. Conventional cytogenetics demonstrated a translocation involving 15q and 19p. Fluorescence in situ hybridization (FISH) studies were positive for fusion of the NUTM1 (15q14) and BRD4 (19p13.12) loci. Although the immunohistochemistry staining was unusual, the FISH studies and cytogenetics are diagnostic of a NUT (nuclear protein of the testis) carcinoma. PET-CT scan showed increased uptake of two cervical lymph nodes. She is currently undergoing treatment with radiation to the sella/sphenoid with concurrent chemotherapy (cisplatin and docetaxol). NUT carcinoma is an exceedingly rare malignancy with fewer than 100 reported cases. It is a poorly characterized squamous cell carcinoma, which arises in midline structures of the head and neck and thorax. The tumor is highly aggressive, with greater than 50% demonstrating metastasis (to lymph nodes and bones) at diagnosis. Diagnosis is made by the demonstration of a pathognomonic translocation of the NUTM1 gene on chromosome 15, most often to BRD4 gene on chromosome 19, forming a BRD4-NUT fusion oncogene on cytogenetic studies. Unfortunately, there is no established or effective treatment regimen and median survival remains between 6.7-9 months. Recent advances in understanding the molecular biology of NUT carcinoma have led to promising novel targeted therapies, such as histone deacetylase (HDAC) inhibitors or bromodomain (BRD) inhibitors which induce squamous differentiation.

### Struggle/Dilemma of the Clinical Presentation Description

Our patient, who was a healthy young adult, initially presented with mundane findings of “sinusitis” and was treated appropriately. No mass lesions were noted on initial CT imaging. A sellar mass was noted only after MRI was performed for neurological deficits. Lastly, the diagnosis of NUT carcinoma was challenging because it is an exceedingly rare malignancy without pathognomonic cytologic and histopathologic features. Cytogenetic studies showing the pathognomonic gene translocation is required for diagnosis.

**Keywords:** Horner's syndrome, Abducens Nerve Palsy, Skull base tumors, Sphenoid sinus

### References

- 1) Bair RJ, Chick JF, Chauhan NR, et al. Demystifying NUT midline carcinoma: radiologic and pathologic correlations of an aggressive malignancy. *AJR*. 2014;203(4): 391-399.
- 2) Duffalha SA, Aukla NA, Hasan S, et al. NUT midline carcinoma: a rare malignancy. *Cancer Control*. 2017;24(2): 202-206.
- 3) Edgar M, Caruso AM, Kim E, et al. NUT midline carcinoma of the nasal cavity. *Head Neck Pathol*. 2016;11: 389-392.
- 4) Hellquist H, French CA, Bishop JA, et al. NUT midline carcinoma of the larynx: an international series and review of the literature. *Histopathology*. 2017;70: 861-868.
- 5) Lemelle L, Pierro G, Freneaux P, et al. NUT carcinoma in children and adults: a multicenter retrospective study. *Pediatr Blood Cancer*. 2017;64(12): 1-9.
- 6) Sun H, McGuire MF, Zhang S, et al. NUT midline carcinoma: morphoproteomic characterization with genomic and therapeutic correlates. *Ann Clin Lab Sci*. 2015;45(6): 692-701.
- 7) Wasserman JK, Purgina B, Sekhon H, et al. The gross appearance of a NUT midline carcinoma. *Int J Surg Pathol*. 2016;24(1): 85-88.



## **“What Don't You See?”**

James O'Brien<sup>1</sup>, Bradley Farris, **Michael Siatkowski**

<sup>1</sup>*Dean McGee Eye Institute / The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA*

### **History & Exam**

A four-year old male presented for evaluation of abnormal eye movements and strabismus which had been present since approximately 6 weeks of age. He was previously diagnosed with nystagmus, ocular torticollis, and esotropia by another provider. An MRI of the brain was performed at approximately 4 weeks of age. The study was reportedly normal, but it was unavailable for our direct review. He underwent right medial rectus recession and right lateral rectus resection for esotropia at age 3. His parents reported exotropia following this strabismus surgery. His medical history otherwise included valve-sparing repair of Tetralogy of Fallot, repair of esophageal atresia, and tracheoesophageal fistula repair. Examination revealed uncorrected visual acuity of 20/200 OD and 20/100 OS. This was not improved by cycloplegic refraction: +2.00 +1.00 x70 OD and +2.00 +1.00 x105 OS. His pupillary exam and gross visual fields by confrontation were normal. His ocular motility revealed pendular nystagmus with predominantly horizontal waveforms but occasional super-imposed see-saw waveforms as well. He had A-pattern exotropia of 8, 15, and 25 prism diopters in up-, primary-, and down-gaze, respectively, with chin-down head posture. There was bilateral overdepression in adduction on motility testing. Anterior segment and dilated fundus examinations were normal bilaterally. A diagnostic test was ordered. (A video demonstrating his ocular motility will be shown)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## **“What Don't You See?”**

*Answer*

### **Final Diagnosis**

See-saw nystagmus secondary to Achromatopsia

### **Summary of Case**

This four-year old male presented with congenital see-saw and horizontal nystagmus. The see-saw component of his nystagmus prompted our investigation into para-sellar pathology. His prior neuroimaging was reportedly normal; however, this study was unavailable for direct review. Repeat MRI of the brain demonstrated achiasma. Achiasma is the congenital absence of the optic chiasm, which may be isolated or associated with other midline central nervous system abnormalities. The first description of mammalian achiasma and its association with ocular motor abnormalities, such as see-saw nystagmus and congenital nystagmus, was reported in the 1990s in a family of mutant Belgian sheepdogs. These observations later led to the association of these findings in humans, prompting analyses of the visual pathways in achiasmatic humans. The lack of crossing fibers at the chiasm results in representation of the entire visual field to each ipsilateral occipital cortex, as has been demonstrated by methods such as visual-evoked potential and functional MRI. Achiasmatic patients described in the literature generally have very poor stereoacuity and moderately reduced visual acuity. In the absence of other visual pathway disease, there is no visual field defect because the entire visual field is represented cortically. There may be associated strabismus and ocular torticollis. Idiopathic infantile nystagmus is present and may have a see-saw and/or horizontal waveform.

### **Struggle/Dilemma of the Clinical Presentation Description**

This patient presented with see-saw nystagmus of unexplained origin. He had a previous MRI of the brain which was reportedly normal. This study was unavailable for our direct review. Subsequent MRI revealed previously-unrecognized anomalous anatomy which accounted for his nystagmus.

**Keywords:** See saw nystagmus, MRI, Optic chiasm, Afferent visual pathways

### **References**

References: 1. Dell'Osso LF, Williams RW. Ocular motility abnormalities in achiasmatic mutant Belgian Sheepdogs: unyoked eye movements in a mammal. *Vis Res* 35:109-116, 1995. 2. Victor JD, Apkarian P, Hirsch J, et al. Visual function and brain organization in non-decussating retinal-fugal fibre syndrome. *Cerebral Cortex* 10:2-22, 2000. 3. Balani A, Kumar AD, Marda SS, et al. Nondecussating retinal-fugal fibre syndrome: clinical and neuroimaging clues to diagnosis. *Indian J Ophthalmol* 63:858-861, 2015. 4. Korff CM, Apkarian P, Bour LJ, et al. Isolated absence of optic chiasm revealed by congenital nystagmus, MRI, and VEPs. *Neuropediatrics* 34:219-223, 2003. 5. Jansonius NM, van der Vliet TM, Cornelissen FW, et al. A girl without a chiasm: electrophysiologic and MRI evidence for the absence of crossing optic nerve fibers in a girl with congenital nystagmus. *J Neuro-Ophthalmol* 21:26-29, 2001.

## **“One Peak is Worth Twenty Finesses”**

Steven Newman<sup>1</sup>, James Mandell<sup>1</sup>

<sup>1</sup>*University of Virginia, Charlottesville, Virginia, USA*

### **History & Exam**

An 8 year old was referred with a one week history of swelling around her left eye. She was not aware of any change in her vision or double vision. Visual acuity was 20/20 OD and 20/25 OS. Visual fields demonstrated minimal scattered desaturation with < ½ dB asymmetry between the two sides. External examination demonstrated Hertels of 14 and 25 with moderate resistance to retropulsion OS. Pupils were reactive without afferent pupillary defect. Motility revealed minimal limitation in elevation OS. Slight lamp examination was unremarkable. Rebound pressures were 18 and 16. OCT demonstrated average nerve fiber layer thickness of 102 microns OD and 101 OS without retinal striae. CT scan and MRI scan were done prior to referral were said to show a meningioma and neurosurgery was consulted. Pediatric Oncology was concerned about the rapid onset and suggested orbitotomy and or craniotomy.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## **“One Peak is Worth Twenty Finesses”**

*Answer*

### **Final Diagnosis**

Ewing's family sarcoma of the orbit and anterior cranial fossa

### **Summary of Case**

FNAB was performed and demonstrated a small blue cell population with negative Immunohistochemical staining for CD3, CD19, CD79a, CD23, TDT, Yf4, desmin and S100. There was staining of FLI1 and significant staining for SMI33, as well as focal patchy staining for NSE and synaptophysin. FISH demonstrated an intact SYT gene. The patient was diagnosed as having a Ewing's like sarcoma and started on chemotherapy with vincristine, Cytosan, and doxorubicin. Ewing sarcoma frequently involves bone, but has rarely involved the orbit. In Reese's book, *Orbital Tumors* (1st edition (1951) 2nd edition (1963)) fails to mention any patient with a Ewing sarcoma involving the orbit. Fred Jacobiec's book on *Ocular and Adnexal Tumor* (1978) discussed metastatic sarcomas but there were no cases that were identified as Ewing sarcoma. Henderson's *Tumors of the Eye* (1994) reviewed the literature, but added no patients with presumed Ewings. A specific diagnosis has been helped by our recognition of the presence of EWSR1 gene rearrangement as well as FLI1 rearrangement. Recently multiple individual case reports have appeared. These tumors often occur in young patients most frequently involving the long bones and only rarely have they involved the bones of the skull base. The rapid presentation here was a clue of a more aggressive process. The greater wing of the sphenoid was involved. Neurosurgical consultation discussed the possibility of a craniotomy and excision. In the 1980s, Jack Kennerdell introduced fine needle aspiration biopsy to the orbit. Obviously in most children fine needle aspiration biopsy, except under general anesthesia would not have been considered, but in select cooperative patients (such as our case) a specific diagnosis can be made without a trip to the operating room, when combined with histochemical staining.

### **Struggle/Dilemma of the Clinical Presentation Description**

CT and MRI scan were read as a meningioma, and a craniotomy was planned. It is important to emphasize the clinical importance of knowing the specifics of a lesion before deciding on a course of treatment. Fine needle aspiration biopsy, while not always positive, even in young patients, may lead to a specific diagnosis. With advances in immunohistochemistry and gene analysis, evaluation of skull base lesions may be specific.

**Keywords:** Chemotherapy, Orbit, Tumor

### **References**

Alfaar AS, Zamzam M, Abdalla B, et al. Childhood Ewing sarcoma of the orbit. *Journal of Pediatric Hematology/Oncology* 2015; 37: 433-7  
Apostolopoulos K; Ferekidis E. Extensive primary Ewing's sarcoma in the greater wing of the sphenoid bone. *Journal of Oto-Rhino-Laryngology & Its Related Specialties* 2003; 65: 235-7  
Dutton JJ, Rose JG Jr., DeBacker CM, Gayre G. Orbital Ewing's sarcoma of the orbit. *Ophthalmic Plastic & Reconstructive Surgery* 2000; 16: 292-300  
Harbert F, Tabor GL, Jr. Ewing's tumor of the orbit, report of 2 cases. *American Journal of Ophthalmology* 1950; 33: 1219-25  
Henderson JW. *Orbital Tumors* 3rd ed. Raven Press, New York 1984: 184-187  
Kano T, Sasaki A, Tomizawa S, et al. Primary Ewing's sarcoma of the orbit. *Brain Tumor Pathology* 2009; 26: 95-100

## “Testing the Hypophysis”

Alberto Distefano<sup>1</sup>, Julie Cho<sup>1</sup>, Adeniyi Fisayo<sup>1</sup>, Mahsa Sohrab<sup>1</sup>, **Mahsa Sohrab, MD**

<sup>1</sup>*Yale School of Medicine, New Haven, Connecticut, USA*

### **History & Exam**

A 60 year-old female with history of hypertension, hyperlipidemia, and Lyme disease 12 years ago treated with doxycycline, developed extreme thirst and polyuria four years ago and was diagnosed with central diabetes insipidus. Magnetic resonance imaging (MRI) at that time showed enhancement of the pituitary gland and stalk. She was treated with DDAVP with clinical improvement. Repeat MRI six months later showed some improvement. She underwent extensive testing including Positron Emission Tomography/Computed Tomography (PET/CT) and lumbar puncture, which were inconclusive or indeterminate. Her disease was categorized as idiopathic hypophysitis and infundibulitis. One year ago, the patient underwent right ear surgery, and afterward developed dizziness. MRI was performed and showed bilateral intraconal enhancing masses with proptosis. The previously noted hypophyseal enhancement had resolved. She was started on oral prednisone 60 milligrams (mg) without significant improvement, and was then referred to our ophthalmology clinic for further evaluation. On exam, best corrected visual acuity was 20/30 in the right eye and 20/25 in the left eye. Pupils were briskly reactive without relative afferent pupillary defect. Intraocular pressure was within normal limits. Motility was severely reduced in supraduction. Color plates were full bilaterally. Exam revealed mild proptosis greater on the left than the right. Otherwise, ophthalmic exam, including dilated fundus exam, was normal. Imaging was reviewed and an orbital biopsy was performed.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## “Testing the Hypophysis”

Answer

### Final Diagnosis

Erdheim-Chester disease

### Summary of Case

The patient underwent left anterior orbitotomy for biopsy. Yellow, friable intraconal masses were noted intra-operatively. Histologic examination of the excised tissue revealed foamy histiocytes on a background of fibrosis with few Touton giant cells and fibrotic infiltrate. Occasional lymphoid aggregates were present. Immunohistochemical stains were positive for CD68, confirming a preponderance of histiocytes, and negative for S-100. Many of the plasma cells were positive for IgG (about 20 per high-power field), but only 5% were positive for IgG4. AFB stain was negative, but highlighted scattered mast cells. These findings were most consistent with Erdheim-Chester disease. Molecular study of the orbital biopsy showed positive BRAF V600E mutation. Systemic work-up with whole body PET/CT revealed involvement of bilateral lower extremities, kidneys, and heart. Skin biopsies from the left popliteal and right posterior thigh demonstrated reticulohistiocytoma consistent with ECD in the skin. The patient was started on peg-interferon alfa-2a (PEGASYS) 180 mg weekly with mild improvement in her PET/CT imaging. She was unable to tolerate further treatment due to weakness, fatigue, vertigo, and nausea. Treatment was changed to dabrafenib, a BRAF inhibitor, 50 mg two times a day. She has been tolerating the treatment thus far, and is following closely with the hematology/oncology team.

### Struggle/Dilemma of the Clinical Presentation Description

The patient presented with hypophyseal involvement many years ago. Histiocytic disorders were on the original differential, but testing was negative, and biopsy was not feasible or necessary given improvement with DDAVP, prednisone, and time. Also, imaging was not repeated until the new presentation with dizziness, which may have incidentally discovered the orbital lesions at an earlier stage. The patient’s prognosis is worsened by her systemic involvement, especially of the heart.

**Keywords:** Erdheim-Chester disease, Orbital tumors, Proptosis,

### References

1. Adam Z, Balsikova K, Krejci M, et al. Central diabetes insipidus in adult patients--the first sign of Langerhans cell histiocytosis and Erdheim-Chester disease. Three case studies and literature review. *Vnitr Lek* 2010;56(2):138-48.
2. Merritt H, Pfeiffer ML, Richani K, Phillips ME. Erdheim-Chester disease with orbital involvement: Case report and ophthalmic literature review. *Orbit* 2016;35(4):221-6.
3. Reithmeier T, Trost HA, Wolf S, et al. Xanthogranuloma of the Erdheim-Chester type within the sellar region: case report. *Clin Neuropathol* 2002;21(1):24-8.
4. Diamond EL, Dagna L, Hyman DM, et al. Consensus guidelines for the diagnosis and clinical management of Erdheim-Chester disease. *Blood* 2014;124(4):483-92.
5. Caparros-Lefebvre D, Pruvo JP, Remy M, et al. Neuroradiologic aspects of Chester-Erdheim disease. *AJNR Am J Neuroradiol* 1995;16(4):735-40.
6. Manaka K, Makita N, Iiri T. Erdheim-Chester disease and pituitary involvement: a unique case and the literature. *Endocr J* 2014;61(2):185-94.

## **“A Sad Story”**

Jason Peragallo<sup>1</sup>

<sup>1</sup>*Emory University, Atlanta, Georgia, USA*

### **History & Exam**

A healthy 6-year-old boy had a two-week history of progressive headaches associated with nausea and vomiting. An ER diagnosed allergic rhinitis, treated with augmentin and steroids, however his symptoms worsened. At a second ER he was febrile to 103F. A classmate was recently diagnosed with Erlichiosis, and our patient was given doxycycline. Brain MRI with and without contrast was normal. CBC was normal. A lumbar puncture revealed 286 WBC (75%lymphs) , 1 RBC, protein 65, glucose 24, negative gram stain. He was diagnosed with aseptic meningitis. Blood culture, CSF culture, CMV, EBV, Arbovirus, RMSF, Erlichia chaffeensis, Bartonella, and West Nile virus were negative. He developed binocular horizontal diplopia. Neuro-ophthalmology was consulted. Afferent visual function was normal, extraocular motility was full, he had horizontal gaze-evoked nystagmus, an alternating esotropia, and mild bilateral disc edema. Diagnosis was mild sixth nerve palsy from elevated ICP in the setting of meningitis. Neurologic examination was otherwise unremarkable. Head CT showed mild communicating hydrocephalus. Repeat LP showed opening pressure 33cmH<sub>2</sub>O, WBC 366 (60% lymphs), 4 RBC, protein 180, glucose 4, negative Cryptococcus, VDRL, HIV, HSV, TB by PCR. IV ceftriaxone and acyclovir were initiated. MRI brain and spine revealed leptomenigeal enhancement and hydrocephalus. His sixth nerve palsies worsened. He developed bowel and bladder incontinence, and clinically deteriorated. Rifampin, isoniazide, pyrazinamide, and ethambutol were initiated, with vancomycin and steroids. A right EVD was placed for hydrocephalus. Quantiferon Gold, urine and blood histoplasma antigen were negative. He began complaining of vision loss. Repeat head CT revealed dilation of the left lateral ventricle, and a left EVD was placed. He was intubated and sedated. Amphotericin was added. At this point the patient was covered for bacterial, viral, TB, and fungal meningitis. His mother noted he was exposed to well water and frequently played outside in the dirt.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** NIH/NEI core grant P30-EY06360 (Department of Ophthalmology)

## **“A Sad Story”**

*Answer*

### **Final Diagnosis**

Balamuthia mandrillaris granulomatous amebic encephalitis

### **Summary of Case**

Our patient was diagnosed initially with aseptic meningitis. However his clinical condition deteriorated over the course of two weeks. Evaluations for more common infectious causes of his meningitis were negative. A wet prep of his CSF revealed only white blood cells. His CSF was sent to the CDC, and PCR was positive for Balamuthia mandrillaris, negative for Naegleria and Acanthamoeba. He was started on pentamidine, sulfadiazine, flucytosine, fluconazole, azithromycin, and miltefosine. Three days later, the patient was found to have cessation of all cerebral and brainstem function, and care was withdrawn. The family elected not to proceed with autopsy. Balamuthia mandrillaris is a free-living amoeba that can produce rare but frequently fatal granulomatous amebic encephalitis. The organism has been isolated from soil, and infection is thought to occur through inhalation of cysts or through broken skin. Prodromal symptoms can last weeks to months, and most cases are fatal. Miltefosine, a drug approved for the treatment of leishmaniasis, has shown promise in treating granulomatous amebic encephalitis.

### **Struggle/Dilemma of the Clinical Presentation Description**

- 1) When does one consider rare causes of meningitis? After deterioration despite broad antimicrobial coverage?
- 2) Would earlier detection of Balamuthia mandrillaris have improved this patient's outcome?

**Keywords:** Meningo-encephalitis, 6th nerve palsy, Infectious, Increased intracranial pressure, Nystagmus

### **References**

- 1) Rowen JL, Doerr CA, Vogel H, Baker CJ. Balamuthia mandrillaris: a newly recognized agent for amebic meningoencephalitis. *Pediatr Infect Dis J* 1995;14:705-10.
- 2) Ong TYY, Khan NA, Siddiqui R. Brain-eating amoebae: Predilection sites in the brain and disease outcome. *J Clin Microbiol* 2017;55:1989-97.
- 3) Roy SL, Atkins JT, Gennuso R, Kofos D, Sriram RR, et al. Assessment of blood-brain barrier penetration of miltefosine used to treat a fatal case of granulomatous amebic encephalitis possibly caused by an unusual Balamuthia mandrillaris strain. *Parasitol Res* 2015;114:4431-39.
- 4) Matin A, Siddiqui R, Jayasekara S, Khan NA. Increasing importance of Balamuthia mandrillaris. *Clin Microbiol Rev* 2008;21:435-8.
- 5) Moriarty P, Burke C, McCrossin D, Campbell R, Cherian S, et al. Balamuthia mandrillaris encephalitis: Survival of a child with severe meningoencephalitis and review of the literature. *J Pediatr Infect Dis Soc* 2014;3:e4-9.



## **“A Giant (Cell) Mistake”**

Behzad Mansouri<sup>1</sup>, Paul Wawryko<sup>2</sup>, Frank Bovell<sup>1</sup>

<sup>1</sup>*University of Manitoba, Winnipeg, Canada*

### **History & Exam**

71-year-old, left-handed woman, who was referred with ptosis, loss of vision in the right eye and headache. In July 2015 she presented to ER with severe right temporal headache and watery right eye. Her exam and head CT was normal. Her ESR/CRP were elevated. She was allegedly diagnosed with GCA and was started on 50mg prednisone/day that improved her headache. Temporal artery biopsy came back inconclusive. Her headache returned and she noticed some blurred vision in the right eye the prednisone dose was reduced to 40mg/day. She was told to increase the prednisone to 50mg/day. Despite being on high dose oral Prednisone, she continued to lose vision in her right eye and her headache worsened. She presented to ER again in early September and had normal head CT, EKG and elevated ESR again. She was told to continue Prednisone (50mg/day) and was referred to neuro-ophthalmology clinic. At her presentation to neuro-ophthalmology clinic, she complained of loss of vision in the right eye, headache and burning sensation and numbness over the right frontotemporal area. She also reported progressive horizontal and binocular double vision since August 2015 that resolved after she lost vision in the right eye. The medical history was significant for breast cancer (1990s) On exam VA: CF (2-feet) OD, 20/20 OS, Color vision (Ishihara): 0/8 plates OD, 8/8 OS, Pupils were equal in size, and RAPD OD. The external examination of the eyes and orbits was normal OU. The lids showed almost complete ptosis OD. The examination of extra-ocular motility revealed a large angle XT/RHT with significant limitation movement in all directions OD. Automated VF showed diffuse visual field loss OD and was normal OS. Dilated stereoscopic funduscopy revealed pale fundus OD and normal fundus OS.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## **“A Giant (Cell) Mistake”**

*Answer*

### **Final Diagnosis**

Orbital apex syndrome caused by Blastomycosis metastasis

### **Summary of Case**

The Patient was sent for an urgent brain and orbit MRI with contrast, which suggested a soft tissue lesion in the right orbital apex, extending in the right cavernous sinus. A dedicated orbital MRI the next day (October 1, 2015) was reported as: Better visualization workup of the already seen the right orbital apex lesions. Based on the contrast enhancement and the extension into the cavernous sinus and the nasal cavity there are multiple differential diagnoses possible. These include lymphoma manifestation or metastatic lesion. Nerve sheath tumor is less likely. The asymmetry of the lacrimal gland has a dimension. The infiltration of e.g. lymphoma cannot be excluded. In her follow up visit after MRI on Oct 5, 2015 she was still on high dose oral prednisone and was found to have more vision loss in the right eye. Neuro-ophthalmic exam showed: VA: LP OD, 20/20 OS. Neuro exam showed reduced pinprick sensation over the right V1 face area. General exam showed a 5cmX5cm skin lesion over the back. She was admitted to hospital with diagnosis of right orbital apex syndrome likely cause by an infiltrative disease such as lymphoma versus metastasis from her old breast cancer. As part of cancer workup a chest CT scan was done which was reported as: Significant increase in the nodular pulmonary opacities in the short interval since the prior study, in a miliary distribution. The dominant pulmonary lesion demonstrates increased cavitation. The rapid rate of progression is suggestive of atypical infection such as TB. A lung biopsy with bronchoscopy was first refused because it was thought but thoracic surgery service that the diagnosis was metastatic lung cancer and therefore the patient received one dose of radiation treatment. Neuro-Ophthalmology insisted on biopsy that showed Blastomycosis. Unfortunately, the patient died in ICU because of respiratory complications.

### **Struggle/Dilemma of the Clinical Presentation Description**

The challenges of this case were at two folds; at first, the patient presented with very typical symptoms and lab findings for GCA and the treatment was started properly but unfortunately the absence of dramatic improvement of symptoms should have prompted the physicians to reevaluate the diagnosis. Furthermore, the patient was thought to have an infiltrative process affecting the eye/brain that caused wrong treatment for a second time that delayed the proper treatment again.

**Keywords:** Optic Neuropathy

### **References**

None.

## “When The Problem Becomes The Solution”

Ari Shemesh<sup>1</sup>, Timo Krings<sup>2</sup>, Dalia Rotstein<sup>2</sup>, David Munoz<sup>2</sup>, Waleed Brinjikji<sup>2</sup>, Laila Al Shafai<sup>3</sup>, **Edward Margolin**

<sup>1</sup>University of Toronto, Dept of Ophthalmology and Vision Sciences, Toronto, Canada, <sup>2</sup>University of Toronto, Toronto, Canada, Dept of Medical Imaging, University of Toronto, Toronto, Canada<sup>3</sup>

### History & Exam

25 year-old man noticed slow progressive decrease in vision in left eye. Vision was 20/20 OD and 20/40 OS, there was swelling of left optic nerve head. MRI demonstrated white matter lesions in left frontal lobe; cerebrospinal fluid composition was normal. Patient was seen in MS clinic and treatment with dimethyl fumarate commenced. Vision continued to deteriorate and when seen by neuro-ophthalmology service 4 months later it was 20/200 in affected eye with brisk left RAPD and dramatically swollen left optic nerve head. Urgent MRV was interpreted as normal and MRI demonstrated white matter changes in deep left frontal lobe, felt to be microischemic, not demyelinating. Dimethyl fumarate was discontinued; serological workup (HIV, Lyme, Toxoplasma, Bartonella, VDRL, ACE, ANA, ds-DNA, ENA and NMO testing) was unrevealing. CT body was normal. Vision remained stable. Dramatic swelling of left optic nerve persisted as he was followed over 2 years. 2.5 years after initial presentation the patient experienced sudden seizure. MRI demonstrated mass lesion surrounded by edema in left frontal lobe. After transfer to our center biopsy of the lesion was interpreted as “indeterminate” but negative for neoplasm. Second opinion on the biopsy commented on findings inconsistent with both demyelination and arterial infarct. Cerebral Angiography (angiogram) reported unusual tortuous left hemispheric cortical veins without arteriovenous shunting lesion. After extensive multidisciplinary consultation, neurosarcoidosis was felt to be a unifying diagnosis despite absence of tissue diagnosis proving it. Treatment with intravenous methylprednisolone and mycophenolate commenced. MRI done 2 months after starting immunosuppression demonstrated dramatic resolution of the left frontal lobe lesion. Unsatisfied with the diagnosis, all neuro-imaging was re-reviewed. On angiogram the unusual tortuous cortical veins in the left hemisphere were reminiscent of the “pseudophlebitic pattern” seen with brain dural AV fistula (BDAVF). Diagnostic procedure was performed.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## “When The Problem Becomes The Solution”

*Answer*

### **Final Diagnosis**

Spontaneously Thrombosed Dural Arterio-Venous Fistula with Cavernous Sinus Thrombosis

### **Summary of Case**

Second angiogram was performed (false-negative rate for angiographic detection of BDAVF is ~10%). Initial report was unchanged from the first one. Third review of biopsy was requested and revealed perivascular macrophages laden with hemosiderin, areas of necrosis, veins with thick hyalinized wall – all consistent with venous congestion. Consultation with interventional neuroradiologist with expertise in BDAVF was sought. All imaging was re-examined. Both angiograms demonstrated unusual tortuous cortical veins in left hemisphere in classic “pseudophlebitic pattern” seen with BDAVF. Spontaneous closure of BDAVF seen in up to 10% of cases was believed to be the reason for no evidence of shunting. Hyperintense T2/FLAIR white matter lesions in left frontal lobe seen on initial MRI were compatible with ischemia secondary to longstanding BDAVF. When initial MRI/V and both angiograms were re-reviewed, definite evidence of subtle left cavernous sinus thrombosis (CST) was seen on all studies. Hypercoagulability work up was performed and significantly elevated level of anticardiolipin IgG antibodies was found that was likely a cause for CST. In summary, in this unique and complicated case longstanding left frontal BDAVF caused surrounding micro-ischemic changes in left frontal lobe. Subsequently, left CST developed because of hypercoagulable state caused by elevated anticardiolipin antibodies. CST caused shifting of the venous drainage from cavernous sinus to BDAVF leading to dramatically swollen left optic nerve. Compartmentalization of cavernous sinus and presence of fistula in only one compartment was the explanation for the unilateral nerve head edema without other signs of CST; it is also possible that BDAVF specifically involved left optic nerve sheath. 2.5 years after initial presentation acute venous hypertension in area supplied by BDAVF led to venous congestion, edema, and ultimately a seizure. BDAVF then spontaneously closed due to underlying predisposition to hypercoagulability, and left frontal mass with surrounding edema completely resolved several months later.

### **Struggle/Dilemma of the Clinical Presentation Description**

Multiple imaging studies were performed, all missing very subtle signs of left cavernous sinus thrombosis. Appearance of the left frontal lobe mass lesion was unexpected and its appearance did not suggest vascular cause. Only after initial imaging, subsequent cerebral angiograms, and pathology slides were re-examined and the diagnosis of dural arterio-venous fistula was entertained, very complicated sequence of events in this case was understood and treatment with immunosuppression for presumed neurosarcoid was discontinued.

**Keywords:** Dural fistula, Cerebral angiography and venography

### **References**

- 1) Geibprasert S, Pongpech S, Jiarakongmun P, Shroff MM, Armstrong DC, Krings T. Radiologic assessment of brain arteriovenous malformations: what clinicians need to know. *Radiographics*. 2010;30(2):483-501.
- 2) Pandey P, Steinberg GK, Westbroek EM, Dodd R, Do HM, Marks MP. Intraoperative angiography for cranial dural arteriovenous fistula. *AJNR Am J Neuroradiol*. 2011;32(6):1091-5.
- 3) Rodriguez FJ, Crum BA, Krauss WE, Scheithauer BW, Giannini C. Venous congestive myelopathy: a mimic of neoplasia. *Mod Pathol*. 2005;18(5):710-8.
- 4) van Rooij WJ, Sluzewski M, Beute GN. Dural arteriovenous fistulas with cortical venous drainage: incidence, clinical presentation, and treatment. *AJNR Am J Neuroradiol*. 2007;28(4):651-5.

## **“Triple Take”**

Johanna Beebe<sup>1</sup>, Liang Cheng<sup>2</sup>, Shira Simon<sup>3</sup>, Michael Wall<sup>3</sup>, Randy Kardon<sup>3</sup>, Alkapalan Deema<sup>4</sup>, Ian Han<sup>3</sup>, Matthew Thurtell<sup>3</sup>

<sup>1</sup>*Park Nicollet, Department of Ophthalmology, St. Louis Park, Minnesota, USA*, <sup>2</sup>*University of Iowa Carver College of Medicine, Iowa City, Iowa, USA*, <sup>3</sup>*University of Iowa, Department of Ophthalmology, Iowa City, Iowa, USA*, <sup>4</sup>*University of Iowa, Department of Pathology, Iowa City, Iowa, USA*

### **History & Exam**

A 42 year-old male noticed difficulty reading labels while stocking shelves at work. Over the next three weeks, he developed a dark “cloud” in his central vision in the left eye, and then the right eye. He did not have associated pain. When evaluated by the retina service, his visual acuities were 20/100 OD and 20/1250 OS without a relative afferent pupillary defect. Goldmann perimetry showed central scotomas OU. His anterior segment was unremarkable. Dilated fundus examination showed subtle telangiectatic vessels on the optic nerve head and in the macula OU. Optical coherence tomography (OCT) showed diffuse inner retinal thinning with focal irregularities in the outer plexiform layer in the macula OU, as well as ganglion cell layer thinning OU. He was evaluated in neuro-ophthalmology for possible Leber’s hereditary optic neuropathy. Repeat visual field, dilated fundus examination, and OCT findings were unchanged from previously. MRI brain and orbits with and without contrast showed subtle bilateral optic nerve enhancement. He was thought to have bilateral optic neuritis. He was admitted for further work-up and management. CSF evaluation showed a minimally elevated protein concentration of 48 mg/dL, with normal constituents otherwise. CSF cytology was negative. NMO antibodies were not detected and a paraneoplastic panel was negative. Further diagnostic testing was performed.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## **“Triple Take”**

*Answer*

### **Final Diagnosis**

Paraneoplastic autoimmune retinopathy and optic neuropathy secondary to a renal oncocytoma

### **Summary of Case**

On admission, his creatinine was noted to be elevated to 3.8 mg/dL. A subsequent renal ultrasound demonstrated adult polycystic kidney disease and a large mass arising from the right kidney, raising concern for neoplastic disease and a paraneoplastic syndrome as the cause for his vision loss. Biopsy of his renal mass showed a benign renal oncocytoma. A full-body PET-CT scan showed no other areas of hypermetabolic activity other than the known right renal mass. ERG demonstrated severe cone greater than rod dysfunction. Anti-retinal and optic nerve antibody testing showed auto-antibodies to multiple proteins, including alpha- and gamma-enolase. Immunohistochemical staining of the oncocytoma biopsy specimen showed positive alpha- and gamma-enolase staining throughout the sample. Ultimately, the unifying diagnosis was a paraneoplastic autoimmune retinopathy and optic neuropathy secondary to a renal oncocytoma. The patient’s treatment involved IV corticosteroids, plasmapheresis, and complete excision of the renal mass with an associated partial nephrectomy. With treatment, he has gained a significant improvement in his vision. At his most recent follow-up visit, his visual acuities were 20/125 OD and 20/200 OS, with improved bilateral central scotomas.

### **Struggle/Dilemma of the Clinical Presentation Description**

The patient presented with subacute, bilateral, painless central vision loss and was thought to have Leber’s hereditary optic neuropathy based on his clinical course and fundus examination. However, neuroimaging showed bilateral optic nerve enhancement. Recognizing the atypical nature of his presentation for optic neuritis prompted admission and the discovery of his renal tumor. Finally, the diagnosis was clinched by obtaining the ERG, auto-antibodies, and staining of his renal biopsy specimen to show the causative relationship.

**Keywords:** autoimmune reinopathy, Optic Neuropathy, Paraneoplastic, Special staining, Electroretinogram

### **References**

1. Fox, A., H.N. Sen, and R. Nussenblatt, Autoimmune Retinopathies, in Ryan’s Retina. 2018, Elsevier. p. 1562-1571.
2. Golovastova, M.O., et al., The cancer-retina antigen recoverin as a potential biomarker for renal tumors. Tumour Biol, 2016. 37(7): p. 9899-907.
3. Wu A. Oncocytic Renal Neoplasms on Resections and Core Biopsies: Our Approach to This Challenging Differential Diagnosis. Arch Pathol Lab Med 2017 Oct;141(10):1336-1341. doi: 10.5858/arpa.2017-0240-RA.

## **“Coming to a Rapid Conclusion.”**

Leanne Stunkel<sup>1</sup>, Namita Sinha<sup>2</sup>, Nathan Kung<sup>3</sup>, Robi Maamari<sup>4</sup>, Cole Ferguson<sup>2</sup>, Sonika Dahiya<sup>2</sup>, George Harocopos<sup>2</sup>, Gregory Van Stavern<sup>4</sup>, **Dr. Gregory Van Stavern**

<sup>1</sup>Washington University in St Louis School of Medicine, St. Louis, Missouri, USA, <sup>2</sup>Department of Pathology & Immunology, Washington University in St. Louis, St. Louis, Missouri, USA, <sup>3</sup>Blue Sky Neurology, Denver, Colorado, USA, <sup>4</sup>Department of Ophthalmology and Visual Sciences, Washington University in St. Louis, St. Louis, Missouri, USA

### **History & Exam**

A 21-year-old man presented to a retina specialist for 2.5 weeks of painless central vision loss OD. His initial examination was notable for visual acuity 20/200 OD and 20/20 OS. Fundus examination was significant for several macular areas of retinal pigment epithelial (RPE) atrophy with associated subretinal whitening. Fundus autofluorescence showed further areas of RPE atrophy centrally and temporally. OCT of the macula showed areas of atrophy of the RPE with adjacent areas of hyperreflectivity and showed choroidal thickening in the involved area. Fluorescein angiogram showed well-circumscribed regions of early hypofluorescence and adjacent regions of transmission defects and late hyperfluorescence. The working diagnosis was acute retinal necrosis, and the patient was offered admission for IV antivirals. When we declined admission, he was started on oral valacyclovir. About 10 days later, he developed a new, frontal headache, followed a few days later by involvement of the other eye (OS). Funduscopic examination showed a new small area of whitening just inferior to the fovea OS. He was admitted to an outside hospital for IV and intravitreal antivirals. An infectious work-up was negative. At that time, he was started on prednisone 80mg daily out of concern for inflammatory etiology. However, his vision continued to decline to count fingers OD with examination notable for a new relative afferent pupillary defect OD and a new inferonasal visual field deficit OS. He continued to have worsening headaches. Approximately 1 week later he had sudden complete loss of vision OD and began to have hallucinations. His mental status declined and he had abnormal limb movements. He was intubated for airway protection. His examination without sedation was notable for hypertension, bradycardia, unresponsiveness, fixed 8mm pupils bilaterally, intact oculocephalic reflexes, intact corneal reflexes, intact cough and gag reflexes, overbreathing the ventilator, and extensor posturing in response to noxious stimuli.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## **“Coming to a Rapid Conclusion.”**

*Answer*

### **Final Diagnosis**

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) with secondary CNS vasculitis causing strokes in multiple vascular territories.

### **Summary of Case**

Head CT showed diffuse effacement of the sulci with diffuse cytotoxic edema and cerebral edema in a right middle, left middle, and left posterior cerebral artery distribution. He was started on mannitol and hypertonic saline. MRI of the brain showed large areas of ischemia in the bioccipital, biparietal, and right frontal regions with associated cytotoxic edema. MR Angiogram showed a left M1 occlusion. Lumbar puncture could not be performed in the setting of active herniation. His family declined decompressive bifrontal craniectomies due to his poor prognosis. Over the next 24 hours, he progressed to brain death despite aggressive treatment with mannitol and hypertonic saline. This was 42 days after the onset of visual changes, and 24 days after his initial visit to a retina specialist. On autopsy, ocular pathology showed granulomatous choroiditis with multinucleated giant cells confined to the posterior pole, with some foci of overlying subretinal fluid (correlating with the active-appearing subretinal infiltrates noted on funduscopy examination, choroidal thickening noted on OCT, and hypofluorescent areas on fluorescein angiogram), with adjacent areas of RPE atrophy (correlating with the areas of RPE atrophy noted on funduscopy examination, OCT, and fluorescein angiogram). HSV-1 and HSV-2 immunostains were negative. In the brain and spinal cord, blood vessels of all sizes, including left MCA tributaries, showed patchy chronic inflammation varying from lymphocytic to lymphohistiocytic to granuloma formation; granulomatous vasculitis was best appreciated in the spinal cord. Some inflamed vessels also displayed focal associated angioneurosis and partially organized luminal thrombi. Most foci of vasculitis were observed in leptomeninges with limited involvement of intraparenchymal vessels. Also noted were multiple ischemic infarcts, evidence of cerebral edema, and Duret hemorrhage.

### **Struggle/Dilemma of the Clinical Presentation Description**

This presented with retinal lesions that were initially misdiagnosed as acute retinal necrosis. This presentation was not initially recognized as APMPPE. This may have been in part because the lesions were initially unilateral. When his retinal lesions were later recognized as APMPPE, his headaches were attributed to treatment with PO valacyclovir and thus were not recognized as neurologic involvement (isolated headache preceded the strokes by 2 weeks).

**Keywords:** vasculopathy, retinopathy, headaches, Neurologic disorders, Outer retinopathies/White dot syndromes

### **References**

Brownlee WJ, Anderson NE, Sims J, Pereira JA. Neurological complications of acute multifocal placoid pigment epitheliopathy. *J Clin Neuroscience*. 13, 76-80, 2016. Comu S, Verstraeten T, Rinkoff JS, Busis NA. Neurological Manifestations of Acute Posterior Multifocal Placoid Pigment Epitheliopathy. *Stroke*. 27, 996-1001, 1996. de Vries JJ, den Dunnen WFA, Timmerman EA, Kruihof, De Keyser J. Acute Posterior Multifocal Placoid Pigment Epitheliopathy With Cerebral Vasculitis: A Multisystem Granulomatous Disease. *Arch Ophthalmol*. 124, 910-3, 2016. Tsang BKT, Chauhan, Haward R, Whiteman I, Judith Frayne J, McLean C. Fatal Ischemic Stroke Complicating Acute Multifocal Placoid Pigment Epitheliopathy: Histopathological Findings. *J Neuro-Ophthalmol*. 34, 10-5, 2014. Wilson CA, Choromokos EA, Sheppard R. Acute Posterior Multifocal Placoid Pigment Epitheliopathy and Cerebral Vasculitis. *Arch Ophthalmol*. 106, 796-800, 1988.



## **“It's Always Been Like That”**

Eric Gaier<sup>1</sup>, William Butler<sup>2</sup>, Joseph Rizzo<sup>1</sup>, **Joseph F Rizzo III MD**

<sup>1</sup>Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, USA, <sup>2</sup>Massachusetts General Hospital, Boston, Massachusetts, USA

### **History & Exam**

An 18 year-old Caucasian boy presented with left upper eyelid ptosis, headaches, and iris heterochromia. The patient and his family reported the left iris being darker than the right since early childhood. Over the 5 years preceding his presentation, the patient's mother noted progressive ptosis of his left upper eyelid. A top student in middle school, his grades had declined through high school, and his family had noticed loss of motivation mixed with intermittent irritability and mood changes. The patient developed headaches 2 years prior that had been worsening steadily and culminated over the preceding week in severity with daily episodes of nausea and vomiting. He noticed increased thirst and voiding frequency and had felt fatigued. He gained 25 lbs in the preceding 3 months. The patient was initially prescribed sumatriptan and cyproheptadine for presumed migraines without symptomatic benefit. In the week prior to presentation, the left side of his face began to droop and he developed binocular, horizontal diplopia. A CT head was abnormal, and the patient was referred for evaluation and admission. External examination revealed ptosis of the left upper eyelid and slate grey circumferential coloration of the sclera (Figure 1). The right iris was hazel, and the left was dark brown. The pupils were equal and reactive without a relative afferent defect. Visual acuities were 20/20 OU without dyschromatopsia or metamorphopsia. Abduction of the left eye was mildly limited, and there was subtle left facial weakness. Automated visual field testing showed enlarged blind spots bilaterally. Funduscopic examination was significant for papilledema with peripapillary flame hemorrhages OU and a striking interocular diffuse choroidal pigmentation disparity with the left eye being darker than the right (Figure 2). The patient was treated with corticosteroids with improvement of his headache and resolution of diplopia. A diagnostic procedure was performed.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## **“It's Always Been Like That”**

*Answer*

### **Final Diagnosis**

Primary central nervous system melanoma, likely leptomeningeal, in association with Nevus of Ota

### **Summary of Case**

MRI showed a 6 cm left frontal enhancing mass causing significant mass effect and displacement of the optic chiasm (Figure 3). CSF cleft and white matter buckling signs suggested an extra-axial origin of the tumor. The patient underwent subtotal neurosurgical resection (80-90%) of the mass, which was felt intraoperatively to be an intraparenchymal tumor without adhesion to the skull base. Histopathologic analysis of the tissue revealed nests of epithelioid cells positive for MART-1 and MITF (Figure 4). Additional stains including GFAP, synaptophysin, Olig2, EMA, PR, Oct3/4, AE1.3/CAM5.2, and desmin were negative. The tumor was positive for pathogenic variants in GNAQ (including Arg183Gln), which are reported to occur in 50% of uveal melanomas Co-Authors[1]. A complete skin examination revealed no evidence of a primary cutaneous melanoma. Follow up examination 3 weeks later revealed stable afferent function, normal intraocular pressures, significant improvement in papilledema, and no evidence of focal lesions in the peripheral fundus. In the following months, the patient graduated high school. He underwent radiation and 4 cycles of ipilimumab and nivolumab that were complicated by high-grade fevers, hemolytic anemia, and that responded to corticosteroid therapy. MRI of the cervical spine 5 months after his initial presentation showed new diffuse nodular leptomeningeal enhancement consistent with metastases that was confirmed on cytology of cerebral spinal fluid. The patient was later hospitalized with headaches and confusion and repeat MRI of the brain showed evidence of hydrocephalus secondary to progressive leptomeningeal disease. A ventriculoperitoneal shunt was placed. Shortly thereafter, the patient had a tonic seizure and hypoxic respiratory failure requiring intubation. A new tumor focus was found near the intracranial portion of the shunt and the shunt was revised. Following extubation and discussion with the family, the patient was discharged home with Hospice care and passed away 1 month later.

### **Struggle/Dilemma of the Clinical Presentation Description**

Nevus of Ota is strongly associated with uveal melanoma Co-Authors[2] and rarely associated with primary central nervous system melanoma [3,4]. The differential for this patient's tumor did not initially include melanoma; the Nevus of Ota was initially felt to be unrelated to his cerebral lesion. The delay in diagnosis was driven by the undue influence of considering statistically more likely etiologies and neglecting the relevant association of Nevus of Ota with melanoma.

**Keywords:** Papilledema, Intracranial tumors, Pediatric, headaches, Ptosis

### **References**

1. Van Raamsdonk CD, Bezrookove V, Green G, et al. Frequent somatic mutations of GNAQ in uveal melanoma and blue naevi. *Nature* 2009;457:599-602.
2. Shields CL, Kaliki S, Livesey M, et al. Association of ocular and oculodermal melanocytosis with the rate of uveal melanoma metastasis: analysis of 7872 consecutive eyes. *JAMA Ophthalmol* 2013;131:993-1003.
3. Balmaceda CM, Fetell MR, O'Brien JL, Housepian EH. Nevus of Ota and leptomeningeal melanocytic lesions. *Neurology* 1993;43:381-6.
4. Goldman-Levy G, Rigau V, Blechet C, et al. Primary Melanoma of the Leptomeninges with BAP1 Expression-Loss in the Setting of a Nevus of Ota: A Clinical, Morphological and Genetic Study of 2 Cases. *Brain pathology (Zurich, Switzerland)* 2016;26:547-50.

## “Light at the End of the Tunnel?”

Noel Chan<sup>1</sup>, Tak Lap Poon<sup>2</sup>, Joyce Chow<sup>2</sup>, Wai Lun Poon<sup>3</sup>, Sherman Lo<sup>3</sup>, Wing Hung Lau<sup>4</sup>, Ka Hong Au<sup>5</sup>, Carmen Chan<sup>1</sup>

<sup>1</sup>Neuro-Ophthalmology Service, Hong Kong Eye Hospital, Hong Kong, Hong Kong, <sup>2</sup>Department of Neurosurgery, Queen Elizabeth Hospital, Hong Kong, Hong Kong, <sup>3</sup>Department of Radiology & Imaging, Queen Elizabeth Hospital, Hong Kong, Hong Kong, <sup>4</sup>Department of Pathology, Queen Elizabeth Hospital, Hong Kong, Hong Kong, <sup>5</sup>Department of Ophthalmology, United Christian Hospital, Hong Kong, Hong Kong

### History & Exam

A 24-year-old Chinese man presented with 1-year history of progressive blurring of vision of the right eye. He had no significant past ocular nor medical history except moderate myopia and migraine. On ophthalmologic examination, his corrected visual acuity at distance was 20/100 OD and 20/30 OS. Ishihara OD failed test plate, OS 3/14. Ocular examination, including intraocular pressure, was normal, except the finding of bilateral disc pallor with enlarged cup-disc ratio of 0.9 OD and 0.7 OS. Visual field examination showed OD general depression and OS tunnel vision. OCT retinal nerve fiber layer analysis confirmed optic atrophy OU. MRI brain and orbit with contrast did not show any optic nerve abnormalities, but there were abnormal T2 hyperintensities at the genu of corpus callosum and the adjacent white matter, which were commented as highly suggestive of demyelinating disease. Other investigations including C-reactive protein, anti-nuclear antibody, rheumatoid factor, vitamin B12, folate levels were all normal. Neuromyelitis optica antibody was not found. Lumbar puncture showed CSF white cell count of 13 (99% lymphocyte), and oligoclonal bands were present. Alpha-fetoprotein (AFP) and beta- human chorionic gonadotropin (b-HCG) levels, in serum and CSF, were normal. Multiple sclerosis was suspected, and intravenous steroid therapy was considered, but withheld since the diagnosis was not certain and there was no definite evidence of acute deterioration. When reviewed 2 months after initial presentation, his visual acuity had dropped to 20/400 OS and 20/100 OS. In view of the rapidly deteriorating visual acuity, the MRI was reviewed. It was felt the nodular ependymal and hypothalamus/ pituitary stalk lesions were atypical for demyelination. A diagnostic procedure was performed.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## “Light at the End of the Tunnel?”

*Answer*

### **Final Diagnosis**

Central nervous system (CNS) Germinoma (non-secreting)

### **Summary of Case**

The patient underwent mini-craniotomy and brain biopsy. Intraoperative findings included diffuse leptomeningeal thickening, atrophic optic nerves and a thickened hyperemic pituitary stalk which was biopsied. Histology showed germinoma (CD117+, OCT3/4+). Pre-operative hormonal profile revealed hypopituitarism and he was also diagnosed with central diabetes insipidus. MRI whole spine did not show germinoma involvement. Ultrasound of scrotum was normal. CT scan of thorax, abdomen and pelvis showed no evidence of malignant lesion. He referred to oncology and planned for radiotherapy (CSI 24Gy/16fr + boost 21Gy/14fr), which is due to start shortly. CNS germ cell tumors (GCT) are classified as germinomas or non-germinoma germ cell tumors. Most patients are diagnosed between the age of 10-21, with a male predominance. The most common presentation of CNS GCT are diabetes insipidus, hypopituitarism and visual field defect. These tumors sometimes secrete AFP and b-HCG and finding elevated levels of these tumor marks may aide diagnosis. On MRI, germinomas are isointense or slightly hypointense on T1-weighted images, and isointense or hyperintense on T2-weighted images, and they enhance with gadolinium. They usually appear as midline mass lesions, most commonly near the pineal gland, and less frequently in the suprasellar region, basal ganglia and thalamus. Diffuse involvement is unusual, and to the best of our knowledge, there has only been one other reported case of germinoma mimicking multiple sclerosis and that case did not present with visual symptoms. Radiotherapy is the first line treatment for germinomas and the 2-year survival is better than 90% with radiotherapy alone. More recently, systemic chemotherapy with reduced doses of radiation has been advocated as alternative treatment, however longer-term follow-up is required to determine if it will replace standard radiotherapy.

### **Struggle/Dilemma of the Clinical Presentation Description**

This patient’s MRI was reported as highly suggestive of demyelinating disease and the CSF oligoclonal bands were positive, pointing to the diagnosis of multiple sclerosis. However careful review of the MRI revealed atypical involvement of the hypothalamus and pituitary stalk, which led to the diagnostic brain biopsy.

**Keywords:** Optic Neuropathy, Tumor

### **References**

1. Jennings MT; Gelman R; Hochberg F. Intracranial germ-cell tumors: natural history and pathogenesis. *J Neurosurg.*; 63(2):155-67, 1985
2. Fujimaki T, Matsutani M, Funada N, Kirino T, Takakura K, Nakamura O et al. CT and MRI features of intracranial germ cell tumors. *J Neurooncol.*;19(3):217-26, 1994.
3. Birnbaum T, Pellkofer H, Buettner U. Intracranial germinoma clinically mimicking chronic progressive multiple sclerosis. *J Neurol.*; 255(5):775-6, 2008.
4. Blakeley JO; Grossman SA. Management of pineal region tumors. *Curr Treat Options Oncol.*; 7(6):505-16, 2006.
5. Shibamoto Y. Management of central nervous system germinoma: proposal for a modern strategy. *Prog Neurol Surg.*; 23:119-29, 2009.

## **“A Can of Worms”**

Ali Hamedani<sup>1</sup>, **Madhura Tamhankar, MD**

<sup>1</sup>*University of Pennsylvania, Philadelphia, Pennsylvania, USA*

### **History & Exam**

A 67 year-old man presented to the ophthalmology clinic with one day of binocular horizontal diplopia. He also complained of one week of bilateral periorbital pain which was worse on the right than the left. Four days prior, he had undergone partial right nephrectomy for grade II papillary renal cell carcinoma. He denied vision loss; other neurologic symptoms including weakness, numbness, or imbalance; or constitutional symptoms such as fever, chills, or weight loss. Visual acuity was 20/20 in each eye with normal color vision and full visual fields to confrontation. Pupils were equally reactive without afferent pupillary defect. External examination was unremarkable without proptosis, ptosis, or eyelid retraction. Motility was mildly limited in abduction bilaterally, and he had a comitant 16 prism diopter esotropia. MRI brain, acetylcholine receptor antibodies, and TSH were ordered, and the patient was referred to neuro-ophthalmology. Two weeks later, he presented to neuro-ophthalmology clinic with worsening diplopia and was found to have complete bilateral abduction deficits and 50 PD esotropia. He was admitted to the neurology service and during his hospital stay developed right upper and lower facial weakness, distal vibratory loss, and mild sensory ataxia. MRI brain revealed a questionable fullness of the right cavernous sinus, but on further review this was reported to be normal. Lumbar puncture revealed an opening pressure of 21cm, WBC 1/mL, RBC 1/mL, glucose 64 mg/dL, protein 98 mg/dL, and normal cytology. Serum GQ1b antibodies were negative, and EMG/NCS revealed evidence of axonal polyneuropathy without demyelinating features. He was treated empirically for Miller-Fisher syndrome with IVIG 2g/kg. Despite treatment, his diplopia continued to worsen over the next three months and he developed a new left supraduction deficit in addition to his bilateral abduction deficits (Figure 1). Further diagnostic testing was then performed.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## **“A Can of Worms”**

*Answer*

### **Final Diagnosis**

CANOMAD (chronic ataxic neuropathy, ophthalmoplegia, M-protein agglutination, and disialosyl antibodies)

### **Summary of Case**

An extended ganglioside antibody panel was obtained that showed asialo GM1, GM2, and GD1a antibodies. In light of these results and the chronicity of his presentation, CANOMAD (chronic ataxic neuropathy, ophthalmoplegia, M-protein agglutination, and disialosyl antibodies) was diagnosed. He was treated with monthly IVIG, oral prednisone, and later rituximab. Ocular motility improved, although at one year of follow up he continues to have diplopia from 25 PD of esodeviation. The temporal association of his symptoms and recent nephrectomy for renal cell carcinoma was initially concerning for an infectious or neoplastic process, but neuroimaging and CSF cytology were normal. Miller-Fisher syndrome was then suspected, but serum GQ1b antibodies, which are present in over 80% of patients with Miller-Fisher syndrome (Ito 2008), were absent. Furthermore, he experienced no clinical improvement over the subsequent three months, which is unusual as the natural history of Miller-Fisher syndrome is for symptoms to peak after one week, plateau for two weeks, and resolve by three months (Mori 2001). The progressive nature of his diplopia and ophthalmoparesis prompted additional testing leading to the correct diagnosis. First described in 1985, CANOMAD is a chronic, often relapsing autoimmune polyneuropathy characterized by prominent ophthalmoparesis. Antibodies against multiple disialosyl-containing gangliosides, including GQ1b, may be present (Willison 2001). The typical neuro-ophthalmic presentation is diffuse, progressive ophthalmoparesis, though there are case reports of optic neuropathy in CANOMAD (Sanvito 2011). The literature is limited to a handful of case reports and case series totaling some 65 patients, and there is no known association with malignancy or recent surgery. The recognition of this rare clinical syndrome had implications for this patient’s treatment, as there are reports of success with both IVIG (Attarian 2010) and rituximab (Delmont 2010).

### **Struggle/Dilemma of the Clinical Presentation Description**

The acute onset of ophthalmoparesis in the perioperative setting following a recent cancer diagnosis created an initial diagnostic dilemma. Later, the diagnosis of Miller-Fisher syndrome was called into question by the absence of GQ1b antibodies and lack of clinical improvement with IVIG. Detection of less commonly recognized antiganglioside antibodies ultimately led to the correct diagnosis and treatment.

**Keywords:** Miller Fisher variant, Diplopia, Guillain-Barré, CIDP

### **References**

1. Ito M, Kuwabara S, Odaka M, Misawa M, Koga M et al. Bickerstaff's brainstem encephalitis and Fisher syndrome form a continuous spectrum: clinical analysis of 581 cases. *J Neurol* 2008; 255(5): 674-82.
2. Mori M, Kuwabara S, Fukutake T, Yuki N, Hattori T. Clinical features and prognosis of Miller Fisher syndrome. *Neurology* 2001; 56(8): 1104-6.
3. Willison HJ, O'Leary CP, Veitch J, Blumhardt LD, Busby M et al. The clinical and laboratory features of chronic sensory ataxic neuropathy with anti-disialosyl IgM antibodies. *Brain* 2001; 124: 1968-77.
4. Sanvito L, Rajabally YA. Optic neuropathy associated with CANOMAD: description of 2 cases. *Muscle Nerve* 2011; 44(3): 451-5.
5. Attarian S, Boucraut J, Hubert AM, Uzenot D, Delmont E et al. Chronic ataxic neuropathies associated with anti-GD1b IgM antibodies: response to IVIg therapy. *JNNP* 2010; 81(1): 61-4.
6. Delmont E, Jeandel PY, Hubert AM, Marcq L, Boucraut J et al. Successful treatment with rituximab of one patient with CANOMAD neuropathy. *J Neurol* 2010; 257(4): 655-7.

## “Cold Fever”

Shannon Beres<sup>1</sup>

<sup>1</sup>*Stanford University, Palo Alto, California, USA*

### **History & Exam**

A 34-year old rock-climbing-mountain man woke with bilateral painless blurry vision along with alternating conjunctival erythema and eyelid edema. A headache began without associated migrainous features. Prior history revealed an untreated mysterious ‘new form of TB’ followed by the CDC at age 2 during a work-up for a large lymph node. He had an aunt with Hodgkin’s lymphoma and no recent insect bites despite hiking internationally. His visual acuity was 20/70 OD, 20/50 OS and there was enlargement of both blind spots. There was conjunctival injection and no cells in the anterior chamber or vitreous. He had significant disc elevation OU with cotton wool spots, no hemorrhage, and bland appearing. A brain MRI was normal. He had elevated inflammatory markers (ESR 104) and leukocytosis (WBC 23). Lumbar puncture had normal opening pressure and showed an aseptic meningitis; CSF WBC (456), protein (229). Extensive infectious and carcinomatous CSF work-up was negative and empiric treatment with antifungals and antibiotics were trialed until cultures returned negative. CSF metagenomics sequencing matched *Borrelia hermsii*, however confirmatory testing was negative. That month, a pruritic head-sparing maculopapular rash appeared and he developed fleeting fevers triggered by cold, tinnitus, progressive severe sensorineural hearing loss, enlarged lymph nodes, and precipitous weight loss >35 lbs. During the hunt for cancer a PET/CT showed diffuse marrow activity and multiple lymph nodes with increased metabolic activity. Lymph node and bone marrow biopsies were negative. Skin biopsies of two different rashes came back as pityriasis rosea and psoriasis. Five months from presentation, his optic disc and vision remained stable and he was without a diagnosis. Repeat MRI brain was performed showing new plaque-like dural enhancement and lacrimal enhancement. Lacrimal biopsy was negative. A repeat bone marrow biopsy initially suggested a plasma cell neoplasm, but cytogenetics was negative. A genetic test was performed.

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None

## “Cold Fever”

### Answer

#### Final Diagnosis

The final diagnosis was optic disc inflammation from cryopyrin-associated periodic syndrome (CAPS).

#### Summary of Case

With no malignant cells, fungus, toxin, or bacteria found, the diagnosis of cryopyrin-associated periodic syndrome (CAPS) was decided in light of the clinical history and negative pathology. CAPS is a rare, 1-3:1,000,000,(1) genetic inflammatory disorder that includes three phenotypes: Muckle–Wells syndrome, neonatal-onset multisystem inflammatory disease and familial cold autoinflammatory syndrome. CAPS diagnosis is made clinically and some phenotypes can be confirmed genetically. Clinical criteria includes increased inflammatory markers and >2 of 6 signs/symptoms (urticarial-like rash, cold/stress triggered episodes, sensorineural hearing loss, arthralgias/myalgias, chronic aseptic meningitis, epiphyseal overgrowth/frontal bossing).(2) The inflammatory symptoms come from a gain-of-function mutation of the NLRP3 gene coding for cryopyrin, which helps regulate the innate immune response by forming intracellular protein complexes called inflammasomes. Defective inflammasomes cause overproduction of interleukin-1 leading to the systemic inflammation. Effective treatment is with anakinra,(3) an interleukin 1-receptor antagonist and canakinumab,(4) a monoclonal antibody that is specific for IL-1b. Gene testing is available but one infant study found 40% without the gene defect, thought to be related to gene heterogeneity.(5) The patient was started on anakinra with significant resolution of his symptoms. His optic disc swelling improved with resulting gliosis. Unfortunately, there was irreversible sensorineural hearing loss and central visual acuity loss likely due to chronic inflammation, remaining at 20/100 OD and 20/80 OS. Gene testing returned negative for our patient.

#### Struggle/Dilemma of the Clinical Presentation Description

This case was difficult to diagnose given that smoldering infection and lymphoma were thought to be the cause in light of his childhood history of mycobacterial infection, extensive hiking history and travel, and family history of lymphoma. The diagnostic dilemma continued after a negative workup until multiple subspecialists came together identifying this rare disorder.

**Keywords:** Optic disc edema, Vision loss: visual field

#### References

1. Cuisset L, Jeru I, Dumont B, et al, Mutations in the autoinflammatory cryopyrin-associated periodic syndrome gene: epidemiological study and lessons from eight years of genetic analysis in France, *Ann Rheum Dis*,70:495–9, 2011.
2. Kuemmerle-Deschner JB, Ozen S, Tyrrell PN, et al, Diagnostic criteria for cryopyrin-associated periodic syndrome, *Ann Rheum Dis*, Jun;76(6):942-947, 2017.
3. Kullenberg T, Lofqvist M, Leinonen M, et al, Long-term safety profile of anakinra in patients with severe cryopyrin-associated periodic syndromes, *Rheumatology*, Aug;55(8): 1499-506, 2016.
4. Lachmann HJ1, Kone-Paut I, Kuemmerle-Deschner JB, et al, Use of canakinumab in the cryopyrin-associated periodic syndrome. *N Engl J Med*, Jun 4;360(23):2416-25, 2016.
5. Aróstegui JI1, Lopez Saldaña MD, Pascal M,et al, A somatic NLRP3 mutation as a cause of a sporadic case of chronic infantile neurologic, cutaneous, articular syndrome/neonatal-onset multisystem inflammatory disease: Novel evidence of the role of low-level mosaicism as the pathophysiologic mechanism underlying mendelian inherited diseases. *Arthritis Rheum*, Apr;62(4):1158-66, 2016





North American Neuro-Ophthalmology Society

# 44th Annual Meeting

March 3– March 8, 2018

The Hilton Waikoloa Village • The Big Island of Hawaii

## Poster Session I: Clinical Highlights in Neuro-Ophthalmology

Sunday, March 4, 2018 1:00 pm – 3:00 pm

*Authors will be standing by their posters during the following times:*

*Odd-Numbered Posters: 1:15 pm - 2:00 pm*

*Even-Numbered Posters: 2:00 pm - 2:45 pm*

Poster #		Presenting Author
<b>Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)</b>		
1	Varicella Zoster Virus Optic Neuritis in a Young, Healthy Female	Amar K Bhat
2	Sequential Non-arteritic Ischemic Optic Neuropathy in a Healthy 19-year-old Male	Larissa K Ghadiali
3	The Dynamics of Retinal Ganglion Cell Loss in Non Arteritic Anterior Ischemic Optic Neuropathy (NAION)	François-Xavier Borruat
4	Combined Folic Acid and Vitamin A Deficiency Optic Neuropathy and Retinopathy	Su Ann Lim
5	Dasatinib-related Haemorrhagic Optic Neuropathy	Chee Fang Chin
6	AZOOB and Brain White Matter Lesions	Theo M Mobach
7	A Case of Concomitant Optic Neuritis and Panuveitis	Venkatesh L Brahma
8	Primary Ewing's Sarcoma Of The Paranasal Sinuses Presenting With Rapidly Progressive Bilateral Visual Loss.	Haydee Martinez
9	An Unusual Presentation of Bilateral Anterior Optic Neuritis	Amrita-Amanda D Lakraj
10	Central Retinal Artery Occlusion Due to Orbital Segment Ophthalmic Artery Aneurysm	Andrew R Carey
11	Achiasma in Kapur-Toriello Syndrome: Two Rare Entities	Grant A Justin
12	Chiasmal Migration of Intraocular Silicone Oil	Anuchit Poonyathalang
13	Isolated Optic Neuritis with Abnormal Trigeminal Nucleus on Imaging: Rare Complication of Herpes Zoster Ophthalmicus	Kavin Vanikieti
14	Enhancement of the Optic Nerve Sheath in Arteritic Ischemic Optic Neuropathy	Sara AlShaker
15	Progressive Normal Tension Glaucoma or Optic Nerve Compression: A Case Report	Ian C Uber
16	Optic Neuropathy Secondary to Allergic Fungal Sinusitis	Peter Daniel
17	The Perfect Storm: Ruptured & Dissecting Cerebral Aneurysms Leading To Acute Macular Neuroretinopathy	Tina R Porzukowiak
18	Irreversible and Severe Vision Loss Despite Aortic and Carotid Revascularization in Takayasu's Arteritis	Michael E Christiansen
19	Atypical Cases of Leber Hereditary Optic Neuropathy	Bo Young Chun
20	Vitreopapillary Traction Associated with Bullous Retinoschisis Masquerading as Optic Disc Edema	Gerard L Hershewe
21	Two Cases of Segmental Disc Edema and Normal Visual Acuity in Giant Cell Arteritis	Ari Shemesh

22	Giant Cell Arteritis Involving Multiple Cranial Nerves	Sara N Reggie
24	A Case of Efferent and Afferent Disease	Andrew J Sumnicht
25	Mitochondrial Translation Optimizer-1 Mutation as a Cause of Hereditary Optic Neuropathy	Emily Li
<b>Disorders of the Posterior Visual Pathway and Visual Processing</b>		
26	Cerebral Stroke Causing Monocular Hemianopia on Automated Perimetry	Samuel K Lee
27	Akinetopsia after Unilateral Surgical Labyrinthectomy	Dr Maryke N Neiberg
28	Homonymous Hemianopsia as the Presenting Sign of Migrainous Infarction	Aroucha Vickers
29	Persistent Visual Field Defects Eight Months After Posterior Reversible Leukoencephalopathy Syndrome	Senem Salar Gomceli
<b>IIH</b>		
30	Improved Transverse Sinus Stenosis After Lumbar Puncture in Idiopathic Intracranial Hypertension	Seo-Young Choi
31	The Utility of Optical Coherence Tomography in the Evaluation of Papilledema	Rahul A Sharma
32	Glomus Jugulare Tumor Induced Intracranial Hypertension	Editha D Johnson
33	Lithium-induced Venous Sinus Anatomy and Pressure Gradient Changes in Pseudotumor Cerebri Syndrome	Aimee J Szewka
34	Nonsyndromic Craniosynostosis Mimicking Primary Pseudotumor Cerebri Syndrome	Elissa K Ortolani
<b>Miscellaneous</b>		
35	Transient Visual Hallucinations with Eye Closure After Gamma Knife Radiosurgery	Leo Kubono
36	Serous Retinal Detachment and Optic Neuropathy Secondary to Intra-operative Venous Congestion	Victoria Leung
37	Rituximab Use In Neurosarcoidosis	Mangayarkarasi Thandampallayam
38	Acrodermatitis Enteropatica (AEZ) and Retinal Ganglion Cell Dysfunction – Is There a Causal Relationship?	Neringa Jurkute
39	Bilateral Ischemic Optic Neuropathy following Benzathine Penicillin: Hoigne Syndrome	Moira R Altszul
<b>Neuro-Imaging</b>		
40	Sudden-onset Blindness from a Spontaneous Carotid-cavernous Fistula with Secondary Central Retinal Artery Occlusion.	Daniel J Oh
41	Non-LETM in MOG-IgG related CNS demyelination	Kemar E Green
42	Extensive Adenoid Cystic Carcinoma (ACC) Presented as Bilateral Vision Loss and Optic Nerve Atrophy	Yu Zhao
43	Intracranial Hypertension From Dural Arteriovenous Fistula	Justin West
44	Decreased Activation of Human Motion Area V5/MT+ During Motion Perception and Attempted Pursuit in Akinetopsia	Eek-Sung Lee
45	Imaging Modalities as an Aide in the Diagnosis of MGDA and Associated Comorbidities	Catalina Cleves-Bayon
46	Giant Dilated Virchow Robin Spaces Causing Midbrain Compression and Obstructive Hydrocephalus	Padmaja Sudhakar
47	Longitudinal Multi-Modal Neuroimaging in Opsoclonus-Myoclonus Syndrome	Sun-Young Oh
<b>Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases</b>		
48	Optic Neuritis and Hemiparesis in a Previously Healthy Young Woman	Dulanji K Kuruppu
49	Visual loss Due to Nutritional Optic Neuropathy Following Gastric Bypass	Xuemin Zhang
<b>Orbital and Eyelid Disorders</b>		
50	A Case of the Orbital Apex Syndrome as Initial Presentation of Acute Myelitic Leukemia	Ji-Yun Park
<b>Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases</b>		
51	Eyes Wide Shut in the Face of Cancer	Arezu Haghighi
52	Fibrous Meningioma with Clinical Resemblance to Inflammatory Pseudotumor	Dae Woong Bae
53	Horner's Syndrome as the Presenting Symptom in Giant Cell Arteritis	Stephanie Figueira

54	Oculomotor Nerve Palsy Due To Clivus Metastasis Of Breast Cancer	Soon Young Cho
55	Neuro-ophthalmologic Findings in a Hemizygous Patient with Spastic Ataxia of Charlevoix-Saguenay	Scott R Haines
57	Isolated Optic Neuropathy Associated with Mycoplasma Pneumoniae	Seo-Young Choi
58	Papilledema Due to Cerebral Venous Sinus Thrombosis	MInsoo Baek
59	A Case of Anti-Glial Fibrillary Acidic Protein (GFAP) Antibody Associated Meningoencephalomyelitis	Thirugnanam Umapathi
60	POSTER WITHDRAWN	
61	Compressive Optic Neuropathy? - A Case of Thyroid-associated Optic Neuropathy without Crowding Orbital Apex	Ko-Jo Lin
62	An Unusual Case of Bilateral Optic Disc Swelling: POEMS syndrome	Gabriele Berman
63	Profound Hemorrhagic Disc Edema as Presenting Manifestation of Acute Myelogenous Leukemia	Gerard L Hershewe
64	Trichinella Nativa Infection from Black Bear Meat: A Rare Cause of Cerebral Venous Sinus Thrombosis	Danah H Albreiki
65	Ataxia, Areflexia, and Ophthalmoplegia in a Patient with AChR Binding Antibody?	Christine Greer
66	Retinal Angiographic Evidence of CJD Prion Disease in Humans	Norah S Lincoff
67	Chronic Lymphocytic Leukemia Presenting as Optic Disc Edema and Branch Retinal Artery Occlusion	Jefferson Berryman
68	Tubular Aggregate Myopathy with Miosis and Rod-Cone Dysfunction	Greg A Richardson
69	Atypical Central Retinal Artery Occlusion As The First Manifestation Of POEMS Syndrome	Thanatporn Threetong
70	Intermittent Colour Vision Loss as the Initial Presentation of Chronic Myeloid Leukemia	Solin Saleh
71	Papilledema and Anterior Granulomatous Uveitis in Congenital HIV despite HAART Therapy	Ryan A Gise
72	Isolated Unilateral Optic Nerve Involvement as Initial Manifestation of Meningeal Carcinomatosis	Amadeo R Rodriguez
73	Optic Neuropathy in Riboflavin Transporter Deficiency (Brown-Vialetto Van Lear syndrome)	Kannan M Narayana
74	Diffusion Weighted Imaging in Non-arteritic Posterior Ischemic Optic Neuropathy	Kristin Miller
75	Reversible Bilateral Optic Disc Edema with Heart Failure, Bacterial Endocarditis and Bicuspid Aortic Valve (BAV)	Adeela M Alizai
76	MOG Positive Optic Neuritis with a Phenotype of CRION Disease	Ama Sadaka
77	Bilateral Optic Disc Edema in a Young, Obese Woman: Pseudotumor Cerebri or Something More?	Laurel N Vuong
78	A Curious Case of Arteritis: Infectious, Inflammatory or Both	Jacob Rullo, MD
79	Alcohol-Responsive Myoclonus In Type I Sialidosis	Julie DeBacker
80	Arteritic Anterior Ischemic Optic Neuropathy and Eosinophilic Granulomatosis with Polyangiitis: Case Report	Kelvin Au, MD
81	Neurosarcoidosis Mimicking Viral Meningoencephalitis	Joseph G Chacko
82	Hemodynamic Neuro-ophthalmic Complications from Hemodialysis	Nailyn Rasool
83	Against the Wall	Abby L Vercio
84	Hypereosinophilia and Neuro-ophthalmological manifestations in Lymphoma	Ehtesham Khalid
85	Traumatic Carotid-Cavernous Fistula in FMD Presenting as Ophthalmoplegia and Status Epilepticus	Scott Grossman
86	Congenital Cranial Dysinnervation Disorder: An Unusual Phenotype	Michael S Salman
87	Check Point Inhibitor (CPI) Related Limbic Encephalitis	Ehtesham Khalid
88	Early Detection of Dural Carotid-cavernous Fistula (CCF) with Rapidly Aggravating Headache and Cranial Nerve Paresis	Yeon Woong Chung
89	A Case of Complete Ophthalmoplegia as the First Manifestation of Primary Pituitary Lymphoma	Hae-ri Yum
90	Axenfeld-Rieger Syndrome with Cerebellar Dysgenesis: A Clinical Association in Patients with FOXC1 Mutation	Laura A Torrado
91	Infectious Cavernous Sinus Thrombosis in a Non-Toxic Patient.	Sanjai Jalaj

92	Sudden Onset Diplopia and Eyeball Pain Diagnosed as Rhino-orbito-cerebral Mucormycosis (ROCM)	Hak Seung Lee
93	A Case of Susac Syndrome with Neuropsychiatric Overtones	Siwei Zhou
94	More than Meets the Eye	Sophie Cai
96	Wernicke Encephalopathy Owing To Vitamin Non-Adherence After Bariatric Surgery	Olivia J Killeen
97	Triple Hit Ophthalmoplegia	Claudia M Prospero Ponce
98	Isolated IV Nerve Palsy as First Sign in the Diagnostic of Lung Carcinoma	Luciana L Iacono
99	Rapid Onset Wernicke's Encephalopathy In A Patient Undergoing Radiation Therapy	Jordan Stanley
100	Neuro-ophthalmological Sequelae of Carbon Monoxide Poisoning: A Brief Case Series	Sangeeta Khanna
101	Glial Fibrillary Acidic Protein Astrocytopathy: The Great Imitator	David Rastall
102	On The Hunt For Sarcoidosis	Kimberly K Gokoffsk
103	A Divergence of Views	Roisin Buckels
104	Bilateral Anophthalmia Associated with Septo-optic Dysplasia.	Omar Solyman
105	Optic Perineuritis, Horner's Syndrome, and Purtscher-Like Retinopathy as an Atypical Presentation of Giant Cell Arteritis	Leonid Zlotcavitch
<b>Ocular Motility Disorders and Nystagmus</b>		
106	Two cases of painful ophthalmoplegia	Hirofumi Emoto
107	Topical Timolol In The Treatment Of Superior Oblique Myokymia: Report Of Two Additional Cases	Jagger C Koerner
108	Dorsal Midbrain Syndrome, a Manifestation of Shunt Malfunction in Aqueductal Stenosis	Xuemin Zhang
109	A Case of Paroxysmal Ocular Tilt Reaction	Ju-Hyang Lee
110	Innervational Upshoot In Duane's Retraction Syndrome - when to suspect and how to treat?	Rawan Omary
111	Novel Recessive Mutations in SLC38A8 Causing Infantile Onset Nystagmus with Foveal Hypoplasia	Kim Bo Ram
112	Monocular Single Saccadic Pulses in Brainstem Inflammation	Jae-Hwan Choi
113	Cerebellar Dysfunction Associated Anti-glutamic Acid decarboxylase Antibody	Seo-Young Choi
114	Bilateral Internuclear Ophthalmoplegia Associated with Anti-GQ1b Antibody	Seung-Han Lee
115	Windmill Nystagmus in a Patient with Visual Loss	Sun-Uk Lee
116	Post-surgical Oculopalatal Tremor with Facial Diplegia and Bilateral Horizontal Gaze Palsy	Anthony J Brune
117	Downbeat and Prominent Progressive cacheXia from anti-DPPX encephalitis	Jonathan A Micieli
118	Facial And Abducens Palsy In Pseudotumor Cerebri. Case Report And Literature Review.	Maria L Braccia Gancedo
119	Periodic Alternating Nystagmus Associated with Joubert Syndrome	Hak-Seung Lee
120	Quite An Odd Pairing: Miller-Fisher Syndrome and Autoimmune Thyroid Diseases	May Al-Ameri
121	Bilateral Complete Sixth Nerve Palsy After Traumatic Left Occipital Bone Fracture	Austin S Nakatsuka
122	A Case of Third Nerve Palsy Caused by Pituitary Carcinoma	Venkatesh Brahma
123	More Than Just Multiple Meningiomas: A Case Report of an Atypical Cause of Nystagmus	Jocelyn Kim
124	Gaze Evoked Nystagmus, Cataracts, Ataxia, and Progressive Hearing Loss: A Unique Syndrome	Devon A Cohen
125	Saccadic oscillations as a possible indicator of dizziness due to cholinesterase inhibitors	Ileok Jung
127	Hodgkin Lymphoma Diagnosed on Work-up for Ocular Myasthenia	Rhiannon Brooks
128	Acquired Comitant Esotropia following Botulinum Toxin Injection: A Brief Case Series	Lisa Bennett
<b>Ocular-Imaging</b>		
129	A Case of Cavernous Sinus Thrombosis with Acute Sinusitis in Children	Young Hoon Jung
130	Optical Coherence Tomography Angiography vs Fluorescein Angiography in Leber's Hereditary Optic Neuropathy (LHON)	Nagham Al-Zubidi
<b>Orbital and Eyelid Disorders</b>		
131	Thyroid-Associated Ophthalmopathy Presenting as Superior Rectus and Levator Palpebrae Enlargement	Angeline M Nguyen

132	Pituitary Adenoma Apoplexy of the Orbit	Nickisa M Hodgson
133	A Longhorn-Induced Superior Orbital Fissure Syndrome: A Case Report	Kimberly K Nguyen
134	Transorbital Embolization of a Thrombosing Carotid Cavernous Fistula	Lance J Lyons
135	Recurrent Fibrous Dysplasia	Nickisa M Hodgson
136	Orbital Apex Syndrome as a Complication of Herpes Zoster Ophthalmicus: Role of Systemic Steroids	Elizabeth A Cretara
137	Eosinophilic Variant of Orbital Granulomatosis with Polyangiitis with Hyperimmunoglobulinemia E: A Case Report	Ji Eun Lee, MD
138	Metastatic Orbital Disease with Positive Immunohistochemical test for Breast Cancer without Primary Tumor	Sheikh M Faheem
139	Headaches And Diplopia Secondary To Ipilimumab Treatment For Stage III Melanoma	Geetha K Athappilly
140	Trochleitis Without Imaging Abnormality	Yan Ning Neo
<b>Pupil</b>		
141	Painful Horner Syndrome as a Presentation of Nasopharyngeal Carcinoma: A Carotid Dissection Mimicking Lesion.	Tanyatuth Padungkiatsagul
142	Bilateral Carotid Body Paragangliomas Presenting with An Isolated Horner's Syndrome	Shuai-Chun Lin
143	A Fluttering Diagnosis	DonRaphael Wynn

## Poster 1

### Varicella Zoster Virus Optic Neuritis in a Young, Healthy Female

Amar Bhat<sup>1</sup>, Adrienne Gomez<sup>1</sup>, Murooj Jumah<sup>1</sup>, Nancy Vilar<sup>1</sup>

<sup>1</sup>George Washington University, Washington, District of Columbia, USA

#### Introduction:

We describe a very rare case of varicella zoster virus (VZV) optic neuritis causing profound vision loss in a young, immunocompetent adult female. The vast majority of VZV optic neuritis cases occur in elderly or immunosuppressed patients.

#### Description of Case(s):

A 29-year-old healthy and immunocompetent Caucasian female presented to her primary ophthalmologist with a right peri-orbital rash in the V1 distribution and a positive Hutchinson's sign. Past medical history was remarkable for chickenpox at age 6. She started taking oral valacyclovir but nonetheless developed pain with eye movements and sudden vision loss of the right eye (OD). She was referred to the hospital for work-up and treatment with IV acyclovir. On admission, she had hand-motion visual acuity and multiple dendritiform corneal epithelial lesions OD. Dilated fundus exam was unremarkable. The diagnosis of herpes zoster ophthalmicus was made and retrobulbar optic neuritis was suspected. MRI confirmed the diagnosis of optic neuritis but showed no signs of demyelinating disease. Cerebrospinal fluid studies were positive for VZV. Extensive work-up revealed no evidence of other infectious, inflammatory, immunosuppressive, ischemic, or hypercoagulable pathologies. Despite treatment with IV acyclovir and corticosteroids, the patient's vision progressed to no light perception within three days. She was discharged on oral prednisone and valacyclovir. Optical coherence tomography revealed progressive thinning of the retinal nerve fiber layer over three months. Fluorescein angiography was unremarkable. The patient underwent a second course of IV acyclovir and corticosteroids followed by a 6 week course of oral prednisone. Visual acuity improved to bare light perception 6 months after presentation.

#### Conclusions, including unique features of the case(s):

This case demonstrates that VZV can be a cause of profound vision loss due to optic neuritis in a young, healthy patient. This case also may represent just one of many cases of VZV optic neuritis to come, given the rising incidence of herpes zoster in young patients.

**References:** Kawai, Yawn, Wollan, Harpaz; Increasing Incidence of Herpes Zoster Over a 60-year Period From a Population-based Study, *Clinical Infectious Diseases*, Volume 63, Issue 2, 15 July 2016, Pages 221–226,

**Keywords:** Optic neuropathy, Neuro-ophth & infectious disease (eg, AIDS, prion), Optic nerve trauma and treatment

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 2

### Sequential Non-arteritic Ischemic Optic Neuropathy in a Healthy 19-year-old Male

Larissa Ghadiali<sup>1</sup>, Aakriti Garg<sup>2</sup>, Jeffrey Odel<sup>2</sup>

<sup>1</sup>Loyola University Medical Center, Maywood, Illinois, USA, <sup>2</sup>Columbia University Medical Center, New York, New York, USA

#### Introduction:

Non-arteritic ischemic optic neuropathy (NAION) is rare among patients below the age of 40. Younger patients tend to experience NAION in the setting of diabetes, optic nerve head drusen, hypercoagulation, or acute hypertension, hypotension, or blood loss. Vision loss is frequently bilateral (1-4). We present a case of a healthy 19-year-old male with sequential NAION.

#### Description of Case(s)

A 19-year-old Polish male presented with a history of painless vision loss of 8 months' duration OS and 1.5 months' duration OD. In Poland, he was treated with steroids without improvement. On our exam, BCVA was 20/25 OD and 20/30 OS with 14/14 Ishihara Color Plates seen OU and a left RAPD. HVF demonstrated an inferior defect OD and an inferior and superonasal defect OS. The right optic nerve was swollen while the left was pale with a crowded optic nerve head. There were no drusen seen on ultrasound or autofluorescence. Fluorescein angiography demonstrated disc leakage and staining OD. OCT showed RNFL thickening OD and thinning OS, while OCT angiography revealed increased vascularity around the optic nerve OD and peripapillary capillary dropout OS. Neurological exam was unremarkable. MRI brain/orbits, MRA head, EEG, CSF profile, and opening pressure were normal. Hypercoagulability and vasculitis work-up as well as optic neuropathy serology including NMO antibodies, anti-MOG antibodies, vitamin levels, and infectious testing were negative. Mitochondrial genome sequencing revealed no abnormalities. Multifocal ERG was normal and multifocal VEP confirmed his HVF defects. His right disc swelling gave way to pallor and his fields and acuity remained stable.

#### Conclusions, including unique features of the case(s):

Though extremely rare in teenagers, NAION does occur in this age group. As likely illustrated in this patient, patients under age 40 have a greater tendency toward sequential NAION than older adults. We feel that NAION at this age is a diagnosis of exclusion and believed an extensive work-up was necessary.

**References:** Chutorian, Winterkorn, Geffner. Anterior Ischemic Optic Neuropathy in Children: Case Reports and Review of the Literature. *Pediatr Neurol.* 26,358-64, 2002. Janáky, Fülöp, Pálffy, Benedek, Benedek. Non-arteritic ischaemic optic neuropathy (NAION) in patients under 50 years of age. *Acta Ophthalmol Scand.* 83, 499-503, 2005. Hamed, Purvin, Rosenberg. Recurrent anterior ischemic optic neuropathy in young adults. *J Clin Neuroophthalmol.* 8, 239-48, 1988. Turkoglu, Ilhan, Cetinkaya, Bilgin, Apaydin. Nonarteritic anterior ischemic optic neuropathy in young patients. *J Fr Ophtalmol.* 38, 421-6,2015.

**Keywords:** Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

### Poster 3

## The Dynamics of Retinal Ganglion Cell Loss in Non Arteritic Anterior Ischemic Optic Neuropathy (NAION)

François-Xavier Borruat<sup>1</sup>, Bao Khanh Tran<sup>1</sup>

<sup>1</sup>University of Lausanne, Ophthalmology department, Jules-Gonin Eye Hospital, Lausanne 1004, Switzerland

### Introduction:

Ischemic optic neuropathy will result in permanent loss of retinal ganglion cells (RGC). The time course of RGC loss has been determined in animal models of experimentally induced optic neuropathy, but is not known precisely in humans. The window of opportunity for neuroprotection of RGC needs to be precisely determined in humans.

### Description of Case(s):

A 47-year-old man presented with NAION in his left eye less than two days before initial examination. Seven years previously he suffered from a similar event in the right eye. We serially examined this patient with SD-OCT to assess the RGC layer (RGCL) thickness, in order to determine the time-course of his RGC loss. From the first examination on, there was an absolute symmetrical inferior altitudinal visual field loss with 20/20 visual acuity in both eyes. Visual function remained unchanged over the next five months. Left eye RGCL thickness was normal on Day 2 after acute NAION and started to decrease significantly on Day 7. We observed three phases of RGC loss : a rapid and linear phase from Day 7 to Day 15 ; a plateau for the next 28 days ; a slower but progressive rate of RGC loss for the next 12 weeks. The RGCL thickness remained then stable and was identical in both eyes.

### Conclusions, including unique features of the case(s):

The time course of RGC loss in human NAION seem to be similar to what has been reported in rodents following experimental injuries to the optic nerve. The RGCL thickness as assessed by SD-OCT start to decrease rapidly 7 days after the ischemic event. Although it is based only on the results of a single case of NAION, we suggest that the best window of opportunity for attempting a rescue to RGC via neuroprotective agents might be limited to the first six days after NAION.

**References:** None.

**Keywords:** Optic neuropathy, Vascular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



## Poster 4

### Combined Folic Acid and Vitamin A Deficiency Optic Neuropathy and Retinopathy

Su Ann Lim<sup>1</sup>, Melissa Chih Hui Tien<sup>1</sup>, Graham Holder<sup>2</sup>

<sup>1</sup>Tan Tock Seng Hospital, Singapore, Singapore, <sup>2</sup>National University Hospital/ Tan Tock Seng Hospital, Singapore, Singapore

#### Introduction:

We describe a case of combined folate and vitamin A deficiency (VAD) related optic neuropathy and retinopathy.

#### Description of Case(s):

A 22 year old Malay male presented with one month history of blurred right eye vision but no nyctalopia. Best corrected visual acuity (VA) was 6/18 OD, and 6/6 OS with no pupillary abnormality. No Ishihara color plates were seen with OD; 12/15 OS. Retinal nerve fiber layer (RNFL) and retinal optical coherence tomography (OCT) was bilaterally normal. At eventual review, VA was light perception OD, finger counting OS accompanied by Bitot spots, punctuate corneal epithelial erosions and white punctuate retinal lesions. He also developed optic disc and retinal swelling which were confirmed with OCT. VAD was suspected and electroretinography revealed a probable cone-isolated retina with no detectable rod function. In addition, there was bilateral optic nerve dysfunction, right much worse than left. Investigation revealed very low vitamin A and folate levels. It transpired that his diet was largely restricted to white bread for approximately 10 years. Replacement therapy gave symptomatic improvement and near normalization of his ERGs. There was post-treatment improvement only on the left in his visual evoked potentials.

#### Conclusions, including unique features of the case(s):

Combined nutritional optic neuropathy and retinopathy related to both folate and VAD has not been previously reported. The presentation was of unilateral optic neuropathy, perhaps surprisingly without nyctalopia. Folate deficiency optic neuropathy usually has a normal optic disc (1), but this patient developed both disc and RNFL swelling. Folate deficiency may result in inadequate detoxification of endogenous formate (2); formate acidemia produces optic disc swelling in monkeys (3). These novel observations may assist our understanding of the pathophysiology of nutritional optic neuropathy.

**References: 1)** Hsu CT et al.. Optic neuropathy from folic acid deficiency without alcohol abuse. *Ophthalmologica* 2002; 216:65-67. **2)** Golnik KC, Schaible ER. Folate responsive optic neuropathy. *J Neuro-ophthalmol* 1994, 14:163-169. **3)** Martin-Amat G et al. Methanol poisoning: Ocular toxicity produced by formate. *Toxicol Appl Pharmacol* 1978, 45:201-208.

**Keywords:** Optic neuropathy, Pupils Retina, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 5

### Dasatinib-related Haemorrhagic Optic Neuropathy

Chee Fang Chin<sup>1</sup>

<sup>1</sup>*Tan Tock Seng Hospital, Singapore, Singapore*

#### **Introduction:**

Dasatinib is a BCR-ABL tyrosine kinase inhibitor (TKI) which also targets platelet-derived growth factor (PDGF). Dasatinib is increasingly used in the treatment of chronic myeloid leukaemia (CML).

#### **Description of Case(s):**

A 47 year-old lady with a history of CML in the accelerated phase was commenced on Dasatinib. She also had a history of well-controlled Type 2 diabetes mellitus and hypertension. One month later, she presented with a 2-day history of painless blurring of vision in the right eye. Concurrently, she also complained of hearing loss, tinnitus and giddiness. She was initially diagnosed with right non-arteritic anterior ischaemic optic neuropathy (ON) and Dasatinib-related vestibulopathy. Although Dasatinib was transiently discontinued, she continued to develop a left ON, while the right eye continued to deteriorate to no perception of light. Investigations including MRI of the brain, orbits and internal auditory meatus, autoimmune screen, infective screen and lumbar puncture were normal. No evidence of infiltrative ON was found. Her visual acuities and vestibulopathy symptoms improved spontaneously. Thereafter, she was recommenced on Dasatinib. She then presented with a drop in her vision again, and developed severe left haemorrhagic optic disc swelling with multiple blot haemorrhages in the retina. She developed intractable tinnitus and giddiness. Investigations were repeated and were normal, with no evidence of any other causes of ON. Dasatinib was discontinued, and she was commenced on oral steroids. Her visual acuities improved, with resolution of the retinopathy in the left eye.

#### **Conclusions, including unique features of the case(s):**

We postulate that this was a case of Dasatinib toxic ON. A possible mechanism is retinal ganglion cell apoptosis secondary to inhibition of the PDGF pathway. The severity and clinical picture was unusual in this case. To our knowledge, there has been one prior published case of optic neuropathy secondary to dasatinib, where the presentation was of disc pallor.

**References:** None.

**Keywords:** Chemotherapy and radiation injury, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 6

### AZOOR and Brain White Matter Lesions

Theo Mobach<sup>1</sup>

<sup>1</sup>University of Calgary, Calgary, Alberta, Canada

#### Introduction:

We present a unique case report of a 25-year-old previously healthy female diagnosed with acute zonal occult outer retinopathy (AZOOR) and brain lesions suspicious for demyelination with asymptomatic left optic neuritis. AZOOR has been previously associated with multiple sclerosis and is thought to share a autoimmune pathophysiologic mechanism.

#### Description of Case(s):

The patient initially developed photopsias in the left superior temporal visual field and was assessed at another site. Approximately 26 months later she was re-assessed with persistent daily photopsia's and visual field changes in the left superior temporal region. Examination showed visual acuities of 20/20 OU, normal colour vision and afferent pupillary function. Visual field testing showed a left eye superior temporal defect on Humphrey 30-2. Ophthalmoscopy showed inferior retinal thinning in the left eye. Both optic nerves, blood vessels and maculae were normal. OCT showed average retinal nerve fiber layer thickness of 112 mcm in the right eye and 123 mcm in the left eye. Retinal OCT showed thinning of outer retinal layers in the left eye inferiorly. Fluorescein angiography revealed left eye inferior nasal increased visibility of the choroid circulation due to overlying atrophy of the retinal layers. ERG demonstrated attenuation of P1 responses in the left inferior nasal quadrant. MRI brain scan demonstrated increased T2 signal and swelling within the left optic nerve in addition to multiple T2/FLAIR lesions within the posterior fossa and periventricular regions suspicious for demyelination. Lumbar puncture showed positive oligo-clonal bands with normal cell count, glucose and protein. Additional testing was negative for anti-AQP4, anti-MOG, syphilis, HIV, and ANA.

#### Conclusions, including unique features of the case(s):

The case above outlines a unique presentation of AZOOR and demyelinating brain/optic nerve lesion. To our knowledge, only one other similar case has been published in the literature. Patients with AZOOR may benefit from neuroimaging to exclude co-existing demyelinating lesions in the brain/optic nerve.

**References:** 1. Hintzen RQ, van den Born LI. Acute zonal occult outer retinopathy and multiple sclerosis. *Journal of neurology, neurosurgery, and psychiatry.* 2006;77(12):1373-5. 2. Wang JC, Finn AP, Grotting LA, Sobrin L. Acute Zonal Occult Outer Retinopathy Associated With Retrobulbar Optic Neuritis. *Journal of Neuro-Ophthalmology : the official journal of the North American Neuro-Ophthalmology Society.* 2017;37(3):287-90.

**Keywords:** Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 7

### A Case of Concomitant Optic Neuritis and Panuveitis

Venkatesh Brahma<sup>1</sup>, Ninani Kombo<sup>1</sup>

<sup>1</sup>Yale-New Haven Hospital, Department of Ophthalmology, New Haven, Connecticut, USA

#### Introduction:

Relationships between multiple sclerosis and optic neuritis as well as between multiple sclerosis and uveitis have previously been described in literature. In fact, a recent study identified higher and comparable prevalence between optic neuritis and intermediate, posterior and pan-uveitis in comparison to anterior uveitis. We describe a case of optic neuritis with associated intermediate uveitis with otherwise unremarkable comprehensive testing.

#### Description of Case(s):

A 31-year-old male with no past medical or ocular history presented to the emergency department with 5 days of blurred vision and pain in the right eye. All other review of systems were negative. Vision was 20/60 pinhole to 20/30 in the right eye and 20/20 in the left eye. He had right eye pain with extraocular movement and a large right sided relative afferent pupillary defect. Anterior segment exam and intraocular pressures were normal in both eyes. Dilated fundus exam revealed mild disc edema in the right eye, as well as snowballs, snowbanking and peri-venular sheathing in both eyes. MRI demonstrated enhancement of the right optic nerve, but was otherwise unremarkable. Lab testing for Lyme, syphilis, sarcoid, cat-scratch, auto-immune diseases, HIV and Tuberculosis was negative. Fluorescein angiography revealed late optic nerve staining in the right eye and patchy phlebitis in both eyes. OCT of the maculae were within normal limits. He was treated with high dose prednisone and continues to be followed by the ophthalmology and neurology teams with stable findings.

#### Conclusions, including unique features of the case(s):

While multiple sclerosis has been associated with both uveitis and optic neuritis, testing should be performed to rule out other etiologies. Cases of optic neuritis and uveitis have been seen with BCG vaccination as well Q fever. Testing for infectious (TB, syphilis, etc.), inflammatory (sarcoid, Bechet's), malignancy (leukemia, lymphoma) and investigation into medication-related (rifabutin) should be performed when patients present with both uveitis and optic neuritis.

**References:** 1) Hegde V, Dean F. Bilateral panuveitis and optic neuritis following Bacillus Calmette-Guérin (BCG) vaccination. *Acta Paediatr.* 94(5):635-6. 2005. 2) Thouvenot E, Mura F, De verdal M, et al. Ipsilateral uveitis and optic neuritis in multiple sclerosis. *Mult Scler Int.* 2012:372361. 2012. 3) Million M, Halfon J, Le lez ML, Drancourt M, Raoult D. Relapsing uveitis and optic neuritis due to chronic Q fever. *Br J Ophthalmol.* 95(7):1026-7, 1038-9. 2011. 4) Channa R, Khurana RN, Speicher MA, et al. Diagnostic and therapeutic challenges: panuveitis and optic neuritis. *Retina (Philadelphia, Pa).* 29(7):1045-51. 2009. 5) Guo D, Liu J, Gao R, Tari S, Islam S. Prevalence and Incidence of Optic Neuritis in Patients with Different Types of Uveitis. *Ophthalmic Epidemiol.* 2017;;1-6. 2017.

**Keywords:** Optic neuropathy, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 8

### Primary Ewing's Sarcoma Of The Paranasal Sinuses Presenting With Rapidly Progressive Bilateral Visual Loss.

Haydee Martinez<sup>1</sup>, Mirta Arana<sup>1</sup>, Lidia Sarotto<sup>1</sup>, Carolina Busquets<sup>1</sup>, Marcelo Rivamonti<sup>1</sup>, Nicolas Zago<sup>1</sup>, Juan Ignacio Antonelli<sup>1</sup>, Mariana de Virgilis<sup>2</sup>, Macarena Clementi<sup>1</sup>

<sup>1</sup>Hospital de Clinicas "Jose de San Martin" – University of Buenos Aires, Buenos Aires, Argentina, <sup>2</sup>Hospital Oftalmológico "Dr. Pedro Lagleyze", Buenos Aires, Argentina

#### Introduction:

To raise awareness on this uncommon etiology of paranasal tumors in adulthood, more frequent in child population, but poorly taken under consideration in compressive optic neuropathy. The diagnosis was established with certainty by means of surgical biopsy.

#### Description of Case(s):

Clinical report of a thirty two year-old male, who consulted for rapid visual loss in his left eye (OS) associated with diplopia, specially in up-gaze. He had undergone otorrinolaringologic treatment for epistaxis ten days prior to the initial eye symptoms, therefore has had an endonasal "polyp" removed. In the neuro-Ophthalmologic exam the visual acuity (VA) arouse 20/20 in right eye (OD), and finger counting in OS associated to RAPD, up-gaze limitation, impaired cromatic vision and swelling optic disc. He also developed left exoftalmos while progressing visual loss to light perception OS and posterior affection of VA in his OD to 20/200. A brief summery of the patient will be presented, and also the studies carried out to diagnose this rare etiology of optice nerve compression. Interdisciplinary consultations were undergone, including Otorhinolaryngology, Neurology and Oncology. Neuroimaging was performed, but the final etiological diagnosis was arrisen after biopsy and anatomopathological analysis, conclusive of a PNET/Ewing's sarcoma of the paranasal sinuses. Therefore, the patient undergone chemo and radiotherapy. In post treatment control, and after one-year follow up, the patient's VA was OD hand movement and OS no light perception, RAPD OD and Marcus Gunn pupil OS, and fundus examination OU with generalized pallor of the optic disk.

#### Conclusions, including unique features of the case(s):

Although PNET/Ewing's Sacoma affects adults rarely, it should be considered in patients presenting with diplopia, associated to VA impairment and otorrinolaringological symptoms, since a rapid diagnose will invariably lead to best results, and biopsy is much less aggressive when done through enodonasal approach.

**References:** None.

**Keywords:** Neuroimaging, Ocular Motility, Optic neuropathy, Orbit/ocular pathology, Tumors

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 9

### An Usual Presentation of Bilateral Anterior Optic Neuritis

Amrita-Amanda Lakraj<sup>1</sup>, Neil Miller<sup>1</sup>, Andrew Carey<sup>1</sup>

<sup>1</sup>Wilmer Eye Institute, Johns Hopkins Hospital, Baltimore, Maryland, USA

#### Introduction:

VKH disease is a granulomatous inflammatory disorder that can be bilateral or unilateral and is associated with a variety of ocular findings, including serous retinal detachments, multifocal retinal pigment epithelial detachments, optic disc swelling, and vitritis.

#### Description of Case(s):

A 62-year-old male dentist with a history of hypertension, cervical stenosis, and long-standing hearing loss presented to the ER with a 1-week history of headache and visual disturbance. Ophthalmologic exam was significant for visual acuity of 20/40 OD and 20/50 OS, normal color vision, and Frisén grade 1-2 disc swelling OU. MRI brain w/wo was normal. MRI orbits showed subtle increased T2 signal of both optic nerves. MR venogram was unremarkable. Lumbar puncture revealed an opening pressure of 16 cm H<sub>2</sub>O with 10-13 WBCs and a protein of 70 mg/dL. The patient was admitted to Neurology. Serum and CSF evaluations for various bacterial and viral infections were unremarkable. CSF cytology demonstrated increased cellularity, with mononuclear cells, predominantly lymphocytes, T>B. Over the next 2 days, the patient's VA worsened to 20/50 OD and 20/100 OS. Given the negative CSF/serum evaluation, he was started empirically on IV methylprednisolone, 1 gram daily. Within 3 days, VA improved significantly to 20/40 OD and 20/20 OS. He was discharged on a steroid taper with presumed diagnosis of NMO. Upon clinic follow up, Heidelberg OCT of the retinal nerve fiber layer and macula showed multifocal retinal pigment epithelial detachments associated with subretinal fluid OU with thickened choroid. The patient was diagnosed with bilateral papillitis due to Vogt-Koyanagi-Harada (VKH) disease and was restarted on oral prednisone.

#### Conclusions, including unique features of the case(s):

Papillitis has only recently been recognized as a presenting sign of VKH. Presence of choroidal thickening on OCT may differentiate the two (3). Ophthalmologists and neurologists should be aware of intraocular causes of optic disc swelling and their systemic associations.

**References:** 1. O'Keefe, Ghazala A. Datto, and Narsing A. Rao. "Vogt-Koyanagi-Harada disease." *Survey of ophthalmology* 62.1:1-25, 2017. 2. Algahtani, Hussein, et al. "Vogt Koyanagi Harada Syndrome mimicking multiple sclerosis: A case report and review of the literature." *Multiple Sclerosis and Related Disorders* 12: 44-48, 2017. 3. Maruko I, Iida T, Sugano Y, Go S, Sekiryu T. "Subfoveal choroidal thickness in papillitis type of Vogt-Koyanagi-Harada disease and idiopathic optic neuritis." *Retina*; 36(5):992-9, May 2016.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 10

### Central Retinal Artery Occlusion Due to Orbital Segment Ophthalmic Artery Aneurysm

Andrew Carey<sup>1</sup>

<sup>1</sup>*Wilmer Eye Institute, Johns Hopkins Medicine, Baltimore, Maryland, USA*

#### **Introduction:**

Central retinal artery occlusions occur in 1 in 100,000 people. Etiologies include vasculitis, local thrombosis, or embolism. It carries an increased risk of stroke and myocardial infarction. There is no proven treatment for central retinal artery occlusion and thus evaluation and treatment is targeted at identifying and treating underlying risk factors to reduce the risk of stroke and myocardial infarction. Embolisms may originate from venous thrombus if a right-left shunt exists; a cardiac thrombus; calcific or septic embolus from diseased cardiac valve; from great vessel, carotid artery, or ophthalmic artery disease including stenosis, arteriosclerotic plaque, dissection, or aneurysm.

#### **Description of Case(s):**

A 60 year-old lady presented with sudden onset vision loss in the right eye following right arm pain, dizziness, and was found to have blood pressure of 224/120. Ophthalmic exam demonstrated visual acuity of Counting Fingers at face OD and 20/20 OS with 0.9 log unit RAPD OD. Fundus exam demonstrated macular whitening with a cherry red spot & perfused nasal macula via short cilioretinal vessels along with arteriolar attenuation and venous box-carring. The patient was diagnosed with central retinal artery occlusion. Computed tomography angiography of the head and neck revealed an orbital segment ophthalmic artery aneurysm on the right just proximal to the branching of the central retinal artery.

#### **Conclusions, including unique features of the case(s):**

Intra-orbital ophthalmic artery aneurysm is an exceptionally rare finding, although compressive lesions causing vision loss have been reported, associated central retinal artery occlusion has not. Intra-orbital ophthalmic artery aneurysm may be an overlooked cause of cryptogenic central retinal artery occlusion because modern non-invasive angiography often poorly images the ophthalmic artery. Ophthalmic artery aneurysm may be associated with other pathology including intracranial aneurysm, arteriovenous fistula or malformation. Treatment of orbital aneurysms is controversial, however in cases of orbital apex syndrome deficits can be reduced or resolved with treatment.

**References:** Della, Sabatino, La Rocca, Sceratti, Maira et al. Intraorbital and intracanalicular ophthalmic artery aneurysms. Literature review and report of a case. *Br J Neurosurg.* 2014 Dec;28(6):787-90. doi: 10.3109/02688697.2014.913776. Epub 2014 May 5.

**Keywords:** Neuroimaging, Orbit, Vascular disorders, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 11

### Achiasma in Kapur-Toriello Syndrome: Two Rare Entities

Grant Justin<sup>1</sup>, Keith Early<sup>2</sup>, Aaron Grant<sup>2</sup>

<sup>1</sup>Brooke Army Medical Center, Fort Sam Houston, Texas, USA, <sup>2</sup>Wilford Hall Ambulatory Surgical Center, San Antonio, Texas, USA

#### Introduction:

We describe a case of achiasma in a 5-year-old male with a constellation of signs demonstrating Kapur-Toriello syndrome. We provide a brief review of achiasma with common findings on examination and imaging studies.

#### Description of Case(s):

A 5-year-old male presented to the Neuro-Ophthalmology clinic after achiasma was noted on an MRI. Visual acuities were 20/250 OD and 20/150 OS. He had a right relative afferent pupillary defect. There was restriction of adduction in the right eye. He had a right exotropia 35 PD at near and 30 PD at distance (Krimsky). This was consistent with either an internuclear ophthalmoplegia or Duane's syndrome. In addition, he had a small amplitude, high frequency pendular horizontal nystagmus with overlying right beating nystagmus. On slit lamp examination, he had an inferior right iris coloboma. His posterior examination demonstrated a large retinal and optic nerve coloboma in the right eye. In addition, consistent with the rare Kapur-Toriello syndrome, he had a right unilateral cleft lip and palate, neurologic abnormality in his achiasma, anal atresia, vesicoureteral reflux, hypospadias, growth deficiency. He would be the 7th described case of Kapur-Toriello syndrome. Chromosome microarray showed a small gene deletion of 6p23, which is not associated with any syndrome. No history of birth defects, severe cognitive impairment, genetic conditions, recurrent miscarriages or sudden death were noted in his family.

#### Conclusions, including unique features of the case(s):

Achiasma and Kapur-Toriello syndrome are both extremely rare. Although visual field testing was not able to be completed on our patient, on review of the literature it is generally normal. Providers should consider treating amblyopia in these patients with patching.

**References:** 1. Sami DA, Saunders D, Thompson DA, et al. The achiasmia spectrum: congenitally reduced chiasmal decussation. *Br J Ophthalmol.* 2005;89(10):1311-7. 2. Breclj J, Sustar M, Pečarič-Meglič N, Skrbec M, Stirn-Kranjc B. VEP characteristics in children with achiasmia, in comparison to albino and healthy children. *Doc Ophthalmol.* 2012;124(2):109-23. 3. Hoffmann MB, Kaule FR, Levin N, et al. Plasticity and stability of the visual system in human achiasma. *Neuron.* 2012; 9;75(3):393-401. 4. Kapur S, Toriello HV. Apparently new MCA/MR syndrome in sibs with cleft lip and palate and other facial, eye, heart, and intestinal anomalies. *Am J Med Genet.* 1991; 41:423-425.

**Keywords:** Pediatric Neuro-Ophthalmology, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



## Poster 12

### Chiasmal Migration of Intraocular Silicone Oil

Anuchit Poonyathalang<sup>1</sup>, Pisit Preechawat<sup>1</sup>, Panitha Jindahra<sup>1</sup>, Piyaphon Cheecharoen<sup>1</sup>, Duangnate Rojanaporn<sup>1</sup>, Wimonwan Chokthaweesak<sup>1</sup>

<sup>1</sup>Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

#### Introduction:

To report a rare neuronal complication of long-term intraocular silicone oil

#### Description of Case(s):

A 62-year-old woman presented to our clinic with sudden painless temporal visual field loss in the right eye. Visual acuity was 20/50 and hand motion in the right and left eye, respectively. Right funduscopy was significant for stable proliferative diabetic retinopathy (PDR) with diffused photocoagulation chorioretinal scar. Funduscopy of the left eye revealed glaucomatous optic atrophy and detached retina with incomplete silicone oil filling of the globe. Visual field testing showed temporal visual field defect in the right eye. Eight months prior to presentation, she was diagnosed with bilateral PDR and severe tractional retinal detachment in the left eye, which was treated with vitrectomy and silicone oil tamponade. Her left eye also developed neovascular glaucoma with high intraocular pressure, ranging from 30-60 mmHg, in spite of maximal antiglaucomatous medication and photocoagulation. Based on magnetic resonance imaging (MRI), silicone oil was observed in left vitreal cavity and along left optic nerve extending to optic chiasm. The diagnosis of retrograde chiasmal migration of intravitreal silicone oil was made. Silicone oil removal was performed in order to prevent further progression of visual field defect. Four months follow-up, visual acuity was 20/40 and hand motion in the right and left eye, respectively. Temporal visual field defect in the right eye remained stable. Hypotony of the left eye was observed. Repeated MRI revealed stable silicone oil along left optic nerve extending to optic chiasm.

#### Conclusions, including unique features of the case(s):

Similar to our case, uncontrolled elevating intraocular pressure and glaucomatous optic atrophy are known to be risk factors of the rare intracranial migration of long-term intraocular silicone oil. Awareness, appropriate management of postoperative glaucoma and early removal of intraocular silicone oil as no longer indicated, are prudent to consider for prevention of this devastating neuronal complication.

**References:** None.

**Keywords:** Optic neuropathy, Pupils Retina, Neuroimaging, Visual fields

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 13****Isolated Optic Neuritis with Abnormal Trigeminal Nucleus on Imaging: Rare Complication of Herpes Zoster Ophthalmicus**

Kavin Vanikieti<sup>1</sup>, Anuchit Poonyathalang<sup>1</sup>, Panitha Jindahra<sup>2</sup>, Piyaphon Cheecharoen<sup>3</sup>, Patchalin Patputtipong<sup>3</sup>, Tanyatuth Padungkiatsagul<sup>1</sup>

<sup>1</sup>Dept. of Ophthalmology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, <sup>2</sup>Dept. of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, <sup>3</sup>Dept. of Radiology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

**Introduction:**

Herpes zoster ophthalmicus (HZO) is related to reactivation of the latent varicella zoster virus (VZV) involving ophthalmic branch of the trigeminal nerve. Optic neuritis (ON) is a rare ocular complication following HZO. Most of the previous cases occurred simultaneously with other ocular complications, especially orbital apex syndrome. Moreover, detailed magnetic resonance imaging (MRI) with diffusion weighted imaging (DWI) of optic nerve and trigeminal nucleus in HZO-related ON are scarcely documented.

**Description of Case(s):**

A healthy 58-year-old woman presented with sudden painful visual loss in right eye for 2 days. Four weeks prior, she was diagnosed as right HZO and received intravenous acyclovir for 10 days. Ophthalmic examination revealed visual acuity of light perception and 20/20 in the right and left eye, respectively. Right relative afferent pupillary defect was present. Otherwise was unremarkable. Neurologic examination was significant for hypoesthesia in the area of HZO. Other causes of atypical ON were excluded. MRI demonstrated enhancement and restricted diffusion of right-sided optic nerve with linear hyperintense T2 of right-sided spinal trigeminal nucleus and tract (STNT) along the brainstem. She received 14-day of intravenous acyclovir and 5-day of methylprednisolone. Both were switched into oral route with a total of 2 months in treatment duration. After the completion of treatment, visual acuity were counting fingers and 20/20 in the right eye and left eye, respectively. Stable brainstem STNT abnormalities and resolution of ON were found radiologically.

**Conclusions, including unique features of the case(s):**

Isolated ON is a very ocular complication following HZO. Furthermore, abnormal high signal of STNT on T2 weighted image may be present. This may be a clue for VZV-associated complications, such as HZO-related ON, especially in the case of lacking obvious history of HZO or other concomitant ocular complications. Prompt treatment with acyclovir and corticosteroids should be started. Restricted diffusion of the optic nerve may be a predictor for poor visual recovery.

**References:** None.

**Keywords:** Optic neuropathy, Neuroimaging, Neuro-ophth & infectious disease (eg, AIDS, prion)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 14****Enhancement of the Optic Nerve Sheath in Arteritic Ischemic Optic Neuropathy**

Sara AlShaker<sup>1</sup>, Ari Shemesh<sup>1</sup>, Laura Donaldson<sup>2</sup>, Edward Margolin<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Canada,* <sup>2</sup>*Department of Ophthalmology, McMaster University, Hamilton, Canada*

**Introduction:**

Giant cell arteritis (GCA) is an inflammatory vasculitis affecting large- and medium-sized arteries. The most common ocular manifestation is arteritic anterior ischemic optic neuropathy (AAION). MRI often shows enhancement of the extracranial and ophthalmic arteries; enhancement of the optic nerve sheath is very uncommon (Geiger et al., 2009). High dose steroids reduce the likelihood of fellow eye involvement, however, deterioration of vision continues in a subset of patients despite prompt treatment (Danesh-Meyer et al., 2005). Recovery of visual acuity occurs in a minority of patients (Foorozan et al., 2003).

**Description of Case(s):**

An 80 year-old female presented with a 5-day history of profound vision loss affecting first the right, then the left eye. She had been completing a taper of oral steroids for biopsy-negative presumed GCA with no prior ocular manifestations. Her BCVA on presentation was counting fingers and 20/150. There was no optic disc edema or pallor. Oral prednisone 50 mg daily was started. Despite this, vision deteriorated over 2 days to NLP and 20/150. Her right optic nerve head now exhibited diffuse pallid edema, with the left eye appearing segmentally swollen. High dose steroid (2g of solumedrol IV for 5 days) was initiated and the BCVA 1 week later was NLP and 20/50. MRI of the orbits revealed avid bilateral optic sheath enhancement with adjacent fat stranding. A repeat temporal artery biopsy confirmed the diagnosis of GCA.

**Conclusions, including unique features of the case(s):**

This is a unique case of severe vision loss secondary to GCA occurring despite initiation of steroids, followed by a significant recovery of vision. The initial normal appearance of the optic nerve heads suggested a posterior ischemic process, rapidly followed by the more common AAION. This unusual case is a reminder that during an acute phase of GCA, gadolinium enhancement of the optic nerve and orbital fat can be observed on MRI.

**References:** Danesh-Meyer, H., Savino, P. J., Gamble, G. G. Poor prognosis of visual outcome after visual loss from giant cell arteritis. *Ophthalmology*, 112(6), 1098-1103, 2005. Foroozan, R., Deramo, V., Buono, L., Jayamanne, D., Sergott, R. et al. Recovery of Visual Function in Patients with Biopsy-proven Giant Cell Arteritis. *Ophthalmology*, 110(3), 593-542, 2003. Geiger, J., Ness, T., Uhl, M., Lagrèze, W. A., Vaith, P. et al. Involvement of the ophthalmic artery in giant cell arteritis visualized by 3T MRI. *Rheumatology (Oxford)*, 48(5), 537-541, 2009.

**Keywords:** Optic neuropathy, Neuroimaging, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 15

### Progressive Normal Tension Glaucoma or Optic Nerve Compression: A Case Report

Ian Uber<sup>1</sup>, Thomas Ableman<sup>1</sup>

<sup>1</sup>Walter Reed National Military Medical Center, Bethesda, Maryland, USA

#### Introduction:

Optic neuropathy resulting from carotid (ICA) compression of the optic nerve anterior to the chiasm and the cavernous sinus is rare (1, 2, 3, 4, 5). Magnetic resonance imaging (MRI) studies of asymptomatic patients have shown that contact between the ICA and optic nerve at this location without optic neuropathy is in fact common. (2) When pathologic compression occurs, retrospective case reviews suggest that it can mimic normal tension glaucoma (1, 5).

#### Description of Case(s):

We present a case of a 37 year old male that was originally diagnosed with normal tension glaucoma (NTG) in his right eye. Visual field loss progressed over 3 years despite topical treatment. MRI was normal other than showing an extra loop in the internal carotid artery without obvious compression or contact of the optic nerve. He was ultimately referred to our Neuro-Ophthalmology clinic. Repeat MRI was obtained showing compression of the right optic nerve by a dolichoectatic right internal carotid artery. His optic neuropathy progressed over the next several years, becoming symptomatic. The decision was made to perform optic nerve decompression. After surgery that patient's visual fields stabilized, and his afferent pupillary defect (APD) and visual acuity improved.

#### Conclusions, including unique features of the case(s):

Conclusions 1. Compression of the optic nerve by the ICA is a rare, potentially treatable cause of optic neuropathy that can be misdiagnosed as NTG. 2. Progression in the setting of treatment for NTG may alert the clinician to reconsider the diagnosis of NTG. 3. Definitively identifying clinically significant compression presents a diagnostic challenge.

**References:** 1. Jacobson, Symptomatic Compression of the Optic Nerve by the Carotid Artery, *Ophthalmology*, 106, 1994-2004, 1999. 2. Jacobson, Warner, and Broste, Optic Nerve Contact and Compression by the Carotid Artery in Asymptomatic Patients, *American Journal of Ophthalmology*, 123, 677-683, 1997. 3. Golnik, Hund, Stroman, and Stewart, Magnetic Resonance Imaging in Patients with Unexplained Optic Neuropathy, *Ophthalmology*, 103, 515-520, 1996 4. Fargan and Blackburn, Surgical Decompression for Optic Neuropathy From Carotid Artery Ectasia: Case Report with Technical Considerations, *World Neurosurgery*, 82, 239.E9-231.E12. 5. Purvin, Kawasaki, Zeldes, Dolichoectatic arterial compression of the anterior visual pathways: neuro-ophthalmic features and clinical course, *Journal of Neurology, Neurosurgery, and Psychiatry*, 75, 27-32, 2004.

**Keywords:** Optic neuropathy, Vascular disorders, Visual fields

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 16

### Optic Neuropathy Secondary to Allergic Fungal Sinusitis

Peter Daniel<sup>1</sup>

<sup>1</sup>UAB, Birmingham, Alabama, USA

#### **Introduction:**

Allergic fungal sinusitis (AFS) may mimic other disorders in Neuro-Ophthalmology. As opposed to invasive fungal disease often associated with an immunocompromised state, AFS generally presents in young immunocompetent individuals with a history of atopy. It is most common in the Mississippi river valley but may present anywhere dematiaceous fungi are found. Allergic mucin, the pathologic hallmark, has been described as “peanut butter” or “axel grease” due to its tenacious viscosity.

#### **Description of Case(s):**

A nineteen year-old African American man presented with four-day history of painless visual loss OD. He had asthma but was otherwise healthy. Examination showed CF vision OD associated with an rAPD, mild proptosis, and optic nerve head pallor. Neuroimaging revealed extensive paranasal sinus dilation with mucoperiosteal changes and chronic inspissated secretions, resulting in orbital cone narrowing and compression of the right optic nerve as well as extension through the planum sphenoidale into the anterior cranial fossa. The patient was promptly referred to ENT for surgical evaluation but ultimately failed to regain vision despite decompression via functional endoscopic sinus surgery.

#### **Conclusions, including unique features of the case(s):**

AFS is a fascinating disease process frequently misdiagnosed due to its indolent nature in relatively young healthy individuals. It may cause proptosis, facial dysmorphism, severe vision loss, and potential cognitive dysfunction if brain compression occurs. Neuroimaging, particularly MRI, demonstrates characteristic findings that may be mistakenly perceived as absence of disease. Treatment is effective and largely surgical but also includes medical therapy. It is of the utmost importance for healthcare providers to have a high index of suspicion for timely diagnosis and treatment.

**References:** Aakalu, Vinay K. et al., “Allergic Fungal Sinusitis Induced Visual Loss and Optic Neuropathy,” *Neuro-Ophthalmology*, 2009. Graham, Scott M. et al., “Response of Visual Loss in Allergic fungal Sinusitis to Oral Corticosteroids,” *Annals of Otolaryngology, Rhinology, and Laryngology*, 2005. Gupta, A.K. et al., “Visual loss in the setting of allergic fungal sinusitis: pathophysiology and outcome,” *Journal of Laryngology and Otology*, 2007. Thakar, A. et al., “Optic Nerve Compression in Allergic Fungal Sinusitis,” *Journal of Laryngology and Otology*, 2011.

**Keywords:** Neuroimaging, Optic neuropathy, Miscellaneous, Orbit

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 17

### The Perfect Storm: Ruptured & Dissecting Cerebral Aneurysms Leading To Acute Macular Neuroretinopathy

Tina Porzukowiak<sup>1</sup>, Brianne Hobbs<sup>1</sup>

<sup>1</sup>Midwestern University Arizona College of Optometry, Glendale, Arizona, USA

#### Introduction:

Acute macular neuroretinopathy (AMNR) is a rare condition resulting in abrupt onset of unilateral or bilateral paracentral scotoma, mild visual acuity reduction, and wedge or oval-shaped lesions in the macula<sup>1-2</sup>. Common associations include antecedent flu-like illness, oral contraceptive or sympathetic agonist use, trauma, hypovolemia, and severe hypotension<sup>1</sup>. We present the first case of AMNR associated with ruptured and dissecting cerebral aneurysms status post neurosurgical repair.

#### Description of Case(s):

A 43-year-old Caucasian female presented to the emergency department with acute respiratory failure, seizure, and loss of consciousness. Spontaneous subarachnoid hemorrhage from a ruptured posterior inferior cerebellar artery aneurysm and right vertebral artery dissecting aneurysm was found. Surgical repair involved embolization and stenting, external ventricular drain placement, and a diagnostic angiogram. Vertebral basilar vasospasm was noted during angiography; this was treated with nicardipine hydrochloride. The post-operative period was complicated by declining cardiac status requiring multiple vasopressors and intra-aortic balloon pump for stress cardiomyopathy. Digital subtraction angiography revealed basilar and bilateral internal carotid artery vasospasm. Post-op blood loss anemia was documented. A paracentral scotoma of the left eye was noted upon awakening post-brain surgery. Best corrected visual acuity was 20/20 right eye (OD) and 20/20- left eye (OS). Pupils were normal without afferent pupillary defect. Deep, focal, yellow pigmentary changes were noted inferior-nasal to the macula. Fundus photographs, optical coherence tomography (OCT), and visual field studies were consistent with AMNR OS.

#### Conclusions, including unique features of the case(s):

Severe hypotension, hypovolemia, vasospasm, and treatment with sympathetic agonists created the perfect storm for reduced retinal capillary plexus perfusion. The pathogenesis of this patient's AMNR presentation may have been complex, but the diagnosis was straightforward using spectral domain OCT. This case highlights a unique presentation leading to AMNR relevant to all eye care providers.

**References:** 1. Bhavsar, Lin, Rahimy, et al. Acute Macular Neuroretinopathy: A Comprehensive Review of the Literature, *Survey of Ophthalmology*, 61,538-65, 2016. 2. Bos, Deutman. Acute Macular Neuroretinopathy, *American Journal of Ophthalmology*,80,573-84,1975. 3. Turbeville, Cowan, Gass. Acute Macular Neuroretinopathy,*Survey of Ophthalmology*, 48,1-11, 2003. 4. Aziz, Kheir, Young, et al. Acute Macular Neuroretinopathy: A Case Report and Review of the Literature, 2002-2012, *Ophthalmic Surgery, Lasers & Imaging Retina*, 46,114-24, 2015. 5. Sarraf, Rahimy, Fawzi, et al. Paracentral Acute Middle Maculopathy: A New Variant of Acute Macular Neuroretinopathy Associated with Retinal Capillary Ischemia, *JAMA Ophthalmology*,131,1275-87, 2013.

**Keywords:** Vascular disorders, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Visual fields, Pupils Retina, Interventional neuroradiology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 18****Irreversible and Severe Vision Loss Despite Aortic and Carotid Revascularization in Takayasu's Arteritis**

Michael Christiansen<sup>1</sup>, Cumara O'Carroll<sup>1</sup>, Oana Dumitrascu<sup>1</sup>

<sup>1</sup>Mayo Clinic, Phoenix, Arizona, USA

**Introduction:**

Takayasu's arteritis (TA) is a large-vessel vasculitis associated with ischemic oculo-cerebral complications. We report a patient with visual loss as initial manifestation and discuss surgical revascularization indication.

**Description of Case(s):**

19-year-old female developed recurrent episodes of transient right eye vision loss triggered by positional changes. Retinal evaluation showed bilateral sludge-like blood-flow. Two-months later, permanent right eye vision loss and new bright-light-induced left amaurosis prompted evaluation in our center. Subclavian bruits, palpable epigastric aortic pulsation, and faint radial pulses were noted. Best-corrected-visual-acuity was 20/200 in the right and 20/25 in the left eye. Right retinal and optic disc pallor, arteriolar narrowing, and bilateral boxcarring were seen. Fluorescein angiogram showed delayed right choroidal and bilateral arm-to-retina and arteriovenous filling. OCT showed inner-retina hyperreflectivity. Head/neck CT angiogram demonstrated left subclavian artery origin and right common carotid artery (CCA) occlusion, severe innominate and left CCA stenosis. Transcranial ultrasound demonstrated right ophthalmic artery flow reversal. Brain MRI showed scattered bi-frontal T2 white-matter hyperintensities. Corticosteroids, methotrexate, infliximab, and dual-antiplatelet therapy were initiated. 11 weeks later, patient underwent aortic aneurysm and bilateral CCAs graft repair. Pathology confirmed chronic active TA. Two weeks post-operatively, left eye visual symptoms and boxcarring resolved; right visual loss persisted and new right optic disc neovascularization was noted.

**Conclusions, including unique features of the case(s):**

Retinal ischemia and boxcarring in young women should prompt emergent inflammatory and vascular evaluation. The pathogenetic mechanisms are: hyperperfusion from ICA occlusion and ophthalmic artery flow reversal away from the eye to the brain; retinal artery occlusion due to microemboli from thickened inflamed proximal vessel; and small retinal arterial branches inflammation and occlusion. Prolonged right retinal ischemia had dismal prognosis despite carotid-aortic revascularization, whereas left retinal boxcarring reversed. Surgical revascularization is recommended for severely symptomatic oculo-cerebrovascular disease, once inflammation is better controlled with immunosuppressive therapy. Chronic ocular ischemia delayed complications may be prevented with surgical revascularization.

**References:** None.

**Keywords:** Vascular disorders, Stroke Trauma, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Pupils Retina

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 19

### Atypical cases of Leber Hereditary Optic Neuropathy

Bo Young Chun<sup>1</sup>, Sook Young Kim<sup>2</sup>, Soolienah Rhiu<sup>3</sup>

<sup>1</sup>Department of Ophthalmology, Kyungpook National University School of Medicine, Daegu, Korea, Republic of, <sup>2</sup>Department of Ophthalmology, Daegu Catholic University Medical Center, Daegu, Korea, Republic of, <sup>3</sup>Department of Ophthalmology, Hallym University Dongtan Sacred Heart Hospital, Dongtan, Korea, Republic of

#### Introduction:

To report atypical cases of Leber hereditary optic neuropathy (LHON)

#### Description of Case(s):

Case 1) A 52 year-old male presented with bilateral progressive visual loss for one month. The visual acuity was 20/200 in his right eye and CF in his left eye. Fundus examination revealed slight hyperemic optic nerve head in his right eye and normal optic disc in his left eye. Both eyes had central scotoma in visual field exam. He was found to have a 14484 mitochondrial point mutation consistent with LHON. Two years before LHON diagnosis, he was diagnosed to have a hepatic cellular carcinoma. Case 2) A 24 year-old female presented with bilateral subtle visual disturbance. Her visual acuities were 20/30 in both eyes. After 7 months later, her visual acuities decreased to 20/40, and fundus exam revealed temporal pallor of optic nerve head in both eyes. OCT demonstrated prominent papillomacular bundle defect in both eyes. She was found to have a 11778 mitochondrial point mutation consistent with LHON. One and half years after LHON diagnosis, her visual acuities decreased to 20/70 in both eyes.

#### Conclusions, including unique features of the case(s):

In Case 1, he was doing well with his 20/20 visual acuity although he had a 14484 mitochondrial point mutation. It is inferred that the trigger factor of the disease conversion may be a mitochondrial dysfunction induced by an increased requirement of ATP due to his hepatic cellular carcinoma. In Case 2, typical clinical feature of LHON is an acute or subacute visual loss in one eye followed by visual loss in the fellow eye at a median interval of 6-8 weeks, however, her bilateral symmetric visual deterioration has slowly progressed during 2 years. Considering that the patient is a young, otherwise healthy female, we speculate that neuroprotective effect of Estrogen might have a certain role in her atypical feature of LHON.

**References:** None.

**Keywords:** Optic neuropathy, Genetic Disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 20****Vitreopapillary Traction Associated with Bullous Retinoschisis Masquerading as Optic Disc Edema**

Gerard Hershewe<sup>1</sup>, Joshua Gratwohl<sup>2</sup>, Nikki Hamada<sup>2</sup>, Jerad Hershewe<sup>2</sup>, Alyssa Eckert<sup>1</sup>, Micaela Koci<sup>1</sup>

<sup>1</sup>University of Nevada, Reno School of Medicine, Reno, Nevada, USA, <sup>2</sup>University of Nevada, Reno, Reno, Nevada, USA

**Introduction:**

Vitreopapillary traction is characterized by persistent attachment of contracting vitreous to the optic nerve head. This may be caused by diabetic vitreoretinopathy, central retinal vein occlusion, and an epiretinal membrane. We report a patient with vitreopapillary traction associated with bullous retinoschisis clinically improved following vitrectomy, ERM and IRM peeling, laser, and gas therapy.

**Description of Case(s):**

81 year old female presented with a six month history of blurred vision OS. The patient also complained of a slight waviness of straight lines. She denied any symptoms consistent with temporal arteritis. The referring physician obtained a VA of 20/25 OD and 20/50 OS. There was reported optic disc edema OS and OCT showed an RNFL of 100 OD and 182 OS. Patient was referred to Neuro-Ophthalmology clinic. Initial examination showed VA of 20/20 OD and 20/30 OS, color vision was normal and there was a 0.3 RAPD OS. Funduscopic examination was normal OD and examination OS showed a serous detachment of the retina extending from the optic nerve to the macula. There was evidence of an epiretinal membrane. In addition there was vitreopapillary traction overlying the optic nerve in combination with bullous retinoschisis extending into the nasal midretinal periphery. There was also evidence of an inferior traction retinal detachment. The OCT confirmed the funduscopic examination and showed a serous detachment of the neurosensory retina extending from the fovea to the peripapillary region, vitreopapillary traction, and a moderate-sized nasal bullous retinoschisis. Subsequently the patient underwent a left vitrectomy with peeling of the epiretinal membrane, endolaser around the retinoschisis, and gas exchange with 10% C3F8. Overall her clinical status remained stable and the OCT improved.

**Conclusions, including unique features of the case(s):**

In patients presenting with optic disc edema, OCT may be a valuable tool in diagnosing vitreopapillary traction and peripapillary retinoschisis leading to appropriate surgical intervention.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 21

### Two Cases of Segmental Disc Edema and Normal Visual Acuity in Giant Cell Arteritis

Ari Shemesh<sup>1</sup>, Jonathan Micieli<sup>1</sup>, Laura Donaldson<sup>2</sup>, Edward Margolin<sup>1</sup>

<sup>1</sup>Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Canada, <sup>2</sup>Department of Ophthalmology, McMaster University, Hamilton, Canada

#### Introduction:

Giant cell arteritis (GCA) involves the ocular circulation in up to 70% of cases. Arteritic anterior ischemic optic neuropathy (AAION) classically causes optic nerve head edema with waxy pallor. Nonarteritic AION (NAION) commonly presents with better central visual acuity and diffuse or segmental disc hyperemia and edema. It is important to distinguish NAION from AAION, as AAION requires immediate treatment to minimize risk to the fellow eye. We describe two cases of biopsy-confirmed GCA presenting with preserved visual acuity and segmental disc edema without pallor.

#### Description of Case(s):

1) A 78 year-old man presented 5 weeks after he was seen by an optometrist for “blurred vision” in the right eye and found to have an altitudinal visual field defect. History was positive for questionable jaw claudication. Visual acuity was 20/20 OU with a right relative afferent pupillary defect (RAPD). The right optic nerve head showed moderate cupping (cup-to-disc ratio of 0.7) but no swelling, the left cup-to-disc ratio was 0.4. There was mild temporal pallor bilaterally. CRP was elevated at 70mg/dl while ESR and CBC were normal. 2) A 61 year-old woman presented with headache, jaw claudication, severe scalp tenderness and a one-week history of a right inferior visual field defect. Visual acuity was 20/30 and 20/20 with no RAPD. The right optic nerve head showed segmental edema superiorly with a single cotton wool spot and no pallor. Optic nerve head on the left appeared normal with cup-to-disc ratio of 0.4. CRP was mildly elevated at 11.1mg/dl, ESR and CBC were normal. Both patients underwent temporal artery biopsy, which confirmed the diagnosis of GCA.

#### Conclusions, including unique features of the case(s):

In cases that seem to fit a pattern for NAION, atypical signs/features should be looked for and a diagnosis of GCA entertained. Normal central visual acuity and absence of optic disc pallor do not rule out GCA.

**References:** Kawasaki A, Purvin V. Giant cell arteritis: an updated review. *Acta Ophthalmol* 87:13-32, 2009.

**Keywords:** Optic neuropathy, Neuro-opth & systyemic disease ( eg. MS, MG, thyroid), Vascular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 22**

**Giant Cell Arteritis Involving Multiple Cranial Nerves**

Sara Reggie<sup>1</sup>, Keirnan Willett<sup>1</sup>

<sup>1</sup>*University of Pennsylvania Scheie Eye Institute, Philadelphia, Pennsylvania, USA*

**PUBLICATION PERMISSION NOT GRANTED**

## Poster 24

### A Case of Efferent and Afferent Disease

Andrew Sumnicht<sup>1</sup>

<sup>1</sup>Loma Linda University, Loma Linda, California, USA

#### **Introduction:**

IgG4-related disease (RD) is a diagnosis of exclusion that manifests as inflammation and fibrosis in any organ, including the meninges and orbits. IgG4-RD has manifested as cranial nerve palsies and vision loss in these settings[1]. These symptoms are reversible with treatment.

#### **Description of Case(s):**

A 49-year-old female with chronic pachymeningitis presented with four weeks of progressive vision loss in the left eye (OS) from 20/20 to 20/400. In the past year she had two cranial nerve palsies in the right eye, each resolving spontaneously. She demonstrated borderline thickening of the retinal nerve fiber layers, a relative afferent pupillary defect, and a severely constricted visual field OS. Vision worsened to no light perception (NLP) OS over three days. Imaging demonstrated a new mass compressing the left optic nerve and diffuse pachymeningeal enhancement. Lumbar puncture showed elevated protein, IgG, IgG index (3.03), and IgG synthesis. Extensive workup revealed normal serum IgG and IgG4 fraction and ruled out known causes of meningitis. Dural biopsy revealed mild fibrosis without plasma cells or IgG4 immunoreactive cells. Her vision improved to 1/200 OS after two weeks of oral prednisone, which the patient self-discontinued due to side effect intolerance. She declined rituximab. Her vision spontaneously improved to 20/60 OS after two more months.

#### **Conclusions, including unique features of the case(s):**

The presumptive diagnosis was IgG4-hypertrophic pachymeningitis (HP). There are at least four other reported cases of biopsy-proven IgG4-HP with ophthalmic symptoms. Elevated IgG and IgG4 indices are reported to be reliable markers of IgG4-HP compared with infectious, rheumatologic, and other autoimmune causes of HP[2]. The diagnostic value of serum elevation of IgG and IgG4 has been questioned since IgG4 is only elevated in as many as 51% of cases and IgG is elevated in even fewer[1]. In this case the patient regained significant vision in a previously NLP eye and had a perplexing clinical course and workup.

**References:** Wallace ZS et al, IgG4-related disease: baseline clinical and laboratory features in 125 patients with biopsy-proven disease, *Arthritis Rheumatol*, 67(9), 2466-2475, 2015 Della-Torre E et al, Diagnostic value of IgG4 indices in IgG4-related hypertrophic pachymeningitis, *J Neuroimmunol*, 266(1-2): 82-86, 2014

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Skull Base, Neuroimaging, Tumors, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 25

### Mitochondrial Translation Optimizer-1 Mutation as a Cause of Hereditary Optic Neuropathy

Emily Li<sup>1</sup>, Francine Testa<sup>1</sup>, Valentina Emmanuele<sup>2</sup>, Christiane De Araujo Martins Moreno<sup>2</sup>, Michio Hirano<sup>2</sup>, Robert Lesser<sup>1</sup>

<sup>1</sup>Yale University School of Medicine, New Haven, Connecticut, USA, <sup>2</sup>Columbia University Medical Center, New York, New York, USA

#### Introduction:

Mitochondrial translation optimizer-1 (MTO1) mutations are a rare cause of hereditary optic neuropathy, with fewer than ten affected families reported in literature. Of these, only one family was reported to have vision loss. We present a case of hereditary optic neuropathy secondary to a mutation in MTO1.

#### Description of Case(s):

A 17-year-old male presented to a neuro-ophthalmologist in 2015 with bilateral progressive visual decline to 20/400 on the right and 20/200; exam was remarkable for optic nerve pallor and circumpapillary telangiectasias. Five years earlier, an exam performed in the context of neonatal hypertrophic cardiomyopathy, intellectual disability, and pulmonary stenosis, established bilateral best-corrected visual acuity of 20/20 bilaterally. Genetic testing for Leber hereditary optic neuropathy was negative. He had continued vision loss to hand motion bilaterally at last visit in 2017. An older brother, who was also born with cardiac and neurologic defects, has not had vision loss. Both developed a generalized epilepsy with photosensitivity. Whole exome sequencing revealed compound heterozygous novel mutations of MTO1 in the patient and his brother; the parents each carried one mutant allele.

#### Conclusions, including unique features of the case(s):

Mitochondrial diseases result in clinical compromise of multiple organ systems that rely on the mitochondrial respiratory chain. Classic manifestations include cardiomyopathy, seizure disorders, and cognitive disability. We report a case of hereditary optic neuropathy due to MTO1 mutations. Better characterization of this disease facilitates awareness, diagnosis, and potential therapeutic development.

**References:** 1. Baruffini E, Dallabona C, Invernizzi F, et al., MTO1 mutations are associated with hypertrophic cardiomyopathy and lactic acidosis and cause respiratory chain deficiency in humans and yeast, *Human Mutation*, 34(11), 1501-9, 2013. 2. Charif M, Titah SM, Roubertie A, et al., Optic neuropathy, cardiomyopathy, cognitive disability in patients with a homozygous mutation in the nuclear MTO1 and a mitochondrial MT-TF variant, *American Journal of Medical Genetics Part A*, 167A(10), 2366-74, 2015. 3. Finnila S, Majamaa K, Lack of a modulative factor in locus 8p23 in a Finnish family with nonsyndromic sensorineural hearing loss associated with the 1555A>G mitochondrial DNA mutation, *European Journal of Human Genetics*, 11(9), 652-8, 2003. 4. Ghezzi D, Baruffini E, Haack TB, et al, Mutations of the mitochondrial-tRNA modifier MTO1 cause hypertrophic cardiomyopathy and lactic acidosis. *American Journal of Human Genetics*, 90(6), 1079-87, 2012. 5. Martin MA, Garcia-Silva MT, Barcia G, et al., The homozygous R504C mutation in MTO1 gene is responsible for ONCE syndrome, *Clinical Genetics*, 91(1), 46-53, 2017.

**Keywords:** Optic neuropathy, Genetic Disease, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Pediatric Neuro-Ophthalmology, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 26**

**Cerebral Stroke Causing Monocular Hemianopia on Automated Perimetry**

Samuel Lee<sup>1</sup>, Yao Wang<sup>1</sup>, Collin McClelland<sup>1</sup>, Michael Lee<sup>1</sup>

<sup>1</sup>*University of Minnesota, Minneapolis, Minnesota, USA*

**Introduction:**

A homonymous hemianopia localizes to the retrochiasmal visual pathway. A monocular hemianopic defect typically localizes anterior to the chiasm. We report three patients with a monocular hemianopia on automated perimetry following cerebral stroke.

**Description of Case(s):**

In this retrospective, consecutive case series, three individuals who suffered a cerebral stroke underwent full neuro-ophthalmic evaluations including automated perimetry. Testing revealed a normal visual field in one eye and a monocular hemianopia in the other eye. No other neurologic or ocular causes for this abnormality were found.

**Conclusions, including unique features of the case(s):**

To our knowledge, this is the first report of monocular hemianopia following cerebral stroke. Brain MRI warrants consideration in patients with a monocular hemianopia on automated perimetry.

**References:** None.

**Keywords:** Visual fields, Stroke Trauma

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 27****Akinetopsia after Unilateral Surgical Labyrinthectomy**

Maryke Neiberg<sup>1</sup>

<sup>1</sup>*Massachusetts College of Pharmacy and Health Sciences, Worcester, Massachusetts, USA*

**Introduction:**

Defective dorsal stream information results in deficits of motion perception. Akinetopsia describes the condition wherein patients perceive moving objects as a succession of still images. In akinetopsia, ability to see running water from a shower as a continuous stream of water is interrupted. Instead the patient sees water drops frozen in the air in discreet freeze frame intervals. A rare sub-classification of akinetopsia is the Zeitraffer phenomenon, in which the perception of the speed of motion is perceived as faster or slower than reality.

**Description of Case(s):**

We present the case of a 62-year-old Caucasian male with torticollis, referred to our clinic for evaluation of lingering visual and postural symptoms after elective unilateral left surgical labyrinthectomy for longstanding Meniere's Disease. The patient's static symptoms had subsided, but impaired perception of visual motion due to retinal slip in the contralateral hemi-field during pursuits persisted, which he described as "ratcheting" of his vision.

**Conclusions, including unique features of the case(s):**

Unilateral surgical labyrinthectomy is typically reserved for older patients with a profound hearing loss on the same side. Post-operative static disequilibrium is well managed by vestibulo-ocular reflex (VOR) adaptation and the neuroplasticity of compensation. Saccadic training augments VOR rehabilitation. Recovery of the vestibular neurons in response to dynamic head movement requires aggressive vestibular rehabilitation and improves somewhat over the first few weeks but symptoms in high acceleration head movements, like akinetopsia, may persist indefinitely.

**References:** None.

**Keywords:** Ocular manifestations of vestibular disorders, Higher visual functions, Vestibular, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 28**

**Homonymous Hemianopsia as the Presenting Sign of Migrainous Infarction**

Aroucha Vickers<sup>1</sup>, Gio Campagna<sup>2</sup>, Claudia Prospero-Ponce<sup>1</sup>, Andrew Lee<sup>3</sup>

<sup>1</sup>Houston Methodist Hospital, Houston, Texas, USA, <sup>2</sup>Baylor College of Medicine, Houston, Texas, USA, <sup>3</sup>Houston Methodist Hospital, Blanton Eye Institute, Houston, Texas, USA

**Introduction:**

Migraine is a clinical diagnosis. Occasionally, unusual presentations make migraine a diagnosis of exclusion, where imaging is required to rule out structural pathologies before the diagnosis of a migraine can be made. This condition presents a great diagnostic challenge for clinicians because the pathophysiology is not entirely clear, and evaluation of a migrainous infarction upon initial presentation lacks nuance. In typical migraine headaches, visual field phenomena are temporary, unlike the case presented here where persistent visual field loss should prompt neuroimaging.

**Description of Case(s):**

A 47-year-old African American female presented with acute onset bilateral visual disturbance consistent with her typical migraine aura. This was followed by the development of a headache, but her visual symptoms persisted, whereas her usual visual aura normally resolved within 20 minutes. Patient was evaluated in the emergency department (ED) three times where cranial CT scans were normal and she was repeatedly discharged with a diagnosis of a “migraine”. Three weeks after the onset of this particular migraine, patient was evaluated in the Neuro-Ophthalmology clinic. Automated perimetry revealed a left congruous denser superiorly macular sparing homonymous hemianopsia. MRI of the brain confirmed an ischemic infarction in the right posterior cerebral artery distribution. An extensive workup for the etiology of her ischemic event was unremarkable and she was diagnosed with a migrainous infarction by IHS criteria.

**Conclusions, including unique features of the case(s):**

Neurologists, ophthalmologists and ED physicians should be aware of the possibility of migrainous infarction in this setting because patients often present to the ED where confrontation visual fields (rather than automated perimetry) and cranial CT scan (rather than MRI) may be the only evaluation tools. This might lead to an inappropriate discharge with the diagnosis of “prolonged” migraine aura rather than migrainous infarction. We recommend the use of other tools such as an amsler grid to better identify visual field defects in the ED.

**References:** None.

**Keywords:** Stroke Trauma, Visual fields, Neuroimaging, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 29****Persistent Visual Field Defects Eight Months after Posterior Reversible Leukoencephalopathy Syndrome**

Senem Salar Gomceli<sup>1</sup>, Pearl Rosenbaum<sup>1</sup>, Nancy Blace<sup>1</sup>

<sup>1</sup>Bronx -Lebanon Hospital Center of Icahn School of Medicine at Mount Sinai, Bronx, NY, USA, Bronx, New York, USA

**Introduction:**

Posterior reversible encephalopathy syndrome (PRES) is not commonly encountered in routine ophthalmologic practice. It is characterized by acute or subacute neurological changes in the form of confusion, lethargy and visual disturbances (1-3), most commonly occurring in the clinical setting of acute hypertension, eclampsia and solid organ transplantation. It is also associated with connective tissue disorders and the use of cytotoxic or immunosuppressive medications. Vision loss occurs as the result of vasogenic edema, primarily involving the parietal and occipital cortex in 98% of cases (4). Diagnosis is based on clinical presentation and the characteristic MRI demonstration of posterior cerebral hyperintensities best seen on FLAIR images (5). Radiographic findings usually resolve partially or completely with treatment of the underlying condition and, in most cases, vision is restored (1).

**Description of Case(s):**

A 43-year-old man with a past medical history of hypertension, dyslipidemia, and chronic alcohol and marijuana abuse was admitted to the ICU for delirium tremens complicated by acute hypoxic respiratory failure, acute renal failure, aspiration pneumonia and urinary tract infection. Three days after extubation, he developed bilateral cortical blindness; ophthalmological exam was otherwise normal. Brain MRI revealed cerebral edema involving both parieto-occipital regions as well as the high frontal lobes and posterior and inferior temporal lobes. One week later, uncorrected distance acuities improved to 20/20 OU. At 1-month follow up, HVF revealed a right homonymous inferior paracentral scotoma. Repeat brain MRI at 2 months showed decreased, but incompletely resolved, cerebral edema. At 8 months, Humphrey 24-2 perimetric defects corresponding to the residual MRI hyperintensities persisted, albeit improved. These were better visualized on 10-2 perimetry.

**Conclusions, including unique features of the case(s):**

Our case demonstrates that visual recovery, even to 20/20, may mask subtle scotomas that may be functionally disabling. Perimetry thus plays an important role in monitoring visual function and recovery in patients with PRES.

**References:** 1. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, et al. A reversible posterior leukoencephalopathy syndrome. *The New England journal of medicine*. 1996;334(8):494-500. 2. Pula JH, Eggenberger E. Posterior reversible encephalopathy syndrome. *Current opinion in ophthalmology*. 2008;19(6):479-84. 3. Kahana A, Rowley HA, Weinstein JM. Cortical blindness: clinical and radiologic findings in reversible posterior leukoencephalopathy syndrome: case report and review of the literature. *Ophthalmology*. 2005;112(2):e7-e11. 4. Bartynski WS, Boardman JF. Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. *AJNR American journal of neuroradiology*. 2007;28(7):1320-7. 5. Gass A, Niendorf T, Hirsch JG. Acute and chronic changes of the apparent diffusion coefficient in neurological disorders-biophysical mechanisms and possible underlying histopathology. *Journal of the neurological sciences*. 2001;186 Suppl 1:S15-23.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Neuroimaging, Visual fields

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 30****Improved Transverse Sinus Stenosis after Lumbar Puncture in Idiopathic Intracranial Hypertension**

Seo-Young Choi<sup>1</sup>, Minji Kim<sup>1</sup>, Yunji Choi<sup>1</sup>, Byung-Kun Kim<sup>2</sup>

<sup>1</sup>Pusan National University Hospital, Pusan, Korea, Republic of, <sup>2</sup>College of Medicine, Eulji University, Eulji Hospital, Seoul, Korea, Republic of

**Introduction:**

Idiopathic intracranial hypertension (IIH) is characterized by elevated intracranial pressure (ICP) without explainable other causes. The pathophysiology is still unclear, but, it is known to be associated with sex and body mass index (BMI). There are some typical image findings, such as empty sella, flattening of the posterior globes at the insertion of the optic nerves, protrusion of the optic nerve head, tortuosity of the intraorbital optic nerve, and bilateral transverse sinus stenosis. We report a patient with IIH showing transverse sinus stenosis, which improved after several times of lumbar puncture.

**Description of Case(s):**

A 36-year-old woman complained the progressive constriction of visual field and repeated visual obscurations for four months. BMI was 30.25kg/m<sup>2</sup>. Lumbar puncture revealed an opening pressure of 340 mmHg. MR T2 image showed protrusion of the optic nerve head, MR venography showed a bilateral narrowing of transverse sinuses. Acetazolamide (2000mg/day) for 10 days could not improve her symptoms. Follow-up CSF drainage showed 390 mmHg as opening pressure at that time. After two days from follow-up lumbar puncture, her visual symptoms were improved subjectively, and the stenosis of transverse sinuses was disappeared in the transfemoral cerebral angiography. At that time, opening pressure of lumbar puncture was 180 mmHg. She discharged with acetazolamide (2000 mg/day).

**Conclusions, including unique features of the case(s):**

Although some patients with IIH have bilateral obstructions of cerebral transverse sinuses, it has not revealed whether the venous stenosis is the cause for IIH or the result from that. Stent insertion in the transverse sinus might reduce venous pressure, that leads to increasing CSF drainage, so could be normalized ICP. Since CSF drainage may reduce ICP, serial lumbar puncture should be considered for patients with uncontrolled ICP.

**References:** None.

**Keywords:** High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 31****The Utility of Optical Coherence Tomography in the Evaluation of Papilledema**

Rahul Sharma<sup>1</sup>, Wayne Cornblath<sup>2</sup>, Lindsey DeLott<sup>2</sup>

<sup>1</sup>The University of Ottawa Eye Institute, Ottawa, Canada, <sup>2</sup>WK Kellogg Eye Center University of Michigan, Ann Arbor, Michigan, USA

**Introduction:**

The clinical assessment of papilledema is highly subjective and often variable, even with formal grading systems like the Modified Frisén Scale. We describe three cases of Idiopathic Intracranial Hypertension (IIH) where optical coherence tomography (OCT) revealed subclinical swelling of the optic nerves not readily apparent on funduscopic examination.

**Description of Case(s):**

(1) A 16-year old male was referred for evaluation of worsening headaches. There was no abnormality in visual acuity, color vision or visual field testing. No optic disc edema was noted on clinical examination, but OCT-RNFL revealed mildly elevated optic nerve heads bilaterally. (2) A 15-year old male was referred for evaluation of episodic blurred vision and headaches. Visual acuity, color vision or visual field testing were normal. No optic disc edema was noted on clinical examination, but OCT-RNFL revealed mildly elevated optic nerve heads bilaterally. (3) A 25-year old female was referred for evaluation of possible bilateral optic disc edema. She reported worsening headaches and transient visual obscurations, both increasing in frequency. There was no abnormality in visual acuity, color vision or visual field testing. Clinical evaluation of her optic nerves revealed clear optic disc edema OS and questionable disc edema OD. OCT indicated asymmetric optic disc swelling, left eye greater than right. In all 3 cases, neuroimaging was normal and lumbar puncture showed elevated opening pressure (33, 45, 27) with normal CSF constituents. After treatment with Acetazolamide, symptoms improved and the OCT showed resolution of papilledema.

**Conclusions, including unique features of the case(s):**

We present three cases of IIH with papilledema that was not recognized clinically but was appreciated with OCT of the RNFL. We propose a diagnosis of Idiopathic Intracranial Hypertension Without Funduscopically Detectable Papilledema (IIHWOPD) in these cases. Given the sensitivity of OCT in detecting and following optic disc edema, it should be readily used in the management of patients with IIH.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Pseudotumor Cerebri

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 32****Glomus Jugulare Tumor Induced Intracranial Hypertension**

Editha Johnson<sup>1</sup>, Evan Schloss<sup>2</sup>, Marc Dinkin<sup>2</sup>, Athos Patsalides<sup>2</sup>, Cristiano Oliveira<sup>2</sup>

<sup>1</sup>University of Illinois College of Medicine at Peoria, Peoria, Illinois, USA, <sup>2</sup>Weill Cornell Medical College, New York, New York, USA

**Introduction:**

Pseudotumor cerebri syndrome (PTCS), the categorical term for primary and secondary causes of raised intracranial pressure (ICP) in the absence of space-occupying lesion, has a characteristic presentation that includes frequent headaches, visual changes, pulsatile tinnitus with papilledema. Neuroimaging is an essential step in PCTS diagnosis. We present a unique case, originally thought to be a presentation of primary PTCS, later revealed as PTCS secondary to a glomus jugulare tumor, causing venous outflow obstruction and consequential intracranial hypertension, which was treated with venous stenting and post-stent balloon angioplasty of the right internal jugular vein.

**Description of Case(s):**

A 38-year-old obese woman who presented with a five-month history of transient visual obscurations, pulsatile tinnitus, intermittent blurred vision and occasional headaches, was found to have bilateral optic disc edema. Subsequent workup with MRI brain followed by MRA revealed a glomus tumor at the right jugular bulb. At this point, she was diagnosed with presumed idiopathic intracranial hypertension (IIH) and referred to our medical center for further evaluation and management of the tumor. She was seen at the Neuro-Ophthalmology service, in preparation for hypofractionated stereotactic radiosurgery (HSR), because of the presumed IIH diagnosis. Due to our concern regarding the cerebral venous anatomy additional MRV head was obtained, which confirmed the presence of a dominant right transverse venous sinus with venous outflow obstruction caused by the glomus jugulare tumor. She underwent venous stenting and post-stent balloon angioplasty of the right internal jugular vein followed by planned HSR.

**Conclusions, including unique features of the case(s):**

In the evaluation of patients presenting with symptoms of elevated ICP, a thorough workup is indispensable. The relevance of the glomus jugulare tumor in the present case, which was initially thought to be incidental, was demonstrated with MRV. The venous outflow obstruction was treated with venous stenting and angioplasty of the right internal jugular vein.

**References:** None.

**Keywords:** High intracranial pressure/headache, Tumors, Pseudotumor Cerebri, Interventional neuroradiology, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 33****Lithium-induced Venous Sinus Anatomy and Pressure Gradient Changes in Pseudotumor Cerebri Syndrome**

Aimee Szewka<sup>1</sup>

<sup>1</sup>*Rush University Medical Center, Chicago, Illinois, USA*

**Introduction:**

Lithium has been reported as a cause of pseudotumor cerebri in several case series. Venous sinus abnormalities and intracranial venous pressure gradients have been associated with intracranial hypertension. This case describes venous anatomy changes in pseudotumor cerebri syndrome after withdrawal and reinitiation of lithium.

**Description of Case(s):**

A 33-year-old woman with past medical history of chronic daily headaches and bipolar disorder, treated with lithium presented with new onset headaches. Examination was remarkable for Grade III papilledema and full visual fields. MRV revealed bilateral venous sinus stenosis and opening pressure (OP) of 33cm H<sub>2</sub>O and normal CSF constituents. Lithium was stopped due to concern for secondary pseudotumor cerebri. She had initial improvement in her headaches and her papilledema, however, within weeks headaches recurred. Repeat LP revealed OP of 33cm H<sub>2</sub>O, but headaches persisted. Due to refractory symptoms on maximum dose of acetazolamide (4g/day) and furosemide, venous angiography was performed and no significant pressure gradient or right transverse sigmoid stenosis was noted. She was treated for chronic daily headache. Lithium was restarted due to recurrent and severe suicidal ideations and three months later, she had increased disc edema despite 4g/day of acetazolamide. LP demonstrated an OP of 65cm H<sub>2</sub>O. Repeat venous angiography revealed a high-grade stenosis in the right transverse sigmoid junction with a pressure gradient of 39mmHg to 17mmHg. Venous sinus stent was placed without complication. The patient reports improved headaches, but continued chronic daily headache. Papilledema has improved and she has tolerated wean of acetazolamide to 2g/day. Weight has remained stable throughout the follow up period.

**Conclusions, including unique features of the case(s):**

This is the first illustration of venous pressure gradient and venous sinus anatomy changes in a patient treated with lithium. This case suggests that lithium directly or indirectly induces the pathophysiology resulting in pseudotumor cerebri, although the mechanism is unclear. Further research is needed to investigate.

**References:** Saul RF, Hamburger HA, Selhorst JB. Pseudotumor cerebri secondary to lithium carbonate. *JAMA*. 1985 May 17;253(19):2869-70. Levine SH, Puchalski C. Pseudotumor cerebri associated with lithium therapy in two patients. *J Clin Psychiatry*. 1990 Jun;51(6):251-3.

**Keywords:** High intracranial pressure/headache, Interventional neuroradiology, Pseudotumor Cerebri

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 34****Nonsyndromic Craniosynostosis Mimicking Primary Pseudotumor Cerebri Syndrome**

Elissa Ortolani<sup>1</sup>, Catalina Cleves-Bayon<sup>1</sup>, Robert Safier<sup>1</sup>, Ellen Mitchell<sup>1</sup>

<sup>1</sup>Childrens Hospital of Pittsburgh of UPMC, Pittsburgh, Pennsylvania, USA

**Introduction:**

Pseudotumor cerebri ( idiopathic intracranial hypertension) is a syndrome of Intracranial hypertension with normal brain parenchyma, normal neurologic exam, normal CSF composition and elevated lumbar puncture opening pressure. The common phenotype observed is young, obese and female [1] . We present a pediatric case of an atypical phenotype, a young pre-pubertal thin male, with refractory pseudotumor despite medical management.

**Description of Case(s):**

3 year and 5-month-old boy presented with one week of daily headache. Past medical history was unremarkable. He was developmentally appropriate and took no medications. Family history significant for grandmother with headaches. On presentation, growth parameters and neurologic exam were normal, including normal body mass index. Eye exam showed normal fields to confrontation, normal visual acuity, optic nerve head swelling with obscuration of disc margin OD>OS. MRI notable for partially empty sella, tortuous optic nerves and flattening of posterior globes. Lumbar puncture confirmed elevated opening pressure at 41mm H<sub>2</sub>O, with a normal CSF analysis. He was diagnosed with primary pseudotumor cerebri and acetazolamide initiated. For 36 months, he had intermittent normalization of funduscopic exam with four unsuccessful attempts to wean medication, resulting in re-emergence of disc edema, and 3 additional elevated lumbar puncture opening pressures. On final admission, imaging included CT scan with 3D reconstruction, revealing bilateral coronal, lambdoid, and sagittal craniosynostosis. He was taken to the operating room for total cranial vault expansion. Since intervention, acetazolamide was discontinued, disc edema resolved and he remains asymptomatic.

**Conclusions, including unique features of the case(s):**

Pseudotumor cerebri is typically a disease of obese, young women. We believe atypical phenotypic patients, in age, sex or body mass, may benefit from a CT scan with 3D reconstruction for evaluation of craniosynostosis. Establishing appropriate diagnosis is essential, as treatment for idiopathic intracranial hypertension vs. craniosynostosis are different : medical vs. surgical management. Early diagnosis is essential to prevent progressive visual loss.

**References:** Friedman, D.I., G.T. Liu, and K.B. Digre, Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology*, 2013. 81(13): p. 1159-65.

**Keywords:** High intracranial pressure/headache, Pediatric Neuro-Ophthalmology, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 35

### Transient Visual Hallucinations with Eye Closure After Gamma Knife Radiosurgery

Leo Kubono<sup>1</sup>, Hirofumi Emoto<sup>2</sup>, Yuko Emoto<sup>3</sup>, Kaoru Tamura<sup>4</sup>, Masaaki Yamamoto<sup>5</sup>, Motohiro Kiyosawa<sup>3</sup>

<sup>1</sup>Shuwa General Hospital, Kasukabe-city, Saitama, Japan, <sup>2</sup>Shuwa General Hospital, Saitama, Japan, <sup>3</sup>Emoto Eye Clinic, Tokyo, Japan, <sup>4</sup>Department of Neurosurgery, Tokyo Medical and Dental University, Tokyo, Japan, <sup>5</sup>Department of Neurosurgery, Katsuta Hospital Mito Gamma House, Ibaraki, Japan

#### **Introduction:**

Visual hallucination with eye closure is rare and we report the case after Gamma Knife radiosurgery.

#### **Description of Case(s):**

Case: 56-year-old woman noticed diplopia and visited our hospital. The left abducens palsy was diagnosed. MRI of the brain showed the left cavernous sinus lesion of intermediate signal intensity on T1-weighted images, and high signal intensity in T2-weighted images. Cavernous hemangioma was suspected and the patient was treated with a single session of Gamma Knife radiosurgery with margin dose of 15 Gy, and maximum dose of 25 Gy. One day after the radiosurgery, severe retro-orbital pain and new diplopia developed. Five days after the radiosurgery, the patient presented with the left oculomotor palsy with ptosis, in addition to the pre-existing left abducens palsy and admitted to the hospital. Pupillary function was normal. Repeat MRI could not detect significant interval change. Intravenous administration of corticosteroid was started. On the day of admission, she complained of visual hallucinations with eye closure. The images disappeared while she opened her eyes. She did not have any past history of psychological disorders or medication. She did not present with altered mental status, disorientation, delirium, agitation or seizure. Neurologic and psychologic exam were normal except the left abducens and oculomotor palsy and the visual hallucination. Electroencephalogram could not detect abnormal findings. On ophthalmologic examination, her best corrected visual acuity, intraocular pressure, fundus, visual field etc were normal. The visual hallucinations were colorful, vivid and complex such as animals and ships. These hallucinations are not stereotyped and vary from one episode to the next. The visual hallucinations resolved in five days and she discharged the hospital.

#### **Conclusions, including unique features of the case(s):**

To our knowledge, this is the first case of visual hallucinations with eye closure after Gamma Knife radiosurgery.

**References:** None.

**Keywords:** Higher visual functions

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 36**

**Serous Retinal Detachment and Optic Neuropathy Secondary to Intra-operative Venous Congestion**

Victoria Leung<sup>1</sup>, Sara AlShaker<sup>1</sup>, Ari Shemesh<sup>1</sup>, Laura Donaldson<sup>2</sup>, Laila Alshafai<sup>3</sup>, Taufik Valiante<sup>4</sup>, Edward Margolin<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Canada,* <sup>2</sup>*Department of Ophthalmology, McMaster University, Hamilton, Canada,* <sup>3</sup>*Department of Medical Imaging, Mount Sinai Hospital, Toronto, Canada,* <sup>4</sup>*Department of Neurosurgery, Toronto Western Hospital, Toronto, Canada*

**Introduction:**

Acute post-operative vision loss is a rare but devastating surgical complication. We describe a unique case where disruption of orbital venous drainage during craniotomy resulted in venous congestion and a large serous retinal detachment (RD), presumed secondary to obstruction of the choroidal vortex veins.

**Description of Case(s):**

A 47 year-old male underwent an uncomplicated craniotomy for resection of a large right frontal meningioma. Three days post-operatively, he developed near complete right ophthalmoplegia with severe chemosis and 3 mm of proptosis. Visual acuity was hand motions with an obvious relative afferent pupillary defect. An extensive macula-involving serous RD was present, as well as optic disc edema. MRI/MRV of the brain and orbits was initially interpreted as normal. Upon subsequent review, hemorrhage in the medial and inferior rectus muscles as well as diffusion restriction in the entire optic nerve were identified. Discussion with the neurosurgeon revealed that when the craniotomy was performed, a prominent anomalous venous plexus was noted in the frontal bone. This plexus did not appear to communicate with the intracranial circulation. It was retracted downward for the duration of the surgery. Two weeks following his initial presentation, the patient's proptosis, chemosis, ophthalmoplegia and serous RD all resolved. Visual acuity, unfortunately, did not improve.

**Conclusions, including unique features of the case(s):**

We hypothesize that the venous plexus identified intra-operatively communicated with the orbital circulation. We suspect that performing the craniotomy caused disruption of the orbital drainage, resulting in prominent orbital venous congestion. Subsequent compression of the choroidal circulation caused a large serous RD. Compressive optic neuropathy accounts for the persistent vision loss. Orbital venous stasis and its complications should be considered in any patient undergoing frontal craniotomy presenting with post-operative vision changes.

**References:** None.

**Keywords:** Orbit, Vascular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 37****Rituximab Use In Neurosarcoidosis**

Mangayarkarasi Thandampallayam<sup>1</sup>, David Kaufman<sup>1</sup>, Lina Nagia<sup>1</sup>

<sup>1</sup>Michigan State University, East Lansing, Michigan, USA

**Introduction:**

Rituximab is a chimeric monoclonal antibody that causes depletion of CD 20+ B cells. There are few documented reports describing successful use of rituximab in refractory neurosarcoidosis. Here we present a case of central nervous system (CNS) sarcoidosis effectively treated with rituximab.

**Description of Case(s):**

Fifty nine year old right handed African American woman with history of rheumatoid arthritis, hypertension, diabetes mellitus type 2 and thyroid nodule was referred for evaluation of tinnitus, hearing loss, left sided Bell's palsy, numbness and leg weakness. On evaluation , there was left sided facial weakness, numbness, VA 20/20 BE , full ocular motility and normal fundus. MRI brain with Gadolinium showed multiple cranial nerve enhancement. Chest CT, abdomen and pelvis were normal. Serum laboratory studies including Calcium, CRP, ACE, ANA were within normal limits except for low vitamin B 12 and elevated ESR. CSF studies revealed 2 oligoclonal bands ,elevated protein and gamma globulins. Diagnosis of neurosarcoidosis was considered carefully given the MRI appearance and the clinical course. Initial therapy with high dose steroids improved the Bell's palsy but other symptoms eventually progressed which prompted initiation of a long-term steroid-sparing agent. About 8 months later, despite immunosuppressant therapy (mycophenolate mofetil 1000 mg BID and prednisone 5 mg / day), symptoms worsened. Adalimumab was added to the treatment regimen but was discontinued shortly thereafter due to lack of insurance coverage. Rituximab was then added and showed significant improvement in symptoms, with no relapses at 3 months follow up.

**Conclusions, including unique features of the case(s):**

Despite sarcoidosis being a T-cell mediated disease, humoral mechanism also appears to play a role in its pathogenesis. In our patient, failure of steroids and mycophenolate mofetil to control the disease, led to trial of rituximab. A significant remission occurred with rituximab and it could be an effective alternative in the management of refractory neurosarcoidosis.

**References:** 1. Timothy Vollmer, Roberto Bomprezzi, Sandidan Pati, Chakorn Chansakul , A case of Neurosarcoidosis successfully treated with Rituximab ( Neurology.2010 Aug 10; 75(6):568-70 doi:10.1212/WNL.0b013e3181ec7ff9) 2. Francesco Cinetto, Nicolo Compagno, Riccardo Scarpa, Giacomo Malipiero, Carlo Agostini , Case report :Rituximab in refractory Sarcoidosis (Clinical and Molecular Allergy 2015 13:19) 3. Marc A Judson, Advances in the diagnosis and treatment of sarcoidosis (F1000 Prime Reports)

**Keywords:** Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 38

### Acrodermatitis Enteropathica (AEZ) and Retinal Ganglion Cell Dysfunction – Is There a Causal Relationship?

Neringa Jurkute<sup>1</sup>, Andrew Webster<sup>2</sup>, Anthony Robson<sup>2</sup>, Graham Holder<sup>3</sup>, Gavin Arno<sup>2</sup>, Naushin Waseem<sup>4</sup>, Patrick Yu Wai Man<sup>2</sup>

<sup>1</sup>University College London, Institute of Ophthalmology; Moorfields Eye Hospital, London, United Kingdom, <sup>2</sup>University College London; Moorfields Eye Hospital, London, United Kingdom, <sup>3</sup>University College London; Moorfields Eye Hospital; National University of Singapore, Singapore, Singapore, <sup>4</sup>University College London, London, United Kingdom

#### Introduction:

AEZ (MIM\_201100) is a rare zinc deficiency disorder caused by mutations in the SLC39A4 gene (MIM\_607059) on chromosome 8q24 with a prevalence of approximately 1 in 500,000 children [1]. A few cases of optic atrophy have been reported in association with AEZ, but it was not clear whether this was caused by ocular drug toxicity or secondary to the zinc deficiency per se [2,3].

#### Description of Case(s):

A 49-year-old woman was seen in the neurogenetics clinic with a clinical diagnosis of AEZ. She had longstanding subnormal vision with visual acuities of 6/18 in both eyes and impaired colour vision. She reported a family history of AEZ without vision loss. This patient was diagnosed with AEZ when she was 1 month old and treatment with diiodohydroxyquinoline was started at a dose of 200 mg three times a day. In the absence of any significant visual benefit, the drug was increased to a total daily dose of 2400 mg before being replaced by zinc supplements when she was 8 months old. Fundus examination showed bilateral optic atrophy with significant thinning of the peripapillary retinal nerve fibre layer on optical coherence tomography (OCT). Visual electrophysiological testing was consistent with primary retinal ganglion cell (RGC) dysfunction. Her younger 44-year-old sister was diagnosed with AEZ as soon as the first symptoms of the disease became apparent and zinc supplements were started without any delay. She was visually asymptomatic and fundus examination was normal, however subtle optic atrophy was noted on OCT. Visual electrophysiological findings were also consistent with mild RGC dysfunction. One novel (c.943\_944delinsA, p.Pro315Thrfs\*34) and previously reported missense mutation (c.599C>T, p.Pro200Leu) and likely benign variant (c.251C>T, p.Pro84Leu) in the SLC39A4 gene were identified.

#### Conclusions, including unique features of the case(s):

Zinc deficiency can lead to progressive RGC dysfunction. The early diagnosis of AEZ and the prompt initiation of zinc supplementation can improve the visual prognosis.

**References:** 1. Küry S, Kharfi M, Blouin E, Schmitt S, Bézieau S. Clinical utility gene card for: acrodermatitis enteropathica – update 2015. *Eur J Hum Genet.* 2016;24(5):10-13. doi:10.1038/ejhg.2015.203. 2. Garcia-Perez A, Castro C, Franco A, Escribano R. A case of optic atrophy possibly induced by quinoline in acrodermatitis enteropathica. *Br J Dermatol.* 1974;90(4):453-455. doi:10.1111/j.1365-2133.1974.tb06433.x. 3. Cameron J, McClain C. Ocular histopathology of acrodermatitis enteropathica. *Br J Ophthalmol.* 1986;70:662-667. <http://bj.o.bmj.com/content/70/9/662.short>.

**Keywords:** Genetic Disease, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 39**

**Bilateral Ischemic Optic Neuropathy following Benzathine Penicillin: Hoigne Syndrome**

Moira Altszul<sup>1</sup>, Camila Challiol<sup>1</sup>

<sup>1</sup>*Hospital Italiano de Buenos Aires, Ciudad Autónoma de Buenos Aires, APO AE, Argentina*

**Introduction:**

Hoigne Syndrome is a pseudoanaphylactic reaction that occurs shortly after intramuscular administration of penicillin G procaine or benzathine. These are embolic toxic reactions possibly due to vascular occlusions by large crystals of the penicillin salts (1), although the mechanism responsible for the development of Hoigne Syndrome, and its incidence, are unknown (2). Clinical manifestations include psychosis, seizures (3), “doom anxiety” (2), visual and auditory hallucinations, dysarthria, dyspnea, tachycardia (1). Other drugs, such as lidocaine (2), clarithromycin (4), and ceftriaxone (5) have been associated with Hoigne syndrome. Management guidelines include prompt recognition, patient reassurance and benzodiazepines (2).

**Description of Case(s):**

A 45 year-old man presented with a month long bilateral loss of vision. He noticed it after 2 days of induced pharmacological coma, due to seizures secondary to benzathine penicillin injection for trophic ulcer debridement following left lower extremity chronic osteomyelitis. He brought a previous OCT which showed severe macular ischemia and optic disc edema in both eyes. MRI, serology and neck doppler ultrasound were normal. Ophthalmic doppler ultrasound showed reduced flow in posterior ciliary arteries. Examination revealed visual acuity of hand motions in both eyes. Fundus showed pale discs and macular hemorrhages with fine deposits and vascular occlusions. Central scotomas in visual fields were present in both eyes. A new OCT and fluorescein angiography were ordered, which showed progressive thinning of retinas and hypofluorescence due to ischemia.

**Conclusions, including unique features of the case(s):**

This case is unique because it is the first reported Hoigne Syndrome secondary to benzathine penicillin with ocular ischemic manifestations. Differential diagnosis from anaphylactic reactions to penicillin is mandatory. In such cases, treatment with that drug is contraindicated as opposed to Hoigne syndrome in which it is allowed.

**References:** 1. Gain P, Paniagua MJ. Síndrome de Hoigne. *Allergol et immunopathol* 2005; 33 (1): 57-8. 2. Thompson TM et col. Hoigne Syndrome: a little known adverse effect of lidocaine. *Am J Emerg Med* 2016; 34 (3): 679de 3-4. 3. Silber TJ, D’Angelo L. Psychosis and Seizures Following the Injection of Penicillin G Procain. Hoigne Syndrome. *Am J Dis Chil* 1985; 139 (4):335-7. 4. Rallis E et col. Clarithromycin-induced Hoigne syndrome in a patient treated for rosacea. *J Eur Acad Dermatol Venereol* 2009; 23 (9): 1093-94 5. Landais A et col. Un cas de syndrome de Hoigne lors d’une injection intraveineuse de ceftriaxone. *Rev Med Interne* 2014; 35 (3): 199-201.

**Keywords:** Optic neuropathy, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 40

### Sudden-Onset Blindness from a Spontaneous Carotid-Cavernous Fistula with Secondary Central Retinal Artery Occlusion

Daniel Oh<sup>1</sup>, Priyanka Chhadva<sup>1</sup>, Levi Kanu<sup>1</sup>, Catherine Liu<sup>1</sup>, Peter MacIntosh<sup>1</sup>

<sup>1</sup>Illinois Eye and Ear Infirmary, University of Illinois at Chicago, Chicago, Illinois, USA

#### Introduction:

High-flow carotid-cavernous fistulas (CCFs) typically present with blurry vision, headache, diplopia and pain with trauma<sup>1</sup>, however a ruptured cavernous carotid artery aneurysm may present similarly.<sup>2</sup> We describe a case of spontaneous high-flow CCF presenting as sudden vision loss, with venous congestion and concomitant central retinal artery occlusion.

#### Description of Case(s):

A 37-year-old woman presented with right eye swelling, throbbing retro-orbital pain, and complete loss of right eye vision for two days. She was diagnosed with orbital cellulitis at an outside hospital and transferred. She had no light perception in the right eye with a fixed, dilated pupil. Her EOMs were restricted in all gazes, and her eyelids were difficult to open. Hertel measurements were 22mm and 18mm in the right and left. Her cornea was edematous and retina was pale with a cherry-red macular spot but without optic disc pallor or edema. Her IOP was high as 86mmHg. Canthotomy and cantholysis were deferred by the primary team due to emergent imaging and angiography. CT brain demonstrated subarachnoid hemorrhage in the basal cisterns and lateral ventricle enlargement. An external ventricular drain was placed and angiogram showed a right complex CCF and right cavernous internal carotid aneurysm which were successfully embolized. Her IOP normalized. She was discharged after EVD trial, but her vision remained NLP.

#### Conclusions, including unique features of the case(s):

Low-flow dural sinus fistulas often occur without trauma, however, high-flow CCFs are usually traumatic with gradual vision loss and EOM restriction over weeks.<sup>3</sup> There are also cases of ruptured cavernous carotid aneurysms as the cause of high-flow CCFs<sup>4,5,6</sup>. Unusually, our patient also presented with a pale retina with a cherry-red spot despite angiographically patent ophthalmic artery. While our patient had congestive symptoms of pain, proptosis, elevated IOP, her retinal findings suggested a simultaneous CRAO likely from prolonged elevated intraocular and intraorbital pressures<sup>1,7</sup> that normalized after embolization.

**References:** 1. Kupersmith MJ. Neuro-vascular Neuroophthalmology. Berlin, Springer-Verlag, 1993. 2. Liu GT, Volpe NJ & Galetta SL. Neuro-Ophthalmology: Diagnosis and Management, 2nd ed. Elsevier, 2010. 3. Das JK, Medhi J, Bhattacharya P, et al. Clinical spectrum of spontaneous carotid-cavernous fistula. Indian J Ophthalmol. 2007;55(4):310-2. 4. Nakagawa S, Murai Y, Wada T, Tateyama K. 4D flow preliminary investigation of a direct carotid cavernous fistula due to a ruptured intracavernous aneurysm. BMJ Case Rep. 2015;2015. 5. Deburun G, Vinuela F, Fox AJ. Indication for treatment and classification of 132 carotid-cavernous fistulas. Neurosurgery 1988;22:285-9. 6. Lewis AI, Tomsick TA, Tew JM Jr. Management of 100 consecutive direct carotid-cavernous fistulas: results of treatment with detachable balloons. Neurosurgery 1995;36:239-45. 7. Karna S, Jain M, Alam MS, Mukherjee B, Raman R. Carotid cavernous fistula with central retinal artery occlusion and Terson syndrome after mid-facial trauma. GMS Ophthalmol Cases. 2017;7:Doc12.

**Keywords:** High intracranial pressure/headache, Neuroimaging, Interventional neuroradiology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 41

### Non-LETM in MOG-IgG Related CNS Demyelination

Kemar Green<sup>1</sup>, Armin Jewell<sup>1</sup>, Daniel Long<sup>1</sup>, Ali Saeed<sup>1</sup>, Christopher Glisson<sup>1</sup>

<sup>1</sup>Michigan State University, Department of Neurology and Ophthalmology, East Lansing, Michigan, USA

#### Introduction:

The initial presentation of a non-LETM without optic neuritis is rather infrequent in MOG-IgG autoimmunity, and lends more to alternate diagnoses.

#### Description of Case(s):

42-year-old African-American male with a Graves' disease presenting with right hemiparesis and aphasia. A few months prior at an outside facility, he was diagnosed with CNS vasculitis via biopsy after presenting with abnormal neuroimaging. Treatment with IVMP was successful, and he was rehabilitated for his motor deficits while continuing a low-dose steroid. In addition to presenting symptoms, his exam showed left lower facial weakness and bilateral internuclear ophthalmoplegia. MRI brain showed multiple rhombencephalic and cortical enhancing white matter lesions. Subsequent cervical spine MRIs showed non-longitudinal extensive T2 lesions of the cord with enhancement. MRI orbits showed no signs of nerve disease. LP was consistent with albuminocytologic disassociation, negative oligoclonal bands and elevated IgG synthesis rate; further CSF studies were within normal limits. He was treated initially with 3 days of high-dose steroids then started on a 14-day course of an oral taper; however, there were no improvements in his symptoms and he developed severe encephalopathy and dysphagia. Significant radiological and clinical improvement occurred after 5 rounds of plasma-exchange with continual oral steroids. Further laboratory studies including inflammatory, infectious and paraneoplastic panels were normal. CT of the chest, abdomen and pelvis showed no evidence of occult malignancy. Cerebral angiogram showed no evidence of vasculitic process. Serum MOG-IgG came back positive 2 weeks later via email for the Mayo Clinic Research lab. Azathioprine with low-dose oral steroid was started but within 8 weeks he developed vision loss OS. 3 months from the onset of vision loss, he was seen in the Neuro-Ophthalmology with significant temporal atrophy OS and mild atrophy OD. No further relapses reported to date.

#### Conclusions, including unique features of the case(s):

The case report highlights an atypical manifestations of a rare CNS demyelinating disease.

**References:** None.

**Keywords:** Optic neuropathy, Demyelinating disease, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuroimaging, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 42

### Extensive Adenoid Cystic Carcinoma (ACC) Presented as Bilateral Vision Loss and Optic Nerve Atrophy

Yu Zhao<sup>1</sup>, John Hinkle<sup>2</sup>, Kyle White<sup>3</sup>, Byron Lam<sup>2</sup>

<sup>1</sup>Minneapolis Clinic of Neurology, Minneapolis, Minnesota, USA, <sup>2</sup>Bascom Palmer Eye Institute, Miami, Florida, USA, <sup>3</sup>University of Miami, Miller School of Medicine, Miami, Florida, USA

#### Introduction:

ACC is rare epithelial tumor of major and minor salivary glands of the head and neck. We presented a case with presenting symptom as blurry vision, who had prior "normal" MRI and CT imaging.

#### Description of Case(s):

68-year-old woman presented with 3-month vision decline. It started with left eye blurry vision then left pupil became dilated. 2 months later her right eye vision decreased. CT and MRI brain in local hospital were "normal". She had stroke work-up for right mid-face and peri-orbital numbness, but was only diagnosed with sinus infection. She did not respond to antibiotics. ROS showed 30 pounds loss. On examination, uncorrected right VA was 20/200, which improved to 20/70-2; left was HM. Left pupil was 6mm, right was 4mm in dark and constricted to 5mm and 3mm to light. There was a left RAPD. Fundus exam showed bilateral optic nerve pallor, worse on the left. Lab were unremarkable except ESR was 40. ANA t was 1:40. MRI showed extensive infiltrative process centered in the central skull base involving the sella, bilateral cavernous sinuses, anterior and middle cranial fossa and extending into the infratemporal fossa, orbital apices, superior nasal cavity, sphenoid and posterior ethmoid sinuses. The bilateral cavernous and supraclinoid internal carotid arteries were encased but no vessel narrowing. CT showed permeative lytic appearance of the central skull base. Pathology showed solid pattern ACC with focal areas of cribriform pattern and bone invasion.

#### Conclusions, including unique features of the case(s):

ACC can be easily missed. The unique feature of this case is that the patient did not have an apparent mass but extensive intracranial lesion centered in skull base. She only presented with painless vision loss without significant other neurological deficits except mild facial sensory changes. The extent and size of the lesion are significantly disproportional to the symptoms.

**References:** 1. Ramsden D, Sheridan BF, Newton NC, De Wilde FW, Adenoid cystic carcinoma of the Head and Neck: a Report of 30 cases, *Aust N Z J Surg.* 1973 Sep;43(2):102-8. 2. Gondivkar SM, Gadbill AR, Chole R, Parikh RV, Adenoid cystic carcinoma: a rare clinical entity and literature review, *Oral Oncol.* 2011 Apr;47(4):231-6. 3. Dantas AN, Morais EF, Macedo RA, Tinôco JM, Morais Mde L, Clinicopathological characteristics and perineural invasion in adenoid cystic carcinoma: a systematic review, *Braz J Otorhinolaryngol.* 2015 May-Jun;81(3):329-35. 4. Van Weert S1, Bloemena E, van der Waal I, de Bree R, Rietveld DH, Adenoid cystic carcinoma of the head and neck: a single-center analysis of 105 consecutive cases over a 30-year period, *Oral Oncol.* 2013 Aug;49(8):824-9. 5. Walsh RD, Vagefi MR, McClelland CM, Alonso-Basanta M, Tamhankar MA, Primary adenoid cystic carcinoma of the orbital apex, *Ophthal Plast Reconstr Surg.* 2013 Jan-Feb;29(1):e33-5. 6. Lee AG1, Phillips PH, Newman NJ, Hayman LA, Tang RA, Neuro-ophthalmologic manifestations of adenoid cystic carcinoma, *J Neuroophthalmol.* 1997 Sep;17(3):183-8.

**Keywords:** Neuroimaging, Tumors

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 43

### Intracranial Hypertension From Dural Arteriovenous Fistula

Justin West<sup>1</sup>, Sally Mathias<sup>2</sup>, Douglas Lukins<sup>3</sup>, Padmaja Sudhakar<sup>4</sup>

<sup>1</sup>University of Kentucky, Lexington, Kentucky, USA, <sup>2</sup>University of Kentucky Department of Neurology, Lexington, Kentucky, USA, <sup>3</sup>University of Kentucky Department of Radiology, Lexington, Kentucky, USA, <sup>4</sup>University of Kentucky Department of Ophthalmology and Department of Neurology, Lexington, Kentucky, USA

#### Introduction:

The clinical presentation of dural arteriovenous fistula (DAVF) is variable and depends on the venous drainage pattern and location. Type I DAVF drains directly into the dural venous sinuses with antegrade flow. DAVF located in the transverse-sigmoid sinus typically present with symptoms of raised intracranial pressure including headache, bruit, pulsatile tinnitus, and visual symptoms. We report a unique case of a 69 year old male who presented with intracranial hypertension secondary to a dural AV fistula that had multiple feeders.

#### Description of Case(s):

A 69 year old man presented with recurrent episodes of headache over 1 year, transient vision loss, dizziness and pulsatile tinnitus. An ophthalmology exam revealed visual acuity of 20/40 OD, 20/25 OS, and bilateral papilledema. Contrast enhanced MR head was unremarkable but contrast enhanced MRV was suspicious but inconclusive for left transverse sinus thrombosis. Spinal tap revealed opening pressure of 46 cm H<sub>2</sub>O with normal CSF composition. He was started on acetazolamide and warfarin. Subsequent conventional cerebral angiography showed a complex arteriovenous fistula of the torcula and left transverse and transverse sigmoid junction fed by multiple arterial feeders mostly from the external carotid branches and a meningeal feeder from the right vertebral artery. Onyx embolization of the most prominent left occipital artery branches was possible but not the smaller feeders. He was then successfully treated with adjuvant radiotherapy with gamma knife. He experienced symptomatic relief and the papilledema resolved.

#### Conclusions, including unique features of the case(s):

Intracranial hypertension in a transverse sinus DAVF may result from decreased CSF absorption secondary to venous hypertension. Venous sinus thrombosis is often associated with DAVFs but the cause-effect relationship is not clear. One hypothesis is that the thrombosis causes opening of congenital channels leading to a fistula. Another is that the sluggish blood flow from venous hypertension leads to thrombus formation. Our case had successful outcomes with embolization followed by radiotherapy.

**References:** Ahmed, Khoury, Wilkinson, Parker, Halamagyi, Venous Hypertension as the Cause of Intracranial Hypertension in Patients With Transverse Sinus Dural Arteriovenous Fistula, *Journal of Neuro-Ophthalmology*, 33, 102-5, 2013 Pham, Khanna, Type 1 Dural Arteriovenous Fistula Mimicking Dural Venous Sinus Thrombosis-Related Intracranial Hypertension, *Letters to the Editor in Journal of Neuro-Ophthalmology*, 0, 1-2, 2017 Cognard, et al, Dural Arteriovenous Fistulas as a Cause of Intracranial Hypertension Due to Impairment of Cranial Venous Outflow. *Journal of Neurology, Neurosurgery, and Psychiatry*. 65(3):308-16. 1998. Zako, Murata, Inukai, Yasuda, Iwaki. Long-term Progressive Deterioration of Visual Function After Papilledema Improved by Embolization of a Dural Arteriovenous Fistula in the Sigmoid Sinus: A Case Report. *Journal of Medical Case Reports*. 8:392. 2014

**Keywords:** Vascular disorders, Interventional neuroradiology, Neuroimaging, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 44****Decreased Activation of Human Motion Area V5/MT+ During Motion Perception and Attempted Pursuit in Akinetopsia**

Eek-Sung Lee<sup>1</sup>, Yeong-Beom Lee<sup>2</sup>, Hyo-Jung Kim<sup>3</sup>, Jin-Ok Lee<sup>3</sup>, Tae-Kyeong Lee<sup>3</sup>, Ji-Soo Kim<sup>3</sup>

<sup>1</sup>Department of Neurology, Soonchunhyang University Bucheon Hospital, Bucheon, Korea, Republic of, <sup>2</sup>KI for Health Science and Technology, KAIST, Daejeon, Korea, Republic of, <sup>3</sup>Department of Neurology, Seoul National University Bundang Hospital, Bundang, Korea, Republic of

**Introduction:**

Akinetopsia refers to selective impairment of motion perception, and may occur in association with bilateral or unilateral posterior brain lesions, epileptic seizure, Alzheimer's disease, and drug intoxication (nefazodone).

**Description of Case(s):**

A 40-year-old man presented with difficult perception of moving objects for three years. He should move his head to read the moving subtitles on television because he could not chase the moving letters with the eyes. Also, he became unable to play table tennis or badminton anymore. His past medical history was unremarkable excepts cured pulmonary tuberculosis. His visual acuity was 20/20 OS and 20/200 OD, but findings were normal for other ophthalmologic examination that included intraocular pressure, slit lamp examination, pupillometry, perimetry, fundus photography, optical coherence tomography, and electroretinogram. His perception of the colors, faces, and static objects was intact without simultanagnosia, optic ataxia, spatial neglect, or ocular motor apraxia. Brain magnetic resonance images were unremarkable. The patient showed prominent impairment of horizontal smooth pursuit and optokinetic responses in the presence of normal saccades, VOR, and VVOR. To evaluate motion perception, he performed random dot kinematogram (RDK) and structure-from motion (SFM) tests with varying levels of background noise. In addition, the patterns of cortical activation were evaluated using fMRI during attempted smooth pursuit and optokinetic responses, and while viewing a moving array of dots, a preferred stimulus for activating the human motion area V5/MT+. These tests revealed increased threshold coherence values for the RDK and SFM tasks when compared to age-matched controls, and decreased activation of the V5 area during attempted pursuit eye movements and motion perception.

**Conclusions, including unique features of the case(s):**

The findings in our patient with idiopathic akinetopsia provide further evidence that V5/MT+ is responsible for motion perception and pursuit eye movements in humans and corresponds to the V5 area in monkeys.

**References:** None.

**Keywords:** Higher Visual Cortical functions, Higher visual functions

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



## Poster 45

### Imaging Modalities as an Aide in the Diagnosis of MGDA and Associated Comorbidities

Catalina Cleves-Bayon<sup>1</sup>, Ken Nischal<sup>1</sup>, Ellen Mitchell<sup>1</sup>, Elissa Ortolani<sup>1</sup>

<sup>1</sup>*Children's Hospital of Pittsburgh of UPMC, Pittsburgh, Pennsylvania, USA*

#### **Introduction:**

Morning Glory disc anomaly (MGDA) is a rare congenital anomaly that is often associated with life-threatening neurovascular complications. Distinguishing its special features from other congenital anomalies such as colobomas is key, as neurovascular diseases such as Moyamoya may be present which carry a high risk of stroke if surgical bypass is not performed. When corneal opacities interfere with visualization of the fundi, additional imaging techniques such as ultrasound, OCT and MRI of the orbits can be extremely helpful. We describe a 2 year old in which such techniques allowed for correct diagnosis, and prompt neurosurgical management.

#### **Description of Case(s):**

2 year old girl adopted from China presented with left microphthalmia and nystagmus. There was a prominent corneal opacity of the left eye that prevented visualization of the fundus. Orbital US was suspicious for funnel shape excavation of the optic nerve, as well as a hyperechoic area suggestive of a glial tuft. ON excavation was confirmed on orbital imaging which also revealed bilateral Moyamoya disease. The patient underwent pial synangiosis and continues to do well.

#### **Conclusions, including unique features of the case(s):**

In patients with congenital disc anomalies in which ophthalmoscopy is challenging, ancillary imaging that combines MRI, US and OCT can be helpful to further delineate the abnormalities and clarify diagnosis and subsequent plan of care. MGDA is frequently associated with ischemic events and, if not recognized promptly can lead to catastrophic neurological complications

**References:** Lee B, Traboulsi EI. Update on the Morning Glory Disc Anomaly. *Ophthalmic Genetics*, 29, 48, 2008. Ceynowa DJ, Wickstrom R, Olsson M, Ek U, Eriksson U. Morning Glory Disc Anomaly in Childhood- a population-based study. *Acta Ophthalmologica*, 93, 623, 2015 Robson SE, Heidary G, Paldino MJ. Morning Glory Disc Anomaly: Characteristic MR Imaging Findings. *AJNR*, 34, 2010, 2013.

**Keywords:** Neuroimaging, Pediatric Neuro-Ophthalmology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 46****Giant Dilated Virchow Robin Spaces Causing Midbrain Compression and Obstructive Hydrocephalus**

Padmaja Sudhakar<sup>1</sup>, Flavius Raslau<sup>1</sup>

<sup>1</sup>*University of Kentucky, Lexington, Kentucky, USA*

**Introduction:**

Virchow Robin spaces (VRSs) are normal perivascular spaces, lined with pia mater, around perforating arteries in the brain parenchyma that act as drainage pathways for interstitial fluid. Giant dilatation of VRS is rare and may produce multicystic giant lesions that can cause pressure effect on surrounding structures and can mimic cystic neoplasms. We describe a 12 year old boy with a giant dilated Virchow robin space centered on the midbrain (type 3- mesencephalic) who presented with lethargy and upbeat nystagmus.

**Description of Case(s):**

A 12 year-old boy with hypothyroidism presented with lethargy after a streptococcal throat infection and hand tremors concerning for Sydenham's chorea. Contrast enhanced MRI head revealed a large multicystic right midbrain mass extending into the thalamus and pons without enhancement or perilesional edema and compression of cerebral aqueduct causing obstructive hydrocephalus. He underwent biopsy with removal of tissue superior to the brainstem and fenestration of some cysts. This ruled out a neoplasm and established a diagnosis of dilated VRSs. Neuro-Ophthalmology exam revealed 20/20 vision in both eyes with full extraocular movements. He had left hyperphoria, saccadic vertical smooth pursuit and upbeat nystagmus with null point in downgaze making him adopt a chin-up position. He had grade 1 papilledema OU. Follow-up imaging after biopsy showed smaller cystic midbrain lesion with compensated hydrocephalus. His papilledema also resolved on follow-up eliminating the need for any shunt. He underwent superior rectus plication 6 mm, inferior rectus recession 6 mm and superior oblique recession 6 mm bilaterally to adjust the null point and correct his chin position. He did well post-operatively

**Conclusions, including unique features of the case(s):**

This case is unique as upbeat nystagmus from midbrain compression has never been previously described in dilated VRSs. Interestingly the fenestration of some cysts lead to marked improvement in papilledema and lethargy, thus deferring the need for any surgical intervention.

**References:** 1. Donaldson C, Chatha G, Chandra RV, Goldschlager T. Obstructive Hydrocephalus Secondary to Enlarged Virchow-Robin Spaces: A Rare Cause of Pulsatile Tinnitus. *World Neurosurg.* 2017 May;101:815.e1-815.e3. 2. Kumar A, Gupta R, Garg A, Sharma BS. Giant Mesencephalic Dilated Virchow Robin Spaces Causing Obstructive Hydrocephalus Treated by Endoscopic Third Ventriculostomy. *World Neurosurg.* 2015 Dec;84(6):2074.e11-4. 3. Fayeye O, Pettorini BL, Foster K, Rodrigues D. Mesencephalic enlarged Virchow-Robin spaces in a 6-year-old boy: a case-based update. *Childs Nerv Syst.* 2010 Sep;26(9):1155-60. 4. Revel F, Cotton F, Haine M, Gilbert T. Hydrocephalus due to extreme dilation of Virchow-Robin spaces. *BMJ Case Rep.* 2015 Jan 6;2015.

**Keywords:** Neuroimaging, Nystagmus, High intracranial pressure/headache, Ocular Motility, Pediatric Neuro-Ophthalmology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 47****Longitudinal Multi-Modal Neuroimaging in Opsoclonus-Myoclonus Syndrome**

Sun-Young Oh<sup>1</sup>, Ji-Soo Kim<sup>2</sup>, Marianne Dieterich<sup>3</sup>, Rainer Boegle<sup>3</sup>, Jae-Il Kim<sup>4</sup>

<sup>1</sup>Department of Neurology, Chonbuk National University, Jeonju-City, Korea, Republic of, <sup>2</sup>Seoul National University, Seong-nam City, Korea, Republic of, <sup>3</sup>Ludwig-Maximilians-University, Munich, Germany, Munich, Germany, <sup>4</sup>Dankuk University Hospital, Cheon-An, Korea, Republic of

**Introduction:**

To investigate structural, metabolic and functional connectivity changes in visual and oculomotor structures throughout a period of involuntary ocular oscillation in a paraneoplastic opsoclonus patient.

**Methods:**

We used serial rs-fMRI and FDG-PET data collected from acute stages to chronic resolution of the opsoclonus to investigate the metabolic and functional changes in the visual and oculomotor systems.

**Results:**

FDG-PET scan demonstrated a substantially increased metabolism in structures around the deep cerebellar nuclei (e.g. fastigial nucleus (FN)) and relatively reduced metabolism in the bilateral occipital lobes during the acute stage of the disease. Functional connectivity increased initially between the seeds of oculomotor and visual system including the primary (V1) and motion-sensitive visual cortex (V5), frontal eye field, superior colliculus, and cerebellar oculomotor vermis (OMV) during the acute phase and then decreased later as the symptom resolved. The functional connectivity between the OMV and FN showed a positive correlation [PzE1] during the acute period and then the connectivity decreased during the resolved phase. [PzE1]With what

**Conclusions:**

Our study provides a descriptive representation for the changes of abnormal functional connectivity throughout the visuo-oculomotor brain in opsoclonus and may suggest directions for further research on the pathogenesis of opsoclonus.

**References:** None.

**Keywords:** Neuroimaging, Ocular Motility, Ocular manifestations of vestibular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 48****Optic Neuritis and Hemiparesis in a Previously Healthy Young Woman**

Dulanji Kuruppu<sup>1</sup>, G Giuliari<sup>1</sup>, Devin Mackay<sup>1</sup>

<sup>1</sup>*Indiana University School of Medicine, Indianapolis, Indiana, USA*

**Introduction:**

A 35-year-old woman from Honduras presented with five days of sudden onset decreased vision in her right eye, pain with extraocular movements, fevers and chills, and three days of right upper and lower extremity weakness and numbness.

**Description of Case(s):**

Visual acuity was no light perception in the right eye and her right pupil was amaurotic. Fundoscopic exam revealed severe optic disc edema, cotton wool spots, extensive flame-shaped peripapillary and intraretinal hemorrhages, and retinal pallor. MRI of the brain with and without contrast showed scattered ring-enhancing lesions in the bilateral thalami and right globus pallidus, and right optic nerve enhancement. The fundus and MRI findings in the context of subjective fevers and recent immigration reinforced the importance of screening for an infectious etiology. Serum HIV testing was positive. Serum CMV PCR and toxoplasmosis PCR and IgG were positive. Her optic disc edema, retinal pallor, and retinal hemorrhages were consistent with CMV retinitis. The presence of multiple ring-enhancing lesions in the deep gray matter on brain MRI was suggestive of toxoplasmosis. She was treated with intravenous and intravitreal ganciclovir for CMV, oral sulfamethoxazole/trimethoprim for toxoplasmosis, and started on antiretroviral therapy. One month after initiation of treatment, her right sided motor/sensory deficits, retinitis, and optic disc edema were improving, but her right eye visual acuity remained at no light perception.

**Conclusions, including unique features of the case(s):**

Optic neuritis and unilateral weakness/numbness initially raised concern for demyelinating disease. However, her fundoscopic exam findings and brain lesions suggested an alternative etiology. Her subjective fevers and recent immigration suggested an infectious cause, which prompted testing for HIV and associated opportunistic infections. This case emphasizes the importance of additional testing in cases of atypical optic neuritis and retinitis, and particularly screening for infectious causes in which immunomodulatory therapies have the potential to put vision and neurologic function at further risk.

**References:** None.

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 49**

**Visual Loss Due to Nutritional Optic Neuropathy Following Gastric Bypass**

Xuemin Zhang<sup>1</sup>, Janet Sunness<sup>2</sup>, Angelique Pillar<sup>2</sup>

<sup>1</sup>University of Maryland School of Medicine, Baltimore, Maryland, USA, <sup>2</sup>GBMC, Baltimore, USA

**Introduction:**

There has been an increase in the number of bariatric gastric bypass surgeries in the United States, leading to an increased number of patients with complications related to nutritional deficiencies. Nutritional optic neuropathy is an uncommon disease caused by damage to the papillomacular bundle due to nutritional deficiencies.

**Description of Case(s):**

We report a case of a 33-year-old male with history of sleeve gastrectomy two years prior who presented with progressive bilateral central scotomas and myelopathy. He was noted to have severe vitamin B12 deficiency a year prior and had been on monthly vitamin B12 injections as well as multivitamin supplementation. He was noted to have reduction of sensitivity near the center of each eye subjectively and on microperimetry. His history of sleeve gastrectomy prompted a laboratory work-up which revealed folate and vitamin B1 deficiency. Visual acuity improved with increased vitamin supplementation.

**Conclusions, including unique features of the case(s):**

The patient developed nutritional optic neuropathy despite being on vitamin B12 injections and multivitamin supplementation. In patients with subacute or chronically progressive optic neuropathy or myelopathy, importance must be placed in history of gastric surgery and proper laboratory work-up should be performed.

**References:** None.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 50**

**A Case of the Orbital Apex Syndrome as Initial Presentation of Acute Myelitic Leukemia**

Jl-Yun Park<sup>1</sup>, Ju-Hyang Lee<sup>1</sup>, Sun-Young Kim<sup>1</sup>

<sup>1</sup>*Ulsan University Hospital, Ulsan, Korea, Republic of*

**Introduction:**

Patients with leukemia often have ocular manifestations. Although nearly all ocular structures can be affected, leukemic retinopathy is often the most clinically apparent manifestation. They sometimes may precede systemic diagnosis or may be a sign of leukemia recurrence. We report a rare case of superior orbital syndrome as initial presentation of adult AML.

**Description of Case(s):**

A 54-year-old man presented with acute onset of ptosis and diplopia in the left eye. On examination, his right eye was nearly complete ophthalmoplegia with ptosis, protrusion and decreased visual acuity (BCVA 0.3). PNS CT showed mucosal thickening of the maxillary, ethmoid, sphenoid sinuses and the mainly the right nasal cavity suggesting chronic sinusitis. His brain MRI and MRA with enhancement showed mild thickening of the medial rectus muscle in the right orbit and pansinusitis without intracranial focal stenosis. Initial laboratory test showed normal CBCs and chemistry. He was initially diagnosed with orbital apex syndrome due to inflammatory or infectious cause. ESS with culture and biopsy were performed and empirical antibiotics (ampicillin/sulbactam) with solumedron IV pulse therapy were received. After steroid and antibiotics therapy, his ocular pain and gaze limitation was partially improved and he discharged. After 20 days of steroid therapy, he visited the emergency department because of aggravating eye pain and diplopia. At that time his CBCs showed pancytopenia and his bone marrow biopsy showed increased lymphocytic histiocytes with erythroid precursor and RBCs that suggested pure erythoid leukemia. Although he received chemotherapy and conservative care, he died three months after the onset of painful diplopia.

**Conclusions, including unique features of the case(s):**

Orbital apex syndromes may result from a variety of inflammatory, infectious, neoplastic, iatrogenic/traumatic, and vascular condition. In this patient, orbital apex syndrome of adult leukemia is rarely the initial sign of the disease even initial CBCs were normal.

**References:** None.

**Keywords:** Adult strabismus with a focus on diplopia, Tumors

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 51

### Eyes Wide Shut in the Face of Cancer

Arezu Haghighi<sup>1</sup>, Kimberly Gokoffski<sup>1</sup>, On-Tat Lee<sup>1</sup>, Vivek Patel<sup>1</sup>

<sup>1</sup>University of Southern California Roski Eye Institute, Los Angeles, California, USA

#### Introduction:

Neuroendocrine tumors are rare, epithelial neoplasms that arise from various organ systems, including the gastrointestinal (GI) tract and tracheobronchial tree [1]. 50-75% of cases present with metastatic disease, most commonly the liver [2]. Metastases to the eyes are rare but can involve the choroid or, with a primary of GI origin, the orbit [3, 4]. Orbital involvement commonly presents with proptosis and motility limitations [4]. Herein we present a case of metastatic carcinoid masquerading at first glance as myasthenia gravis (MG).

#### Description of Case(s):

A 38-year-old man with remote TBI was referred for subacute onset diplopia and fluctuating ptosis OD concerning for MG. Patient endorsed generalized weakness, weight loss, and lower trunk pain. Visual acuity was 20/20 OU. Adnexal exam was notable for 2 mm ptosis OD with normal levator function, negative lid fatigue, and absent Cogan lid twitch. No lateral flare or proptosis was noted. Sensorimotor exam revealed a large angle intermittent RXT and LHT. Saccadic velocities, pupillary and fundoscopic examination were normal. Careful inspection revealed a conjunctival salmon patch infiltrate and palpable mobile masses of the orbit OS as well as the scalp. MRI brain/orbits revealed extraconal masses in the left orbit as well as involvement of right superior rectus/levator complex. CT scan as part of malignancy work-up showed multiple hypoattenuated liver lesions. A biopsy of both liver and scalp lesions revealed a low-grade carcinoid tumor. PET scan demonstrated additional spinal and renal metastases. Chemotherapy with capecitabine/temozolomide for metastatic carcinoid with presumed GI origin was begun.

#### Conclusions, including unique features of the case(s):

Seldom are ophthalmologists at the frontline of diagnosing neuroendocrine tumors which are not only rare but infrequently present with ocular signs. A broad differential and careful integration of both ocular and systemic clues as well as a multi-disciplinary approach are critical in such challenging cases.

**References:** [1] Klimstra D, Modlin I, Coppola D, Lloyd R, Suster S. The Pathological Classification of Neuroendocrine Tumors. *Pancreas* (2010); 39(6): 707-712. [2] Jensen RT, Norton JA. Carcinoid tumours and the carcinoid syndrome. In: De Vita VT, Hellman S, Rosenberg SA, editors. *Cancer Principles and practice of Oncology*. Philadelphia: Lippincott- Raven Publishers, 1997;1704–23 (5th ed.). [3] Shetlar DJ, Font RL, Ordonez N, el-Naggar A, Boniuk M. A clinicopathologic study of three carcinoid tumors metastatic to the orbit. Im- munohistochemical, ultrastructural, and DNA. *Ophthalmology*. 1990 Feb;97(2):257-64 [4] Fan JT, Buettner H, Bartley GB, Bolling JP. Clinical features and treatment of seven patients with carcinoid tumor metastatic to the eye and orbit. *Am J Ophthalmol* 1995;119:211–8.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Orbit, Orbit/ocular pathology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 52**

**Fibrous Meningioma with Clinical Resemblance to Inflammatory Pseudotumor**

Dae Woong Bae<sup>1</sup>, Seunghee Na<sup>2</sup>

<sup>1</sup>*Department of Neurology, St. Vincent's hospital, the Catholic University of Korea, Suwon, Korea, Republic of,* <sup>2</sup>*Department of Neurology, Incheon St. Mary's hospital, the Catholic University of Korea, Incheon, Korea, Republic of*

**Introduction:**

Inflammatory pseudotumor is a nonneoplastic process of unknown etiology most frequently involving the lungs and orbits. Primary intracranial inflammatory pseudotumors are exceptionally rare. The authors report a rare case of meningioma in posterior cavernous sinus mimicking clinical characteristics for inflammatory pseudotumor.

**Description of Case(s):**

A 55-year-old man presented with binocular diplopia involving right cranial nerve VI and III palsy and headache in Rt. frontal and periorbital area. MR imaging revealed a mass in posterior cavernous sinus, clivus and protruding to right prepontine cistern. Considering possibility of inflammatory pseudotumor, he was treated with prednisolone 60mg daily for 2weeks. He showed dramatic response with full recovery of his symptom and no focal neurological deficit. After 10 months later, he complained of the same binocular diplopia symptom with previous attack. He showed right cranial nerve VI palsy and follow-up MR imaging documented the same mass lesion with strong enhancement. Treatment with prednisolone was not effective at that time so surgical decompression and tumor removal was performed. Histopathology confirmed the diagnosis of fibrous meningioma. Radiation therapy was also applied and the patient is doing well at 4 months' follow-up with resolution of diplopia and cranial neuropathy.

**Conclusions, including unique features of the case(s):**

Meningioma can mimic inflammatory pseudotumor both radiologically and clinically. The treatment options consist of surgery, high-dose steroids, irradiation, and chemotherapeutic agents with variable therapeutic response. The importance of recognizing and appropriately diagnosing this rare intracranial pathology lies in prognostication and avoidance of overzealous treatment. This case indicates that meningioma may manifest peculiar biological behavior more typical of intracranial granulomas than of meningiomas.

**References:** Toshiaki Yamaki et al., Lymphoplasmacyte-rich meningioma with clinical resemblance to inflammatory pseudotumor, *J Neurosurg* 86:898–904, 1997 Manish K. et al., Sphenoid wing inflammatory pseudotumor mimicking a clinoidal meningioma: case report and review of the literature, *Surgical Neurology* 70 (2008) 509–513 Atsushi Okano et al, Intracranial Inflammatory Pseudotumors Associated with Immunoglobulin G4-Related Disease Mimicking Multiple Meningiomas: A Case Report and Review of the Literature, *World Neurosurg.* (2015) 83, 6:1181.e1-1181.e4

**Keywords:** Tumors, Pseudotumor Cerebri

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 53**

**Horner's Syndrome as the Presenting Symptom in Giant Cell Arteritis**

Stephanie Figueira<sup>1</sup>, Benjamin Farley<sup>1</sup>, Brooke Hartenstein<sup>1</sup>, Charles Maitland<sup>1</sup>

<sup>1</sup>Florida State University College of Medicine, Tallahassee, Florida, USA

**Introduction:**

An etiology for isolated Horner's syndrome is found in approximately 60% of patients and rarely associated with Giant Cell Arteritis (GCA). In five previously reported cases, each had associated constitutional symptoms, other neurological signs and/or elevated inflammatory markers. We examined a 73 year old woman free of constitutional symptoms other than mild temporal headaches who developed Horner's syndrome without other neurological symptoms and normal inflammatory markers. Bilateral ischemic optic neuropathies subsequently developed despite steroid treatment.

**Description of Case(s):**

A 73 year old female complained of left temporal headaches sensitive to touch. Over a period of two months, left lid ptosis appeared without orbital or neck pain. She denied prior TIA like symptoms, she felt constitutionally well. Past history was negative for migraines, head or neck trauma. She had no chronic medical conditions. Physical examination: corrected visual acuity 20/25- OU; full confrontation fields. Funduscopy revealed normal appearing discs with 0.3 cup/disc ratios. Motility was full, tracking smooth, refixational saccades accurate. Both pupils were reactive, the right measured 3mm, the left 2mm. Pupillometry revealed dilator lag in the left pupil. There was a 3 mm ptosis, non-fatiguing of the left lid. Pharmacologic testing supported the diagnosis of left Horner's syndrome. Diagnostic: ESR 2, CRP 0.6, platelets 192,000. MRI of head, orbits, and neck with/without contrast unremarkable. MRA chest normal. Temporal artery biopsy demonstrated partial segmental loss of elastic lamina with focal inflammation. The patient was started on 80mg prednisone QID with gradual reduction monthly. After 5 months, on 30mg QID, she developed slight disc head elevation (OCT 116Um OD, 110Um OS) and arcuate bundle defects bilaterally. Steroids were increased and the condition stabilized.

**Conclusions, including unique features of the case(s):**

Giant cell arteritis presents in many forms. An isolated Horner's syndrome, particularly in the elderly, even in the absence of other constitutional symptoms and signs may be the only manifestation of GCA.

**References:** None.

**Keywords:** Optic neuropathy, Vascular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 54**

**Oculomotor Nerve Palsy Due To Clivus Metastasis Of Breast Cancer**

Soon Young Cho<sup>1</sup>, Ho Chang Kim<sup>1</sup>, Eok Soo Suh<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology, Dongguk University College of Medicine, Gyeongju, Korea, Republic of*

**Introduction:**

Tumors of the clivus and metastases to the clivus are very rare. We experienced a case of oculomotor nerve palsy due to clivus metastasis of breast cancer.

**Description of Case(s):**

A 51-year-old woman visited the ophthalmology clinic with a 5-day history of diplopia. She had a history of breast cancer for 7 years and a metastasis of the liver and bone. She had a partial mastectomy and systemic chemotherapy. Ophthalmic evaluation showed visual acuity of 20/25 of both eyes and intraocular pressure of 17 mm Hg on right eye and 18 mm Hg on left eye. Ptosis or anisocoria was not observed. Exodeviation of the left eye in the primary position, and ocular movement limitation in all directions except abduction were observed. Brain magnetic resonance angiography demonstrated an enhancing lesion in clivus. We diagnosed oculomotor nerve palsy due to clivus metastasis of breast cancer. She had conventional radiotherapy on clivus. No symptom relief or tumor size decrease was observed. She died three weeks after her visit due to systemic complication of the breast cancer metastasis.

**Conclusions, including unique features of the case(s):**

Although not common, oculomotor nerve palsy can be the first sign of metastasis of the clivus in breast cancer patient. We should consider magnetic resonance angiography and magnetic resonance imaging of brain in oculomotor nerve palsy patient in metastatic breast cancer.

**References:** 1.Pallini R, Sabatino G, Doglietto F, Lauretti L, Fernandez E, Maira G. Clivus metastases: report of seven patients and literature review. *Acta Neurochir (Wien)* 2009;151:291-6 2.Kimura F, Kim KS, Friedman H, Russell EJ, Breit R. MR imaging of the normal and abnormal clivus. *AJNR Am J Neuroradiol.* 1990;11:1015–21 3. McDermott RS, Anderson PR, Greenberg RE, Milestone BN, Hudes GR. Cranial nerve deficits in patients with metastatic prostate carcinoma: clinical features and treatment outcomes. *Cancer* 2004;101:1639–43 4.Altman KW, Mirza N, Philippe L. Metastatic follicular thyroid carcinoma to the paranasal sinuses: a case report and review. *J Laryngol Otol* 1997;111:647–51 5.Alessi G, Lemmerling M, Vereecken L, De Waele L. Benign metastasising leiomyoma to skull base and spine: a report of two cases. *Clin Neurol Neurosurg* 2003; 105:170–4

**Keywords:** Tumors, Adult strabismus with a focus on diplopia, Neuroimaging, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 55**

**Neuro-ophthalmologic Findings in a Hemizygous Patient with Spastic Ataxia of Charlevoix-Saguenay**

Scott Haines<sup>1</sup>, Amy Harper<sup>1</sup>

<sup>1</sup>*Virginia Commonwealth University, Richmond, Virginia, USA*

**Introduction:**

Like all genetic ataxias, autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) is a rare diagnosis. However, it is being more frequently recognized as a cause of inherited cerebellar dysfunction. Classic findings of ARSACS include certain features relevant to Neuro-Ophthalmology. Nystagmus and other eye movement abnormalities can be present. There is also a characteristic prominence of the peripapillary retinal nerve fiber layer.

**Description of Case(s):**

A 12 year old African American boy with a longstanding gait abnormality presented to pediatric neuromuscular clinic for evaluation. He was also noted to also have increased tone and poor coordination. EMG showed sensory predominate axonal neuropathy. MRI showed superior cerebellar vermis atrophy and striated “footprints” in the pons. A chromosome micro-array was performed which found a deletion in the long arm of chromosome 13. The SACS gene is located within this region. Neuro-ophthalmologic evaluation was notable for gaze evoked nystagmus and limited upgaze. There was also prominent thickening of the retinal nerve fiber layer around the optic disc.

**Conclusions, including unique features of the case(s):**

ARSACS is a rare condition, with certain neuro-ophthalmologic features which may be pathognomonic. Recognizing these features may help lead to what can otherwise be a difficult diagnosis. ARSACS is most common in French Canada. There have been additional reports in other populations worldwide, but not previously reported in the African American population of the southern United States. Furthermore, the genetic finding of hemizygous state due to a microdeletion is unique compared to the usual homozygous autosomal recessive genetics. Therefore, this was a rare presentation of a rare disease, but the neuro-ophthalmologic features significantly contributed to confirming this diagnosis.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Pediatric Neuro-Ophthalmology, Nystagmus

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 57**

**Isolated Optic Neuropathy Associated with Mycoplasma Pneumoniae**

Seo-Young Choi<sup>1</sup>, Yunji Choi<sup>1</sup>, Kwang-Dong Choi<sup>1</sup>, Jae-Hwan Choi<sup>2</sup>

<sup>1</sup>*Pusan National University Hospital, Pusan, Korea, Republic of*, <sup>2</sup>*Pusan National University Yangsan Hospital, Pusan, Korea, Republic of*

**Introduction:**

Mycoplasma pneumoniae is a major pathogen of primary atypical pneumonia and has been known to cause various kinds of extrapulmonary manifestations involving almost all organs of the human body. Optic neuritis associated with M. pneumoniae infection has rarely been described and mostly, it combined other neurological complications including meningitis, meningoencephalitis, myelitis, and peripheral neuropathy.

**Description of Case(s):**

We report two patients who presented with isolated optic neuritis due to M. pneumoniae infection, seven-year-old girl and 20-year-old woman. Previously, five additional patients were reported the isolated optic neuritis associated with M. pneumoniae. All patients are child or young adults, and optic neuritis was unilateral (n = 3) or bilateral (n = 4). Remarkably, four patients did not have preceding history of respiratory M. pneumoniae infection, and ocular pain or headache was accompanied in only three. Although initial visual acuities were severely reduced in most cases, visual outcome was excellent after systemic steroid and/or antibiotics treatment.

**Conclusions, including unique features of the case(s):**

M. pneumoniae infection should be considered in the differential diagnosis of isolated optic neuritis, especially when occurring in a child or young adults, even though there was no preceding pneumonia, accompanying ocular pain, or headache. Various mechanisms including direct local inflammation, vascular occlusion, or indirect immune modulation due to M. pneumoniae infection can lead to isolated neurological manifestations without pneumonia.

**References:** None.

**Keywords:** Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 58

### Papilledema due to Cerebral Venous Sinus Thrombosis

Minsoo Baek<sup>1</sup>, Changhwan Lee<sup>1</sup>, moohwan Chang<sup>1</sup>, jiho Chang<sup>2</sup>, Sungeun Kyung<sup>1</sup>

<sup>1</sup>Dankook University, Cheonan-City, Chungchungnam-Do, Korea, Republic of, <sup>2</sup>Sunchunhyang University(Bucheon), Bucheon, Korea, Republic of

#### Introduction:

The diagnosis of cerebral venous thrombosis is challenging due to a wide range of clinical manifestations. Headache is the most common presenting symptom. Papilledema is present in about 28% of patients with cerebral venous thrombosis. We report the diagnosis of sinus thrombosis in two patients with blurred vision and asymptomatic optic disc swelling.

#### Description of Case(s):

A 27 - year - old man presented with blurred vision for 2 months. The best corrected visual acuity was 1.0 in the right eye and 0.7 in the left eye. The intraocular pressure was normal. Visual field examination revealed peripheral constriction and fundus revealed optic disc swelling in both eyes. Brain magnetic resonance imaging was normal and magnetic resonance Venography revealed a filling defect in the transverse sinus, suspected sinus thrombosis. The intracranial pressure was 36cmH<sub>2</sub>O. A 54-year-old man visited our hospital due to suspected bilateral optic nerve head swelling. The best corrected visual acuity was 0.9 in the right eye and 1.0 in the left eye. Visual field examination revealed inferior temporal defect in right eye. The optical coherence tomography and fundus examination revealed bilateral optic disc edema. MR imaging was normal. The venography showed a decrease in blood flow in the right transverse sinus, sigmoid sinus vein, and right internal carotid artery. The intracranial pressure was 22 cmH<sub>2</sub>O.

#### Conclusions, including unique features of the case(s):

Cerebral venous sinus thrombosis (CVST) is a disease caused by various causes such as coagulopathy, infection, vasculitis, and head trauma. We report cases of bilateral optic disc swelling due to sinus thrombosis without underlying disease. Magnetic resonance venography in combination with MRI is recommended to identify patients with papilledema due to cerebral venous sinus thrombosis in ophthalmologic clinic.

**References:** 1. Ferro JM, Canhao P, Stam J, Boussier MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: Results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) Stroke. 2004;35:664–70. 2. Saposnik G, Barinagarrementeria F, Brown RD, Jr, Bushnell CD, Cucchiara B, et al. Diagnosis and management of cerebral venous thrombosis: A statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011;42:1158–92. 3. Boussier MG, Chiras J, Bories J, Castaigne P. Cerebral venous thrombosis: Review of 38 cases. Stroke. 1985;16:199–213 4. O'Rourke TL, Slagle WS, Elkins M, Eckermann D, Musick A. Papilloedema associated with dural venous sinus thrombosis. Clin Exp Optom. 2014;97:133-9.

**Keywords:** Neuroimaging, Optic neuropathy, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 59**

**A Case of Anti-Glial Fibrillary Acidic Protein (GFAP) Antibody Associated Meningoencephalomyelitis**

Thirugnanam Umapathi<sup>1</sup>, Ambihai Sivalingam<sup>1</sup>, Peng Soon Ng<sup>1</sup>

<sup>1</sup>*National Neuroscience Institute, Singapore 308433, Singapore*

**Introduction:**

A novel antibody, anti-Glial Fibrillary Acidic Protein (anti-GFAP), is a biomarker for a corticosteroid-responsive, occasionally paraneoplastic, meningoencephalomyelitis. It has distinctive neuroradiological findings and is associated with bilateral papillitis.

**Description of Case(s):**

A 68-year-old lady presented with a week of fever, cough, headache, vomiting and altered mental state. Clinical examination was consistent with acute meningoencephalomyelitis. Optic discs were not swollen. MRI brain showed diffuse leptomeningeal enhancement extending to brainstem and spinal cord. Multiple segmental, intramedullary, T2 hyperintense, enhancing lesions were seen at the medulla and the entire length of spinal cord. Spinal fluid revealed lymphocytic pleocytosis, raised protein and low glucose. Standard bacteriological and virologic evaluation was unyielding. She was given meningitic doses of antibiotics. She continued to deteriorate neurologically. Anti-tuberculous (TB) treatment was started with high-dose dexamethasone. She started to improve. However, within two weeks of weaning dexamethasone she became confused again. TB cultures had returned negative. MRI brain showed persistent leptomeningeal enhancement and a radial pattern of perivascular enhancement in the periventricular region. The radiologic features raised the possibility of anti-GFAP antibody associated meningoencephalomyelitis. Fundoscopy showed equivocal disc swelling on the right. Anti-GFAP antibody was detected at high titres in the spinal fluid. PET scan did not indicate an underlying neoplasm. TB treatment was stopped and high dose corticosteroids started. Over next few weeks her cognition, limb strength and coordination gradually improved. She is currently on mycophenolate and tapering doses of corticosteroid.

**Conclusions, including unique features of the case(s):**

We describe a typical case of a recently characterized, treatable, dysimmune meningoencephalomyelitis associated with anti-GFAP antibody. Neuro-ophthalmologists are likely to encounter this condition because of its association with bilateral papillitis and its mimicry of conditions such as TB, sarcoidosis, acute disseminated encephalomyelitis (ADEM), primary progressive multiple sclerosis, primary CNS or intravascular lymphoma, CLIPPERS syndrome and progressive encephalomyelitis with rigidity and myoclonus (PERM).

**References:** None.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Neuroimaging, Paraneoplastic syndromes, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 61****Compressive Optic Neuropathy? - A Case of Thyroid-associated Optic Neuropathy without Crowding Orbital Apex**

Ko-Jo Lin<sup>1</sup>

<sup>1</sup>Taipei Municipal Wan Fang Hospital, Taipei, Taiwan

**Introduction:**

Thyroid-associated optic neuropathy is a serious complication in patient with thyroid eye disease. The common cause was direct compression of optic nerve by enlarged extraocular muscles, or compromised blood supply by increased orbital pressure. In this case report, we demonstrate a case of thyroid-associated optic neuropathy without crowding orbital apex.

**Description of Case(s):**

A 54-year-old male with Graves' ophthalmopathy suffered from right eye decrease vision for 1 month. Eye examination revealed proptosis with bilateral exposure keratopathy, mild impaired color vision was also noted. There was no optic disc edema nor RAPD sign at first visit. Laboratory data of systemic inflammation work-up and VEP was arranged, but the result showed no significant abnormality. MRI revealed enlarged extraocular muscles with tendon sparing, no contrast enhancement on optic nerve was noted. Oral prednisolone (20mg/day) was prescribed for 1 week with slow-tapering, his vision was improved after our treatment. However, after discontinuation of steroid, his vision deteriorated again. Visual field defect progressed and his optic disc became swelling with significant impaired of color vision. The VEP also showed prolong P100 latency. The second MRI was similar to previous report. Oral prednisolone was regained (40mg/day) for 2 week. The visual acuity and disc edema dramatically improved after the steroid treatment.

**Conclusions, including unique features of the case(s):**

The first line therapy of thyroid-associated optic neuropathy is parental or oral steroid. In our patient, we gave him suboptimal dose of oral steroid due to his underlying diabetes mellitus and hepatitis B virus infection. But the response(both vision improvement and decrease optic disc edema) seemed to be satisfying. We demonstrate series of RNFL thickness change by OCT during this course, which was correlated with the disease severity. Last but not least, we want to remind that: in patient with thyroid eye disease always keep "compressive optic neuropathy" in mind, even if their orbital apex were not crowded!

**References:** None.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 62****An Unusual Case of Bilateral Optic Disc Swelling: POEMS syndrome**

Gabriele Berman<sup>1</sup>, Dalia Berman<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology, Aalborg University Hospital, Aalborg, Denmark*

**Introduction:**

Bilateral optic disc swelling with preserved visual function prompts a list of differential diagnoses. In an older patient the diagnostic process may be quite cumbersome, and unless meticulous observations are undertaken, a delayed diagnosis of a systemic disease may ensue. POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, and Skin changes) is a rare multisystemic disease that occurs in the setting of a plasma cell dyscrasia.

**Description of Case(s):**

A 57-year-old woman was noticed having bilateral optic disc swelling at a yearly screening for diabetic retinopathy. The patient had no visual complaints. Increased skin pigmentation was noticed. Her laboratory findings showed a tendency towards thrombocytosis. She was initially observed for presumed subclinical diabetic papillopathy, but as her disc appearance did not change, she underwent an unrevealing brain MRI and liquor dynamic examination. Her GFR appeared to be decreasing over time. Additionally, she reported a sensory loss and pain in her feet as well as Raynaud phenomenon. A diagnosis of POEMS syndrome was entertained. Serum electrophoresis demonstrated an M-band with isolated IgA lambda chains and prompted a hematologic evaluation. Both bone marrow flowcytometry and inguinal lymph node biopsy failed to show any monoclonality. CT thorax/abdomen was significant for ascites and pleural effusion, spleno- and hepatomegaly. PET-CT showed an avid increase of FDG uptake and enlargement of the portacaval lymph node. Histopathology confirmed Castleman disease.

**Conclusions, including unique features of the case(s):**

This case illustrates that clinical findings quite common in a diabetic patient (i.e. peripheral neuropathy, impaired renal function) in the setting of unusual signs (persistent optic disc swelling) or unexplainable symptoms (increased skin pigmentation, newly onset Raynaud phenomenon) should warrant a multidisciplinary approach. We do as well wish to argue whether "optic disc swelling" as opposed to papilledema might be a more suitable term in describing optic disc morphology in POEMS syndrome.

**References:** POEMS syndrome: 2017 Update on diagnosis, risk stratification, and management. Dispenzieri A. Am J Hematol. 2017 Aug;92(8):814-829.

**Keywords:** Paraneoplastic syndromes

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



## Poster 63

### Profound Hemorrhagic Disc Edema as Presenting Manifestation of Acute Myelogenous Leukemia

Gerard Hershewe<sup>1</sup>, Joshua Gratwohl<sup>2</sup>, Nikki Hamada<sup>2</sup>, Micaela Kocia<sup>1</sup>, Hershewe Jerad<sup>2</sup>, Alyssa Eckert<sup>1</sup>

<sup>1</sup>University of Nevada, Reno School of Medicine, Reno, Nevada, USA, <sup>2</sup>University of Nevada, Reno, Reno, Nevada, USA

#### Introduction:

Acute Myelogenous Leukemia (AML) is an acute form of leukemia caused by the neoplastic proliferation of hematopoietic stem cells. There are several neuro-ophthalmic manifestations of AML, including retinal hemorrhages, papilledema, and optic nerve infiltration. We present a patient with severe hemorrhagic disc edema as the initial manifestation of AML.

#### Description of Case(s):

58-year-old male presented with vertigo, light headedness, disequilibrium, left orbital pain, rare TVO's, and VA of 20/20 OU. Color vision was slightly reduced OS, and there was a 0.3 RAPD OD. Funduscopic examination showed severe bilateral hemorrhagic disc edema. There were several intraretinal and subhyaloid hemorrhages OU along the posterior poles. HVF showed bilateral paracentral scotomas and RNFL thickness was elevated at 160 microns OD and 171 microns OS. MRI scan of the brain and orbits were normal. Laboratory studies showed a WBC count of 9.6, hemoglobin was 5.6, platelet count was 8k (140-440k). There were 20% blast cells. Bone marrow biopsy and aspiration showed an increase number of blast cells with an 8:21 translocation. The patient was treated with chemotherapy, platelets, and red blood cell transfusions and improved clinically. Repeat examination 6/25/08, the patient reported that his central vision had improved bilaterally. VA remained 20/20 OU. Color vision and pupillary reaction were normal. Funduscopic examination showed almost complete resolution of the hemorrhagic disc edema and intraretinal hemorrhages. HVF showed mild to moderate blind spot enlargement OU. OCT showed an average RNFL thickness of 106 microns OD, and 108 microns OS. Fundus photography showed complete resolution of the hemorrhagic disc edema and resolution of the intraretinal hemorrhages.

#### Conclusions, including unique features of the case(s):

We present a patient with profound hemorrhagic disc edema as a presenting manifestation of AML. The major contributing factor to the disc hemorrhage was the profound thrombocytopenia. Leukocytosis with increased blast cells and anemia also correlate well with the severity of the intraretinal hemorrhages.

**References:** 1. Abuhelwa, Ziad, Al Shaer, Qasem, Taha, Sari, Ayoub, Khubaib, Amer, Riad, Characteristics of De Novo Acute Myeloid Leukemia Patients in Palestine: Experience of An-Najah National University Hospital. Asian Pacific Journal of Cancer Prevention, 2017, 18(9): 2459-2464. 2. Sharma, T, Gupta, S, Murray, PI, Ophthalmic manifestations of acute leukaemias: the ophthalmologist's role. Eye, 2004, 18: 663-672.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 64****Trichinella Nativa Infection from Black Bear Meat: A Rare Cause of Cerebral Venous Sinus Thrombosis**

Danah Albreiki<sup>1</sup>, Rahul Sharma<sup>1</sup>, Daniel Boucher<sup>2</sup>, Daniel Dalcin<sup>3</sup>, Dante Zarlenga<sup>4</sup>

<sup>1</sup>The University of Ottawa Eye Institute, Ottawa, Canada, <sup>2</sup>Northern Ontario School of Medicine, Thunder Bay, Canada, <sup>3</sup>The University of Calgary, Calgary, Canada, <sup>4</sup>Animal Parasitic Diseases Laboratory, USDA-Agricultural Research Service, Beltsville, Maryland, USA

**Introduction:**

Trichinellosis is a rare helminthiasis caused by nematodes of the *Trichinella* genus. Human infection occurs following the consumption of undercooked meat infected with cysts of *Trichinella* larvae. Clinical manifestations range from asymptomatic presentations to fatal disease; frequent signs and symptoms include eosinophilia, fever, periorbital edema and myalgias. We report a rare complication of *Trichinella nativa* infection: a cerebral venous sinus thrombosis (CVST) and subsequent bilateral abducens nerve palsy, resulting from the ingestion of dried meat from a black bear hunted in Northern Ontario.

**Description of Case(s):**

A previously-healthy 41-year old man presented to the emergency department with a three-day history of abdominal pain, nausea, diarrhea and a diffuse maculopapular rash. His symptoms were attributed to viral gastroenteritis. Two weeks later, he returned with diffuse myalgias and periorbital edema. Bloodwork revealed a leukocytosis with peripheral eosinophilia. At this visit, he reported prior consumption of dehydrated black bear meat that preceded his initial presentation. Given this history, Trichinellosis was suspected, and he was treated empirically with Prednisone and Mebendazole. Nine days after beginning treatment, he began to experience binocular diplopia, worsened headaches and transient visual obscurations. The patient was sent for an urgent computed tomography (CT) scan, which suggested an acute CVST. An MRI brain indicated a partially occlusive thrombosis in the superior sagittal sinus, complete occlusion of the left transverse sinus and thrombi in the inferior sagittal and straight sinuses. Subsequent neuro-ophthalmic assessment revealed bilateral papilledema. Oculomotor evaluation indicated a bilateral abducens nerve palsy.

**Conclusions, including unique features of the case(s):**

Cases of Trichinellosis are uncommon. We report 1 of 10 recent cases of Trichinellosis occurring in Northern Ontario in March 2016. Suspicion of *T. nativa* infection should occur in patients with a compatible clinical history. It should be recognized that thromboembolic complications, such as CVST, may rarely occur.

**References:** None.

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion), Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 65****Ataxia, Areflexia, and Ophthalmoplegia in a Patient with AChR Binding Antibody?**

Christine Greer<sup>1</sup>, Vivek Patel<sup>1</sup>, Kimberly Gokoffski<sup>1</sup>

<sup>1</sup>University of Southern California, Los Angeles, California, USA

**Introduction:**

We report a case 72 yo M who presented with one week of progressive weakness, multiple falls and 3 days of diplopia.

**Description of Case(s):**

Afferent exam was unremarkable. No anisocoria was appreciated. There was mild bilateral ptosis. Ductions were limited in the right eye: impaired abduction and adduction (-0.5), supraduction (-2), but infraduction full. There was no limitation of the left eye. Cranial nerves V, VII-XII otherwise intact. Patient had normal strength and tone proximally and distally. Deep tendon reflexes were 1+ in the upper extremity and absent in the lower extremity bilaterally, and ataxic on finger-to-nose, heel-to-shin, displayed a wide-based, unsteady gait. MRI brain, cervical spinal cord with and without contrast, MRA of the head and neck were normal. CSF studies were remarkable for cytoalbuminologic dissociation (WBC 5, RBC 104, glucose 62, protein 1925). All infectious, inflammatory, and paraneoplastic serology and CSF studies were negative. Anti-GQ1B antibodies were also negative. Over a few days, the patient developed weakness, predominately left shoulder abduction, and left hand grip. His bilateral ptosis was now near complete OD. His symptoms and examination did not fluctuate. Anti-AChR binding antibodies returned positive (0.7 nM). A bedside Tensilon test (2mg IV q 1 minute as tolerated) was negative. Repetitive nerve stimulation of the right ulnar and left facial nerves was normal and without a decremental response. Nerve conduction study of the right median, ulnar, peroneal, and tibial nerves demonstrated severely low amplitude compound muscle action potentials (CMAP), with severe distal latency prolongations, conduction velocity slowing and distal CMAP temporal dispersion. These EMG findings suggest an acquired demyelinating process and support the clinical picture of Guillian-Barre variant or Miller Fisher syndrome. The patient was started on IVIG, with gradual improvement.

**Conclusions, including unique features of the case(s):**

This case highlights an unusual circumstance of Anti-AChR binding antibody false positivity, which demonstrates reproducible specificities up to 99%(1)

**References:** 1. F E Somnier. Clinical implementation of anti-acetylcholine receptor antibodies. Journal of Neurology, Neurosurgery, and Psychiatry. 1993;56:496-504.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 66****Retinal Angiographic Evidence of CJD Prion Disease in Humans**

Norah Lincoff<sup>1</sup>, Lucia Balos<sup>1</sup>, Charles Chung<sup>1</sup>, Osman Farooq<sup>1</sup>

<sup>1</sup>Jacobs School of Medicine and Biomedical Sciences, SUNY at Buffalo, Buffalo, New York, USA

**Introduction:**

We report a unique case of retinal angiographic evidence of CJD prion disease, which, to our knowledge has not previously been reported. Significant retinal changes have been reported in the Veterinary literature and also on post-mortem human donor tissue. To our knowledge this is a unique case describing retinopathy in CJD prior to the classic development of cortical visual loss and ophthalmoplegia.

**Description of Case(s):**

A 57 year old man experienced a change in behavior, including the diagnosis of a fugue state, and depression. Seven months later he noted blurring of vision R>L eye and unsteadiness, causing him to fall twice. He was found to have 20/70 vision bilaterally, but an otherwise normal exam. Neuro-Ophthalmology questioned maculopathy R>L eye, which was confirmed on fluorescein angiography. He died within 11 months of his initial symptoms. Autopsy and immunohistochemical staining confirmed frontal lobe spongiform change and reactive astrocytosis. CSF analysis later confirmed the presence of very high levels of T-tau protein and 14-3-3 protein.

**Conclusions, including unique features of the case(s):**

CJD is a rare fatal neurodegeneration. Sporadic CJD originates from chance conversion of the normal form of the prion protein to an abnormal form in the brain of affected individuals. Early symptoms of CJD are often memory loss, personality changes, OCD symptoms, and depression. Retinal angiographic evidence of CJD prion disease in humans has never been reported. Significant retinal changes though have been reported, in the Veterinary literature, but also on post mortem human donor tissue. Fluorescein angiogram is a valuable test to order early in the work up of patients presenting with idiopathic progressive encephalopathy. It is our hope that this becomes a more recognized finding that will allow earlier diagnosis in patients with this unfortunate condition.

**References:** 1. Mead MW, Prion protein accumulation in eyes of patients with Sporadic and Variant Creutzfeldt Jakob Disease. Investigative Ophthalmology and Visual Sciences: Vol 44, 342-346, Jan 2003 2. Greenlee MHW, Changes in retinal function and morphology are early clinical signs of disease in cattle with bovine spongiform encephalopathy. Plos ONE; 10(3): E0119431, 2015 3. Brazis PW, Lee AG, Eggenberger ER, Homonymous visual field defects in patients without corresponding structural lesions on Neuroimaging: J Neuro-Ophthalmol; 20:92-96, 2000 4. Satoshi K et al, A case of homonymous hemianopia without corresponding anomalies on MRI. Poster 23, NANOS 2009 5. Derrick P, Lee AG et al, A case of CJ with periaqueductal grey involvement and upgaze paresis. Poster 124, NANOS 2011 6. TianG et al, CJ disease with cortical blindness. Poster 131, NANOS 2012. 7. Habib L, Sun L, Odel J, CJ disease an important differential diagnosis of supranuclear palsy. Poster 54, NANOS 2016

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 67****Chronic Lymphocytic Leukemia Presenting as Optic Disc Edema and Branch Retinal Artery Occlusion**

Jefferson Berryman<sup>1</sup>, Melinda Chang<sup>1</sup>, Ala Moshiri<sup>1</sup>

<sup>1</sup>University of California, Davis, Sacramento, California, USA

**Introduction:**

Optic nerve involvement in chronic lymphocytic leukemia (CLL) is rare and typically occurs late. We present a case of an otherwise healthy 52-year-old man who developed optic disc edema and a branch retinal artery occlusion (BRAO). Further workup confirmed the diagnosis of CLL with CNS involvement.

**Description of Case(s):**

A 52-year-old previous healthy male presented to the emergency department after experiencing sudden onset blurry vision in the inferior visual field of the left eye. Initial examination revealed a visual acuity of 20/40, 2+ RAPD, and inferior hemi-field deficit to confrontation in the left eye. Slit lamp examination was notable for 2+ cells in the anterior chamber bilaterally. Funduscopic exam revealed superior and nasal optic disc edema with peripapillary cotton wool spots and hemorrhage. Additionally, there was retinal whitening along the superotemporal and superonasal vascular arcades, consistent with a large BRAO sparing the foveal center. The patient underwent fluorescein angiography, optical coherence tomography (OCT), and OCT angiography. OCT suggested possible compression of the retinal arteriole at the optic disc. Workup revealed a WBC count of 62,100/mm<sup>3</sup>, and flow cytometry confirmed the diagnosis of CLL. MRI of the orbits did not show thickening or enhancement of the optic nerve, but lumbar puncture was positive for atypical lymphocytes. The patient was treated with systemic and intrathecal chemotherapy and intravenous steroids with improvement in optic disc edema.

**Conclusions, including unique features of the case(s):**

Optic nerve involvement as the presenting symptom of CLL is extremely uncommon. Our patient had unilateral optic disc edema and BRAO, suggestive of optic nerve infiltration causing compressive arterial occlusion. Alternatively, BRAO may be related to hyperviscosity, although our patient had no evidence of venous occlusion, which is more typical of hyperviscosity. To our knowledge, this is the first case report of this combination of ocular complications in a patient with CLL.

**References:** 1. Currie JN, Lessell S, et al. "Optic neuropathy in chronic lymphocytic leukemia." *Archives of Ophthalmology*. 1988 May;106(5):654-60. 2. Khan K, Malik AI, et al. "Optic Neuropathy Due to Chronic Lymphocytic Leukemia Proven With Optic Nerve Sheath Biopsy." *Journal of Neuroophthalmology*. 2016 Mar;36(1):61-6 3. Moisseiev E(1), Ling J, Morse LS. "Leukemic Optic Nerve Infiltration Complicated by Retinal Artery and Vein Occlusions." *Retina*. 2017 Feb;37(2):e10.

**Keywords:** Optic neuropathy, Vascular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 68****Tubular Aggregate Myopathy with Miosis and Rod-Cone Dysfunction**

Greg Richardson<sup>1</sup>, Apeksha Shah<sup>1</sup>, Aleksandar Radunovic<sup>1</sup>, Naz Raoof<sup>1</sup>

<sup>1</sup>The Royal London Hospital, Barts Health NHS Trust, London, United Kingdom

**Introduction:**

Tubular aggregate myopathy (TAM) is a rare condition primarily affecting skeletal muscles. Abnormal proteins build up in type I and II fibres forming bundles of tube-like structures called tubular aggregates. It is characterized by muscle pain, cramps, weakness and fatigability. There have been reports of pupil miosis, ophthalmoplegia and retinal degeneration in patients with TAM. Two genes have been implicated in TAM; STIM1 gene encodes a protein which acts as endoplasmic reticulum calcium sensor, and ORAI1 gene which encodes calcium release-activated calcium channel. We report a patient with miosis, rod-cone dysfunction and TAM with heterozygous Pro245Leu mutation in the ORAI1 gene.

**Description of Case(s):**

A 57-year-old Indian male taxi driver presented with a several year history of myalgia, distal weakness, raised creatine kinase level varying between 540-2500, EMG which showed myopathic changes in proximal and distal muscles, and muscle biopsy which showed tubular aggregates. Genetic analysis revealed previously described heterozygous Pro245Leu mutation in the ORAI1 gene. There were concerns regarding poor night vision whilst driving. Visual acuity was 6/9 bilaterally with microcoria, but an otherwise unremarkable iris. On instillation of mydriatic eye-drops, his pupils did not dilate beyond 2mm. Due to poor pupil dilation, there was limited fundal view. Visual fields were full. Eye movements were unaffected. Electroretinogram (ERG) testing demonstrated no response to pattern ERG, and moderate-markedly subnormal bright flash, flicker and photopic single flash ERGs, suggesting moderate-severe dysfunction of rods and cones. These results could not be attributable to poor pupil dilation alone.

**Conclusions, including unique features of the case(s):**

ORAI1 mutations have been associated with TAM and congenital miosis. There is less evidence that it can cause retinal dystrophy. Ca<sup>2+</sup> is known to be a second messenger within the retina, and ORAI1 encoded Ca<sup>2+</sup> channels have been shown to be expressed in the RPE, so it is plausible that mutations in ORAI1 could affect retinal function.

**References:** None.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Pupils Retina

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 69

### Atypical Central Retinal Artery Occlusion As The First Manifestation Of POEMS Syndrome

Thanatporn Threetong, MD.<sup>1</sup>, Panitha Jindahra, MD. PhD.<sup>2</sup>, Jariya Waisayarat, MD.<sup>3</sup>, Piyaphon Cheecharoen, MD.<sup>4</sup>, Pimjai Niparuck, MD.<sup>2</sup>, Narong Samipak, MD.<sup>1</sup>, Purit Petpiroon, MD.<sup>1</sup>, Tharikarn Sujirakul, MD.<sup>1</sup>, Charungthai Dejthevaporn, MD.PhD.<sup>2</sup>, Anuchit Poonyathalang, MD.<sup>1</sup>, Kavin Vanikieti, MD.<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, Faculty of Medicine Ramathibodi Hospital, Bangkok, Thailand, <sup>2</sup>Department of Internal Medicine, Faculty of Medicine Ramathibodi Hospital, Bangkok, Thailand, <sup>3</sup>Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Bangkok, Thailand, <sup>4</sup>Department of Radiology, Faculty of Medicine Ramathibodi Hospital, Bangkok, Thailand

#### Introduction:

POEMS syndrome is a plasma cell disorder, which clinically manifests from paraneoplastic syndrome: polyradiculoneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes. The most common ocular manifestation is optic disc edema, whereas other ocular manifestations; cystoid macular edema, serous macular detachment, anterior ischemic optic neuropathy, optic disc drusen, peripapillary choroidal neovascularization, uveitis and infiltrative orbitopathy, had also been reported.

#### Description of Case(s):

A 52-year-old Thai man presented with 1-day sudden painless visual loss in the left eye. Ophthalmic examination revealed visual acuity of 20/20 and no light perception in the right and left eye, respectively. Right fundoscopic examination was significant for hyperemic with generalized optic disc edema. Left fundoscopic examination revealed cherry red spot with opaque edematous retina and pallid optic disc edema. Fluorescein angiography showed profound leakage of bilateral optic nerve heads and arteriolar filling defect in macula area along with leakage of small retinal arterioles in the left eye. Magnetic resonance imaging showed diffused and enhanced dural thickening along with acute left middle/posterior cerebral artery watershed infarction. Cerebrospinal fluid analysis revealed high protein level with normal opening pressure. Intravenous methylprednisolone was initially started without any benefit. After extensive investigations, diagnosis of "POEMS syndrome" was made based on polyneuropathy, elevated lambda light chain level, elevated plasma vascular endothelial growth factor (VEGF), hepatosplenomegaly, spinal sclerotic bone, and thrombocytosis. Furthermore, sural nerve biopsy demonstrated positive VEGF staining. He was treated with eight cycles of bortezomib, cyclophosphamide and dexamethasone (BorCyDex). Polyneuropathy and thrombocytosis had remarkably improved after 2nd cycle, whereas, visual impairment had shown no recovery. Hepatosplenomegaly was significantly reduced after the completion of BorCyDex. Our case eventually received autologous hematopoietic stem cell transplantation with high dose melphalan.

#### Conclusions, including unique features of the case(s):

To our knowledge, this case illustrated the first case given central retinal artery occlusion as the first presentation and ocular finding ever reported in POEMS syndrome.

**References:** None.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuroimaging, Vascular disorders, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 70****Intermittent Colour Vision Loss as the Initial Presentation of Chronic Myeloid Leukemia**

Solin Saleh<sup>1</sup>, Kaisra Esmail<sup>1</sup>, Danah Albreiki<sup>1</sup>

<sup>1</sup>*University of Ottawa Department of Ophthalmology, Ottawa, Canada*

**Introduction:**

Leukemia encompasses several malignant proliferative disorders, and is characterized by over-crowding of mature or immature neoplastic leukocytes in the bone marrow, with subsequent infiltration of organs, tissues and peripheral blood. Ocular involvement in leukemia may be a result of direct invasion or secondary associated hematologic abnormalities, including hyperviscosity syndrome. Chronic myeloid leukemia (CML) is one such variant which accounts for 15-20% of adult leukemias. Ophthalmologists play a unique role in caring for these patients in that ocular manifestations may rarely be the only presenting sign of this life-threatening condition. We report a case of bilateral intermittent colour vision loss as the presenting symptom of CML.

**Description of Case(s):**

A 70-year-old man presented to the Neuro-Ophthalmology clinic with subacute decrease in visual acuity as well as intermittent colour vision loss upon waking, a symptom that had been dismissed by previous healthcare providers. Ophthalmic examination revealed multiple peripheral Roth spots in both eyes, in the context of chronic night sweats and recent intermittent fevers. This raised suspicion for a lymphoproliferative process. CBC with differential was promptly ordered, which revealed a markedly increased WBC count. The patient was diagnosed with CML through a bone marrow biopsy and initiated on cytoreduction therapy. He experienced complete resolution of his visual symptoms and had a normal WBC count at his most recent follow up appointment.

**Conclusions, including unique features of the case(s):**

We report, to our knowledge, the first case of intermittent colour vision loss as the initial presenting symptom of CML in the current literature, and reiterate the importance of a thorough history, neuro-ophthalmic examination and relevant investigations in patients with unusual visual symptoms, including intermittent loss of colour vision. In this case, we speculate that hyperviscosity syndrome secondary to CML was the cause of this patient's peculiar visual disturbance.

**References:** None.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 71****Papilledema and Anterior Granulomatous Uveitis in Congenital HIV Despite HAART Therapy**

Ryan Gise<sup>1</sup>, Erin Walsh<sup>1</sup>, Jacqueline Busingye<sup>1</sup>

<sup>1</sup>Montefiore Medical Center/ Albert Einstein College of Medicine, New York, New York, USA

**Introduction:**

Human Immunodeficiency Virus is a known cause of granulomatous uveitis as well as various ophthalmologic and neurologic manifestations. We present a case of a female with congenital HIV who developed papilledema, granulomatous anterior uveitis, and HIV associated encephalopathy despite excellent adherence to HAART therapy.

**Description of Case(s):**

A 19 year old female with congenital HIV, well controlled with Viral Load 152, and CD4 736, was brought to the emergency department from school for 3 months of progressive decline in mental status. On arrival to the ED, the patient was difficult to arouse and would only respond to questions with one word answers. Ophthalmology was consulted after initial opening pressure of lumbar puncture was found to be greater than 60 cmH<sub>2</sub>O. On initial exam, visual acuity at near was 20/20 OD and 20/40 OS. Her anterior segment was notable for diffuse bilateral granulomatous keratic precipitates with 1+ anterior chamber cell and flare and rare vitreal cell OU. She had chronic appearing grade 3 disc edema OD and grade 2 OS with vascular sheathing OU on dilated fundus exam. She could not perform either Humphrey Visual Field or Optical Coherence Tomography. Extensive work up for uveitis and papilledema was undertaken and found to be negative. Cerebrospinal fluid (CSF) was notable for lymphocytic pleocytosis and an HIV viral load of 20,000. She was diagnosed with HIV Associated Neurocognitive Disease (HAND), switched to CNS penetrating anti-retrovirals, and also started on topical prednisolone for her anterior uveitis. Following treatment, her opening pressure decreased to 17 cmH<sub>2</sub>O and CSF viral load to 587 in 1 month. Her anterior uveitis resolved and her mental status recovered.

**Conclusions, including unique features of the case(s):**

Despite excellent adherence to HAART therapy, HIV infection of the CNS can occur and be associated with both papilledema and granulomatous uveitis.

**References:** Clifford DB and Ances BM. HIV-Associated Neurocognitive Disorder (HAND). *Lancet Infect Dis*; 13(11): 976-986, 2013. Kunavisarut P, Siriirungsi W, Pathanapitoon KM, Rothova A. Clinical Manifestations of Human Immunodeficiency Virus-Induced Uveitis. *Ophthalmology*; 119: 1455-1459, 2012. Patel K, Ming X, Williams PL et al. Impact of HAART and CNS-Penetrating antiretroviral regimens on HIV Encephalopathy among Perinatally Infected Children and Adolescents. *AIDS*; 23(14): 1893-1901, 2009. Roseberger DF, Heinemann MH, Friedberg DN and Holland GN. Uveitis Associated with Human Immunodeficiency Virus Infection. *Am J Ophthalmol*; 125: 301-305, 1988. Soulie C, Descamps D, Grude M et al. Antiretroviral-naïve and -treated HIV-1 Patients Can Harbour More Resistant Viruses in CSF than In Plasma. *J Antimicrob Chemother*; 70: 566-572, 2015

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion), High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 72****Isolated Unilateral Optic Nerve Involvement as Initial Manifestation of Meningeal Carcinomatosis**

Amadeo Rodriguez<sup>1</sup>

<sup>1</sup>*Division of Ophthalmology and Neurology, McMaster University, Canada, Hamilton, Canada*

**Introduction:**

Meningeal carcinomatosis results from dissemination of malignant cells to the leptomeninges. This case is about a patient who presented with isolated unilateral optic nerve involvement as the initial manifestation.

**Description of Case(s):**

A 79-year old woman consulted for painless vision loss in the left eye over the course of two weeks. She did not have any other complaint. She had a history of breast cancer treated with surgery, chemotherapy and radiation 12 years before. There was left eye vision loss and ipsilateral RAPD with normal optic discs. Her neurological exam was otherwise unremarkable. Sedimentation rate and C-reactive protein were normal. MRI of the brain and orbits showed thickening and enhancement of the left optic nerve sheath with no signal abnormality of the optic nerve substance. She was empirically treated with high dose intravenous methylprednisolone for three days followed by oral prednisone with no improvement. Other investigations were normal including complete blood count, ANA, cANCA, pANCA, ACE, syphilis serology and chest x-ray. The patient remained stable for approximately two months when she developed unsteadiness, poor appetite and weight loss. Exam again revealed left optic neuropathy, this time with optic atrophy. In addition there were bilateral abduction defects. Repeat MRI study showed persistent left optic nerve abnormality with minimal leptomeningeal enhancement in the cerebellum. CSF analysis from her second lumbar puncture showed elevated protein level and malignant cells. Her CA 15-3 was elevated. A diagnosis of meningeal carcinomatosis from breast cancer was made and the patient was treated with whole brain radiation with palliative intent.

**Conclusions, including unique features of the case(s):**

Isolated, unilateral optic neuropathy can be the initial manifestation of meningeal carcinomatosis even in the absence of other neurological manifestations. The diagnosis is challenging but a high index of suspicion is recommended, in particular in patients with previous history of cancer.

**References:** 1) McFadzean R, Brosnahan D, Doyle D, Going J, Hadley D, Lee W. A diagnostic quartet in leptomeningeal infiltration of the optic nerve sheath. *J Neuroophthalmol* 1994;14(3):175-82 2) DeAngelis M. Current diagnosis and treatment of leptomeningeal metastasis. *J Neurooncol* 1998;38(2-3):245-252 3) Grossman SA, Krabak M. Leptomeningeal carcinomatosis. *Cancer Treat Rev* 1999;25(2): 103-119 4) Lanfranconi S, Basilico P, Trezzi I, et al. Optic Neuritis as Isolated Manifestation of Leptomeningeal Carcinomatosis: A Case Report and Systematic Review of Ocular Manifestations of Neoplastic Meningitis. *Neurol Res Int* ; 2013:892523. doi:10.1155/2013/892523.

**Keywords:** Optic neuropathy, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Tumors

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 73

### Optic Neuropathy in Riboflavin Transporter Deficiency (Brown-Vialetto Van Lear syndrome)

Kannan Narayana<sup>1</sup>, Jaime Vengoechea<sup>1</sup>, Michael Silver<sup>1</sup>

<sup>1</sup>Emory University School of Medicine, Atlanta, Georgia, USA

#### Introduction:

Brown-Vialetto-Van-Laere syndrome (BVVL), is a rare autosomal recessive degenerative disorder, associated with mutations in the SLC52A2 and SLC52A3 genes, thought to be involved in the transport of riboflavin. Manifestations include motor neuropathy ( proximal / distal limb weakness, severe distal wasting and can lead to paralysis of the diaphragm), sensory neuropathy ( gait ataxia) and cranial neuropathy (manifesting as optic atrophy, sensorineural deafness, bulbar palsy). Onset is usually in infancy or in childhood. Typical initial finding is sensorineural deafness, which is usually progressive and severe.

#### Description of Case(s):

A 26-year-old Caucasian woman with findings of ataxia, loss of proprioception, muscle weakness, hearing loss, anorexia, peripheral neuropathy was evaluated for vision loss since a very young age. Her whole exome sequencing was noted to show one copy of c.916G>A (p.G306R) pathogenic variant and one copy of c.1258G>A (p.A420T) likely pathogenic variant in the SLC52A2 gene. Ophthalmological examination showed corrected vision of counting fingers in right eye and 20/300 in the left eye, sluggish pupils, severe loss of color vision and optic disc pallor bilaterally. Manual perimetry showed generalized depression in both eyes, along with superior arcuate scotoma in the right, and central/ superior arcuate scotoma in the left. Her findings were consistent with bilateral optic neuropathy.

#### Conclusions, including unique features of the case(s):

This is an illustrative case of a rare genetic disorder for which riboflavin supplementation may be beneficial. She has noted some subjective improvement with riboflavin supplementation. Our patient had slightly late onset, around 8 or 9 years. She was strongly suspected to have unknown mitochondrial disorder for a long time. Although rare, familiarity of this disorder is important. This disorder is being increasingly recognized (1). It is also important to note that this can be confused with other pediatric neurological disorders including neuro-immunological disorders (2,3) . Not only stabilization, but improvement has been reported in this disorder (1,2,4).

**References:** 1. Bosch AM, Abeling NG, Ijlst L, Knoester H, Ludo van der Pol, et al. Brown-Vialetto-Van Laere and Fazio Londe syndrome is associated with a riboflavin transporter defect mimicking mild MADD: a new inborn error of metabolism with potential treatment. *J Inher Metab Dis.* 2011;34:159–164 2. Bosch AM, Stroek K, Abeling NG, Waterham HR, Ijlst L, et al. The Brown-Vialetto-Van Laere and Fazio Londe syndrome revisited: natural history, genetics, treatment and future perspectives. *Orphanet J Rare Dis.* 2012;7:83. 3. Allison T, Roncero I, Forsyth R, Coffman K, Pichon JL. Brown-Vialetto-Van Laere syndrome as a mimic of neuroimmune disorders: 3 cases from the clinic and review of the literature. *J Child Neurol.* 2017;32:528–532 4. Shashi V, Petrovski S, Schoch K, et al. Sustained therapeutic response to riboflavin in a child with a progressive neurological condition, diagnosed by whole-exome sequencing. *Cold Spring Harb Mol Case Stud.* 2015;1(1):a000265

**Keywords:** Genetic Disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 74**

**Diffusion Weighted Imaging in Non-arteritic Posterior Ischemic Optic Neuropathy**

Kristin Miller<sup>1</sup>, Stephanie Lyden<sup>1</sup>, Aimee Szewka<sup>1</sup>, Milena Stosic<sup>1</sup>, Rima Dafer<sup>1</sup>

<sup>1</sup>Rush University Medical Center, Chicago, Illinois, USA

**Introduction:**

Posterior ischemic optic neuropathy (PION) is a rare cause of vision loss and restricted diffusion in the affected optic nerve is a rare finding on MRI. Several etiologies have been proposed for non-arteritic PION, including microangiopathy, acute volume loss, hypotension, and acute carotid occlusion.

**Description of Case(s):**

A 43 year old woman with Sweet's syndrome on prednisone, chronic hypotension, end stage renal disease, and atrial fibrillation on apixaban presented with a 4-day history of acute painless vision loss of the left eye. Examination was remarkable for light perception only in the left eye with a consensual but no direct pupillary response. She had normal ocular motility and alignment, and fundoscopic examination. She was empirically treated for presumed inflammatory optic neuropathy with methylprednisolone, followed by oral steroids. MRI orbits demonstrated restricted diffusion of the left optic nerve near the orbital apex corresponding with an area of ischemia, with lack of nerve enhancement on contrast images. There were microvascular ischemic changes on MRI brain. Except for elevated protein to 117 in the cerebrospinal fluid and mildly elevated serum ACE level which later normalized, work-up including CTA head and neck, CT chest, and temporal artery biopsy was non-contributory. Ten days later, vision in the left eye improved to hand motion at 4 feet inferiorly and finger count at one foot superotemporally.

**Conclusions, including unique features of the case(s):**

This is a rare imaging finding of a complicated presentation of PION with restricted diffusion in the affected optic nerve. We hypothesize that the etiology of PION in our patient is likely hypoperfusion related to chronic hypotension exacerbated by hemodialysis, in the setting of multiple vascular risk factors.

**References:** None.

**Keywords:** Neuroimaging, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Vascular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 75**

**Reversible Bilateral Optic Disc Edema with Heart Failure, Bacterial Endocarditis and Bicuspid Aortic Valve (BAV)**

Adeela Alizai<sup>1</sup>

<sup>1</sup>Franciscan Saint Anthony Memorial Hospital, Michigan City, Indiana, USA

**Introduction:**

Bicuspid Aortic Valve (BAV) is present in 1-2 % of population. Given its prevalence and significant complications, it is estimated that BAV is responsible for more mortality and morbidity than the combined effects of all the other congenital heart defects.

**Description of Case(s):**

26 y/o hispanic male presented with blurry vision OU x 4 weeks. He had 10 lbs. unintentional weight loss over 12 weeks, mild nocturnal cough and joint pains with anemia. BMI was 21. Visual acuity was sc OD 20/40, OS 20/25, normal neuro-ophthalmic exam other than severe optic disc edema, right greater than left with vascular engorgement. MRI brain and chest x-ray were normal. MRI orbits showed fullness of optic nerve sheaths and slight flattening of the posterior globes bilaterally, worse on the right. The CSF opening pressure was 24cm H2O in lateral decubitus with normal formula. MRV demonstrated possible embolic infarct in left parietal lobe but no venous thrombosis. Medical exam revealed systolic murmur. Patient's ESR was 53 and CRP was 49. Final diagnosis was decompensation of congenital bicuspid aortic valve, chronic Strep Viridins endocarditis, aortic root abscess, ventricular septal defect and systolic heart failure class IV. Patient had a dental procedure few weeks before presentation, not reported in the initial history. Complete reversal of visual complaints and bilateral disc edema was seen after urgent aortic root abscess debridement, St Jude's mechanical valve replacement and treatment with IV antibiotics.

**Conclusions, including unique features of the case(s):**

1. Severe bilateral optic disc edema can be a presenting sign of life threatening heart failure associated with bacterial endocarditis despite minimal systemic complaints. 2. Family and personal history of BAV should be elicited in thin young patients with unexplained bilateral optic disc edema, especially in the absence of headache. These patients should be auscultated for a cardiac murmur and antibiotic prophylaxis be given prior to dental procedures.

**References:** GE Beaumont . A case of reversible papilloedema in heart failure. British Medical Journal, 1948 Jan 10; 1(4560) : 50

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Optic neuropathy, Miscellaneous, Vascular disorders, Pediatric Neuro-Ophthalmology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 76****MOG Positive Optic Neuritis with a Phenotype of CRION Disease**

Ama Sadaka<sup>1</sup>, Jaspreet Jakhu<sup>2</sup>, Nagham Al-Zubidi<sup>3</sup>, Rosa Tang<sup>3</sup>, Jade Schiffman<sup>4</sup>

<sup>1</sup>University of Beirut, Beirut, Lebanon, <sup>2</sup>Neuro-Ophthalmology of Texas, Houston, Texas, USA, <sup>3</sup> Neuro-Ophthalmology of Texas / Blanton Eye Institute, Houston Methodist Hospital, Houston, Texas, USA, <sup>4</sup>Neuro-Ophthalmology of Texas/ MS Eye Care, HOUSTON, Texas, USA

**Introduction:**

CRION is a recurrent, isolated, steroid dependent optic neuritis, without any associated neurological deficits or known systemic autoimmune diseases. MOG is a component of myelin and an antigen target in central nervous system demyelinating disease. There is growing evidence that the MOG antibody is linked to multiple central nervous system diseases such as anti-aquaporin-4 (AQP4)-negative NMO spectrum disorder with several phenotypical expressions. Similarly, cases of CRION, have been found to be positive for the MOG antibody.

**Description of Case(s):**

Our patient is a 22-yr F previously healthy who presented with multiple episodes of recurrent optic neuritis, the initial event was bilateral and there was a total of 4 optic neuritis events over a 7-month period all exquisitely steroid responsive and each event reoccurred soon after steroid withdrawal. MRI of the brain failed to show any evidence of inflammatory or demyelinating disease. CSF was normal with no oligoclonal bands. Blood work was negative for infectious and inflammatory causes of optic neuritis. NMO antibodies were negative, but MOG antibodies were positive. Given the recurrent and steroid-responsive and dependent course of her disease, a diagnosis of MOG-IgG-related CRION disease was made. She was started on Rituximab and has been doing well with no relapses and still with no other neurologic disease. Her final visual acuity was 20/20 in both eyes with a left relative afferent pupillary defect.

**Conclusions, including unique features of the case(s):**

There is growing evidence that MOG antibodies are involved in several NMO-related CNS diseases, including recurrent optic neuritis. According to the Mayo clinic, they have collected patient's serum with the "CRION type-phenotype" and have found MOG positivity in a good percentage of these cases. Our case highlights the importance of testing for MOG antibodies in cases of suspected CRION since failure to diagnose the disorder and start treatment can cause sustained and progressive nerve fiber loss and vision loss.

**References:** None.

**Keywords:** Demyelinating disease, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Optic neuropathy, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 77

### Bilateral Optic Disc Edema in a Young, Obese Woman: Pseudotumor Cerebri or Something More?

Laurel Vuong<sup>1</sup>, Adam Chin<sup>1</sup>

<sup>1</sup>Tufts-New England Eye Center, Boston, Massachusetts, USA

#### Introduction:

A 23-year-old obese, woman presented with new headaches, bilateral eye strain and decreased inferior vision OS. Bilateral optic disc edema was seen with no other findings. Pseudotumor cerebri was highly suspected due to her body habitus and symptoms. However, progression on high dose acetazolamide suggested reconsideration of her diagnosis was needed.

#### Description of Case(s):

On presentation, her visual acuities were 20/20-1 OD and 20/30-1 OS. Color vision was slightly decreased OS. There was no rAPD. Automated perimetry showed an inferior altitudinal defect OS. Asymmetric optic disc edema, left worse than right, was seen. Due to her body habits, only a CT brain and CTV head could be obtained urgently; the imaging was notable for findings associated with elevated ICP. She was started on acetazolamide 1 gram twice daily. When she returned 3 days later, her optic disc edema worsened and acetazolamide was increased to three times daily. The opening pressure from a lumbar puncture under fluoroscopy was only 18cm H<sub>2</sub>O. When she returned a few days later, her optic disc edema and visual fields worsened. MRI obtained showed only bilateral optic nerve enhancement. NMO, sarcoidosis, syphilis, and tuberculosis testing were negative. Chest CT was unremarkable. Lyme IgM titers were positive. In review, the patient, who lives in New Hampshire, recalled a rash on her leg and experiencing myalgia prior to the onset of her symptoms. She was treated with IV ceftriaxone and steroids. At 2-month follow up, her vision was 20/20-1 bilaterally with complete resolution of disc edema and visual field defects.

#### Conclusions, including unique features of the case(s):

When routine cases take an atypical course, alternative diagnoses need to be considered. Optic neuritis associated with Lyme is a rare, but treatable, cause of optic neuritis. It should be considered in patients living in endemic regions with other manifestations of Lyme disease.

**References:** Balcer LJ, Winterkorn JM, Galetta SL. Neuro-ophthalmic manifestations of Lyme disease. *J Neuroophthalmol.* 1997 Jun;17(2):108-21. Review. Fedorowski JJ, Hyman C. Optic disk edema as the presenting sign of Lyme disease. *Clin Infect Dis.* 1996 Sep;23(3):639-40. Kan L, Sood SK, Maytal J. Pseudotumor cerebri in Lyme disease: a case report and literature review. *Pediatr Neurol.* 1998 May;18(5):439-41. McVeigh K, Vakros G. Case report: papillitis as the sole ocular sign in Lyme disease. *Clin Ophthalmol.* 2012;6:1093-7. Rothermel H, Hedges TR 3rd, Steere AC. Optic neuropathy in children with Lyme disease. *Pediatrics.* 2001 Aug;108(2):477-81. Träisk F, Lindquist L. Optic nerve involvement in Lyme disease. *Curr Opin Ophthalmol.* 2012 Nov;23(6):485-90.

**Keywords:** Optic neuropathy, Lyme, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** This work was supported in part by a Research to Prevent Blindness Unrestricted Award to the New England Eye Center/Department of Ophthalmology, Tufts University School of Medicine

**Poster 78****A Curious Case of Arteritis: Infectious, Inflammatory or Both**

Jacob Rullo<sup>1</sup>, Nadil Zeiadin<sup>1</sup>, Ambika Gupta<sup>1</sup>, James Farmer<sup>1</sup>, Marie Clements-Baker<sup>1</sup>, Martin ten Hove<sup>1</sup>

<sup>1</sup>Queen's University, Kingston, Canada

**Introduction:**

Takayasu arteritis is a large-vessel vasculitis affecting the aorta and its primary branches resulting in fibrosis and stenosis. The ocular manifestations of Takayasu's arteritis include arteriovenous irregularities, ocular ischemic syndrome, and reduced perfusion of the retina and choroid. Takayasu's arteritis rarely manifests in the eye as a first presentation.

**Description of Case(s):**

A 57-year-old woman was referred for a history of floaters. On examination, visual acuity was OD 20/30 and OS 20/20. Posterior segment examination: OD revealed a region of retinal pallor extending from the disc to the para-foveal region; OS showed two white-centered hemorrhages. Urgent blood work: ESR 59, CRP 60, WBC 13, PLT 266. Additional probing into the patient's medical history revealed a previous diagnosis of untreated Takayasu's arteritis, managed for 30 years with naturopathic remedies. The patient was started on oral prednisone. Twelve hours later, she returned mildly anxious and diaphoretic. Vitals: Temperature: 37.1. HR: R110; L 111. BP: R 156/61; L BP 179/77. A cyanotic left hand with absent radial and ulnar pulses was noted. She was admitted to hospital. Urgent imaging revealed focal stenosis involving the aorta, subclavian and carotid arteries. The left brachial artery was occluded at the forearm. Surgical exploration revealed a thrombosed brachial artery with purulent material. Histopathology: transmural inflammation with scattered gram positive cocci consistent with an infectious aneurysm. Blood cultures: gram positive cocci, streptococcus mitis. Endocarditis and vegetative growths were ruled out. Discussion with the patient revealed a one-month history of a recent febrile illness after a dental procedure.

**Conclusions, including unique features of the case(s):**

The diagnostic and surgical findings are in keeping with a combined ischemic, infectious process; untreated vasculitis resulting in a nidus for bacterial overgrowth. This case highlights the ischemic complications of active Takayasu's arteritis with concurrent acute bacteremia. White centered hemorrhages with associated ischemic infarcts should prompt a broad differential including infectious aetiologies.

**References:** Foote EA, Postier RG, Greenfield RA, Bronze MS. Infectious Aortitis. *Current Treat Options Cardiovascular Medicine*. 7, 89–97, 2005. Virmani R, Burke A. Nonatherosclerotic Diseases of the Aorta and Miscellaneous Disease of the Main Pulmonary Arteries and Large Veins. In: Silver M, Gotlieb A, Schoen F, editors. *Cardiovascular Pathology*. 3rd ed. Churchill Livingstone; Philadelphia, pp.107–137, 2001. Chun YS, Park SJ, Park IK, Chung H, Lee J. The ocular manifestations of takayasu's arteritis. *Retina*, 21(2): 132-40, 2001.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Neuro-ophth & infectious disease (eg, AIDS, prion), Vascular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



## Poster 79

### Alcohol-Responsive Myoclonus In Type I Sialidosis

Julie DeBacker<sup>1</sup>, Steven Frucht<sup>1</sup>, Laura Balcer<sup>1</sup>, Steven Galetta<sup>1</sup>, Janet Rucker<sup>1</sup>

<sup>1</sup>NYU Langone Health, Brooklyn, New York, USA

#### Introduction:

Sialidosis type I is in the differential diagnosis for cherry red spots, along with other lysosomal storage disorders such as Gangliosidosis I (GMI), Tay Sachs disease, Sandhoff disease, Niemann Pick disease Type A, B, C, and D, Sialidosis type II, Farber lipogranulomatosis, Goldberg Syndrome, Metachromatic leukodystrophy, multiple sulfatase deficiency, and Wolman disease plus vascular conditions such as a central retinal artery occlusion, dapsone poisoning, and traumatic ischemia. Visual findings in Sialidosis type I include lens opacities, color vision impairment, night blindness, nystagmus, corneal opacities, loss of visual acuity, and a macular cherry red spot. In lysosomal storage disorders, such as Sialidosis, cherry red macular spots are caused by the storage of oligosaccharides and sphingolipids in the retinal ganglionic cell layer leading to a pale macula surrounding the fovea. Patients with Sialidosis type I may have visual impairment, progressive myoclonus, ataxia, epilepsy, and usually normal intellect. Correct identification of involuntary limb movements as myoclonus as well as accurate recognition of a cherry red spot in the retina in various ethnicities may be challenging. Then, proper generation of a differential diagnosis and targeted diagnostic work up for a combination of cherry red spots, cerebellar dysfunction, and myoclonus is required. Confirmation of the diagnosis may be made by urinary oligosaccharides, urinary bound sialic acid excretion, and enzyme assay in leukocytes and cultured fibroblasts – or with multigene sequencing. In this case, we describe a man with a macular cherry red spot and alcohol-responsive myoclonus who ultimately received the correct diagnosis of Sialidosis Type I.

#### Description of Case(s):

A 30-year-old man presented for neuro-ophthalmologic consultation. He developed visual impairment at age 12 that progressively worsened in his 20's, when he noted reduced color vision and nyctalopia. He had associated slurred speech and balance difficulties with frequent falls. In his 20's, he developed seizures, difficulty putting on clothes and manipulating objects due to impaired arm coordination and abnormal movements in his limbs. Clonazepam and alcohol dramatically improved his abnormal motor movements. There was no family history of visual or neurologic disease, however, his mother had two miscarriages and he had a sister who died in infancy. On examination, visual acuity was 20/30+2 OD and 20/40-2 OS at distance. Visual fields were intact to confrontation. He perceived all Ishihara color plates correctly with each eye. Pupils were brisk and equal without an APD. He had a mild right sixth nerve palsy and convergence insufficiency. Pursuit was saccadic horizontally, normal vertically. Saccades were slightly hypometric. No nystagmus was observed. Fundoscopy revealed normal optic discs and an abnormal retinal appearance (photographs will be shown). Abnormal spontaneous movements were seen in the upper extremities (video will be shown). He had bilateral upper extremity dysmetria, worse on the left. Gait was mildly unsteady with a normal base, with deterioration in darkness. Prior test results included: Normal CBC, CMP, ESR, vitamin B12, folate, thyroid function tests, and EEG. EMG/NCS showed a distal motor neuropathy or neuronopathy. Brain MRI showed cerebellar vermis atrophy and a cavum septum pellucidum. He was treated with oral sodium oxybate with significant improvement in his action myoclonus and functional performance, and continues to take it daily.

#### Conclusions, including unique features of the case(s):

This patient had progressive neurological dysfunction with epilepsy, myoclonus, ataxia and bilateral cherry red spots. Genetic testing revealed two mutations in the NEU1 gene, confirming a diagnosis of Sialidosis Type I (aka., cherry red spot myoclonus syndrome), an autosomal recessive lysosomal storage disease. MRI revealed cerebellar atrophy, which may be a late finding in this condition. Alcohol responsiveness is atypical for Sialidosis, but is increasingly recognized, and based on this, the patient was treated with (and received benefit from) sodium oxybate. Alcohol responsivity appears to be a novel and therapeutically important feature of the disorder. Additionally, he was found to have a peripheral neuropathy, which is also atypical for Sialidosis.

**References:** Franceschetti S, Canafoglia L. Sialidoses. *Epileptic Disorders*, 18(S2):89-93, 2016 Nirenberg MJ, Frucht SJ. Myoclonus. *Current Treatment Options in Oncology*, 7: 221–230, 2005 Ospina LH, Lyons CJ, McCormick AQ. "Cherry-red spot" or "perifoveal white patch"? *Canadian Journal of Ophthalmology*. 40(5):609-10, 2005 Leavitt JA, Kotagal S. The "cherry red" spot. *Pediatric Neurology*. 2007 Jul; 37 (1): 74-5 Steinman L, et al. Peripheral neuropathy in the cherry-red spot-myoclonus syndrome (sialidosis type I). *Annals of Neurology*. 7(5):450-6), 1980

**Keywords:** Genetic Disease, Pupils Retina

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 80****Arteritic Anterior Ischemic Optic Neuropathy and Eosinophilic Granulomatosis with Polyangiitis: Case Report**

Kelvin Au<sup>1</sup>

<sup>1</sup>*University of Calgary, Calgary, Canada*

**Introduction:**

We report a case of a 60-year-old female with a history of asthma, chronic sinusitis and nasal polyps presenting with acute vision loss and numbness in her extremities.

**Description of Case(s):**

On the background of a 6-month history of pan-sinusitis and progressive jaw claudication, our patient developed sudden onset numbness involving her left hand and right wrist. Shortly after, she had obscuration of upper and lower portions of her visual fields, primarily in her right eye. She was found to have segmental pallid edema of her right optic disc with flame hemorrhages in keeping with arteritic anterior ischemic optic neuropathy (AION). Nerve conduction studies revealed evidence for mononeuritis multiplex affecting the left median nerve, bilateral peroneal and bilateral tibial nerves. She had eosinophilia, elevated ESR, positive P-ANCA with elevated anti-MPO titers. MRI brain and orbits showed enhancement of the optic nerve sheaths. There was extensive exudate and inflammation noted in the frontal, maxillary, sphenoid, and ethmoid sinuses. Nasal and sural nerve biopsies were unrevealing. Given the clinical presentation, laboratory and diagnostic imaging findings, she was given the diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA). Treatment included high dose IV methylprednisolone and cyclophosphamide induction with immediate improvement. She was placed on azathioprine maintenance therapy but subsequent relapse prompted switch to rituximab therapy. Despite this, she has had recurrent relapses but fortunately remains prednisone sensitive. She is currently on mycophenolate mofetil.

**Conclusions, including unique features of the case(s):**

Our case highlights the rare, but previously reported(1) manifestation of arteritic AION due to EGPA, and the need for aggressive treatment with immunosuppressive therapy. Previous cases of AION secondary to EGPA have typically been stabilized with corticosteroids, cyclophosphamide, and/or azathioprine(1). Our case is unique in that multiple immunotherapy agents, including cyclophosphamide, azathioprine and rituximab have been unable to achieve remission from EGPA. Further investigation into appropriate immunotherapy for these high risk patients is needed.

**References:** 1. Padovano I, Pazzola G, Pipitone N, Cimino L, Salvarani C. Anterior ischaemic optic neuropathy in eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome): a case report and review of the literature. *Clin Exp Rheumatol*. 2014 May-Jun;32(3 Suppl 82):S62-5. 2. Groh M, Pagnoux C, Baldini C, Bel E, Bottero P, et al. Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA) Consensus Task Force recommendations for evaluation and management. *Eur J Intern Med*. 2015 Sep;26(7):545-53.

**Keywords:** Optic neuropathy, Neuro-opth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 81****Neurosarcoidosis Mimicking Viral Meningoencephalitis**

Joseph Chacko<sup>1</sup>, Hans Wang<sup>1</sup>, Rudy Van Hemert<sup>31</sup>, Murat Gokden<sup>1</sup>, Sarkis Nazarian<sup>1</sup>

<sup>1</sup>UAMS, Little Rock, Arkansas, USA

**Introduction:**

Neurosarcoidosis is a rare disease more commonly associated with systemic sarcoidosis and affects the cranial nerves preferentially (1). In a retrospective study of sarcoidosis patients, isolated neurosarcoidosis has been cited to have an incidence of around ten percent, making its diagnosis problematic (2).

**Description of Case(s):**

A 43-year-old Caucasian woman presented with cognitive slowing and headache. She attributed this to a sinus infection and was treated. Two weeks later she returned with a fluctuating headache, difficulty concentrating, and right hemifield visual blurring. MRI showed diffuse vasogenic edema in the left occipital, parietal, and temporal lobes suspicious for viral meningoencephalitis. CSF studies showed mildly elevated protein and WBC count with lymphocytic predominance. She was treated with IV antivirals and antibiotics. Several days later she felt at baseline and was discharged. Three weeks later she was readmitted for word-finding difficulties, right visual field defects, and worsening headaches. Repeat MRI showed nodular enhancement with contrast and worsened T2 and FLAIR hyperintensities in the periventricular right parieto-occipital lobe and left parietal, occipital, and temporal lobes. Repeat LP showed worsened protein and WBC levels with lymphocytic predominance. Brain biopsy via L parietal craniotomy showed multiple vascular-centered granulomata and leptomeningeal involvement with reactive gliosis, indicating a diagnosis of Neurosarcoidosis.

**Conclusions, including unique features of the case(s):**

The presentation can be varied and nonspecific, making diagnosis a challenge. Without definitive histopathology, there is no constellation of signs or symptoms which point to a high probability of Neurosarcoidosis, and it often exists as a diagnosis of exclusion if biopsy is not undertaken (4). Sarcoidosis is also more prevalent in the African American population, which complicated the diagnosis (5). The patient was eventually treated with high dose tapering steroids with good response. On last clinic visit, she has a mild residual right inferior quadrantanopia but is able to function independently.

**References:** Lacomis. Neurosarcoidosis. *Current Neuropharmacology*. 2011; 3:429-436. Nozaki, Scott, Sohn, Judson. Isolated Neurosarcoidosis: Case series in 2 sarcoidosis centers. *The Neurologist*. 2012; 6:373-377. Mayer, Yim, Onesti, et al. Biopsy-proven isolated sarcoid meningitis: case report. *Journal of Neurosurgery*. 1993; 6:994-996. Hoitsma, Faber, Drent, Sharma. Neurosarcoidosis: a clinical dilemma. *The Lancet Neurology*. 2004; 7:397-407. Baughman, Field, Costabel, et al. Sarcoidosis in America. Analysis based on health care use. *Annals of the American Thoracic Society*. 2016; 8:1244-1252.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 82**

**Hemodynamic Neuro-ophthalmic Complications from Hemodialysis**

Nailyn Rasool<sup>1</sup>, Philip Meyers<sup>1</sup>, Jason Horowitz<sup>1</sup>, Sara Rostanski<sup>1</sup>, Roman Nowygrad<sup>1</sup>, Dean Cestari<sup>2</sup>, Avni Patel<sup>2</sup>, Benjamin Gallagher<sup>1</sup>, Jeffery Odel<sup>1</sup>

<sup>1</sup>*Columbia University, New York, New York, USA*, <sup>2</sup>*Harvard University, Boston, Massachusetts, USA*

**PUBLICATION PERMISSION NOT GRANTED**

**Poster 83**  
**Against the Wall**

Abby Vercio<sup>1</sup>, Timothy Winter<sup>1</sup>

<sup>1</sup>Loma Linda University Eye Institute, Loma Linda, California, USA

**Introduction:**

Melanoma associated retinopathy is a paraneoplastic processes involving auto-antibodies against normal retinal tissues, specifically the bipolar cell layer. This adversely affects rod systems as neuroretinal transmission from the photoreceptors through the inner retina is disrupted. This yields a characteristic electronegative ERG pattern helpful in diagnosis of this life-threatening disease.

**Description of Case(s):**

A 63 year old female was evaluated for vision changes with shimmering photopsias. She was found to have inferior disc edema OD, "at-risk" C/D and tortuous vessels OU. Visual fields were abnormal with altitudinal defect OD and superior arc OS. OCT NFL confirmed thickening OD. CBC, ESR and CRP were normal. She was diagnosed with NAION OD and started on PO prednisone. 2 months later she had decline in night vision; multifocal and full field ERGs were performed showing intact macular cone function and abnormal rod system response to scotopic flash conditions OU, concerning for electronegative response. Given her tobacco abuse concern arose for a cancer associated retinopathy. Prednisone was tapered and she began extensive imaging workup.

**Conclusions, including unique features of the case(s):**

Following a series of imaging studies including MRI brain/orbits, whole body NM PET and CT chest/abdomen/pelvis, the patient was found to have a left pelvic wall mass, for which diagnostic laproscopy with excisional biopsy was pursued, resulting in a diagnosis of metastatic melanoma, primary source yet unconfirmed. Given this, a secondary diagnosis of melanoma-associated retinopathy was made in light of the associated ocular symptoms and pathology. Visual field deficits improved with PO prednisone. This case showcases a unique case of an unknown primary melanoma with metastasis to the pelvic wall with the uncommon presenting sign of unilateral optic disc edema.

**References:** Keltner J, Thirkill C, Yip P, Clinical and Immunologic Characteristics of Melanoma-Associated Retinopathy Syndrome: Eleven New Cases and a Review of 51 Previously Published Cases, *Journal of Neuro-Ophthalmology*, 21, 173-187, 2001. Singh A, Et Al, Melanoma-associated Retinopathy, *American Journal of Ophthalmology Brief Reports*, 119, 369-370, 1995. Trout A, Rabinowitz R, Platt J, Elsayes K, Melanoma metastases in the abdomen and pelvis: Frequency and patterns of spread, *World Journal of Radiology*, 5, 25-32, 2013. Borowski L, Grover S, Fishman G, Jampol L, Retinal Findings in Melanoma-associated Retinopathy, *American Journal of Ophthalmology Brief Reports*, 132, 273-275, 2001. Thirkill C, Roth A, Keltner J, Cancer-associated Retinopathy, *Archives of Ophtahlmology*, 105, 372-375, 1987.

**Keywords:** Paraneoplastic syndromes, Neuro-opth & systyemic disease ( eg. MS, MG, thyroid), Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 84****Hypereosinophilia and Neuro-ophthalmological Manifestations in Lymphoma**

Ehtesham Khalid<sup>1</sup>, Alexandra May<sup>1</sup>, Woon Chow<sup>2</sup>, John Bond<sup>1</sup>

<sup>1</sup>Vanderbilt University Medical Center, Nashville, Tennessee, USA, <sup>2</sup>Virginia Common Wealth University, Richmond, Virginia, USA

**Introduction:**

While hypereosinophilia is commonly associated with allergies, parasitic and fungal infections, it is an uncommon manifestation of hematological malignancies. Here is a case of idiopathic hypereosinophilia in a patient who presented with neurologic signs but remarkably found to have no imaging abnormalities initially.

**Description of Case(s):**

66-year-old gentleman presented with year-long symptoms of pruritus, failure to thrive, weight loss, dry cough and double vision. Physical examination revealed some notable ophthalmic findings, including right eye junctional scotoma with patchy but reduced visual field bilaterally and esotropia in all directions with minimal limitation of abduction and adduction in each eye (right greater than left). His laboratory workup showed increased absolute eosinophil count (7670 cells/mm<sup>3</sup>) with morphologically abnormal eosinophils and eosinophilic precursors on bone marrow biopsy. Unremarkable cytogenetic studies were reported. Initial brain imaging was negative but later manifested leptomeningeal enhancement and bilateral occipital lobe changes with normal orbital MRI; Positron emission tomography also showed uptake in jejunal loops and mesenteric lymph nodes. Lumbar puncture findings were minimally abnormal. The patient eventually succumbed and a postmortem examination revealed and confirmed the diagnosis of peripheral T-cell lymphoma, not otherwise specified (PTCL, NOS; CD3+, CD4-) with diffuse serositis and visceral infiltration.

**Conclusions, including unique features of the case(s):**

Inflammatory and neoplastic pathology is very hideous and occasionally challenging to confirm without tissue diagnosis. My patient had extensive negative work up leaving the official diagnosis elusive until confirmation on autopsy. His hypereosinophilia was thought to be related to paraneoplastic phenomena that is secondary to cytokine expression by the malignant cells. PTCL, NOS constitutes 25% of PTCL in adults and 4% of non-hodgkin lymphoma overall. Bone marrow is only involved in 22% cases. Hypereosinophilia is a paraneoplastic marker of lymphomas and can be seen in 29% of cases with PTCL but it's a nonspecific finding making diagnosis challenging.

**References:** 1. Broccoli, A., & Zinzani, P. L. Peripheral T-cell lymphoma, not otherwise specified. *Blood* 2017; 129(9): 1103-1112. 2. V Mehta et al. Peripheral T Cell Lymphoma Presenting with Hypereosinophilia. *MJAFI* 2008; 64 : 89-91 3. Falini B et al. Peripheral T-cell lymphoma associated with hemophagocytic syndrome. *Blood*. 1990;75(2):434-444.

**Keywords:** Paraneoplastic syndromes, Tumors, Visual fields

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 85**

**Traumatic Carotid-Cavernous Fistula in FMD Presenting as Ophthalmoplegia and Status Epilepticus**

Scott Grossman<sup>1</sup>, Alexandra Kvernland<sup>1</sup>, Steven Galetta<sup>1</sup>, Miguel Litao<sup>1</sup>

<sup>1</sup>New York University, NYC, New York, USA

**Introduction:**

Carotid-cavernous fistulas (CCFs) are abnormal vascular shunts in which blood flows either directly or indirectly from the ICA into the cavernous sinus. They occur either traumatically (70%) or spontaneously (30%). The most common presenting complaints of CCFs are neuro-ophthalmic: proptosis, chemosis, orbital bruit, ophthalmoplegia, and orbital pain. Cerebral abnormalities including seizures are uncommon. Angiography remains the gold standard in diagnosis, and interventional neuro-radiologic approaches have transformed CCFs into conditions with low morbidity and mortality.

**Description of Case(s):**

A 51 year old woman presented to the ER via ambulance after she had multiple generalized seizures in a restaurant. She received 10mg diazepam twice and had an additional convulsive event in the ER, where she received 2mg IV lorazepam and was intubated. Emergent head CT demonstrated severely dilated ophthalmic vein in the left orbit. Levetiracetam was loaded and on exam she had mild left eye proptosis with diminished horizontal VOR response OS and a large minimally reactive pupil with severe orbital bruit OS. vEEG showed no ongoing seizure activity, but angiogram showed large left-sided CCF draining via basal vein of Rosenthal, multiple small aneurysms and irregular contouring of bilateral ICAs, suggestive of FMD. Over the ensuing 12 hours she became increasingly proptotic and chemotic OS, with new complete ophthalmoplegia. Trans-fistulous endovascular coiling was performed. On awakening she reported an altercation one week prior when she was punched in the left eye, with progressive eye pain and blurred vision. Her FHx was notable for a mother and sister with multiple aneurysms and diagnoses of FMD.

**Conclusions, including unique features of the case(s):**

This is a case of traumatic CCF in a genetically pre-disposed individual. New onset status epilepticus in the emergency room is a rare presentation of CCF, perhaps occurring here due to deep drainage via basal vein of Rosenthal. Post-intervention, complete ophthalmoplegia with severe proptosis resolved with only residual left abduction deficit.

**References:** Ellis, Goldstein, Connolly and Meyers, Carotid-cavernous fistulas, *Neurosurgery Focus*, 32, (5):E9, 2012. Poloskey, Olin, Mace and Gornik, Fibromuscular Dysplasia, *Circulation*, 125:e636-639, 2012

**Keywords:** Interventional neuroradiology, Stroke Trauma, Vascular disorders, Orbit

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 86**

**Congenital Cranial Dysinnervation Disorder: An Unusual Phenotype**

Michael Salman<sup>1</sup>, Samantha Marin<sup>1</sup>, Conor Mulholland<sup>1</sup>, Jens Wrogemann<sup>1</sup>

<sup>1</sup>*Winnipeg Children's Hospital and the University of Manitoba, Winnipeg, Canada*

**PUBLICATION PERMISSION NOT GRANTED**



**Poster 87****Check Point Inhibitor (CPI) Related Limbic Encephalitis**

Ehtesham Khalid<sup>1</sup>, James Mcguirk<sup>1</sup>, Kassandra Stubblefield<sup>1</sup>

<sup>1</sup>Vanderbilt University Medical Center, Nashville, Tennessee, USA

**Introduction:**

Checkpoint inhibitors have been reported to cause varied autoimmune manifestations including autoimmune encephalitis. Here we describe the development of limbic encephalitis in a patient with renal cell carcinoma following treatment with nivolumab and its resolution following corticosteroid therapy.

**Description of Case(s):**

A 56-year-old Caucasian man with metastatic renal carcinoma was being treated with Nivolumab for 1 year when he presented with abnormal eye movements and intermittent confusion. Electroencephalogram confirmed seizures originating in the right temporal lobe. A contrasted brain MRI showed prominent T2 hyper-intensities in the mesial temporal lobes, consistent with limbic encephalitis. CSF was acellular, with elevated protein (102 mg/dL) and normal glucose. Paraneoplastic panel in serum was positive for N-type voltage gated calcium channel (VGCC) antibodies- 0.08 (ref<0.03). All other autoantibodies known to be associated with autoimmune encephalitis were absent. Treatment with steroids resulted in significant reduction in the frequency of clinical and electrographic seizures. Nivolumab was stopped and repeat MRI showed resolution of radiologic changes; repeat paraneoplastic panel was negative for N-type VGCC antibodies after 2 months.

**Conclusions, including unique features of the case(s):**

Nivolumab is a humanized IgG4 anti- PD-1 monoclonal antibody which works as a checkpoint inhibitor, blocking the inhibitory signals which normally result in reduction in T cell activation. The overall incidence for neurological side effects is 0.4-1%. Development of autoantibodies following therapy with CPI is a phenomenon reported with variable paraneoplastic antibodies including AGNA, NMDAR Ab, Anti- CASPR2. The time interval for development of these autoimmune reactions after starting CPI is also variable and can range from weeks to 21 months. So far, the association of these antibodies with limbic encephalitis is not a common occurrence specially in the setting of Nivolumab which makes this case unique.

**References:** 1 Williams, T J. JAMA Neurol. 2016;73(8):928-933. 2 Blackmon, JT. J Neurol Neuromed (2016) 1(4): 39-45. 3 Brown, M. Journal of Neuroimmunology 305 (2017) 16–18. 4 Zalewski, N L. Muscle Nerve. 2016 Aug;54(2):220-7. 5 Xia, Z. J Med Case Rep 2010; 4:95.

**Keywords:** Paraneoplastic syndromes, Nystagmus

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 88**

**Early Detection of Dural Carotid-cavernous Fistula (CCF) with Rapidly Aggravating Headache and Cranial Nerve Paresis**

Yeon Woong Chung<sup>1</sup>, Jae Hoon Sung<sup>2</sup>, Tae Yoon La<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology, College of Medicine, St. Vincent's Hospital, Suwon, Korea, Republic of,* <sup>2</sup>*Department of Neurosurgery, College of Medicine, St. Vincent's Hospital, Suwon, Korea, Republic of*

**Introduction:**

Dural carotid cavernous fistulas (CCF) are defined as abnormal communications between the cavernous sinus and one or more internal or external carotid artery branches. When a dural CCF drains posteriorly into inferior or superior petrosal sinus, even typical corkscrew vessels are rarely detected, and the correct diagnosis is not easy. In this report, we present a patient with dural CCF whose initial symptom was rapidly aggravating headache, oculomotor and trigeminal ophthalmic branch paresis without any ocular symptom or sign.

**Description of Case(s):**

A 63 year-old woman was referred to Neuro-Ophthalmology by a neurologist with new onset of right-sided headache which had not been relieved by analgesics, right medial canthal area pain and double vision for 4 days. Computed tomography with enhancement showed only bilateral mild maxillary sinusitis. The next day, she visited again and said that she could not sleep at all due to both severe headache and right frontal and parietal tingling sensation was newly developed. Right upper lid complete ptosis was accompanied and right pupil became 1 mm larger than left pupil without relative afferent pupil defect. Exodeviation and right hyperdeviation at primary position and right inferior rectus muscle partial paralysis (-1), which were not shown yesterday, occurred. Brain magnetic resonance imaging/angiography showed bright flow signal of right cavernous sinus in time-of-flight view and bright flow signal around right internal carotid artery C4 segment in maximum-intensity-pixel projection imaging, without dilatation of superior ophthalmic vein. Cerebral angiography disclosed a right dural CCF, Barrow classification type D. A microcatheter was introduced into the cavernous sinus and coil embolization was performed. In 3 months, her symptoms disappeared completely.

**Conclusions, including unique features of the case(s):**

If new onset headache is rapidly aggravating and accompanied with other neurologic symptoms and/or signs such as oculomotor and trigeminal nerve, the cavernous sinus should be evaluated with MRA for detecting a dural CCF.

**References:** 1. Miller NR. Dural carotid-cavernous fistulas: epidemiology, clinical presentation, and management. *Neurosurg Clin N Am* 23(1), 179-92, 2012. 2. Yamada SM, Masahira N, Shimizu K. A migraine-like headache induced by carotid-cavernous fistula. *Headache* 47(2), 289-93, 2007. 3. Acierno MD, Trobe JD, Cornblath WT, Gebarski SS. Painful oculomotor palsy caused by posterior-draining dural carotid cavernous fistulas. *Arch Ophthalmol* 113(8), 1045-9, 1995. 4. Wu HC, Ro LS, Chen CJ, Chen ST, Lee TH, et al. Isolated ocular motor nerve palsy in dural carotid-cavernous sinus fistula. *Eur J Neurol* 13(11), 1221-5, 2006. 5. Miyachi S, Negoro M, Handa T, Sugita K. Dural carotid cavernous sinus fistula presenting as isolated oculomotor nerve palsy. *Surg Neurol* 39(2), 105-9, 1993.

**Keywords:** Vascular disorders, Neuroimaging, Adult strabismus with a focus on diplopia, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 89**

**A Case of Complete Ophthalmoplegia as the First Manifestation of Primary Pituitary Lymphoma**

Hae-ri Yum<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology, Konyang University College of Medicine, Daejeon, Korea, Republic of*

**Introduction:**

Primary pituitary lymphoma represents a rare condition with emerging clinical entity. Primary pituitary lymphoma should be considered as a distinct entity from primary CNS lymphoma because of different embryological origins and blood brain barrier. We experienced a case of complete ophthalmoplegia as the first manifestation of primary pituitary lymphoma.

**Description of Case(s):**

A 62-year-old female visited the ophthalmology clinic with the right upper eyelid ptosis and binocular diplopia for 2 weeks. Her corrected visual acuity was 20/40 OD and 20/20 OS. Ophthalmologic evaluation showed ptosis of the right upper eyelid, anisocoria with right relative afferent pupillary defect. She manifested about 70 prism diopters right exotropia in the primary position. In her right eye, we found limited ocular motility in adduction (-4), upgaze (-4), downgaze (-4), and abduction (-2). She was alert without remarkable neurologic findings. To differentiate the causes of diplopia, we performed laboratory studies including thyroid function test and acetylcholine receptor antibody and brain imaging. Brain magnetic resonance imaging showed a pituitary macroadenoma with invasion to right cavernous sinus and internal carotid artery. Trans-sphenoidal surgery was performed and the pathology confirmed an infiltration of the pituitary gland by a diffuse large B-cell lymphoma. A bone marrow biopsy, abdomen, pelvis and chest CT, and total body PET-CT confirmed the absence of systemic involvement. The final diagnosis was primary pituitary lymphoma. The patient underwent systemic chemotherapy with R-MPV (Rituximab, Methotrexate, Procarbazine, Vincristine). By 2 months postoperatively, the patient had marked improvement in her visual symptoms including ptosis, visual acuity, and diplopia.

**Conclusions, including unique features of the case(s):**

Although not common, complete ophthalmoplegia can be the first manifestation of the primary pituitary lymphoma without other neurologic symptoms. With proper diagnosis and rapid treatment, the visual symptoms of primary pituitary lymphoma can be fully recovered.

**References:** 1. A. Tarabay, G. Cossu, M. Berhouma, M. Levivier, R. T. Daniel, M. Messerer. Primary pituitary lymphoma: an update of the literature. *J neuroncol.* 130:383-95 (2016).

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 90**

**Axenfeld-Rieger Syndrome with Cerebellar Dysgenesis: A Clinical Association in Patients with FOXC1 Mutation**

Laura Torrado<sup>1</sup>, Michael Brodsky<sup>1</sup>, Mai Lan Ho<sup>1</sup>

<sup>1</sup>*Mayo Clinic, Rochester, Minnesota, USA*

**PUBLICATION PERMISSION NOT GRANTED**

**Poster 91****Infectious Cavernous Sinus Thrombosis in a Non-Toxic Patient.**

Sanjai Jalaj<sup>1</sup>, Nailyn Rasool<sup>1</sup>, Jeffrey Odel<sup>1</sup>

<sup>1</sup>*Columbia University, New York, New York, USA*

**Introduction:**

Cavernous sinus syndromes are characterized by multiple cranial nerve palsies from a lesion in the cavernous sinus. Causes range from tumors, vascular abnormalities, trauma, to infectious or inflammatory conditions. Infectious cavernous sinus syndrome usually results from infections of the face, sinuses, oral cavity, orbit, or even middle ear. Patients typically present with a toxic appearance with symptoms of headache, subjective fevers, chills, nausea, vomiting, somnolence, and signs of sepsis such as fever, tachycardia, and altered mental status. We herein describe a case of infectious cavernous sinus thrombosis in which the patient did not present with typical toxic signs and symptoms.

**Description of Case(s):**

A 54-year-old male with no significant past medical history presented to the ED with a 24-hour history of moderate left-sided headache accompanied by left eye pain and redness. He described increased pain and blurry vision on left gaze and upgaze. He denied fevers, chills, photophobia, neck stiffness, nausea, fatigue, recent illness, or local trauma. On exam, the patient was non-toxic and otherwise well-appearing and in good spirits. He was 20/20 bilaterally without a relative afferent pupillary defect. His gaze was restricted on abduction and supraduction of the left eye with increased intraocular pressure to 33mmHg and upper lid edema and temporal chemosis. A non-contrast CT head was performed revealing paranasal sinus disease. The initial concern was for orbital cellulitis from spread of a sinus infection. However, because of the elevated intraocular pressure, a CTA was performed revealing a partial thrombosis of the cavernous sinus. A sinus washout was performed and he was treated successfully with ceftriaxone and warfarin.

**Conclusions, including unique features of the case(s):**

Cavernous sinus thrombosis usually presents with dramatic signs and symptoms. However, as demonstrated above, suspicion ought to remain high even for well-appearing patients. Without venous imaging, this patient likely would have received only a sinus washout and antibiotics without anticoagulation.

**References:** None.

**Keywords:** Vascular disorders, Neuro-ophth & infectious disease (eg, AIDS, prion), Neuroimaging, Ocular Motility, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 92**

**Sudden Onset Diplopia and Eyeball Pain Diagnosed as Rhino-orbito-cerebral Mucormycosis (ROCM)**

Hak Seung Lee<sup>1</sup>, Sang Hak Lee<sup>1</sup>, Jin Sung Cheong<sup>1</sup>, Hyun Young Park<sup>1</sup>

<sup>1</sup>*Department of Neurology, Wonkwang University School of Medicine, Iksan-si, Korea, Republic of*

**Introduction:**

Orbital apex syndrome (OAS) is an uncommon clinical presentation consisting of complete ophthalmoplegia with vision loss, involving cranial nerves II, III, IV, V1 and VI. Some of these conditions, particularly infectious causes, can be life-threatening with delayed diagnosis and treatment. Rhino-orbito-cerebral mucormycosis (ROCM) is an invasive and fatal fungal infection. We present a case of a successfully treated diabetic patient with OAS resulting from ROCM who presented to the department of neurology because of eyeball pain and diplopia.

**Description of Case(s):**

A 60-year-old male presented to the department of neurology for severe headache, dizziness, and diplopia. Medical history revealed poorly controlled type 2 DM. He was noted to have significantly decreased ocular motility and loss of vision in his left eye. Ophthalmologic examination revealed no light perception and complete ophthalmoplegia with left eye ptosis. Orbit MRI showed inflammatory change in left optic nerve and diffuse T2 high signal intensity with enhancement in left preseptal area, retromaxillary fossa and masticator space suggesting diffuse inflammatory or infectious condition. Endoscopic surgical resection was performed and a pathology sample was taken. Histopathology of tissue stains showed positivity for mucormycosis. The patient subsequently underwent aggressive endoscopic removal of the involved tissue. The patient was treated with liposomal amphotericin B 400 mg, IV, postsurgery.

**Conclusions, including unique features of the case(s):**

OAS is a common presentation of ROCM, but unfortunately blindness is permanent and the risk of mortality is increased at this stage of progression. Mucormycosis is a highly aggressive infection known to have a high mortality rate when not treated. Survival rates depend on the interval period from appearance of symptoms to onset of treatment or surgery, extent and location of the infection, type of treatment, and amount of immunosuppression. Patients with ROCM need extensive surgical and medical treatment to maximize outcomes. Success requires multidisciplinary management.

**References:** None.

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion), Orbit, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 93

### A Case of Susac Syndrome with Neuropsychiatric Overtones

Siwei Zhou<sup>1</sup>, Leonid Zlotcavitch<sup>1</sup>, Tigran Kostanyan<sup>1</sup>, Gabrielle Bonhomme<sup>1</sup>

<sup>1</sup>University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA

#### Introduction:

Susac Syndrome is a rare autoimmune disorder, which is often misdiagnosed for years given the odd constellation of symptoms and neuropsychiatric overtones.

#### Description of Case(s):

A 31-year-old female with prior history of neoplasm, anxiety and depression presented with ophthalmic, neurologic, and psychiatric complaints. Exam was notable for Brun's Nystagmus and left fourth nerve palsy localizing to the brainstem. Ophthalmoscopy was largely unremarkable. Neurologic workup of her various neurologic complaints, including lumbar puncture, electromyogram and nerve conduction study, infectious and inflammatory serologies, and metabolic and endocrine lab work revealed elevated protein in the cerebrospinal fluid. She had elevated thyroid stimulating hormone with decreased T3 and free T4, suggesting hypothyroidism. Copper and ceruloplasmin were initially elevated, but Wilson's disease was excluded. Despite normalization of thyroid and copper studies, her symptoms persisted. Magnetic resonance imaging (MRI) revealed globular T2 hyperintense lesions in the bilateral temporal lobes, corpus colosum region, and cerebral white matter. Fluorescein angiography demonstrated multiple occluded arterioles and areas of nonperfusion in bilateral retinæ. Audiogram exhibited bilateral sensorineural hearing loss.

#### Conclusions, including unique features of the case(s):

The patient had the classic features of Susac Syndrome: encephalopathy, low-frequency hearing loss, and multiple branch retinal artery occlusions. Neuroimaging was consistent with the classic lesions in the corpus colosum of Susac Syndrome. She was started on immunosuppressive therapy with IV methylprednisone and intravenous immunoglobulin, then transitioned to an oral corticosteroid taper and azathioprine with significant improvement in her symptoms and retinal perfusion, as documented by repeat fluorescein angiography. Her history was clouded by neuropsychiatric overtones, including anxiety and depression, further confounded by daily marijuana use and poor short-term memory. Due to the complexity of disease and involvement of multiple organ systems, Susac Syndrome patients require multidisciplinary care with neurology, ophthalmology, rheumatology, psychiatry, and a primary care provider with frequent communication among the teams.

**References:** 1. Susac J. Susac's syndrome: the triad of microangiopathy of the brain and retina with hearing loss in young women. *Neurology*. 1994;44(4):519-593. 2. Lim CCT, Tan C, Umapathi T, et al. MRI findings in Susac's syndrome. *Neurology*. 2004;761-763. 3. Vodopivec I, Prasad S. Treatment of Susac Syndrome. *Curr Treat Options Neurol*. 2016;18(1):1-8.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Nystagmus, Vascular disorders, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 94

### More than Meets the Eye

Sophie Cai<sup>1</sup>, Roksolyana Tourkevich<sup>2</sup>, Rima Tulbah<sup>2</sup>, Steven Rowe<sup>2</sup>, Timothy McCulley<sup>1</sup>, Daniel Gold<sup>2</sup>, Amanda Henderson<sup>1</sup>

<sup>1</sup>Wilmer Eye Institute, Baltimore, Maryland, USA, <sup>2</sup>Johns Hopkins Hospital, Baltimore, Maryland, USA

#### Introduction:

The diagnosis of Heidenhain variant of Creutzfeldt-Jakob Disease (CJD), marked by early and often isolated visual disturbances, can be challenging to make.

#### Description of Case(s):

An 81-year-old man with history of coronary artery disease and prostate cancer in remission presented with 2 months of progressive vision loss, 10-pound weight loss, memory changes, and difficulty walking requiring a cane. Ophthalmic exam revealed hand motions vision in both eyes, brisk bilateral pupillary reaction to light without relative afferent pupillary defect, periodic alternating nystagmus, and dense right homonymous hemianopia. Dilated fundus exam revealed only mild optic nerve cupping and mild epiretinal membrane of the right eye. Neurologic exam showed full motor strength, decreased vibration sense and proprioception in the feet, and positive Romberg sign. Mini- Mental Status Examination score was 6/30. MRI brain and orbits with and without contrast, MRA head and neck, and EEG were unrevealing. Lumbar puncture sent for routine infectious studies, cytology, flow cytometry, and a paraneoplastic panel was notable for a mildly elevated protein of 58.3 (normal range 98% estimated probability of prion disease).

#### Conclusions, including unique features of the case(s):

Early isolated ophthalmic manifestations can lead to delayed evaluation by a neurologist and difficulty meeting the 2010 CDC diagnostic criteria for probable CJD (1,2). Although not yet incorporated into formal diagnostic criteria, the CSF RT-QuIC assay has emerged as a test with >85% sensitivity and 98-100% specificity for CJD compared to gold-standard neuropathologic diagnosis (3).

**References:** 1. Baiardi S, Capellari S, Ladogana A, et al. Revisiting the Heidenhain variant of Creutzfeldt-Jakob Disease: Evidence for prion type variability influencing clinical course and laboratory findings. *J Alzheimers Dis.* 50(2):465-76, 2016. 2. CDC's diagnostic criteria for Creutzfeldt-Jakob Disease (CJD), 2010. Centers for Disease Control and Prevention. <https://www.cdc.gov/prions/cjd/diagnostic-criteria.html>. [updated Feb 11, 2015] 3. McGuire LI, Poggio A, Poggiolini I, et al. Cerebrospinal fluid real-time quaking-induced conversion is a robust and reliable test for sporadic Creutzfeldt-Jakob disease: An international study. *Ann Neurol.* 80(1):160-5, 2016.

**Keywords:** Visual fields, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Neuroimaging, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 96**

**Wernicke Encephalopathy Owing To Vitamin Non-Adherence After Bariatric Surgery**

Olivia Killeen<sup>1</sup>, Robert O'Rourke<sup>2</sup>, Jonathan Trobe<sup>3</sup>

<sup>1</sup>St. Joseph Mercy Hospital and University of Michigan, Kellogg Eye Center, Ann Arbor, Michigan, USA, <sup>2</sup>University of Michigan, Ann Arbor, Michigan, USA, <sup>3</sup>University of Michigan Kellogg Eye Center, Ann Arbor, Michigan, USA

**Introduction:**

Wernicke encephalopathy (WE) is increasingly recognized as a complication of bariatric surgery precipitated by non-adherence to vitamin supplementation in the setting of pre-surgical hypovitaminosis, nausea, vomiting, gastrointestinal dysmotility, and the high cost of vitamins. Anticipation of this phenomenon allows prompt diagnosis and treatment, which can prevent serious neurologic morbidity and even death.

**Description of Case(s):**

Eleven months after undergoing Roux-en-Y gastric bypass, a 34 year old woman developed weakness and diplopia, including horizontal saccadic slowing, bilateral abduction deficits, and multidirectional nystagmus. She had not taken prescribed vitamins owing to high cost, nausea, and depression. Serum thiamine was low, confirming a diagnosis of WE. Treatment with IV thiamine rapidly eliminated diplopia but nystagmus and weakness persisted.

**Conclusions, including unique features of the case(s):**

To our knowledge, this is the first reported case of bariatric WE in which the high cost of nutritional supplementation contributed to medication non-adherence. Because there is a lifelong need for vitamin supplementation following bariatric surgery, and because such supplementation is typically not covered by insurance, it is imperative that patients understand the importance of and costs associated with vitamin supplementation before undergoing surgery. Furthermore, providers must maintain a high level of suspicion for vitamin non-adherence in post-bariatric surgery patients and should always consider WE in their differential diagnosis when these patients present with symptoms like weakness and oculomotor abnormalities. As ophthalmic signs are prominent, ophthalmologists are positioned to make an early diagnosis. WE after bariatric surgery is likely to become more common as these procedures increase in frequency. Anticipation of post-bariatric WE allows prompt diagnosis and treatment, preventing morbidity and death.

**References:** None.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 97

### Triple Hit Ophthalmoplegia

Claudia Prospero Ponce<sup>1</sup>, Aroucha Vickers<sup>1</sup>, Joshua Suelflow<sup>2</sup>, Andrew Lee<sup>1</sup>

<sup>1</sup>Houston Methodist Hospital, Houston, Texas, USA, <sup>2</sup>Baylor College of Medicine, Houston, Texas, USA

#### Introduction:

Complete bilateral ophthalmoplegia is an uncommon presentation of lymphoma metastasis but to carry a “triple hit” lymphoma (THL) is even more. We present a very unique case of complete ophthalmoplegia secondary to bilateral cavernous sinus (CVS) infiltration of diffuse B cell lymphoma with three different mutations: c-MYC (cell proliferation), BCL2 (anti-apoptotic), and BCL6 (oncogene). The patient was treated with several innovative chemotherapies and survived for almost a year. Local radiation therapy significantly improved ophthalmoplegia.

#### Description of Case(s):

A 54 year old male with stage IV triple hit pelvic diffuse large B-cell lymphoma developed bilateral ophthalmoplegia. He had received intrathecal methotrexate, systemic chemotherapy including SYK inhibitor– TAK659, and radiation to the lower back and pelvis prior to presentation. Nine months after systemic therapy, the patient presented with subacute bilateral sequential ptosis, proptosis, and ophthalmoplegia. His past medical history included hypertension. Ophthalmologic exam showed visual acuity of 20/40 in the right eye (OD) and 20/30 in the left eye(OS). Pupil exam measured 8mm and was fixed OD, and 6mm with a sluggish response to light OS. No relative afferent pupillary defect was noted. He had a bilateral and almost complete ophthalmoplegia, proptosis, and ptosis. The rest of the exam was unremarkable. MRI brain and orbits with contrast revealed enhancement in both cavernous sinuses extending to the orbital apices. Positron emission tomography (PET) scan showed abnormal uptake. Lumbar puncture confirmed CD10 positive, kappa light chain restricted B cells. External beam radiation to both cavernous sinuses and intrathecal cytarabine treatment was given. Repeated lumbar puncture was negative for any B cells. Ocular motility improved significantly in the left eye and minimally in the right eye. He continued with systemic ibrutinib (Bruton’s tyrosine kinase inhibitor) and nivolumab(PD1 blocker) but succumbed to his disease.

#### Conclusions, including unique features of the case(s):

Triple hit lymphoma can metastasize to the cavernous sinus and present to the ophthalmologist.

**References:** Pemmaraju, Naresh, Javed Gill, Saurabh Gupta, and John R. Krause. "Triple-hit Lymphoma." Proceedings (Baylor University. Medical Center). Baylor Health Care System, Apr. 2014. Web. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3954668/>  
• Akyurek, Nalan, Aysegul Uner, Mustafa Benekli, and Ibrahim Barista. "Prognostic Significance OfMYC,BCL2, AndBCL6rearrangements in Patients with Diffuse Large B-cell Lymphoma Treated with Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone plus Rituximab." *Cancer* 118.17 (2011): 4173-183. Web. • "Diffuse Large B-Cell Lymphoma (DLBCL)." Diffuse Large B-Cell Lymphoma - Lymphoma Research Foundation. Lymphoma Research Foundation, Dec. 2016. Web.

**Keywords:** Tumors, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 98**

**Isolated IV Nerve Palsy as First Sign in the Diagnostic of Lung Carcinoma**

Luciana Iacono<sup>1</sup>, Mariana De Virgiliis<sup>1</sup>, M. Laura Braccia Gancedo<sup>1</sup>, Haydée Martínez<sup>2</sup>

<sup>1</sup>Hospital Oftalmológico Dr. Pedro Lagleyze, Buenos Aires, Argentina, <sup>2</sup>Hospital de Clínicas Jose de San Martin, Buenos Aires, Argentina

**Introduction:**

The two most common causes of fourth nerve palsy are trauma and decompensation of a congenital palsy. The nerve can be affected in the midbrain (nucleus of fascicle), in the subarachnoid space, in the cavernous sinus or in the orbital apex. Other non common causes of fourth nerve palsy include infarction, hemorrhage, demyelination, inflammation, infection, tumor and metastasis. The purpose of this poster is to present a case report of an atypical cause of isolated IV nerve palsy due to metastasis of a primary lung tumor unknown until then.

**Description of Case(s):**

A 60-year-old male, with no significant past medical history, presented with a 2 weeks story of binocular vertical diplopia. He denied hypertension, Diabetes Mellitus, traumas and smoking. The only positive clinical sign revealed during the examination was the hypertropia of his left eye with the typical spontaneous tilt head compensation to the right side. The evaluation of the eyes movements showed the palsy of the left superior oblique. A gadolinium enhanced cranial and orbital MRI was performed. T1-weighted MRI without and with contrast demonstrated multiples enhancing brain ring lesions with surrounding vasogenic edema in FLAIR sequence (metastatic lesions). One of these lesions was clearly identified in the left cavernous sinus, in contact with the IV nerve. A thoracic CT was performed and a mass in the left lower pulmonary lobe was diagnosed. The lung biopsy confirmed an adenocarcinoma as the primary tumor.

**Conclusions, including unique features of the case(s):**

Although most common causes of isolated IV nerve palsy are traumatic and congenital, other atypical causes, such as metastasis, must be considered. In this case the IV nerve palsy due to metastatic lesions was the first clinical sign of a pulmonary adenocarcinoma.

**References:** None.

**Keywords:** Tumors, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Ocular Motility, Neuroimaging, Adult strabismus with a focus on diplopia

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 99**

**Rapid Onset Wernicke's Encephalopathy In A Patient Undergoing Radiation Therapy**

Jordan Stanley<sup>1</sup>, Lanning Kline<sup>1</sup>

<sup>1</sup>University of Alabama at Birmingham (UAB), Birmingham, Alabama, USA

**Introduction:**

A 54-year-old man with history of squamous cell carcinoma (SCC) of the tongue base presented with the chief complaint of bilateral visual blurring. Having received chemotherapy previously, he was currently undergoing radiation therapy with increasing weakness. He reported being unable to eat for the past three weeks secondary to nausea and vomiting. Three days prior to presentation, he noted visual blurring of his left eye which proceeded to involve both eyes. Past medical history included tobacco abuse and gastroesophageal reflux in addition to SCC of the tongue base.

**Description of Case(s):**

On exam, his visual acuity was 20/200 bilaterally limited by upbeat nystagmus. Nystagmus was observed to be conjugate, uniplanar, jerk with superior fast phase which worsened in downgaze. The remainder of the exam including pupils, intraocular pressure, extraocular movements, confrontational visual fields, anterior and posterior segment evaluation was normal. The clinical history and exam findings were highly suggestive of Wernicke's encephalopathy. The differential diagnosis also included focal areas of infarction, tumor or demyelinating lesions within the medulla or cerebellum along with cerebellar degeneration. An urgent course of high-dose intravenous thiamine and magnesium was initiated with marked improvement of nystagmus in the following days. Brain MRI obtained after initiation of therapy demonstrated classic radiographic findings of increased T2 signal in the region of mammillary bodies, paraventricular thalamus, and periaqueductal grey matter.

**Conclusions, including unique features of the case(s):**

Wernicke's encephalopathy is a life-threatening neurological condition often initially diagnosed by an ophthalmologist. Diagnosis remains clinical as MRI is only 53% sensitive. [1] When present, brain MRI findings demonstrate areas with high thiamine turnover [2] and the pathophysiology of thiamine utilization is reviewed. [3] Thiamine stores are rapidly depleted with hyperemesis and must be considered in cancer patients [4], pregnancy, as well as those undergoing gastrointestinal banding procedures. [5]

**References:** 1. Sechi, G. and A. Serra, Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. *Lancet Neurol*, 6(5), 442-55, 2007. 2. Hazell, A.S., K.G. Todd, and R.F. Butterworth, Mechanisms of neuronal cell death in Wernicke's encephalopathy. *Metab Brain Dis*, 13(2), 97-122, 1998. 3. Martin, P.R., et al., Alcoholic organic brain disease: nosology and pathophysiologic mechanisms. *Prog Neuropsychopharmacol Biol Psychiatry*, 10(2), 147-64, 1986. 4. Isenberg-Grzeda, E., et al., Palliative treatment of thiamine-related encephalopathy (Wernicke's encephalopathy) in cancer: A case series and review of the literature. *Palliat Support Care*, 13(5), 1241-9, 2015. 5. PUNCHAI, S., et al., Neurologic Manifestations of Vitamin B Deficiency after Bariatric Surgery. *Obes Surg*, 27(8), 2079-82, 2017.

**Keywords:** Nystagmus, Neuro-opth & systemic disease ( eg. MS, MG, thyroid), Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 100**

**Neuro-ophthalmological Sequelae of Carbon Monoxide Poisoning: A Brief Case Series**

Sangeeta Khanna<sup>1</sup>, Gillian Roper Hall<sup>2</sup>, Jafar Kafaie<sup>3</sup>

<sup>1</sup>*Saint Louis University, St Louis, Missouri, USA*, <sup>2</sup>*Saint Louis University Department of Ophthalmology, Saint Louis, USA*, <sup>3</sup>*Saint Louis University Department of Neurology, Saint Louis, USA*

**Introduction:**

Carbon-monoxide (CO) exposure causes brain damage by hypoxia resulting from binding to hemoglobin to form carboxy-hemoglobin reducing oxygen delivering capacity of blood, increasing free radical formation and cardiovascular compromise related hypotension (1). Neuro-imaging has identified basal ganglia, cortical and deep white matter injury with the latter being attributed to chronic symptoms more than the gray matter injury (2). While varying neuro-psychiatric (impaired cognitive ability, memory loss, mood disorder, personality change) and movement disorders (Parkinsonism, tremors, dystonia) have been reported, descriptions of ocular manifestations of CO poisoning are rare in our literature (3, 4). We report three patients who presented with delayed neurological sequelae (DNS) 2.5 years after accidental carbon monoxide poisoning with emphasis on their neuro-ophthalmological findings.

**Description of Case(s):**

All three patients complained of asthenopia, intermittent diplopia, blurred vision, headache and memory problems, with photophobia, hyperacusis and motion-intolerance in two. MRI abnormalities included T2 hyperintensities in the globus pallidus, hippocampal atrophy, and thinning of corpus callosal fiber tracks consistent with CO poisoning. All three had complete neurological, neuro-psychiatric and neuro-ophthalmological evaluation. The most notable finding was convergence dysfunction and all three patients benefited from wearing base in prisms at near. One patient showed decreased accommodation. Visual acuity, visual fields, color vision, pursuit and saccades were clinically normal. In addition, there was no nerve fiber layer or ganglion cell layer loss detected on OCT.

**Conclusions, including unique features of the case(s):**

DNS of CO poisoning can manifest as vergence, accommodation and vestibulo-ocular dysfunction. These findings are remarkably similar to patients with post-concussion syndrome and likely relate to diffuse injury to cerebral white matter tracts common to these two etiologies. Comprehensive ocular motor assessment in patients with CO poisoning can provide a measure of diffuse axonal damage and assist with correction of asthenopic symptoms.

**References:** 1. Raub JA, Benignus VA. Carbon monoxide and the nervous system. *Neurosci Biobehav Rev.* 26(8), 925-40, 2002. 2. T. Beppu. The Role of MR Imaging in Assessment of Brain Damage from Carbon Monoxide Poisoning: A Review of the Literature. *American Journal of Neuroradiology*, 35 (4), 625-631, 2014. 3. Stabile JR, Weaver LK, Deru K, Price R. Delayed visual disturbances in carbon monoxide poisoning: Identification and evaluation. *Undersea Hyperb Med.* 42(4), 307-12, 2015. 4. Fielding J, Lang W, White OB. Carbon monoxide poisoning: impact on ocular motility. *Cogn Behav Neurol.* 23(4), 256-61, 2010.

**Keywords:** Ocular Motility, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 101****Glial Fibrillary Acidic Protein Astrocytopathy: The Great Imitator**

David Rastall<sup>1</sup>, Ali Saeed<sup>2</sup>, Tarig Gheith<sup>2</sup>, Daniel Long<sup>2</sup>, Rany Aburashed<sup>2</sup>, Talal Derani<sup>2</sup>

<sup>1</sup>Michigan State University, Williamson, Michigan, USA, <sup>2</sup>Michigan State University Dept. of Neurology, East Lansing, Michigan, USA

**Introduction:**

Glial fibrillary acidic protein (GFAP) astrocytopathy is a newly discovered antibody-mediated autoimmune encephalitis in which autoantibodies against GFAP cause a range of central nervous system (CNS) symptoms, potentially mimicking diseases including multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD). GFAP astrocytopathy was discovered less than a year ago and here we present two cases of GFAP astrocytopathy which mimicked NMOSD.

**Description of Case(s):**

Case 1: A 51 year-old man presented with hypersomnolence and dysesthesia progressing to quadriplegia and urinary retention. Exam confirmed quadriplegia with hyperreflexia and clonus. He developed diplopia and ophthalmic examination revealed painless ophthalmoplegia. MRI revealed enlargement and central signal hyperintensity within the cord extending from C4 to T3 without enhancement, and T2 signal hyperintensities in the right cerebellopontine peduncle and posterior pons bilaterally. An LP showed CSF WBC of 453 (98% mononuclear), protein of 124 and normal glucose. An extensive work-up for autoimmune causes was negative. He was started on high-dose IVMP and after one day he had full ocular movement, no diplopia, and an improvement in limb strength. Further evaluation of the CSF revealed anti-GFAP antibody. Case 2: A 40 year-old woman presented with a similar complaint of weakness in four extremities and urinary retention. She had had a similar episode in the past diagnosed as MS. Exam showed weakness in right upper and lower extremities with hyperreflexia. Blood work was WNL and CSF was normal except for elevated WBCs. MRI showed lesions in the R frontal lobe, L frontal lobe, and cervical spine. Again NMO was considered, however GFAP serum antibodies were confirmed and high-dose IVMP treated the disorder.

**Conclusions, including unique features of the case(s):**

GFAP astrocytopathy can mimic many CNS disorders and can even meet the criteria for antibody negative NMOSD. It has characteristic MRI findings and responds immediately to high-dose IVMP, so should be considered in the differential of autoimmune encephalitis.

**References:** 1. Fang, B. et al. Autoimmune Glial Fibrillary Acidic Protein Astrocytopathy: A Novel Meningoencephalomyelitis. *JAMA Neurol.* 73, 1297 (2016). 2. Flanagan, E. P. et al. Glial fibrillary acidic protein immunoglobulin G as biomarker of autoimmune astrocytopathy: Analysis of 102 patients: Autoimmune GFAP Astrocytopathy. *Ann. Neurol.* 81, 298–309 (2017). 3. Yang, X. et al. Treatment of Autoimmune Glial Fibrillary Acidic Protein Astrocytopathy: Follow-Up in 7 Cases. *Neuroimmunomodulation* 24, 113–119 (2017).

**Keywords:** Ocular Motility, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 102

### On The Hunt For Sarcoidosis

Kimberly Gokoffski<sup>1</sup>, Christine Greer<sup>1</sup>, Vivek Patel<sup>1</sup>

<sup>1</sup>University of Southern California, Los Angeles, California, USA

#### Introduction:

This is a case of a 55 year-old Hispanic male with hypertension, HIV, on HARRT (CD4 count 754), with acute onset subjective fever, double vision, and severe left sided, boring headache and eye pain for 3 days.

#### Description of Case(s):

Patient had a complete, pupil sparing CN3 palsy of the left side. MRI imaging showed slight asymmetry in the cavernous sinus without abnormal enhancement. All infectious, inflammatory, and paraneoplastic serology and CSF studies were negative, including flow cytometry and cytospin. CT chest was negative. Day 5 the patient was discharged with Tylenol with a presumed diagnosis of Tolosa Hunt Syndrome (THS), he was not given steroids at this point because his quantiferon gold result was pending. Day 19 the patient returned for follow up and was found to have developed a pupil sparing complete cranial nerve III palsy of his right side (now bilateral), as well as cranial nerve VII palsy on the right with preserved lacrimation and normal taste. Cranial nerves IV-VI otherwise intact bilaterally. Repeat imaging demonstrated enhancement of bilateral VII/VIII nerve complexes and bilateral trigeminal nerve involvement at the level of the foramen ovale. The radiologic findings did not correlate with the patient's clinical exam. We felt the risks of biopsy outweighed benefits, especially without a discrete area of enhancement or focal lesion to target. Patient was given 1 g IV solumedrol for 5 days followed by slow oral taper. His symptoms resolved rapidly during treatment and he did not relapse during slow taper. The patient remains free of symptoms 1 month after discontinuing steroids.

#### Conclusions, including unique features of the case(s):

Case reports of bilateral painful ophthalmoplegia are rare, and often due to an underlying structural abnormality<sup>1 2 3</sup>. We propose this case as a rare entity of bilateral THS, in the setting of longstanding, controlled HIV.

**References:** 1. Gladstone J, Dodick D. Painful ophthalmoplegia: Overview with a focus on tolosa-hunt syndrome. Current Science Inc. 2004;8(4):321-329. <http://www.ncbi.nlm.nih.gov/pubmed/15228894>. doi: 10.1007/s11916-004-0016-x. 2. Kastirr I, Kamusella P, Andresen R. Bilateral painful ophthalmoplegia: A case of assumed tolosa-hunt syndrome. Journal of clinical and diagnostic research : JCDR. 2016;10(3):TD16. <http://www.ncbi.nlm.nih.gov/pubmed/27134970>. 3. Nieri A, Bazan R, Almeida L, et al. Bilateral painful idiopathic ophthalmoplegia: A case report. Headache: The Journal of Head and Face Pain. 2007;47(6):848-851. <http://onlinelibrary.wiley.com/doi/10.1111/j.1526-4610.2007.00798.x/abstract>. doi: 10.1111/j.1526-4610.2007.00798.x.

**Keywords:** Adult strabismus with a focus on diplopia, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 103

### A Divergence of Views

Roisin Buckels<sup>1</sup>, Nadeem Ali<sup>1</sup>

<sup>1</sup>Moorfields Eye Hospital, London, United Kingdom

#### Introduction:

The presence of a divergence centre in the brain and an associated divergence palsy remain an area of contention within neuro – ophthalmology. We present the case of a pure divergence palsy in the context of Wernicke’s Encephalopathy (WE) with very localised MRI changes.

#### Description of Case(s):

A 19 year old morbidly obese female (BMI 41kg/sqm) presented with a two week history of leg pain, weakness and ataxia which rapidly progressed. She had undergone gastric bypass surgery several months earlier with little bariatric success. When admitted to the neurology ward, Miller-Fisher syndrome was suspected. Whilst on the ward she developed oscillopsia and diplopia. Orthoptic examination revealed fine, rapid gaze-evoked nystagmus and on motility testing ductions were full in both eyes. When testing convergence her visual axes aligned at 8cm from the nose with single vision. She had normal convergent and divergent eye movements between her nose and 8cm. Beyond 8cm she developed a large angle alternating esotropia with diplopia which increased gradually up to a maximum of 60 base out prism dioptres at approximately 8m. Following inpatient investigations, the diagnosis was changed to WE secondary to gastric surgery and vitamin B therapy was commenced. MRI showed focal, symmetrical signal abnormality in the medial thalami, periaqueductal midbrain and ependymal surface of the tegmental pons and upper medulla. She showed minimal recovery in her neurological signs over a year after commencing vitamin replacement therapy.

#### Conclusions, including unique features of the case(s):

This patient presented with an unusual oculomotor finding of divergence palsy in the context of Wernicke’s Encephalopathy following gastric bypass surgery. Thiamine deficiency can present as a Miller-Fisher picture with ataxia, diplopia and areflexia. We believe this case demonstrates what we would term pure divergence palsy, defined as an increasing esotropia beyond a point of binocularity close to the nose with full ductions of either eye.

**References:** Aasheim. Wernicke Encephalopathy After Bariatric Surgery: A Systematic Review.. Ann Surg, Volume 248, pp. 714-720. 2008. Cogan. Divergence paralysis and paralysis of the near reflex associated with a malnutrition syndrome (presumably Wernicke's poliioencephalitis).. American Medical Association. Archives of Ophthalmology., Volume 46(4), pp. 436-437. 1951. Harper, Giles, Finlay-Jones. Clinical signs in the Wernicke-Korsakoff complex: a retrospective analysis of 131 cases diagnosed at necropsy. Journal of Neurology, Neurosurgery & Psychiatry, Volume 49(4), pp.341-345. 1986. Lepore. Divergence paresis: a nonlocalizing cause of diplopia. Journal of Neuro-Ophthalmology : the official journal of the North American Neuro-Ophthalmology Society, Volume 19(4), pp. 242-245. 1999.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Ocular Motility, Adult strabismus with a focus on diplopia, Neuroimaging, Nystagmus

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 104**

**Bilateral Anophthalmia Associated with Septo-optic Dysplasia.**

Omar Solyman<sup>1</sup>, Mohamed Attya<sup>2</sup>, Peter MacIntosh<sup>1</sup>

<sup>1</sup>University of Illinois at Chicago, Illinois Eye and Ear Infirmary, Chicago, Illinois, USA, <sup>2</sup>Cairo University Hospitals, Cairo, Egypt

**PUBLICATION PERMISSION NOT GRANTED**

**Poster 105**

**Optic Perineuritis, Horner's Syndrome, and Purtscher-Like Retinopathy as an Atypical Presentation of Giant Cell Arteritis**

Leonid Zlotcavitch<sup>1</sup>, Kenneth Taubenslag<sup>1</sup>, Ronald Hamilton<sup>2</sup>, Gabrielle Bonhomme<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA,* <sup>2</sup>*Department of Pathology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA*

**PUBLICATION PERMISSION NOT GRANTED**

## Poster 106

### Two Cases of Painful Ophthalmoplegia

Hirofumi Emoto<sup>1</sup>, Leo Kubono<sup>1</sup>, Yuko Emoto<sup>2</sup>, Yuichiro Inaba<sup>3</sup>, Yuko Takahashi<sup>4</sup>, Daisuke Ono<sup>4</sup>, Motohiro Kiyosawa<sup>5</sup>

<sup>1</sup>Shuwa General Hospital, Kasukabe, Saitama, Japan, <sup>2</sup>Emoto Eye Clinic, Tokyo, Japan, <sup>3</sup>Department of Otorhinolaryngology, Tokyo Medical and Dental University, Tokyo, Japan, <sup>4</sup>Department of Neurology, Tokyo Medical and Dental University, Tokyo, Japan

#### Introduction:

Even though painful ophthalmoplegia may be attributable to serious diseases, sometimes it is difficult to make a diagnosis. We present two cases of painful ophthalmoplegia.

#### Description of Case(s):

Case 1: 54-year-old man had headache and visited several hospitals. Two months after the onset, the right abducens palsy developed. Tolosa-Hunt syndrome was suspected and administration of oral prednisone was initiated. It was effective at first, but the symptoms were worsened one week after the initiation of the therapy. MRI of the brain revealed the lesions in the cavernous sinus and the right masticator space. The biopsy of the masticator space showed abscess and *Fusobacterium* spp. grew in the culture. The dental caries in the right maxilla was thought to be the source of infection. The patient was recovered with extraction of the dental caries, drainage to the lesion and administration of antibiotics Case 2: 69-year-old man had headache and diplopia and visited several hospitals. Right abducens palsy was diagnosed. MRI of the brain could not detect the responsible lesion. The diagnosis of Tolosa-Hunt syndrome was made and oral prednisone therapy was started. The symptoms were improved at first, but worsened two weeks after initiation of the therapy. One month after the onset, the right oculomotor palsy developed. The follow-up MRI with enhancement revealed the cavernous sinus lesion. Blood culture detected aspergillus antigen. The cavernous sinus lesion spread into the right sphenoid sinus. Diffuse large B-cell lymphoma was diagnosed with the biopsy to the sphenoid sinus. The potent chemotherapy was initiated but the symptoms were progressive and the patient was died seven months after the onset.

#### Conclusions, including unique features of the case(s):

If the etiology is unknown, Tolosa-Hunt syndrome is suspected and clinicians may try corticosteroid therapy. We need to pay attention to that it can be caused by infection or infiltration.

**References:** None.

**Keywords:** Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 107

### Topical Timolol In The Treatment Of Superior Oblique Myokymia: Report Of Two Additional Cases

Jagger Koerner<sup>1</sup>, Charles Rheeman<sup>2</sup>, Gregory Krohel<sup>2</sup>

<sup>1</sup>Albany Medical College, Albany, New York, USA, <sup>2</sup>Saratoga Ophthalmology, Saratoga, New York, USA

#### Introduction:

Superior oblique myokymia (SOM) is characterized by spontaneous recurrent bouts of superior oblique contraction that can cause blurred vision, diplopia, and oscillopsia (1). This is a monocular condition and historically has been considered benign and idiopathic, though ominous causes such as cerebellar tumor, stroke, and arterio-venous malformation have been reported (2). Vascular compression of the trochlear root exit zone has also been associated with SOM (3). Both pharmacologic and surgical treatment options exist, with surgery reserved for cases refractory to medical management. Six cases in the literature describe topical beta blocker use (Table 1). The only large case series describing medical management (n=20) did not discuss topical beta blockers (4).

#### Description of Case(s):

Two male patients, aged 38 and 70, presented to a Neuro-Ophthalmology clinic with intermittent oscillopsia and a sense of the right eye "jumping". Eye movements consistent with SOM were observed at the slit lamp in the right eye of each patient. The remainder of the exams were normal. Both patients were started on timolol 0.5% twice daily, and were followed up after one month. No objective signs of SOM could be elicited at follow up and the patients reported symptom resolution within one week. Prior to treatment, one patient was symptomatic for six months, and the other for thirty years.

#### Conclusions, including unique features of the case(s):

Four prior successful descriptions of topical beta blocker use in SOM exist. In two of these, the effect was rapid and dramatic (2,5). Our two cases are consistent with these reports. SOM is rare and has an unpredictable clinical course that includes spontaneous remission and recurrence. Topical beta blockers can be a fast-acting effective treatment for a subset of patients with SOM. They have a favorable side effect profile and could be used as initial treatment in many cases. Patients who do respond often have dramatic improvement within one week.

**References:** (1) Strupp M, Dieterich M, Brandt T, Feil K. Therapy of Vestibular Paroxysmia, Superior Oblique Myokymia, and Ocular Neuromyotonia. *Curr Treat Options Neurol.* 2016 Jul;18(7):34. (2) Borgman CJ. Topical timolol in the treatment of monocular oscillopsia secondary to superior oblique myokymia: a review. *J Optom.* 2014 Apr-Jun;7(2):68-74. (3) Hashimoto M, Ohtsuka K, Hoyt WF. Vascular compression as a cause of superior oblique myokymia disclosed by thin-slice magnetic resonance imaging. *Am J Ophthalmol.* 2001 May;131(5):676-7. (4) Williams PE1, Purvin VA, Kawasaki. Superior oblique myokymia: efficacy of medical treatment. *J AAPOS.* 2007 Jun;11(3):254-7. (5) Bibby K et al. Superior Oblique Myokymia –a topical solution? *Br J Ophthalmology.* 1994;78(11):882.

**Keywords:** Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 108**

**Dorsal Midbrain Syndrome, a Manifestation of Shunt Malfunction in Aqueductal Stenosis.**

Xuemin Zhang<sup>1</sup>

<sup>1</sup>*University of Maryland School of Medicine, Baltimore, USA*

**Introduction:**

Dorsal midbrain syndrome is known to be a manifestation of elevated intracranial pressure associated with ventriculomegaly. The mechanism is unclear and has been speculated to be due to rapid expansion of ventricles or to a trans-tentorial pressure gradient.

**Description of Case(s):**

We report a case of a 19-year-old female with history of aqueductal stenosis and obstructive hydrocephalus of the lateral and third ventricles status-post ventriculo-peritoneal shunt placement, who presented with dorsal midbrain syndrome one year later. Despite a CT scan that had shown markedly decreased hydrocephalus and shunt series showing patent shunt, 7 cc shunt tap resulted in marked improvement of her dorsal midbrain syndrome. Shunt revision revealed restriction of flow due to distal shunt tip adherence to parietal peritoneum.

**Conclusions, including unique features of the case(s):**

This case provides evidence that dorsal midbrain syndrome warrants further evaluation and may be a sign of ventriculo-peritoneal shunt malfunction despite lack of findings noted on CT scan and shunt series.

**References:** None.

**Keywords:** High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 109**

**A Case of Paroxysmal Ocular Tilt Reaction**

Ju-Hyang Lee<sup>1</sup>, Jiyeon Park<sup>2</sup>

<sup>1</sup>*Department of Ophthalmology, Ulsan University Hospital, Ulsan University of Medicine, ULSAN, Korea, Republic of,* <sup>2</sup>*Department of Neurology, Ulsan University Hospital, Ulsan University of Medicine, Ulsan, Korea, Republic of*

**Introduction:**

The ocular tilt reaction (OTR) consists of skew deviation, head tilt toward the hypotrophic eye, and binocular torsion. It is a prenucler disorder due to imbalance in otolithic pathways from the vestibular nucleus to the rostral midbrain. We report one case with intermittent paroxysmal OTR episodes and normal ocular movement after clipping operation of the internal carotid arterial (ICA) aneurysm.

**Description of Case(s):**

A 41-year-old man presented with a one-year history of intermittent diplopia and dizziness. He had suffered from intracranial hemorrhage due to an aneurysmal rupture of a distal ICA and had undertaken two clipping operations 3 year and 2 year before alternatively. On initial prism and alternate cover test, he had 4 prism diopter exophoria and 8 prism diopter right hypertropia at distant straight ahead. During head tilt test, he was orthotropic and symptom was disappeared. Skew deviation and head tilt to the left were revealed for symptomatic periods, and right incyclotorsion and left excyclotorsion were showed on fundus examination. Ocular tilt reaction was all disappeared in asymptomatic episode. The paroxysms occurred 2-3 times an hour and lasted several minutes. Episodes of symptom and resting were repeated at variable intervals. On the video nystagmography (VNG), paroxysms of dissociated vertical deviation and conjugate torsional eye movement were shown and persisted for 2-3 minutes. He was diagnosed as paroxysmal ocular tilt reaction. Baclofen decreased the episodes by approximately 50%.

**Conclusions, including unique features of the case(s):**

Paroxysmal OTR is distinctly rare, which only a few case reports were described. Since quiescent period and ocular tilt reaction episode repeated alternatively, there is a difficulty in diagnosis. Paroxysmal OTR can be caused by intermittent hyperactivity of the mesodiencephalic lesions. To suppression of abnormal neural firing, anticonvulsants can be applied for the patients.

**References:** None.

**Keywords:** Adult strabismus with a focus on diplopia, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 110

### Innervational Upshoot In Duane's Retraction Syndrome - When to Suspect and How to Treat?

Rawan Omary<sup>1</sup>, Konrad Weber<sup>1</sup>, Corina Klaeger<sup>2</sup>, Klara Landau<sup>1</sup>

<sup>1</sup>University Hospital Zürich, Zürich, Switzerland, <sup>2</sup>Augenaerzte Gurtengasse, Bern, Switzerland

#### Introduction:

In Duane's retraction syndrome, upshoot is commonly attributed to a mechanical bridle effect caused by the co-contracting lateral rectus muscle leading to an abrupt upshoot of the eye in adduction. Different patterns of synergistic innervations of the lateral rectus muscle from different divisions of the oculomotor nerve have been reported and supported by evidence from single motor unit electromyography studies. Here we report a case of innervational upshoot due to synergistic innervation of the superior rectus muscle as demonstrated by electromyography.

#### Description of Case(s):

A 32-year-old male with Duane's retraction syndrome type 2 complained of his "left eye disappearing upwards" on right gaze. He had a right head turn, slight left exotropia and hypertropia in primary gaze, globe retraction on adduction with gradual, but severe upshoot. Left lateral rectus muscle recession of 8mm was performed with improvement in primary position and head turn, but almost no effect on upshoot in adduction. Synergistic superior rectus muscle innervation was suspected, and the patient underwent needle electromyography with single motor unit recording from the superior rectus muscle, which demonstrated markedly increased muscle activity on adduction.

#### Conclusions, including unique features of the case(s):

Upshoot on adduction in Duane's retraction syndrome may be the result of synergistic innervation of the superior and medial rectus muscles. In such cases surgery on the lateral rectus muscle will not improve the upshoot as it is the case in the mechanical variant of upshoot caused by a bridle effect of the lateral rectus. If the vertical deviation gradually increases as the eye moves from abduction to adduction, surgery may be required on the abnormally innervated superior rectus muscle.

**References:** 1. Scott, A. B. & Wong, G. Y.: Duane's syndrome. An electromyographic study. Arch. Ophthalmol. Chic. Ill 1960 87, 140–147 (1972). 2. Von Noorden G.K.: Recession of both horizontal recti muscles in Duane's retraction syndrome with elevation and depression of the adducted eye. Am J Ophthalmol 114:311-3 (1992) 3. Mohan K., Saroha V.: Vertical rectus recession for the innervational upshoot and downshoot in Duane's retraction syndrome. J Pediatr Ophthalmol Strabismus 39:94-9 (2002). 4. Kekunnaya R, Kraft S, Rao VB, Velez FG, Sachdeva V, Hunter DG.: Surgical management of strabismus in Duane retraction syndrome. J AAPOS 19:63-9 (2015).

**Keywords:** Pediatric Neuro-Ophthalmology, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 111****Novel Recessive Mutations in SLC38A8 Causing Infantile onset Nystagmus with Foveal Hypoplasia**

Kim Bo Ram<sup>1</sup>, Jun Ikhyun<sup>1</sup>, Kim Hye Young<sup>2</sup>, Park Hye Won<sup>1</sup>, Han Sueng-Han<sup>1</sup>, Han Jinu<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, Yonsei University College of Medicine, Seoul, Korea, Republic of, <sup>2</sup>Department of Ophthalmology, National Health Insurance Service Ilsan Hospital, Goyang, Korea, Republic of

**Introduction:**

Foveal hypoplasia is a developmental eye disorder, often associated with aniridia, ocular albinism or retinopathy of prematurity. We report a rare case of a patient with nystagmus and foveal hypoplasia caused by autosomal recessive SLC38A8 (OMIM: 615585) mutations.

**Description of Case(s):**

A 4-year-old male presented with nystagmus. Upon first examination, 2~3 Hz left beating jerk nystagmus accompanied by infrequent right beating jerk nystagmus. Cycloplegic refraction revealed a refractive error of +sph3.50 -cyl2.50 axis180 in both eyes and his best-corrected visual acuity was 20/125 in both eyes. The patient had no foveal reflex upon dilated fundus examination. Optical coherence tomography revealed an absence of a normal foveal pit, extrusion of the inner retinal layer and outer-segment lengthening at the fovea centralis, all consistent findings with grade 4 foveal hypoplasia. No iris trans-illumination defect was seen. Electroretinography showed normal scotopic responses and an attenuated 30Hz flicker in the photopic responses. Electro-oculography showed bidirectional jerk pattern nystagmus. Targeted next-generation sequencing revealed compound heterozygous mutations c.964C>T:p.Gln322Ter and c.692G>A:p.Cys231Tyr (CADD score: 27.2, minor allele frequency: 0.0000099 in Exome Aggregation Consortium) in SLC38A8. No pathogenic variants were found in both PAX6 and GPR143 genes.

**Conclusions, including unique features of the case(s):**

We found novel SLC38A8 mutations in a patient with foveal hypoplasia and nystagmus. SLC38A8 is a putative glutamine transporter protein that, when a mutation is present, can cause foveal hypoplasia and optic nerve misrouting. The reduced 30Hz flicker response and bidirectional jerk pattern of the nystagmus could be characteristic features of a SLC38A8 mutation. If a patient with nystagmus has isolated foveal hypoplasia and no family history of nystagmus, sequencing of SLC38A8 should be undertaken. Our case demonstrates that molecular diagnosis with next-generation sequencing could provide more accurate genetic counseling in patients with foveal hypoplasia. However, the precise role of SLC38A8 in eye development and foveal formation still remains to be elucidated.

**References:** None.

**Keywords:** Genetic Disease, Nystagmus

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 112****Monocular Single Saccadic Pulses in Brainstem Inflammation**

Jae-Hwan Choi<sup>1</sup>, Eun Hye Oh<sup>1</sup>, Seo Young Choi<sup>1</sup>, Kwang-Dong Choi<sup>1</sup>, Sang-Ho Kim<sup>2</sup>, Hak-Seung Lee<sup>3</sup>

<sup>1</sup>*Department of Neurology, Pusan National University Yangsan Hospital, Yangsan, Korea, Republic of,* <sup>2</sup>*Department of Neurology, Dong-A University Hospital, Busan, Korea, Republic of,* <sup>3</sup>*Department of Neurology, Wonkwang University Hospital, Iksan, Korea, Republic of*

**Introduction:**

Saccadic pulses are brief, usually small eye movements away from the fixation point followed by rapid back. They may be single saccadic pulse (SSP) or double saccadic pulse (DSP). We report a patient with brainstem inflammation showing monocular SSPs.

**Description of Case(s):**

A 40-year-old women presented with progressive gait disturbance, dysarthria, dysphagia and diplopia for 2 months. On neurological examination, there was limitation of adduction and abduction in the left eye, and adduction in the right eye. During attempted primary gaze, fixation of the right eye was continuously interrupted by saccadic eye movements. Video-oculography demonstrated intermittent SSPs in the right eye, which were initially directed rightward without vertical and torsional components. The returning eye movement showed a decreasing velocity waveform toward the initial position. Other findings included dysarthria, decreased soft palate elevation in the left side, and truncal ataxia. Brain MRI showed circumscribed lesions in the dorsal portion of pons and medulla which were more severe on the left side. After intravenous steroid injection, his ophthalmoplegia gradually improved. However, the SSPs were still observed in the right but not in the left eye.

**Conclusions, including unique features of the case(s):**

Monocular SSPs in our patient may be ascribed to the asymmetric damage of the inhibitory projections from the omnipause neurons to the burst neurons generating saccadic pulse.

**References:** None.

**Keywords:** Ocular Motility, Demyelinating disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 113****Cerebellar Dysfunction Associated Anti-glutamic Acid Decarboxylase Antibody**

Seo-Young Choi<sup>1</sup>, Yunji Choi<sup>1</sup>, Minji Kim<sup>1</sup>

<sup>1</sup>*Pusan National University Hospital, Pusan, Korea, Republic of*

**Introduction:**

Glutamic acid decarboxylase (GAD) is an enzyme that catalyzes the decarboxylation of excitatory neurotransmitter, glutamate. Past couple decades, the autoimmunity against this enzyme was found to be related to many neurological conditions; stiff-person syndrome, limbic encephalitis, cerebellar ataxia, epilepsy, and abnormal eye movements. In this report, we describe a patient with history of subacute spontaneous dizziness with downbeat nystagmus and oscillopsia, who was diagnosed anti-GAD antibody-related cerebellar dysfunction.

**Description of Case(s):**

A 38 year-old woman with no previous medical history was referred to Pusan national university hospital because of continuous spontaneous vertigo, nausea and oscillopsia for five months. Two weeks before her visit, the oscillopsia had exacerbated, especially when she was looking downward and on both lateral gaze. Initial neurologic examination revealed spontaneous downbeat nystagmus augmented on downward and both lateral gaze. Other than these, she showed no sign of ataxia, muscle rigidity or myoclonus. Brain MRI revealed no definite abnormality. Cerebrospinal fluid study showed no sign of infection. The initial serum anti-GAD antibody titer was 202.36 U/mL and 18F-FDG PET/CT of brain showed decreased metabolism in both cerebellum. She was diagnosed as anti-GAD antibody-related cerebellitis and systemic intravenous steroid (dexamethasone 5mg/day for three days and tapered for two weeks) and immunoglobulin (0.4g/kg for five days) were started as the initial treatment. However, her symptoms were not improved. So, plasmapheresis for five consecutive every other day was performed, but it failed to improve her symptoms other than the dizziness. After all the immunosuppressive therapies, video-oculography revealed no objective improvement of oscillopsia or spontaneous nystagmus from the initial one. She was discharged with gabapentin (600mg/day).

**Conclusions, including unique features of the case(s):**

Randomized control studies of the therapy for the anti-GAD antibody-related neurological conditions are in need to prove its effectiveness, regarding the role of anti-GAD antibody to validate the use of immunotherapies in these patients.

**References:** None.

**Keywords:** Vestibular

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 114****Bilateral Internuclear Ophthalmoplegia Associated with Anti-GQ1b Antibody**

Seung-Han Lee<sup>1</sup>, Sang-Hoon Kim<sup>1</sup>, Myung-Ho Park<sup>1</sup>, Sang-Jun Park<sup>2</sup>

<sup>1</sup>Department of Neurology, Chonnam National University Hospital, Gwangju, Korea, Republic of, <sup>2</sup>Department of Neurology, Cheomdan Medical Center, Gwangju, Korea, Republic of

**Introduction:**

Anti-GQ1b antibody is often associated with acute ophthalmoplegia, and various diseases which have this antibody and ophthalmoplegia, including Miller Fisher syndrome, Bickerstaff's brainstem encephalitis, Guillain-Barre syndrome, acute ophthalmoplegia (without ataxia) are referred to as anti-GQ1b antibody syndrome. Internuclear ophthalmoplegia (INO) is a disorder of conjugate lateral gaze in which the affected eye shows impairment of adduction that is caused by a lesion in the medial longitudinal fasciculus (MLF). Common etiologies of INO are stroke and demyelinating disorders invading the MLF. Previously, Miller Fisher syndrome has manifested as an INO; however, it is usually called a pseudo-INO since it might not be related to a true MLF lesion. We report a case of anti-GQ1b antibody syndrome with atypical clinical manifestations; true MLF syndrome.

**Description of Case(s):**

A 32-year-old-man presented with diplopia and dizziness. Neurologic examination revealed bilateral INO and gaze-evoked nystagmus while gazing upward. A video head impulse test showed decreased vestibulo-ocular reflex (VOR) gains on the vertical canals. We expected a bilateral MLF lesion caused by stroke or demyelination, but the brain MRI was normal. Several days later, the patient showed gait ataxia and paresthesia during the course of hospitalization. Serum IgG anti-GQ1b antibody was strongly positive. The patient was diagnosed as having anti-GQ1b antibody syndrome, and treated with intravenous immunoglobulin.

**Conclusions, including unique features of the case(s):**

We think that the bilateral INO with vertical gaze-evoked nystagmus and VOR gain deficit in the vertical canals documented by the video head impulse test are suggestive of a true lesion in the MLF. Anti-GQ1b antibody syndrome may cause true INO since the MLF is a heavily myelinated composite tract. Detailed neuro-ophthalmologic examinations including head impulse test and video-oculography may help to document the involvement of the MLF.

**References:** None.

**Keywords:** Ocular manifestations of vestibular disorders, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Nystagmus, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 115

### Windmill Nystagmus in a Patient with Visual Loss

Sun-Uk Lee<sup>1</sup>, Sungyang Jo<sup>2</sup>, Hyo-Jung Kim<sup>1</sup>, Sea-Won Oh<sup>1</sup>, Jeong-Yoon Choi<sup>1</sup>, Ji-Soo Kim<sup>1</sup>

<sup>1</sup>Seoul National University Bundang Hospital, Seongnam-si, Korea, Republic of, <sup>2</sup>Asan Medical Center, Seoul, Korea, Republic of

#### Introduction:

Windmill nystagmus is characterized by a clock-like rotation of the direction of nystagmus. The typical pattern of windmill nystagmus has only once been described in a patient with acquired blindness. We report a second case of windmill nystagmus in a patient with visual loss.

#### Description of Case(s):

A 47-year-old previous healthy man was referred for evaluation of progressive visual loss in both eyes for three months. Under the suspicion of atypical optic neuritis, he had been treated with methylprednisolone 1000 mg per day for 10 days, but his visual loss continued to deteriorate after slight improvement initially. On examination, he was unable to perceive light in the left eye, and was only able to count fingers at 50 cm in the right eye. Both pupils were dilated at 5 mm without a response to light. The optic disc was pale in both eyes. He showed one cycle of clockwise rotation of beating direction of nystagmus, starting from nystagmus beating downward, rightward, upward, leftward, and then finally returning downward. This pattern of nystagmus directions was consistent with windmill nystagmus. The duration of nystagmus in each direction was 10-16 seconds, and it took about 40 seconds to complete one clockwise cycle of windmill nystagmus. Video head-impulse tests and bithermal caloric tests were normal. Findings of CSF analyses, and brain MRIs and MR angiography were unremarkable. Genetic analyses for Leber's hereditary optic neuropathy were negative for mitochondrial DNA 3460, 4171, 11778, and 14484. Anti-aquaporin 4 antibodies and other serologic markers for viral or autoimmune disorders were also all negative.

#### Conclusions, including unique features of the case(s):

The development of windmill nystagmus within 3 months of acquired visual loss in our patients indicates that a malfunction within the visual-motor "adaptation" pathways may occur earlier than expected previously when the vision is lost.

**References:** Sanders MD, Glaser JS (1973) Alternating windmill nystagmus. In: Smith JL (ed) Neuro-Ophthalmology. Mosby, St. Louis  
Choi KD, Shin HK, Kim JS, Kim SH, Choi JH, Kim HJ, et al. Variants of windmill nystagmus. Journal of neurology. 2016;263(7):1375-81.  
Kömpf D, Piper H-F. Eye movements and vestibulo-ocular reflex in the blind. Journal of neurology. 1987;234(5):337-41.

**Keywords:** Nystagmus

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 116****Post-Surgical Oculopalatal Tremor with Facial Diplegia and Bilateral Horizontal Gaze Palsy**

Anthony Brune<sup>1</sup>, Daniel Gold<sup>1</sup>

<sup>1</sup>*Johns Hopkins University, Baltimore, Maryland, USA*

**Introduction:**

An otherwise healthy female presented initially at age 49 with the acute onset of right sixth and seventh nerve palsies and left hemiparesis. Imaging studies revealed two cavernomas within the right pons including one in the region of the facial colliculus. Her deficits improved but did not resolve over several months. Five years after her initial presentation she developed recurrent right facial palsy and dysphagia. Imaging revealed acute pontine hemorrhage and she underwent surgical resection of the cavernoma.

**Description of Case(s):**

Post-operatively, she had facial diplegia and bilateral horizontal gaze palsy. Several months later, she presented with vertical oscillopsia. She also reported a diagonal binocular diplopia that transitioned over time to horizontal diplopia. On examination, she had a continuous vertical pendular nystagmus and symmetric palatal myoclonus. She had bilateral horizontal gaze palsies that were not overcome with oculocephalic maneuvers. Review of her MRI done two months post-operatively revealed surgical changes to the floor of the fourth ventricle as well as marked hyperintensities of the bilateral inferior olivary nuclei.

**Conclusions, including unique features of the case(s):**

This patient presented with classic features of oculopalatal tremor (OPT), including vertical pendular nystagmus, palatal myoclonus, and MRI evidence of olivary hypertrophy. In cases of acquired pendular nystagmus, observation of palatal myoclonus determines localization to the Guillain-Mollaret triangle and can narrow the differential diagnosis. Given the proximity of the central tegmental tract to the abducens nucleus and facial nerve fascicle, she also had complete horizontal gaze palsy and facial diplegia. This case and cases of OPT with other associated features demonstrate the relevant neuroanatomy in relationship to other pathways of neuro-ophthalmologic importance.

**References:** None.

**Keywords:** Nystagmus, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 117

### Downbeat and Prominent Progressive cacheXia from anti-DPPX encephalitis

Jonathan Micieli<sup>1</sup>, Carols Kase<sup>1</sup>, Damian Berezovsky<sup>2</sup>, Nancy Newman<sup>1</sup>, Valerie Biousse<sup>1</sup>

<sup>1</sup>Emory University School of Medicine, Atlanta, Georgia, USA, <sup>2</sup>Barrow Neurological Institute, Phoenix, Arizona, USA

#### Introduction:

Anti-DPPX encephalitis is a recently described paraneoplastic syndrome characterized by the triad of weight loss/gastrointestinal symptoms, cognitive or mental dysfunction and symptoms of CNS hyperexcitability. A large proportion of patients with DPPX antibody-associated encephalitis have ocular findings including nystagmus, skew deviation, and abnormalities in saccades and smooth pursuit.

#### Description of Case(s):

A 49-year old previously healthy white man presented with a 16-month history of severe weight loss, headaches, myalgias, memory loss, tremor, difficulty walking and binocular diplopia and oscillopsia. He developed an upper respiratory tract infection in 06/2015, followed by loss of appetite, severe unintentional weight loss (60lbs in 4 weeks), myalgias, headache, memory loss, tremors and binocular diplopia. He was admitted to an outside hospital from 12/18/2015 to 01/04/2016 and had normal investigations. He continued to worsen and was seen in our Neuro-Ophthalmology service on 10/11/2016. He had lost over 100lbs and was unable to ambulate without assistance. Afferent visual function was normal. Voluntary eye movements were slow and were limited in all directions of gaze especially in upgaze with a small esotropia in primary position. He had saccadic pursuit and dysmetric saccades and he was unable to maintain fixation. He had episodic bursts of opsoclonus with intermittent downbeat nystagmus. Neurological examination showed severe ataxia with a cerebellar syndrome, intention tremor and occasional myoclonic jerks. He had diffuse amyotrophy and was overall very weak. He was admitted to the hospital and intravenous thiamine was immediately started for suspected Wernicke's encephalopathy. He had normal neuroimaging and a normal duodenal biopsy for suspected Whipple's disease. CSF obtained earlier during his admission was tested for antibodies against DPPX and was positive. A diagnosis of autoimmune encephalitis secondary to anti-DPPX was made. He responded well to plasmapheresis and IVIG.

#### Conclusions, including unique features of the case(s):

DPPX-associated encephalitis requires a high index of suspicion in patients with ocular and gastrointestinal symptoms.

**References:** 1. Piepgras J, Höltje M, Michel K, et al. Anti-DPPX encephalitis: pathogenic effects of antibodies on gut and brain neurons. *Neurology* 2015;85(10):890-7. 2. Kim J, Nadal MS, Clemens AM, et al. Kv4 accessory protein DPPX (DPP6) is a critical regulator of membrane excitability in hippocampal CA1 pyramidal neurons. *J Neurophysiol* 2008;100(4):1835-47. 3. Tobin WO, Lennon VA, Komorowski L, et al. DPPX potassium channel antibody: frequency, clinical accompaniments, and outcomes in 20 patients. *Neurology* 2014;83:1797-18093 4. 4. Hara M, Ariño H, Petit-Pedrol M, et al. DPPX antibody-associated encephalitis Main syndrome and antibody effects *Neurology* 2017;88(14):1340-1348. 5. Balint B, Jarius S, Nagel S, et al. Progressive encephalomyelitis with rigidity and myoclonus: a new variant with DPPX antibodies. *Neurology* 2014;82(17):1521-8.

**Keywords:** Paraneoplastic syndromes

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** This study was supported by a grant from Research to Prevent Blindness

**Poster 118****Facial And Abducens Palsy In Pseudotumor Cerebri. Case Report And Literature Review.**

Maria Braccia Gancedo<sup>1</sup>, Haydee Martinez<sup>2</sup>, Mariana de Virgiliis<sup>1</sup>, Luciana Iacono<sup>1</sup>

<sup>1</sup>Hospital Oftalmológico Dr. Pedro Lagleyze, Buenos Aires, Argentina, Lomas de Zamora, Argentina, <sup>2</sup>Hospital de Clínicas José de San Martín. Buenos Aires. Argentina, Buenos Aires, Argentina

**Introduction:**

Pseudotumor cerebri (PTC) or Idiopathic intracranial Hypertension (IIH) revised criteria, included sixth nerve palsies as the most common neurological deficit due to raised intracranial pressure. There are isolated reports, more frequent in children, of peripheral facial palsy in PTC, often combined with sixth nerve deficit. We report a case of VIth and VIIth nerve palsy in PTC in an adult patient, and a literature review.

**Description of Case(s):**

A 22 years old overweight woman (BMI- 27.1), under treatment with oral contraceptives (OC), complaining with headache, double vision and facial asymmetry was diagnosed with PTC with bilateral abducens paresis, right peripheral facial palsy and severe papilledema (grade V frisen scale). Imaging evaluation ruled out cerebral venous thrombosis. The opening pressure (OP) was 52 mmHg, and both VIth and VIIth compromise improved after the lumbar puncture (LP) was performed. Complete motor function was obtained within two weeks with weight loss, oral contraceptives suspension and acetazolamide. In a five years follow up period, in association with mild weight gain and anemia, there was two events of headache and papilledema without VIth or VIIth compromise.

**Conclusions, including unique features of the case(s):**

Facial palsy is a poorly described sign in PTC patients. In case reports, it is almost always associated with unilateral or bilateral VIth commitment and more frequently in pediatric population. In this case, the VIth and VIIth palsy occurred in the context of a severe increase in the OP, with immediate improvement after LP, so it could be considered that the motor commitment was directly proportional to the increase in the OP, given that did not repeat the complete picture in the successive relapses where the symptomatology was mild. We should take into account the rare but likely VIIth nerve compromise in this entity, correlate with the OP values, in order to use it as a prognosis sign when present.

**References:** None.

**Keywords:** High intracranial pressure/headache, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 119**

**Periodic Alternating Nystagmus Associated with Joubert Syndrome**

Hak-Seung Lee<sup>1</sup>, Jae-Hwan Choi<sup>2</sup>, Eun Hye Oh<sup>2</sup>, Jae-Ho Jung<sup>3</sup>, Seo Young Choi<sup>4</sup>, Kwang-Dong Choi<sup>4</sup>, Min-Ji Kim<sup>4</sup>, Sang-Ho Kim<sup>5</sup>

<sup>1</sup>Department of Neurology, Wonkwang University Hospital, Iksan, Korea, Republic of, <sup>2</sup>Department of Neurology, Pusan National University Yangsan Hospital, Busan, Korea, Republic of, <sup>3</sup>Department of Ophthalmology, Pusan National University Yangsan Hospital, Yangsan, Korea, Republic of, <sup>4</sup>Department of Neurology, Pusan National University Hospital, Busan, Korea, Republic of, <sup>5</sup>Department of Neurology, Dong-A University Hospital, Busan, Korea, Republic of

**Introduction:**

Joubert syndrome is a rare autosomal recessive genetic disorder characterized by ataxia, hypotonia, development delay, and “molar tooth sign” on a MRI scan. Since it affects the brainstem and cerebellar vermis, various oculomotor abnormalities have been described. We report a patient with Joubert syndrome showing torsional pendular nystagmus (PN) and periodic alternating nystagmus (PAN).

**Description of Case(s):**

A 51-year-old women presented with binocular oscillopsia for 4 years. On neurological examination, corrected visual acuities were 20/100 in both eyes. With visual fixation, there was intermittent cyclotorsional PN with low frequency in both eyes. In darkness, the nystagmus became jerky toward the left side, but the direction was changed to the right side intermittently. The nystagmus toward the left side had a longer duration and greater maximal slow-phase velocity. Other oculomotor examinations including saccade, smooth pursuit, and vestibule-ocular reflex were unremarkable. Fundus photograph revealed bony spicule-shaped pigment deposits in the periphery of the retina. Brain MRI showed a deep cleft in the isthmus of the brainstem, prominent thickened elongated superior cerebellar peduncles, and the atrophy of the cerebellar vermis, which combined to give the “molar tooth sign”.

**Conclusions, including unique features of the case(s):**

Our patient with Joubert syndrome showed the torsional PN and PAN without abnormalities of saccades, smooth pursuit and VOR. The PAN in our patient may be ascribed to visual impairments due to retinitis pigmentosa or the abnormalities in the velocity storage system by malformation of the cerebellum.

**References:** None.

**Keywords:** Nystagmus

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



## Poster 120

### Quite An Odd Pairing: Miller–Fisher Syndrome and Autoimmune Thyroid Diseases

May Al-Ameri<sup>1</sup>, Jaspreet Jakue<sup>2</sup>, ROSA TANG<sup>3</sup>, Jade Schiffman<sup>4</sup>, Nagham Al-Zubidi<sup>3</sup>

<sup>1</sup>University of Houston, Houston, Texas, USA, <sup>2</sup>Neuro- ophthalmology of Texas / Eye Wellness Center, Houston, Texas, USA, <sup>3</sup>Neuro- Ophthalmology of Texas / Blanton Eye institute Houston Methodist Hospital, Houston, Texas, USA, <sup>4</sup>Neuro-Ophthalmology of Texas/ MS Eye Care, Houston, Texas, USA

#### Introduction:

The concurrence of Miller–Fisher syndrome and autoimmune thyroid diseases (AITD) (Hashimoto's thyroiditis and graves' disease) is scarce with only few reported cases in literature. Immune system dysfunction may underlie this association, and linked by a common immunogenetic susceptibility. Immune system dysfunction was determined by serologic measurements of antibodies to anti-GQ1b antibody, thyroglobulin and thyroid peroxidase. We herein presenting an interesting case with positive antibodies to anti-GQ1b, thyroglobulin and thyroid peroxidase.

#### Description of Case(s):

**METHOD:** This is a case report with a retrospective chart review. A Literature search was performed and the following terms were used: Thyroid disease, Hashimoto's Thyroiditis, Graves' Disease, Miller–Fisher Syndrome, autoimmune diseases **RESULTS:** We described a 35 year- old Hispanic presented with double vision, numbness, and slurred speech which started 2 weeks after a bout of diarrhea. Exam showed bilateral complete external ophthalmoplegia, areflexia and CSF showed albumino-cytological dissociation otherwise exam was negative. Work-up suggested the Miller Fisher syndrome with a positive anti-GQ1b with the co-occurrence of positive thyroglobulin and thyroid peroxidase antibodies. No clinical evidence of TED. Further work up included a normal MRI of brain, orbit, and spine. The blood work for myasthenia gravis was negative. The patient was treated with IV immunoglobulin and plasmapheresis with good recovery.

#### Conclusions, including unique features of the case(s):

We hypothesize that MF concurrence with autoimmune thyroid antibodies may occur due to a common immunogenetic source. The findings in this patient raises an interesting question about their parthenogenesis with the possibility that previous activation of the immune system may predispose to the development of autoantibodies against other antigens.

**References:** · Lau KK, Goh KJ, Lee HC et al (2009) The co-occurrence of serologically proven myasthenia gravis and Miller Fisher/Guillain Barre overlap syndrome: a case report. J Neurol Sci 276:187–188 PubMed · Marino M, Ricciardi R, Pinchera A et al (1997) Mild clinical expression of myasthenia gravis associated with autoimmune thyroid diseases. J Clin Endocrinol Metab 82:438–443PubMed · Kizilay F, Ryan HF Jr, Oh SJ (2008) Myasthenia gravis and Guillain-Barre syndrome occurring simultaneously in the same patient. Muscle Nerve 37:544–546 PubMed · Kung SL, Su JM, Tsai SJ et al (2009) Concurrent Guillain–Barre syndrome and myasthenia gravis: the first case in Taiwan. Acta Neurol Taiwan 18:193–197PubMed · Ercolini AM, Miller SD (2005) Role of immunologic cross-reactivity in neurological diseases. Neurol Res 27:726–733PubMed · Mak W, Chan KH, Ho SL (2005) A case of ocular myasthenia gravis and Miller–Fisher syndrome. Hosp Med 66:116–117PubMed · Polizzi A, Ruggieri M, Vecchio I et al (2001) Autoimmune thyroiditis and acquired demyelinating polyradiculoneuropathy. Clin Neurol Neurosurg 103:151–154PubMed

**Keywords:** Ocular Motility, Genetic Disease, Graves (systemic disease), Orbit, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 121****Bilateral Complete Sixth Nerve Palsy After Traumatic Left Occipital Bone Fracture**

Austin Nakatsuka<sup>1</sup>, Hossein Nazari<sup>2</sup>, Brian Wong<sup>2</sup>

<sup>1</sup>University of Texas Medical Branch, Houston Methodist Hospital, Houston, Texas, USA, <sup>2</sup>University of Texas Medical Branch, Galveston, Texas, USA

**Introduction:**

We present a case of a bilateral complete sixth nerve palsy after traumatic left occipital bone fracture.

**Description of Case(s):**

A previously healthy 60-year old woman developed binocular horizontal diplopia following a motor vehicle collision. Diplopia was worse on lateral gazes. Examination was notable for bilateral severe abduction deficit, consistent with a bilateral sixth nerve palsy. BCVA was 20/20 OU and anterior segment and fundus examinations were unremarkable. Computed tomography imaging of the head, neck and face was significant for a left occipital condyle fracture. MRI of the orbit, head and neck was unremarkable. The patient was observed without intervention and did not show any improvement in ocular motility on one and six months follow-up examinations.

**Conclusions, including unique features of the case(s):**

Occipital condyle fractures have been reported to be associated with lower cranial nerve palsies of the 9th through 12th nerves but are very rarely concurrent with unilateral sixth nerve palsies.<sup>1-3</sup> No clinical or radiologic signs of increased intracranial pressure or direct compression of the abducens nerves were noted in this patient. It is possible that the shearing forces at the level of Dorello's canal, the petrous ridge, or the dural entry points caused permanent nerve injury. To our knowledge, this is the first reported case of a bilateral sixth nerve palsy concurrent with a traumatic occipital condyle fracture.

**References:** 1. Utheim NC, Josefsen R, Nakstad PH, Solgaard T, Roise O, Occipital condyle fracture and lower cranial nerve palsy after blunt head trauma: a literature review and case report, *J Trauma Manag Outcomes*, 9, 2, 2015. 2. Lehn AC, Lettieri J, Grimley R, A case of bilateral lower cranial nerve palsies after base of skull trauma with complex management issues: case report and review of the literature, *Neurologist*, 18(3),152-4, 2012. 3. Kim SH, Kim SW, Sixth and twelfth cranial nerve palsies following Basal skull fracture involving clivus and occipital condyle, *J Korean Neurosurg Soc*, 51(5), 305-7, 2012.

**Keywords:** Adult strabismus with a focus on diplopia, Neuroimaging, Ocular Motility, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 122****A Case of Third Nerve Palsy Caused by Pituitary Carcinoma**

Venkatesh Brahma<sup>1</sup>, Adeniyi Fisayo<sup>2</sup>

<sup>1</sup>*Yale-New Haven Hospital, Department of Ophthalmology and Visual Sciences, New Haven, Connecticut, USA,* <sup>2</sup>*Yale-New Haven Hospital, Department of Ophthalmology, Department of Neurology, New Haven, Connecticut, USA*

**Introduction:**

Pituitary carcinomas are rare entities that account for approximately 0.1% of all pituitary tumors (1). Usually presenting in the third to fifth decade of life, pituitary carcinomas, may initially begin as benign tumors that later become aggressive and unresponsive to conventional therapy (1). We present a case of pituitary carcinoma in a female with previously treated hyperprolactinoma.

**Description of Case(s):**

A 52-year-old woman presented left eye pain and diplopia. Her past medical history was significant for left breast cancer (T1aN0M0, ER/PR Positive, Her2 Negative s/p partial mastectomy, on tamoxifen); as well as hyperprolactinemia. Head imaging between 2004 and 2012 was otherwise unremarkable. She was treated with cabergoline from 2004 until the diagnosis of breast cancer was made in June 2016. In April 2017, she developed left sided headaches and eye pain along with binocular diplopia. At that time, neuro-ophthalmologic exam was significant for intact vision in both eyes, mild left upper lid ptosis, anisocoria with a larger left pupil, as well as supra-duction, infra-duction and adduction deficits of the left eye. She was diagnosed with a left third nerve palsy and admitted. MRI of the Brain and Orbits was significant for a non-enhancing lesion of the left cavernous sinus extending lateral to the left ICA. Bloodwork was significant for elevated prolactin levels. She was started on intravenous steroids and oral cabergoline, as it was thought that the mass was possible an ectopic pituitary gland that had grown during the time period that cabergoline was discontinued. In June 2017, she underwent biopsy of the lesion; the pathology was consistent with atypical prolactinoma, with increased proliferative activity, consistent with malignant pituitary carcinoma. Further imaging in the following months revealed metastases throughout the central nervous system.

**Conclusions, including unique features of the case(s):**

This is a rare case of pituitary carcinoma which may have become aggressive in the setting of discontinuation of cabergoline.

**References:** 1) Heaney AP. Clinical review: Pituitary carcinoma: difficult diagnosis and treatment. *J Clin Endocrinol Metab.* 2011;96(12):3649-60.

**Keywords:** Ocular Motility, Tumors, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 123****More Than Just Multiple Meningiomas: A Case Report of an Atypical Cause of Nystagmus**

Jocelyn Kim<sup>1</sup>, Benjamin Osborne<sup>1</sup>

<sup>1</sup>Medstar Georgetown University Hospital, Washington, District of Columbia, USA

**Introduction:**

Paraneoplastic cerebellar degeneration (PCD) is a syndrome of subacute severe pancerebellar dysfunction resulting in ataxia, dysarthria, dysphagia, nystagmus, diplopia, opsoclonus, and progressive visual field loss. PCD is most commonly associated with lung, ovarian, breast cancer, and Hodgkin disease. We describe a patient with an unusual cause of nystagmus, paraneoplastic cerebellar degeneration (PCD) with a negative malignancy work-up.

**Description of Case(s):**

87 year-old female with multiple meningiomas presented with 3 months of binocular horizontal and vertical diplopia. During this time she had also experienced oscillopsia, dizziness, imbalance, but no vertigo. She was referred by neurosurgery to evaluate the cause of her diplopia in the setting of her meningiomas. Repeat MRI suggested that the meningioma in the right occipital lobe had grown in size. She was 20/30 in both eyes, pupils brisk, no afferent pupillary defect. Visual fields were full to confrontation. Her exam was notable for nystagmus, dysmetria in the extremities, mildly slow rapidly alternating movements, ataxic gait, and diminished deep tendon reflexes. Typical lab work-up for downbeat nystagmus which included thiamine, B12, folate, immunofixation, ESR, CRP, syphilis, RF, CCP, GAD65 Ab, ANA and Kappa/Lambda was unremarkable. Paraneoplastic panel was positive for Neuronal Voltage Gated P/Q Type Calcium Channel. Malignancy work-up was negative, which included CT of the chest/abdomen/pelvis, PET scan, and mammogram.

**Conclusions, including unique features of the case(s):**

2 months later, visual acuity decreased to 20/50 in the right eye and 20/60 in the left eye with slight loss of visual fields. She had no change in diplopia, oscillopsia, and ataxia. She received IVIG over 5 days followed by rituximab and had improvement in her symptoms. Previous reports described patients with known malignancy and PCD who responded to IVIG. To the best of our knowledge this is the first reported case of P/Q Type Calcium Channel associated PCD without malignancy treated with IVIG.

**References:** None.

**Keywords:** Nystagmus, Paraneoplastic syndromes

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 124****Gaze Evoked Nystagmus, Cataracts, Ataxia, and Progressive Hearing Loss: A Unique Syndrome**

Devon Cohen<sup>1</sup>, John Chen<sup>1</sup>, Jacqueline Leavitt<sup>1</sup>

<sup>1</sup>Mayo Clinic, Rochester, Minnesota, USA

**Introduction:**

Several rare syndromes characterized by the combination of mental retardation, cataracts, and hearing loss have been described in the literature. We describe a case series of three family members presenting with a distinct constellation of features potentially representing a unique syndrome.

**Description of Case(s):**

Three of the six offspring from a consanguineous marriage were evaluated for a progressive neuro-ophthalmologic syndrome. The patients ranged from ages 19 to 35. Two were female and one was male. All patients presented with bilateral cataracts, nystagmus, gait difficulty, and progressive hearing loss in childhood. Two patients underwent neuro-ophthalmologic evaluation that was significant for gaze evoked nystagmus, jerky smooth pursuits, and star-shaped cortical cataracts. There were no retinal abnormalities. Neurologic exam was remarkable for dysarthria, hyporeflexia, truncal ataxia, and impaired gait. All three patients were found to have marked cerebellar and brainstem atrophy on magnetic resonance imaging, evidence of length-dependent demyelinating sensorimotor peripheral neuropathy on electromyography, and profound bilateral sensorineural hearing loss on audiometry. Speech pathology demonstrated oropharyngeal dysphagia. One sibling underwent mitochondrial DNA testing that revealed a homoplasmic variant of uncertain significance in the gene MTND2. The mitochondrial change is m.4890A>G. Cryopreserved samples were obtained from the remaining family members and the results of further work up are pending. Outside genetic testing was negative for Friedreich's ataxia. Unlike other previously described syndromes involving cataracts and hearing loss, these patients had no evidence of intellectual disability, which was a prominent feature among other cases reviewed in the literature.

**Conclusions, including unique features of the case(s):**

This unique phenotype of gaze evoked nystagmus, cataracts, ataxia, and progressive hearing loss was present in three out of six siblings from a consanguineous marriage. Mitochondrial DNA testing revealed a previously unreported homoplasmic variant that could represent the underlying etiology of this syndrome.

**References:** Begeer, J. H., Scholte, F. A., van Essen, A. J. Two sisters with mental retardation, cataract, ataxia, progressive hearing loss, and polyneuropathy. *J. Med. Genet.* 28: 884-885, 1991. Pfeiffer RA, Stefan J. Familial cataract, non-progressive neurological disorders and mental deficiency: a new X-linked syndrome? *Ophthalmic Paediatr Genet.* 5: 201-203, 1985.

**Keywords:** Genetic Disease, Nystagmus, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 125**

**Saccadic Oscillations as a Possible Indicator of Dizziness Due to Cholinesterase Inhibitors**

Ileok Jung<sup>1</sup>, Moon Ho Park<sup>1</sup>, Jin-Man Jung<sup>1</sup>, Ji-Soo Kim<sup>2</sup>

<sup>1</sup>*Department of Neurology, Korea University Ansan Hospital, Ansan, Korea, Republic of,* <sup>2</sup>*Department of Neurology, Seoul National University Bundang Hospital, Seoung-nam, Korea, Republic of*

**PUBLICATION PERMISSION NOT GRANTED**

**Poster 127**

**Hodgkin Lymphoma Diagnosed on Work-up for Ocular Myasthenia**

Rhiannon Brooks<sup>1</sup>, Nadeem Ali<sup>1</sup>

<sup>1</sup>*Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom*

**Introduction:**

We present a case of inferior rectus weakness with myasthenic features which led to a diagnosis of classic Hodgkin lymphoma.

**Description of Case(s):**

A 47-year-old male in good general health gave a two week history of vertical double vision with diurnal variation. He had recently been treated for a rash on his hands and had succeeded in losing 17lb in weight over 6 months on a calorie-controlled diet. His grandfather had myasthenia gravis. There was no history of ptosis or other neurological symptoms. Examination revealed a small right hypertropia which increased in down-and-right gaze, with moderate underaction of the right inferior rectus. Ductions were full in both eyes. Ptosis was absent but there was mild orbicularis weakness and mild droop of the left side of the mouth. This combination of signs prompted investigation for myasthenia. Acetyl-choline receptor antibodies were negative. Computer tomography (CT) of the thymus revealed no thymoma but incidentally showed mediastinal lymphadenopathy, raising the possibility of malignancy, sarcoid or tuberculosis. Bloods showed neutrophilia, thrombocytosis, mild lactate dehydrogenase elevation, and elevated C-reactive protein. Erythrocyte sedimentation rate, angiotensin-converting enzyme and quantiferon test were normal/negative. Computer tomography (CT) orbits showed subtle thickening of the right inferior rectus, with asymmetry in the calibre of the horizontal recti. Endobronchial ultrasound biopsy revealed classic Hodgkin lymphoma. Full body CT-PET confirmed extensive disease above the diaphragm and possible increased uptake in the extraocular muscles, of uncertain significance. He was commenced on standard (ABVD) chemotherapy and within 10 days his double vision had improved.

**Conclusions, including unique features of the case(s):**

In this case, the diagnosis of Hodgkin lymphoma was made serendipitously during work-up for presumed myasthenia. The cause of the diplopia remains unclear: either direct involvement of the inferior rectus by lymphoma or neuro-muscular junction dysfunction. Myasthenia has been reported to occur in patients with lymphoma, making it another of lymphoma's masquerade presentations.

**References:** 1. Quilichini R1, Fuentes P, Metge G, Lafeuillade A, Albatro J. Myasthenic syndrome disclosing Hodgkin disease. *Rev Neurol (Paris)*, 150(1), 81-2, 1994. 2. Abrey LE. Association of myasthenia gravis with extrathymic Hodgkin's lymphoma: complete resolution of myasthenic symptoms following antineoplastic therapy. *Neurology*, 45(5), 1019, 1995. 3. Tranchant C, Racamier E, Warter JM. Seronegative myasthenia gravis and familial Hodgkin's disease. *Eur Neurol*, 33(1), 17-19, 1993. 4. Roche JC, Capablo JL, Ara JR. Myasthenia gravis in association with extrathymic neoplasia. *Neurologia*, 29(8), 507-9, 2014.

**Keywords:** Myasthenia, Ocular Motility, Tumors, Neuro-opth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 128**

**Acquired Comitant Esotropia following Botulinum Toxin Injection: A Brief Case Series**

Lisa Bennett<sup>1</sup>, Sangeeta Khanna<sup>1</sup>, Onur Melen<sup>2</sup>, Mitchell Strominger<sup>3</sup>, Michael Rosenberg<sup>2</sup>

<sup>1</sup>*Saint Louis University, St Louis, Missouri, USA*, <sup>2</sup>*Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*, <sup>3</sup>*Tufts University Medical Center, New England Eye Center, Boston, Massachusetts, USA*

**Introduction:**

Diplopia is an uncommon but well described side effect of botulinum toxin treatment to the eyelids with an incidence ranging from 1.7 to 2.1%, with small cohorts reporting as high as 14%[1]. Diplopia is typically transient and has been previously described as the result of paresis of one of the extraocular muscles due to diffusion of toxin beyond the orbital septum[2] and most commonly involves the inferior oblique[3] and less frequently the inferior, superior, and lateral rectus[4] leaving an incomitant deviation. To contrast this, we are presenting three cases of comitant esotropia following injection of botulinum toxin to the eyelids and periocular areas.

**Description of Case(s):**

We describe three cases of acute-onset comitant esotropia 1-2 weeks after injection of botulinum toxin to the eyelids and/or periocular areas. Comitant esotropia was noted in each case, ranging from 4 to 25 prism diopters. Esotropia was noted to be worse at distance. There was no evidence of paresis of the lateral recti or any extraocular muscles, including the levator. The diplopia resolved in all three cases over 6-10 weeks, recurring in one after repeat injection.

**Conclusions, including unique features of the case(s):**

Transient comitant esotropia can be a complication of botulinum toxin diffusion beyond the orbital septum. This is similar to divergence insufficiency-type comitant esotropia in older patients related to sagging eye syndrome[5]. We hypothesize that there is a differential susceptibility to botulinum toxin of the orbital layer of the extraocular muscles[6] that inserts on the orbital connective tissue compared to the global layer. This manifests as a divergence insufficiency-type of esotropia without clinically appreciated paresis of muscle in patients with susceptible orbital tissue laxity.

**References:** 1. Ababneh O, Cetinkaya A, Kulwin D. Long-term efficacy and safety of botulinum toxin A injections to treat blepharospasm and hemifacial spasm. *Clinical and Experimental Ophthalmology* 2014; 42:254-261. 2. Aristodemou, P, Watt L, Baldwin C, Hugkulstone C. Diplopia Associated with the Cosmetic Use of Botulinum Toxin A for Facial Rejuvenation. *Ophthal Plast Reconstr Surg* Vol 22, No. 2, 2006. 3. Wutthiphan, O'Day, Price. Diplopia Following Subcutaneous Injections of Botulinum A Toxin for Facial Spasms. *J Pediatr Ophthalmol Strabismus* 1997;34:229-234. 4. Soo-Keun Lee, Hee Jin Jun. Esotropia following botulinum toxin type A injection for facial wrinkles. *Journal of Cosmetic and Laser Therapy*. DOI: 10.1080/14764172.2017.1349322 5. Chaudhuri Z, Demer JL. Sagging Eye Syndrome: Connective Tissue Involution as a Cause of Horizontal and Vertical Strabismus in Older Patients. *JAMA ophthalmology*. 2013;131(5):619-625. 6. Ugalde I, Christiansen SP, McLoon LK. Botulinum Toxin Treatment of Extraocular Muscles in Rabbits Results in Increased Myofiber Remodeling. *Investigative ophthalmology & visual science*. 2005;46(11):4114-4120.

**Keywords:** Adult strabismus with a focus on diplopia, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 129**

**A Case of Cavernous Sinus Thrombosis with Acute Sinusitis in Children**

Young Hoon Jung<sup>1</sup>, Hae-ri Yum<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology, Konyang University College of Medicine, Daejeon, Korea, Republic of*

**Introduction:**

Cavernous sinus thrombosis is a rare disease that can occur as a complication of orbital cellulitis and sinusitis. We report a case of unilateral cavernous sinus thrombosis with acute sinusitis in children suffering upper lid ptosis, a limitation of ocular movement, and visual disturbance.

**Description of Case(s):**

A 6-year-old girl presented with monocular ptosis and binocular diplopia for 2 days. The patient received oral antibiotic agent for 3 days at the otorhinolaryngology department, as diagnosed with acute sinusitis. However, ptosis of the left eye and diplopia occurred. On the alternative prism cover test, she manifested above 50 prism diopter (PD) exotropia in the primary position with ocular movement limitation in adduction (-3), upgaze (-4), and downgaze (-4) of her left eye. Brain magnetic resonance imaging revealed inflammatory infiltration involving left orbital apex and left cavernous sinus. Asymmetric enlargement of left superior ophthalmic vein and dural thickening suggested left cavernous sinus thrombosis. Functional endoscopic sinus surgery was performed immediately. Systemically, the patient was treated with intravenous antibiotic injection for 4 weeks. The Gram stain of the specimen revealed Gram-positive cocci but no specific strain was cultured. By 3 months postoperatively, the patient had marked improvement in visual acuity, ptosis, diplopia and ocular movement limitation.

**Conclusions, including unique features of the case(s):**

Cavernous sinus thrombosis is a rare complication of orbital and sinus inflammatory disease. Accurate clinical suspicion, early neurologic imaging, and an appropriate approach to treatment are important factors in reducing aftereffect.

**References:** Frank GS, Smith JM, Davies BW, Mirsky DM, Hink EM, Durairaj VD. Ophthalmic manifestations and outcomes after cavernous sinus thrombosis in children. *J AAPOS*. 2015 Aug;19(4):358-62.

**Keywords:** Pediatric Neuro-Ophthalmology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 130**

**Optical Coherence Tomography Angiography vs Fluorescein Angiography in Leber's Hereditary Optic Neuropathy (LHON)**

Nagham Al-Zubidi<sup>1</sup>, Joseph Nayfach<sup>2</sup>, Jaspreet Jakhu<sup>1</sup>, Jade Schiffman<sup>3</sup>, AMA SADAKA<sup>4</sup>, Rosa Tang<sup>1</sup>

<sup>1</sup>Neuro-Ophthalmology of Texas/ Blanton Eye Institute, Houston Methodist Hospital, Houston, Texas, USA, <sup>2</sup>University of Optometry, Houston, Texas, USA, <sup>3</sup>Neuro-Ophthalmology of Texas/MS Eye Card, Houston, Texas, USA, <sup>4</sup>University of Beirut, Beirut, Lebanon

**Introduction:**

LHON is a mitochondrial disease with sequential, bilateral and dramatic vision loss. The initial clinical presentation of LHON is often subtle with optic disc and peripapillary vascular changes that are frequently missed on funduscopy. In addition, the typical lab work for optic neuropathies, are usually unremarkable and can lead to challenging delays in diagnosis. Further the genetic marker for Leber's disease may take quite some time to process. While current treatment may not reverse the dramatic vision loss, it may slow the disease process in hopes of preserving some vision. Given the inherent challenge in diagnosing LHON. Optical Coherence Tomography Angiography (OCT-A) is a novel technique for non-invasive visualization of retinal, optic nerve and choroidal vasculature. While identification of vascular changes in LHON, including peripapillary telangiectasia without leakage, can be made with Fluorescein Angiography (FA), the recent availability of OCT-A offers a rapid diagnostic technique that can aid clinicians to be cognizant of the possibility that the patient may harbor LHON.

**Description of Case(s):**

A 16-year-old male presented with acute onset of sequential bilateral vision loss. He was treated locally with IV MP for 5 days and PLEX with no response. Work up includes MRI of brain, orbit, spine, CSF, OCB, and NMO were negative. Neuro-ophthalmic exam revealed bilateral cecocentral scotomas and minimal disc pallor. Final diagnosis was LHON with positive chromosomal mutation of rs781448429. Herein we are describing the changes on OCT-A compared with traditional FA over an extended observational period of the patient on Idebenone. We also describe findings on OCT-A for the patient's asymptomatic mother and brothers.

**Conclusions, including unique features of the case(s):**

We hypothesize that optical Coherence Tomography Angiography (OCT-A) offers a noninvasive diagnostic technique that can aid clinicians to detect subtle optic disc changes in LHON.

**References:** 1. Carelli, V. et al. International Consensus Statement on the Clinical and Therapeutic Management of Leber's Hereditary Optic Neuropathy. *J. Neuro-Ophthalmol. Off. J. North Am. Neuro-Ophthalmol. Soc.* (2017). doi:10.1097/WNO.0000000000000570 2. Chalam, K. V. & Sambhav, K. Optical Coherence Tomography Angiography in Retinal Diseases. *J. Ophthalmic Vis. Res.* 11, 84–92 (2016). 3. Jurkute, N. & Yu-Wai-Man, P. Leber hereditary optic neuropathy: bridging the translational gap. *Curr. Opin. Ophthalmol.* 28, 403–409 (2017). 4. Rojas, J. O. D., Rasool, N., Chen, R. W. S., Horowitz, J. & Odel, J. G. Optical coherence tomography angiography in Leber hereditary optic neuropathy. *Neurology* 87, 2065–2066 (2016). 5. Takayama, K. et al. Optical coherence tomography angiography in leber hereditary optic neuropathy. *Acta Ophthalmol. (Copenh.)* 95, e344–e345 (2017). 6. Gaier, E. D., Gittinger, J. W., Cestari, D. M. & Miller, J. B. Peripapillary Capillary Dilation in Leber Hereditary Optic Neuropathy Revealed by Optical Coherence Tomographic Angiography. *JAMA Ophthalmol.* 134, 1332–1334 (2016).

**Keywords:** Genetic Disease, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy, Orbit/ocular pathology, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 131**

**Thyroid-Associated Ophthalmopathy Presenting as Superior Rectus and Levator Palpebrae Enlargement**

Angeline Nguyen<sup>1</sup>, Timothy McCulley<sup>1</sup>, Amanda Henderson<sup>1</sup>

<sup>1</sup>*Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, USA*

**Introduction:**

Enlargement of the extraocular muscles, most commonly the inferior and medial rectus muscles, is a hallmark of thyroid-associated ophthalmopathy (TAO). In this report, we describe an unusual presentation, with involvement limited to the superior rectus and levator palpebrae muscles.

**Description of Case(s):**

A 53-year-old previously healthy man presented with three months of right eye proptosis and upper eyelid retraction. Exam revealed 20/20 visual acuity in both eyes, no relative afferent pupillary defect, 50% deficit in elevation and abduction of the right eye, and 4.5mm of right-sided proptosis. MRI of the orbits revealed diffuse enlargement of the right superior rectus muscle body and tendon with mild inflammation in the surrounding fat. Notably, the levator palpebrae was distinctly enlarged. TSH, total T3, and free T4 were normal. TSI was elevated to 419 (normal <140). Treatment with prednisone 80mg daily was initiated for possible orbital inflammatory syndrome. His symptoms and examination did not improve. Moreover, repeat MRI four months later demonstrated increased superior rectus and levator palpebrae enlargement. Biopsy revealed chronic non-specific inflammation, consistent with TAO. Visual acuity and perimetry findings declined, consistent with a compressive optic neuropathy, prompting orbital decompression and orbital radiation daily for two weeks. Afferent visual function (acuity/perimetry) returned to normal. His thyroid function remained unchanged.

**Conclusions, including unique features of the case(s):**

This case illustrates the potential for TAO to present initially as unilateral superior rectus and levator palpebrae enlargement in the absence of thyroid dysfunction. Motility also was atypical, in that it more closely mimicked a paretic than restrictive pattern. In the setting of an otherwise atypical presentation, levator palpebrae enlargement causing upper eyelid retraction supports a diagnosis of TAO. Recognition of this presentation is critical to the institution of appropriate therapy and vigilance in monitoring for endocrinopathy.

**References:** None.

**Keywords:** Orbit, Orbit/ocular pathology, Graves (systemic disease), Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 132

### Pituitary Adenoma Apoplexy of the Orbit

Nickisa Hodgson<sup>1</sup>, Jessica Chang<sup>1</sup>, Adelita Vizcaino<sup>1</sup>, Sarah DeParis<sup>1</sup>, Lilangi Ediriwickrema<sup>5</sup>, Charles Eberhart<sup>1</sup>, Timothy McCulley<sup>1</sup>

<sup>1</sup>The Wilmer Eye Institute Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

#### Introduction:

Descriptions of pituitary adenomas invading the orbit are extremely uncommon with patients presenting with diminishing visual function and proptosis.[1,2] In this report, we describe an elderly patient with hemorrhage of a pituitary tumor within the orbit. To our knowledge this is the only description of a patient diagnosed with pituitary apoplexy of the orbit. We present the first reported case of a female with a large invasive and hemorrhagic prolactinoma of the orbit.

#### Description of Case(s):

A 71-year-old female with a history of prolactinoma treated with transphenoidal resection, chemotherapy, and radiation in 1990, presented with progressive proptosis of the right eye over several weeks. Right globe displacement with ipsilateral optic nerve dysfunction had slowly progressed for several years. Weeks prior to presentation, proptosis and visual loss rapidly progressed (Figure 1). Notable findings on evaluation of the right eye included right visual acuity of 20/200, a relative afferent pupillary defect, 12 mm of relative proptosis, and markedly restricted extraocular movements. MRI demonstrated a 4.2 cm heterogeneous, contrast enhancing intraconal mass. CTA findings were consistent with a cystic hemorrhagic mass (Figure 2). Biopsy demonstrated a highly vascular, poorly defined infiltrative tumor with large hemorrhage-filled cavities (Figure 3). Histopathology was consistent with pituitary adenoma apoplexy, with cells staining positive for prolactin admixed with hemorrhage. A right orbital exenteration was performed as the patient continued to have worsening proptosis and pain.

#### Conclusions, including unique features of the case(s):

We describe a patient who presented with progressive proptosis due to orbital involvement of a hemorrhagic prolactinoma. Orbital invasion of a prolactinoma portends a poor visual prognosis. Symptomatic control or improvement may be achieved with surgical resection or radiation therapy.[3] Rapidly worsening proptosis in orbital prolactinomas may suggest apoplexy of the tumor, and CTA may be useful in confirming the diagnosis.[4] To our knowledge this is the first description of pituitary adenoma apoplexy of the orbit.

**References:** 1. Karcioğlu ZA, Aden LB, Cruz AA, Zaslow L, Saloom RJ. Orbital invasion with prolactinoma: a clinical review of four patients. *Ophthal Plast Reconstr Surg.* 18(1):64-71, 2002. 2. Siddiqui A, Chew N, Miszkiel K. Case report: Unusual orbital invasion by a giant prolactinoma. *Br J Radiol.* 81(971):e259-62, 2008. 3. Vaudaux J, Portmann L, Maeder P, Borruat FX. Orbital invasion by a pituitary macroadenoma without visual loss: case report and view of the literature. *Eye.* 17, 1032-1034, 2003. 4. Van de Straete S, Githeko J, Demaerel P, Wilms G, Lammens M, Plets C, Bouillon R, Baert AL. Aggressive pituitary macroadenoma: CT and MR appearances. *J Belge Radiol.* 79(6):255-7, 1996.

**Keywords:** Orbit, Orbit/ocular pathology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 133**

**A Longhorn-Induced Superior Orbital Fissure Syndrome: A Case Report**

Kimberly Nguyen<sup>1</sup>, Ama Sadaka<sup>2</sup>, Amina Malik<sup>2</sup>

<sup>1</sup>University of Texas Health Science Center at Houston, Houston, Texas, USA, <sup>2</sup>Houston Methodist Hospital, Houston, Texas, USA

**Introduction:**

Superior orbital fissure syndrome is a rare condition with a well-defined clinical presentation. Key clinical features include ophthalmoplegia, ptosis, impaired extraocular muscle function, proptosis, and paresthesia of the frontal region. These symptoms arise from damage to the neurovascular contents in the fissure. Standard treatment protocol does not currently exist due to the rarity of the condition. Treatment options described include conservative observation, versus steroids or surgery.

**Description of Case(s):**

We report an unusual case of a 74-year-old male who suffered a penetrating eyelid injury that occurred when a longhorn abruptly turned his head, broke the patient's eyeglasses, and hit him directly in the left eyelid. The patient had diplopia, ptosis, and pain, but no loss of consciousness. Ocular motility exam showed complete ophthalmoplegia in the left eye. External examination of the left eye revealed complete ptosis, moderate periorbital ecchymosis and edema, and a one centimeter laceration on the nasal upper eyelid with fat prolapse, indicating violation of the orbital septum. Computed tomography scan revealed mild left proptosis and a small, superonasal air pocket adjacent to the medial rectus postseptally, without evidence of globe injury. These findings were consistent with superior orbital fissure syndrome. Eyelid laceration exploration revealed no foreign body in the wound. The wound was irrigated with bacitracin solution and the skin was sutured. The patient did not receive steroids or surgical intervention. He showed progressive improvement of diplopia and extraocular motility throughout follow up, and his symptoms resolved completely without complications over a 4-month period.

**Conclusions, including unique features of the case(s):**

No other studies demonstrate upper eyelid laceration with superior orbital fissure syndrome caused by a longhorn injury, resolving completely with conservative management. This case demonstrates that observation alone may be effective and prevents risks associated with steroid use and surgical complications in geriatric patients.

**References:** None.

**Keywords:** Orbit, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 134****Transorbital Embolization of a Thrombosing Carotid Cavernous Fistula**

Lance Lyons<sup>1</sup>, Andrew Lee<sup>2</sup>

<sup>1</sup>University of Texas Medical Branch, Galveston, Texas, USA, <sup>2</sup>Blanton Eye Institute; University of Texas Medical Branch; Baylor College of Medicine, Houston, Texas, USA

**Introduction:**

Transorbital embolization of carotid cavernous fistulas (CCFs) is uncommon but remains an option in cases of constricted or tortuous ophthalmic veins.[1]

**Description of Case(s):**

An 86 year old man presented with acute unilateral severe proptosis, pain and vision loss. Over the past year he had episodes of left sided blurry vision and mild eyelid swelling; additionally, he was recently diagnosed with glaucoma and started on pressure-lowering medications. Cerebral angiogram performed one year prior revealed an incidental small right sided type D CCF with drainage exclusively via the petrosal sinuses. At the time it was asymptomatic and treated with observation. The vision was hand motion and the intraocular pressure too high to be measured. The left eye was swollen shut with a relative afferent pupillary defect and complete ophthalmoplegia. Fundus exam after lateral canthotomy revealed neither retinal artery nor vein occlusion, nor anterior ischemic optic neuropathy. Catheter angiogram identified the fistula in the intercavernous sinus draining into the partially thrombosed left cavernous sinus and orbit. Transarterial embolization was unsuccessful, and upon transvenous attempt the superior ophthalmic vein was also partially thrombosed; the inferior ophthalmic vein was inaccessible. Therefore, the patient underwent successful percutaneous transorbital direct cavernous sinus puncture and fistula embolization.

**Conclusions, including unique features of the case(s):**

Risks of subarachnoid hemorrhage, globe puncture, internal carotid artery laceration and cranial nerve injury with transorbital puncture exist but are low in reported studies of the technique.[2] Treatment was warranted to prevent cortical venous drainage, venous hypertension or hemorrhage, and contralateral involvement.

**References:** [1] Phan K, Xu J, Leung V, Teng I, Sheik-Ali S, Maharaj M, Mobbs R, Rao P. Orbital approaches for treatment of carotid cavernous fistulas: a systematic review. *World Neurosurg.* 2016;96:243-251. [2] White JB, Layton KF, Evans AJ, Tong FC, Jensen ME, Kallmes DF, Dion JE, Cloft HJ. *Am J Neuroradiol.* 2007;28(7):1415-1417

**Keywords:** Interventional neuroradiology, Neuroimaging, Orbit, Skull Base, Vascular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 135

### Recurrent Fibrous Dysplasia

Nickisa Hodgson<sup>1</sup>, Jessica Chang<sup>1</sup>, Adelita Vizcaino<sup>1</sup>, Charles Eberhart<sup>1</sup>, Andrew Carey<sup>1</sup>, Amanda Henderson<sup>1</sup>, Timothy McCulley<sup>1</sup>

<sup>1</sup>The Wilmer Eye Institute Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

#### Introduction:

Fibrous dysplasia is a benign disease of the bone characterized by the replacement of normal bone with fibro-osseous tissue. We present an aggressive case of a recurrent fibro-osseous lesion.

#### Description of Case(s):

A 29-year-old male presented with three months of right proptosis and diplopia. His visual acuity was 20/20 in both eyes and there was no afferent pupillary defect. He had 3 mm of relative proptosis, restriction in upgaze in the right eye, and a firm lesion over the right zygoma. Computed tomography (CT) imaging revealed a partially calcified and lytic lesion of the right lateral orbital wall displacing the right globe with extension in the infratemporal fossa (Figure 1). Orbitotomy with biopsy revealed a fibro-osseous lesion consistent with fibrous dysplasia and the patient underwent subsequent resection of the mass. He presented three months later with inability to elevate the right brow and recurrent right globe displacement that developed over one month. CT imaging revealed significant progression of the osseous lesion with lytic lesions in the bone (Figure 2). A biopsy after local recurrence demonstrated fibrous dysplasia with areas of hypercellularity; however, there was no atypia and MDM2 stain for osteosarcoma was negative. Given the rapid recurrence and areas of hypercellularity, he underwent complete wide excision for tumor control.

#### Conclusions, including unique features of the case(s):

Cortical bone destruction and soft tissue extension on imaging suggests malignant transformation into a sarcoma.[1] An extremely rare form of locally aggressive fibrous dysplasia has been reported that demonstrates cortical destruction and extension into soft tissue without malignant transformation.[2,3] It is crucial to distinguish between locally aggressive disease and malignant transformation. Radiologic features are non-specific and do not differentiate between locally aggressive fibrous dysplasia and malignant transformation. A biopsy is necessary for definitive diagnosis and pathologic features indicative of malignant transformation include hypercellularity, nuclear atypia, and positive immunohistochemistry for CDK2, MDM2 and GNAS mutations.[4]

**References:** 1. Qu N, Yao W, Zhang H. Malignant transformation in monostotic fibrous dysplasia: clinical features, imaging features, outcomes in 10 patients, and review. *Medicine (Baltimore)*. 94(3):e369, 2015. 2. Muthusamy S, Subhawong T, Conway SA, Temple HT. Locally aggressive fibrous dysplasia mimicking malignancy: A report of four cases and review of the literature. *Clin Orthop Relat Res*. 473(2): 742-750, 2015. 3. Kashima TG, Gamage NM, Ye H, Amary MF, et al. Locally aggressive fibrous dysplasia. *Virchows Arch*. 463(1):79-84, 2013. 4. Dujardin F, Binh MB, Bouvier C, Gomez-Brouchet A. MDM2 and CDK4 immunohistochemistry is a valuable tool in the differential diagnosis of low grade osteosarcomas and other primary fibro-osseous lesions of the bone. *Mod Pathol*. 24(5):624-627, 2011.

**Keywords:** Orbit, Neuroimaging, Orbit/ocular pathology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 136**

**Orbital Apex Syndrome as a Complication of Herpes Zoster Ophthalmicus: Role of Systemic Steroids**

Elizabeth Cretara<sup>1</sup>, Wendy Chen<sup>1</sup>

<sup>1</sup>*The Warren Alpert Medical School of Brown University, Providence, Rhode Island, USA*

**Introduction:**

Orbital apex syndrome (OAS) manifesting as optic neuritis with multiple cranial nerve palsies is an uncommon complication of Herpes Zoster Ophthalmicus (HZO).

**Description of Case(s):**

A 65-year-old man with chronic obstructive pulmonary disease (COPD) presented to a tertiary care center with six days of left eye irritation and redness followed by a vesicular rash involving his left eyelid. The patient's best corrected visual acuity was 20/25 OD 20/40 OS. His exam was significant for eyelid edema and conjunctival injection. A computed tomography scan without contrast showed induration of the preseptal and periorbital soft tissues. The patient was admitted for management of HZO and a concurrent COPD exacerbation. His pre-admission dose of oral prednisone was increased from 30 to 40 mg and intravenous acyclovir was started. On hospital day three, the patient developed left-sided ptosis, ophthalmoplegia and a mid-dilated fixed pupil. A magnetic resonance imaging of the brain with and without contrast demonstrated enhancement of the left optic nerve sheath, pre-septal and post-septal soft tissues, and inferior and medial rectus muscles. Upon diagnosis of OAS, the prednisone dose was increased to 60 mg which was continued at discharge along with oral valacyclovir. At two weeks, prednisone was tapered to 40 mg daily. After two months, his orbital symptoms resolved and the patient was tapered off prednisone.

**Conclusions, including unique features of the case(s):**

This case underscores the difficulty in determining the role of systemic steroids in treating HZO-OAS. The patient developed OAS while taking a chronic dose of oral prednisone for COPD. While the evidence base is poor, antivirals are commonly used for HZO-OAS, while use of systemic corticosteroid varies. More studies are needed to determine the role of systemic steroids in the management of HZO-OAS.

**References:** None.

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion), Orbit/ocular pathology, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 137**

**Eosinophilic Variant of Orbital Granulomatosis with Polyangiitis with Hyperimmunoglobulinemia E: A Case Report**

Ji Eun Lee<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology, Maryknoll Medical Center, Busan, Korea, Republic of*

**Introduction:**

The eosinophilic variant of granulomatosis with polyangiitis (GPA) is rare condition with unknown etiology. To describe a patient with limited orbital GPA who had significant eosinophilia and hyperimmunoglobulinemia E (hyper-IgE).

**Description of Case(s):**

A 61-year-old man with a history of diabetes mellitus complained of left ptosis and periorbital edema for 2 days. He had no history of allergy, atopy, asthma, sinonasal disease, respiratory disease, or renal disease. On examination, visual acuity was 20/20 in both eyes. On slit lamp examination, severe conjunctival injection and chemosis of left eye was noted but there was no tenderness or proptosis. He had a left hypertropia of 4 prism diopters with limitation of abduction, supraduction and infraduction. Laboratory studies revealed normal urinalysis and creatinine, an elevated level of high-sensitivity C-reactive protein, normal WBC count with 28.3% eosinophils and high serum IgE levels 400 IU/ml. Anti-neutrophil cytoplasmic antibody (ANCA) was proteinase 3 (PR3) positive and myeloperoxidase negative. Parasite and allergy testing as well as chest X-ray, nasal endoscopy were normal. Magnetic resonance imaging identified an inferolateral orbital mass with an enlarged lacrimal gland, myositis of lateral rectus muscle, high signal intensity of the retrobulbar fat, linear signal change of the optic nerve sheath in his left eye. Lacrimal gland biopsy revealed that nonspecific chronic inflammation interspersed with eosinophilic infiltrate. The existence of PR3-ANCA with the clinical and pathologic findings led to the diagnosis of eosinophilic variant of limited orbital GPA with hyper-IgE.

**Conclusions, including unique features of the case(s):**

High level of IgE and eosinophilia in limited form of GPA may represent a local hypersensitivity reaction toward an unrecognized exogenous allergen suggesting an etiologic mechanism of this disease. This unique presentation may attribute to identify its association with underlying pathogenesis.

**References:** None.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 138****Metastatic Orbital Disease with Positive Immunohistochemical test for Breast Cancer without Primary Tumor.**

Sheikh Faheem<sup>1</sup>, Joshua Pasol<sup>1</sup>, Byron Lam<sup>1</sup>

<sup>1</sup>Bascom Palmer Eye Institute, University of Miami, FL, Miami, Florida, USA

**Introduction:**

Metastatic orbital disease is rare but it must be considered in the differential diagnosis of any patient with known history of cancer, presenting with ophthalmic symptoms. (1-4). Most ocular metastases of breast cancer are located in the choroid, while an extrabulbar localization within the orbit is rare, with only 3-10% of all ocular metastases. Breast carcinoma is the most prevalent primary tumor in metastatic orbital tumor, accounting for 28.5%–58.8% of all metastases followed by lung, prostate, gastrointestinal, kidney and skin (melanoma) cancers (4). Ocular metastasis can be initial manifestation of breast carcinoma, in some data up to 26% of orbital breast metastases (5).

**Description of Case(s):**

A 79-year-old woman with history of colon mass diagnosed as adenocarcinoma with positive HER-2 receptor but unknown primary and negative breast mass was evaluated for worsening diplopia. Her exam was remarkable for progressive restrictive strabismus. Her preliminary diagnosis was thyroid ophthalmopathy vs. idiopathic orbital inflammatory pseudotumor and recommended prednisone that she refused until evaluation by Neuro-Ophthalmology. Repeat MRI showed enlargement of multiple extraocular muscles with mild enhancement. Pattern was not consistent with typical thyroid ophthalmopathy. Patient underwent medial orbitotomy with left exploration and biopsy of extraocular muscle (LMR). Pathology report was significant for orbital metastatic disease with breast primary (immunohistochemical staining demonstrated ER/PR positivity, negative staining for HER-2/neu). She was referred to oncology for further systemic chemotherapy and orbital radiation therapy. Patient received radiation therapy (total dose delivered 3910 cGy), hormonal therapy (Anastrozole & Tamoxifen) and chemotherapy (Paclitaxel and Carboplatin). Her cancer marker (CA 27-29) decreased from 200 to 78. Her diplopia improved with Fresnel prism.

**Conclusions, including unique features of the case(s):**

This case highlights the difficulty in identifying a metastatic orbital tumor that initially mimics inflammatory orbital disease and thyroid ophthalmopathy. In a patient with atypical clinical course, imaging and biopsy are critical for diagnosis and management.

**References:** 1. Dieing A, Schulz CO, Schmid P, Roever AC, Lehenbauer-Dehm S, Jehn C, et al. Orbital metastases in breast cancer: report of two cases and review of the literature. *Journal of cancer research and clinical oncology*. 2004;130(12):745-8. 2. Raap M, Antonopoulos W, Dammrich M, Christgen H, Steinmann D, Langer F, et al. High frequency of lobular breast cancer in distant metastases to the orbit. *Cancer medicine*. 2015;4(1):104-11. 3. Tabai M, Hazboun IM, Sakuma ET, Sampaio MH, Sakano E. Orbital Metastasis of Breast Cancer Mimicking Invasive Fungal Rhinosinusitis. *Case reports in otolaryngology*. 2016;2016:2913241. 4. Vlachostergios PJ, Voutsadakis IA, Papandreou CN. Orbital metastasis of breast carcinoma. *Breast cancer : basic and clinical research*. 2009;3:91-7. 5. Goldberg RA, Rootman J, Cline RA. Tumors metastatic to the orbit: a changing picture. *Survey of ophthalmology*. 1990;35(1):1-24.

**Keywords:** Ocular Motility, Neuroimaging, Chemotherapy and radiation injury, Orbit/ocular pathology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 139****Headaches And Diplopia Secondary To Ipilimumab Treatment For Stage III Melanoma**

Geetha Athappilly<sup>1</sup>

<sup>1</sup>*Lahey Hospital and Medical Center, Burlington, Massachusetts, USA*

**Introduction:**

Diplopia and headaches is an ominous sign for intracranial spread in patients with malignancy. However, it is important for clinicians to review chemotherapy medications as a potential cause of symptoms.

**Description of Case(s):**

A 28-year old female with stage III melanoma and a prior history of a clinically isolated, steroid responsive, optic neuritis OD, began treatment with Ipilimumab. After her second treatment of Ipilimumab she developed severe throbbing headaches, nausea and vomiting. Initial MRI brain showed slight prominence of the pituitary gland with intact pituitary function. Re-imaging two weeks later due to persistent headaches showed clear enlargement and enhancement of the pituitary gland and stalk suggestive of autoimmune hypophysitis. Her headaches temporarily resolved with IV solumedrol but she developed recurrence of headaches and painful diplopia on a lower prednisone dose. MRI of the orbits revealed enlargement and enhancement of the right inferior and lateral rectus. At time of presentation, her exam showed findings of prior optic neuritis with a right APD, vision of 20/25 OD and limitation of her extra-ocular movements. Extraocular movements revealed complete limitation of abduction and infraduction on the right with positive forced ductions. Within 24 hours of retreatment with IV methylprednisolone she had complete resolution of her eye pain, headaches and improvement of her motility. After 1 month, while on prednisone, her diplopia nearly resolved. Repeat imaging revealed resolution of enlarged and enhancing pituitary gland and extra-ocular muscles.

**Conclusions, including unique features of the case(s):**

This case describes a rare immune related side effect of Ipilimumab. Although Ipilimumab can be associated with a variety of Immune related adverse effects (IRAE), orbital pathology is not common. Treatment with IV steroids often leads to rapid improvement of pain, symptoms and abnormal imaging findings, differentiating the disease from spread of melanoma.

**References:** 1. Pushkarevskaya A, Neuberger U, Dimitrakopoulou-Strauss A et al. Severe Ocular Myositis After Ipilimumab Treatment for Melanoma: A Report of 2 Cases. *J Immunother* . 2017;00:1-4. 2. Borodic G, Hinkle DM, Cia Y. Drug-induced Graves disease from CTLA-4 receptor suppression. *Ophthal Plast Reconstr Surg*. 2011;27:e87–e88. 3. Henderson AD, Thomas DA. A case report of orbital inflammatory syndrome secondary to ipilimumab. *Ophthal Plast Reconstr Surg*. 2014:e68–e69. 4. Papavasileiou E, Prasad S, Freitag SK, et al. Ipilimumab-induced Ocular and Orbital Inflammation—A Case Series and Review of the Literature. *Ocular Immunology & Inflammation*, 2016; 24(2): 140–146 5. Lecouflet M, Verschoore M, Giard C, et al. Orbital myositis associated with ipilimumab. *Ann Dermatol Venereol*. 2013; 140:448–451.

**Keywords:** Ocular Motility, Neuroimaging, Adult strabismus with a focus on diplopia

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 140****Trochleitis Without Imaging Abnormality**

Yan Ning Neo<sup>1</sup>, Ashok Adams<sup>1</sup>, Greg Richardson<sup>1</sup>, Naz Raoof<sup>2</sup>

<sup>1</sup>The Royal London Hospital, Barts Health NHS Trust, UK, London, United Kingdom, <sup>2</sup>The Royal London Hospital, Barts Health NHS Trust; Moorfields Eye Hospital, London, United Kingdom

**Introduction:**

Trochleitis is an uncommon inflammation of the trochlea/peritrochlear region, and there are relatively few reports to guide management in the scientific literature. Clinically, there is characteristic pain and tenderness over the trochlea and pain on vertical ductions. Orbital imaging can show localised swelling and superior oblique inflammation. We report a case of trochleitis, diagnosed clinically, with no demonstrable radiological features, successfully managed by peritrochlear injection of dexamethasone/lidocaine.

**Description of Case(s):**

A 38-year-old female physician presented with a month history of increased pain in the left supra-nasal orbital area, with exquisite pain on direct trochlear palpation, aggravated by vertical ductions. She had an existing diagnosis of left trochleitis 6 years prior and used oral indomethacin during episodes of trochlear pain. In childhood, she had undergone left horizontal muscle strabismus surgery for Duane's syndrome with good ocular alignment. The past medical history included sero-negative arthropathy and recurrent plantar fasciitis. A MRI of the brain and orbits demonstrated no abnormalities. The patient had self-prescribed a course of low dose oral prednisolone, with no effect. Based on the history and examination findings, with exquisite tenderness directly over the trochlea, she underwent a left peritrochlear injection of dexamethasone 3.3mg and lidocaine. Her symptoms resolved immediately and 2 months following the procedure she remains pain free with no post-procedural complication.

**Conclusions, including unique features of the case(s):**

Although a largely clinical diagnosis, neuro-imaging is useful in diagnosing trochleitis as it may reveal confirmatory signs, as well as exclude differentials such as orbital inflammatory disorders or frontal sinus pathology. Our patient, who had a normal MRI brain and orbits, responded very well to peritrochlear injection of dexamethasone/lidocaine, which abolished all the symptoms and signs of trochleitis. Our case report adds to the evidence that MRI trochlear/peritrochlear changes do not have to be present for a local injection to be worthwhile.

**References:** Smith JH, Garrity JA, Boes CJ. Clinical features and long-term prognosis of trochlear headaches. *Eur J Neurol.* 21(4):577-85, 2014 Apr. Jarrín E, García-García Á, Hurtado-Ceña FJ, Rodríguez-Sánchez JM. Clinical Characteristics, Treatment, and Outcome of Trochleitis. *Strabismus.* 25(1):1-4. 2017 Mar.

**Keywords:** Orbit/ocular pathology, Orbit, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 141****Painful Horner Syndrome as a Presentation of Nasopharyngeal Carcinoma: A Carotid Dissection Mimicking Lesion.**

Tanyatuth Padungkiatsagul<sup>1</sup>, Anuchit Poonyathalang<sup>1</sup>, Panitha Jindahra<sup>1</sup>, Piyaphon Cheecharoen<sup>1</sup>, Kavin Vanikiet<sup>1</sup>

<sup>1</sup>*Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

**Introduction:**

Horner syndrome refers to a set of clinical presentations resulting from disruption of sympathetic innervation to ocular and adnexa. Classically, clinical triad consists of ipsilateral blepharoptosis, pupillary miosis and facial anhidrosis. The lesion responsible for Horner syndrome can occur anywhere along ocular sympathetic pathway. Ocular sympathetic denervation may signify the life-threatening causes such as carotid dissection, brainstem infarction and malignancies. A patient with painful oculosympathetic denervation, timely accurate investigation and diagnosis are essential.

**Description of Case(s):**

A 33-year-old Asian male presented with ptosis in his left eye for 3 weeks, along with dull pain on left-sided of his face. Visual acuity was 20/20 bilaterally. Intraocular pressure and ocular movement were unremarkable. His ophthalmic examination was significant for mild ptosis in his left eyelid and anisometropic pupil, which greater in the dark. Both pupils were reacted to light briskly without afferent pupillary defect. Anhidrosis was found on the medial side of left forehead. 10% cocaine test was positive. His neurologic examination revealed hypoesthesia in the area of CN V1-3 territories. Emergency computerized tomography angiography (CTA) showed luminal narrowing of petrous part of left internal carotid artery (ICA); ICA dissection was suspected. Further magnetic resonance imaging (MRI) demonstrated enhancing infiltrative lesion epicenter at central skull base and left sphenoid bone. The lesion encased the left ICA and invaded left Meckel's cave and left sphenoid wing. Rhinoscopy with incisional biopsy was performed, which showed squamous cell nasopharyngeal carcinoma (NPC) pathologically.

**Conclusions, including unique features of the case(s):**

This is an unusual presentation of NPC, including Horner syndrome, facial pain and trigeminal hypoesthesia. Lesion involving Meckel's cave and ICA at the foramen lacerum can present with postganglionic Horner syndrome associated with trigeminal pain and hypoesthesia. These clinical findings may mimic carotid artery dissection. Detailed MRI with careful attention to base of skull should be further performed.

**References:** None.

**Keywords:** Skull Base, Tumors, Neuroimaging, Pupils Retina

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 142**

**Bilateral Carotid Body Paragangliomas Presenting with An Isolated Horner's Syndrome**

Shuai-Chun Lin<sup>1</sup>, Richard Becker<sup>2</sup>, Robert Lesser<sup>3</sup>

<sup>1</sup>The Eye Care Group, Orange, Connecticut, USA, <sup>2</sup>Department of Radiology, Yale University School of Medicine, New Haven, Connecticut, USA, <sup>3</sup>Department of Ophthalmology and Visual Science, Yale University School of Medicine, New Haven, Connecticut, USA

**Introduction:**

Paragangliomas are rare causes of Horner's syndrome. We reported a patient with bilateral carotid body paragangliomas presenting with an isolated Horner's syndrome.

**Description of Case(s):**

A 63-year-old women had been aware of ptosis of the right upper lid for the past few years, but not aware of any pupillary changes. On routine examination, a right Horner's syndrome was noted and she was referred for neuro-ophthalmic evaluation. Examination confirmed an isolated right Horner's syndrome. Magnetic resonance imaging (MRI) revealed bilateral mass lesions located at the level of the carotid bifurcation, identified as carotid body paragangliomas with the characteristic salt and pepper appearance.

**Conclusions, including unique features of the case(s):**

Although the clinical presentation for carotid body paragangliomas is often an asymptomatic neck mass, they can be locally aggressive and lead to lower cranial nerve palsies or malignant transformation.<sup>3</sup> Bilateral carotid body paragangliomas related Horner's syndrome has never been reported in the literature. Our report demonstrates the benefit of thorough imaging investigation for a patient with an isolated Horner's syndrome.

**References:** 1. Chen Y, Morgan ML, Barros Palau AE, Yalamanchili S, Lee AG. Evaluation and neuroimaging of the Horner syndrome. *Can J Ophthalmol.* 2015;50(2):107-111. 2. Sadaka A, Schockman SL, Golnik KC. Evaluation of Horner Syndrome in the MRI Era. *J Neuroophthalmol.* 2017;37(3):268-272. 3. Naik SM, Shenoy AM, Nanjundappa, et al. Paragangliomas of the carotid body: current management protocols and review of literature. *Indian J Surg Oncol.* 2013;4(3):305-312.

**Keywords:** Pupils Retina, Tumors, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 143

### A Fluttering Diagnosis

DonRaphael P. Wynn<sup>1</sup>, Judith Warner<sup>1</sup>, Bradley Katz<sup>1</sup>, Alison Crum<sup>1</sup>, Kathleen Digre<sup>1</sup>

<sup>1</sup>*John A Moran Eye Center, University of Utah*

#### **Introduction:**

Ocular flutter is often associated with infectious or paraneoplastic disorders. Here we describe a patient with confirmed Rabies infection who developed ocular flutter.

#### **Description of Case(s):**

A 77-year-old woman developed rapid onset weakness, myalgias, dysarthria, and dysphagia. Her clinical course rapidly declined, she was intubated and then transferred to our facility. On arrival her neurological examination was remarkable for a decreased level of consciousness, with symmetric facial and tongue weakness, upper and lower extremity flaccid paralysis with frequent, symmetric myoclonus. Brain and spinal cord MRI studies showed enhancement of the left trigeminal nerve, pachymeninges, and spinal nerve roots at the cauda equina. A lumbar puncture revealed a normal opening pressure with 13 WBCs (predominantly lymphocytes), protein 121 mg/dL, and normal glucose. CSF cultures were negative for bacterial growth, and VZV, HSV, and West Nile virus were all negative. The patient's mental status declined, becoming completely unresponsive. Her myoclonus evolved into frequent, generalized choreoathetosis. After 8 days of hospitalization she developed tongue and orofacial dyskinesias and ocular flutter.

#### **Conclusions, including unique features of the case(s):**

About 6 days after transferring to our facility, the family revealed that about 1 month prior to onset of her symptoms, the patient had woken up to find a bat fluttering around her face. Spinal fluid, serum, saliva and nuchal skin punch biopsy samples were sent to the CDC for analysis. All tests were positive for Rabies virus, and additional testing isolated a Rabies virus variant common to the silver-haired bat (*Lasionycteris noctivagans*). Large numbers of silver-haired bats were found to be infesting the eaves and attic of the patient's house. The patient passed away after 11 days in the hospital. One of the most unique aspects of this case is that she developed ocular flutter - this has not been formally reported in prior cases of rabies infection.

**References:** 1. Hemachudha T, Mitrabhakdi E. Rabies. In: Davis LE, Kennedy PGE, eds. Infectious diseases of the nervous system. Oxford: Butterworth-Heinemann, 2000: 401-44. 2. Wynn D, McCorquodale D 3rd, Peters A, Juster-Switlyk K, Smith G, Ansari S. Rapidly progressive quadriplegia and encephalopathy. *JAMA Neurol.* 2016 Nov 1;73(11):1363-1366. 3. Fishbein DB, Robinson LE. Rabies. *N Engl J Med.* 1993 Nov 25;329(22) 1632-38.

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion)

**Grant Support:** Supported in part by an Unrestricted Grant from Research to Prevent Blindness, Inc., New York, NY, to the Department of Ophthalmology & Visual Sciences, University of Utah.

## MONDAY, MARCH 5

6:00 am - 6:45 am	Yoga Class (Pre-registration required, SOLD OUT) .....	Ocean View Terrace
6:30 am - 7:30 am	Breakfast.....	Grand Promenade
6:30 am - 7:30 am	NOVEL Editorial Board/Curriculum Committee Meeting .....	Kona 1
6:30 am - 5:30 pm	Registration/Help Desk .....	Grand Promenade
6:30 am - 2:30 pm	Exhibits .....	Grand Promenade
7:30 am - 9:30 am	Literature Review .....	Grand Ballroom
	<i>Moderators: Y. Joyce Liao, MD, PhD, Heather Moss, MD, PhD</i>	

This session will provide an overview of inflammatory optic neuropathies but will focus on a rational approach to treating these challenging optic neuropathies by addressing evidence-based as well as anecdotal treatment options. The second part of this session will discuss evidences to support mechanical deformation of the optic nerve due to eye movement as a cause of optic neuropathy. This new concept will raise interesting questions such as: can extraocular muscles be a contributing factor to glaucoma?

At the conclusion of this course, the attendees should be able to: 1) describe advances in the understanding the biology of afferent visual pathway; 2) discuss progress in elucidation of mechanisms of diseases affecting neuro-ophthalmic structures and; 3) integrate advances in neurology, neurosurgery and ophthalmology clinical sciences into their management of neuro-ophthalmic presentations.

7:30 am - 7:45 am	<b>RGC and Optic Nerve</b> , Nitza Goldenberg-Cohen, MD, PhD
7:45 am - 8:00 am	<b>Mechanisms of Disease and Treatment</b> , Leonard Levin, MD, PhD
8:00 am - 8:15 am	<b>Visual Processing and Perception</b> , Gregory Van Stavern, MD
8:15 am - 8:30 am	<b>Wild Card</b> , Lynn Gordon, MD, PhD
8:30 am - 8:45 am	<b>Neurology</b> , Caroline Tilikete, MD
8:45 am - 9:00 am	<b>Neurosurgery</b> , Neil Miller, MD, FACS
9:00 am - 9:15 am	<b>Ophthalmology</b> , Helen Danesh-Meyer, MD, PhD
9:15 am - 9:30 am	<b>Q &amp; A</b>

9:30 am - 10:00 am	Coffee Break with Support from EMD Serono .....	Grand Promenade
10:00 am - 12:00 pm	Hot Topics .....	Grand Ballroom
10:00 am - 11:00 am	What's New in the Orbit? <i>Moderators: Howard Krauss, MD, Roger Turbin, MD, FACS</i>	

The first portion of this session concentrates on the clinical characteristics and disease manifestations of six orbital inflammatory diseases that range in incidence from uncommon to rare (Sarcoidosis, Churg Strauss Syndrome, Wegener's Granulomatosis: Granulomatosis with Polyangiitis (GPA), Giant Cell Arteritis, Adult Xanthogranulomatous Diseases and Rosai-Dorfman. The discussion is followed by an update on advances in the understanding of immunologic mechanisms leading to strategies and the predominantly biologic agents engineered to interfere in pathophysiologic immune pathways of the most common orbital inflammatory disease, Graves orbitopathy. Last, we will discuss new developments, diagnostic modalities in the more common orbital inflammatory syndromes, and advances in their treatment. There will be a combined dedicated short session of audience questions to follow the discussion.

At the conclusion of this course, the attendees should be able to: 1) identify rare systemic inflammatory diseases and association with orbital inflammation by presence or absence of key clinical symptoms or signs and; 2) determine which diagnostic tests are required.

10:00 am - 10:20 am	<b>Thyroid Eye Disease Update</b> , Jim Garrity, MD
10:20 am - 10:40 am	<b>Histiocytosis and Other Oddballs of the Orbit</b> , Steven Feldon, MD
10:40 am - 11:00 am	<b>What's New with Orbital Inflammatory Syndrome: Best Approaches and Rx</b> , Howard Krauss, MD



## MONDAY, MARCH 5 (Continued)

**11:00 am - 12:00 pm**      **What's New in the Optic Nerve?**  
*Moderators: Lynn Gordon, MD, PhD, Julie Falardeau, MD*

This session will provide an overview of inflammatory optic neuropathies but will focus on a rational approach to treating these challenging optic neuropathies by addressing evidence-based as well as anecdotal treatment options. The second part of this session will discuss evidences to support mechanical deformation of the optic nerve due to eye movement as a cause of optic neuropathy. This new concept will raise interesting questions such as: can extraocular muscles be a contributing factor to glaucoma?

At the conclusion of this course, the attendees should be able to: 1) name various types of inflammatory optic neuropathy; 2) describe best treatment options for each type of inflammatory optic neuropathy; 3) describe a novel and evolving theory about the etiology of glaucoma and; 4) define key elements of the scientific observations that may yield new therapeutic directions in treatment of glaucoma.

11:00 am - 11:20 am      **A Rational Approach to Treating Inflammatory Optic Neuropathies: Which Treatment and Why,**  
*Jeffrey Bennett, MD, PhD*  
 11:20 am - 11:40 am      **Optic Nerve Deformity as a Possible Contributor to Optic Neuropathy,** *Joseph Demer, MD, PhD*  
 11:40 am - 12:00 pm      **Q & A with all Hot Topics Speakers**

**12:00 pm - 12:30 pm**      **Announcements.....Grand Ballroom**  
 12:00 pm - 12:15 pm      **JNO Update**  
 12:15 pm - 12:20 pm      **NOVEL Update**  
 12:20 pm - 12:30 pm      **Additional Meeting Announcements**

**12:30 pm - 12:50 pm**      **Impact and Advantages of the New Specialty Designation.....Grand Ballroom**  
*Speaker: Michael Repka, MD*

**12:30 pm - 1:00 pm**      **International Relations Committee Meeting.....Kona 1**

**12:50 pm - 2:00 pm**      **Lunch Break (on your own)**

**2:00 pm - 4:00 pm**      **Neurodegenerative Diseases and Neuro-Ophthalmology .....Grand Ballroom**  
*Moderator: Gregory Van Stavern, MD*

Visual dysfunction is an under-recognized and important cause of overall disability and reduced quality of life in neurodegenerative diseases and neuro-ophthalmologists are frequently involved in the diagnosis and management of these patients. This program will

review visual dysfunction (including the afferent and efferent systems as well as the cognitive visual manifestations of disease) in several neurodegenerative disorders, with special focus on clinical neuro-ophthalmic testing and vision disability in AD, Posterior Cortical Atrophy, PD and other neurodegenerative conditions. Our goal is to provide NANOS members with an update on the visual manifestations of these disorders, from both a clinical and research standpoint, and discuss diagnostic and management tools to use in their practices.

At the conclusion of this course, the attendees should be able to: 1) identify patterns of afferent and efferent visual dysfunction in patients with neuro-degenerative disease; 2) identify diagnoses and treatments of visual dysfunction in neurodegenerative disorders and; 3) define new advances and breakthroughs in the field.

2:00 pm - 2:05 pm      **Introduction,** *Gregory Van Stavern, MD*  
 2:05 pm - 2:25 pm      **Cortical Visual Dysfunction: Clinical Pearls,** *Victoria Pelak, MD*  
 2:25 pm - 2:45 pm      **Scientific Aspects of Afferent Visual Dysfunction in Neuro-degenerative Diseases:**  
**Recent Advances,** *Geoff Aguirre, MD, PhD*  
 2:45 pm - 3:05 pm      **Efferent Visual Dysfunction in Neuro-degenerative Diseases: Clinical Pearls,**  
*Matthew Thurtell, MBBS, MSc, FRACP*  
 3:05 pm - 3:25 pm      **Scientific Aspects of Efferent Visual Dysfunction in Neuro-degenerative Diseases:**  
**Recent Advances,** *Heather Moss, MD, PhD*  
 3:25 pm - 3:45 pm      **Using the Visual System as a Biomarker for Neuro-degenerative Diseases,**  
*Gregory Van Stavern, MD*  
 3:45 pm - 4:00 pm      **Q&A**

## MONDAY, MARCH 5 (Continued)

**2:00 pm - 4:00 pm**      **Forum for New and Future Neuro-Ophthalmologists**.....Kona 4-5

All are welcome to attend. This gathering, however, is especially for students, residents, fellows and neuro-ophthalmologists in the early years of their career. There will be small group discussions that provide an opportunity to ask questions, or listen to the questions and advice of others. Attendees can rotate between tables during the session. The first hour of discussions will be led by members of the Young Neuro-ophthalmology (YONO) Committee who are recently out of fellowship, and is geared towards trainees, residents, and fellows. The second hour will be led by senior neuro-ophthalmologists, and is geared towards those in their first years of practice. Attendees can come for one or both hour-long sessions.

**Hour 1: Session I: What Do You Want to Know About Becoming a Neuro-Ophthalmologist?**

**Table 1: Financial Advice for the Young Physician: Do's and Don'ts** with *Kaushal Kulkarni, MD and Barbara Yates, MD*

**Table 2: Starting and Building a Practice** with *Collin McClelland, MD*

**Table 3: Finding Balance as a Neuro-Ophthalmologist: A Practical Approach** with *Evan Price, MD*

**Hour 2: Session II: What Do You Want to Know About Your First Few Years of Practice?**

**Table 1: Publishing Pearls** with *Laura Balcer, MD, MSCE*

**Table 2: Our Foundations and Founders** with *Edmond FitzGibbon, MD and Steven Newman, MD*

**Table 3: International Neuro-Ophthalmology** with *Karl Golnik, MD*

**Table 4: Research Goals** with *Y. Joyce Liao, MD, PhD and Mark Kupersmith, MD*

**4:00 pm - 5:00 pm**      **Free Hour**

**5:00 pm - 7:00 pm**      **Scientific Platform Presentations: Session I** .....Grand Ballroom

*Moderators: Marc Dinkin, MD, Billi Wallace, MD*

5:00 pm - 5:15 pm      **Does Optic Nerve Appearance Predict Visual Outcome in Patients with Idiopathic Intracranial Hypertension (IIH)?**, *Jonathan A. Micieli, MD*

5:15 pm - 5:30 pm      **Safety and Efficacy of an 11 $\beta$ -Hydroxysteroid Dehydrogenase Type-1 Inhibitor (AZD4017) in Idiopathic Intracranial Hypertension**, *Keira A. Markey, MD*

5:30 pm - 5:45 pm      **Next Generation Sequencing Results in an Italian Cohort of Hereditary Optic Neuropathies Patients**, *Chiara La Morgia, MD, PhD*

5:45 pm - 6:00 pm      **Interocular Phase Delay Shifts Visual Cortical Dominance: a Potential New Therapeutic Approach for Amblyopia**, *Eric D. Gaier, MD, PhD*

6:00 pm - 6:15 pm      **eFOCUS Phase 2: Comparative Clinical Performance of Smartphone & Traditional Funduscopy**, *Hamish P. Dunn, MD*

6:15 pm - 6:30 pm      **Assessment of a Fully-Automated RAPD Test as a Routine Screening Tool**, *Lael J. Stander, MD*

6:30 pm - 6:45 pm      **Ocular Motor Abnormalities During Saccadic Reading in Different Neuro-Ophthalmic Diseases**, *Angela J. Oh*

6:45 pm - 7:00 pm      **General Q&A**

**7:00 pm - 7:15 pm**      **Safety/Acuity Outcomes 96-Weeks Post-Treatment with rAAV2/2-ND4; Gene Therapy for ND4 LHON: a Phase I/II Trial**, *Barrett Katz, MD, MBA (Non CME)*

## LITERATURE RELEVANT TO OPTIC NERVE AND RETINAL GANGLION CELLS

**Nitza Goldenberg-Cohen, MD**  
**Ophthalmology, Bnai Zion Medical Center; Technion, Israel Institute of Technology**  
**Haifa, Israel**

### LEARNING OBJECTIVES

1. The attendee will know the latest advances in optic nerve regeneration, and the morphologic criteria and strategies that may take part in the differentiation of spared versus regenerated RGC axons in the injured optic nerve.
2. The attendee will know the intrinsic epigenetic barrier for functional axon regeneration. Will be familiar with various molecular pathways relevant to RGC and axonal regeneration.
3. The attendee will know about new potential treatment targets, such as chelating zinc, inhibition of caspases, the role of different transcription factors in specific types of RGC death (SOX11, GSK3 activity).
4. The attendee will learn about the role of Wnt signaling and Damage-induced neuronal endopeptidase (DINE)/endothelin-converting enzyme-like 1 (ECE1), a metalloprotease that is a nerve regeneration-associated molecule.
5. The attendee will know the debate regarding inflammation and axonal regeneration. Are microglia relevant for neuronal and axonal regeneration after acute injury?
6. The attendee will learn of a dedicated population of RGCs that signals rapidly in the presence of visual threats.
7. The attendee will understand the cell sources for RGC replacement and methods to optimize integration and survival; stimulation of functional neuronal regeneration from Müller glia in adult mice and the role of miRNA-Dependent mechanisms in promoting survival of RGCs.
8. The attendee will understand the role of mitochondrial transport during axon regeneration.

### CME QUESTIONS

1. What is true regarding Sox 11
  - a. Sox11 promotes robust axon regeneration from injured adult RGCs
  - b. Sox11 re-activates a developmental axon growth program
  - c. Sox11 kills  $\alpha$ -RGCs and promotes regeneration from other types
  - d. PTEN deletion enhances axon regeneration induced by Sox11 expression
2. What is not true regarding mitochondrial protein Armcx1
  - a. The mitochondrial protein Armcx1 is upregulated during RGCs axonal regeneration
  - b. Armcx1 overexpression mobilizes mitochondria
  - c. In vivo, Armcx1 overexpression enhances neuronal survival and axonal regeneration
  - d. Armcx1 upregulation is not necessary for mouse model with high regenerative capacity
3. The most harmful substance that is released after optic nerve injury is:
  - a. Calcium
  - b. Copper
  - c. Iron
  - d. Zinc

4. The type of retinal cells responsible for releasing harmful amounts of zinc after optic nerve injury is:
  - a. Photoreceptors
  - b. bipolar cells
  - c. amacrine cells
  - d. ganglion cells
  
5. Chelators:
  - a. Bind to metal ions making them chemically inert
  - b. Detoxify metal ions
  - c. Prevent metal poisoning
  - d. All of the above
  
6. New treatment modalities?
  - a. ZINC chelation
  - b. Caspases inhibition
  - c. Muller re-differentiation
  - d. Anti-inflammatory agent

#### **KEYWORDS**

1. Axonal regeneration
2. Axonal growth
3. Optic nerve injury
4. Mitochondrial protein Armcx1
5. Zinc toxicity and RGCs loss
6. Transcription factor SOX11
7. GSK3 activity
8. Inflammatory caspases
9. Wnt signaling and Damage-induced neuronal endopeptidase (DINE)/endothelin-converting enzyme-like 1 (ECE1)
10. RGC replacement
11. miRNA-Dependent mechanisms and RGCs survival

#### **HIGHLIGHTS**

Notable original publications within the last year relevant to optic nerve and retinal ganglion cells regeneration, transcription factors, enzymes and stem cells are reviewed. The knowledge gained could provide important insights into the cellular and molecular mechanisms required to promote axonal regeneration, thereby directing future research towards which molecular targets are critical to promoting regeneration in the adult CNS.

**Publications reviewed (January 2017 through January 2018):** Nature, Neuron, Experimental Neurology, Sci Reports, Proc Natl Acad Sci U S A, Experimental Eye Research, Stem Cells Translational Medicine, J neuro science, Neuroscience, Progress in Retinal and Eye Research, Cell Death Discovery, Translational Vision Science & Technology, PLoS One, Nature communications.

#### **OPTIC NERVE MODELS AND RGC REGENERATION.**

**Spared versus regenerated RGC axons<sup>1</sup>**

Retinal ganglion cells (RGC) are terminally differentiated CNS neurons that possess limited endogenous regenerative capacity after injury. Under normal circumstances, RGCs cannot regenerate axons after optic nerve damage induction, undergo cell death and lead to permanent visual loss. Recent studies using appropriate genetic manipulations have revealed remarkable abilities of mature RGC axons to regenerate after optic nerve injury, with some studies demonstrating that axons can then go on to re-innervate a number of central visual targets with partial functional restoration. However, one confounding factor inherent to optic nerve crush injury is the potential incompleteness of the initial lesion, leaving spared axons that could later be interpreted erroneously as regenerating distal to the injury site.<sup>1</sup> Careful examination of axonal projection patterns and morphology may facilitate distinguishing spared from regenerating RGC axons.<sup>1</sup>

### **PROFILING TRANSCRIPTION FACTORS, ENZYMES AND PATHWAYS**

#### **Turning Muller glia into retinal cells post injury by genetic activation of the *Ascl1* gene.<sup>2</sup>**

Recent research of regenerative therapies has resulted in multiple breakthroughs that may unlock the regenerative potential of the optic nerve. As in humans, mice cannot repair damage to their retinas. However, because zebrafish can, researchers created in mice a version of the fish gene called *Ascl1*, that is responsible for turning Muller glia into retinal cells post injury.<sup>2</sup> The Müller glia differentiate into stem cells and then into retinal interneurons. In this study, not only they managed to overcome the epigenetic suppression of this gene for unlimited duration (using histone deacetylase inhibitor), the new interneurons formed the proper connections.

#### **Recently identified transcription factor SOX11 that selectively kills $\alpha$ - type RGCS.<sup>3</sup>**

Transcription factor Sox11 appeared to help axons grow past the site of injury. RGCs' functional degeneration in optic nerve injury is subtype dependent.<sup>4</sup> Different subtypes of neurons may respond differently to the same factors<sup>3</sup>. Transcription factor Sox11 efficiently killed the  $\alpha$ -type RGCs, although  $\alpha$ -type of RGCs preferentially survive injury.<sup>3</sup> Sox11 activates genes involved in cytoskeletal remodeling and axon growth. Remarkably,  $\alpha$ -RGCs, which preferentially regenerate following treatments such as PTEN deletion, were killed by Sox11 overexpression. Transcription factor SOX11 has pro regenerative effects on other RGCs.<sup>3</sup> Thus, Sox11 promotes regeneration of non- $\alpha$ -RGCs, which are refractory to PTEN deletion-induced regeneration. At least 30 types of RGCs communicate with the brain through the optic nerve. The goal is to regenerate as many subtypes of neurons as possible. Different subtypes of neurons may respond differently to the same factors. Pro survival and anti regeneration mechanisms through brain derived neurotrophic factor (BDNF) and leucine zipper kinase (DLK) via PTEN were previously described.<sup>4</sup> mTOR is also important for axonal regeneration, and deletion of PTEN, a negative regulator of mTOR, promotes robust RGC axon regeneration within the injured optic projection<sup>4,5</sup>

#### **Mitochondrial protein, RGC survival and axonal regeneration.<sup>6</sup>**

Cartoni et al.<sup>6</sup> demonstrated that the mammalian-specific mitochondrial protein *Armcx1* mobilizes mitochondria and promotes neuronal survival and axonal regeneration in an optic nerve injury model, revealing a new mechanism for regulating responses to neuronal injury. *Armcx1* controls mitochondrial transport during neuronal repair. Following PTEN deletion, *Armcx1* overexpression further increased the number of regenerating axons.<sup>6</sup>

#### **Wnt3a elevates transcription factor Stat3 activity level, protects RGC and enables axonal regeneration.<sup>7</sup>**

The Wnt/ $\beta$ -catenin signaling pathway is an essential signal transduction cascade that regulates axon growth and neurite extension in the developing mammalian embryo. In this study, researchers investigated whether a Wnt/ $\beta$ -catenin signaling activator could be repurposed to induce regeneration in

the adult CNS after axonal injury. Using a RGC axon crush injury model in a transgenic Wnt reporter mice followed by intravitreal injections of Wnt3a or saline, demonstrated that Wnt3a induced Wnt signaling in RGCs and resulted in significant axonal regrowth. Axonal regrowth extended beyond the lesion site within four weeks post injury. Wnt3a-injected eyes showed increased survival of RGCs and significantly higher PERG amplitudes compared to controls. Wnt3a-induced axonal regeneration and RGC survival was associated with elevated activation of the transcription factor Stat3. Reducing expression of Stat3 using a conditional *Stat3* knock-out mouse line led to diminished Wnt3a-dependent axonal regeneration and RGC survival.<sup>7</sup>

### **PTEN deletion induced axonal regeneration of mature RGCs but was attenuated upon TET1 knockdown.<sup>8</sup>**

Mature mammalian neurons exhibit little axonal growth. Weng et al.<sup>8</sup> uncovered an epigenetic mechanism wherein axonal injury elevates the active DNA demethylation pathway to induce regeneration-associated gene expression, which in turn promotes functional axonal regeneration of peripheral sensory neurons. Peripheral nerve lesions elevate Tet3 and 5-hydroxymethylcytosine (5hmC) levels in mature dorsal root ganglion (DRG) neurons. Tet3 is required for axon regeneration of DRG neurons and behavioral recovery. TET3 and TDG mediate injury-induced DNA demethylation and expression of RAGs. TET1 is required for PTEN-deletion-induced axonal regeneration of mature RGCs, and constitutes an epigenetic barrier that can be removed by active DNA demethylation to permit axon regeneration in the adult mammalian nervous system.

### **Zinc increases post injury and kills RGCs and axons.<sup>9</sup>**

#### **Zinc: A surprise target in regenerating the optic nerve after injury.**

Another major factor that suppresses optic nerve regeneration is the massive elevation of ionic zinc that occurs in the synaptic space between amacrine cells and RGCs within an hour after nerve injury<sup>4,10</sup>. Chelating zinc dramatically increases levels of axon regeneration in a mouse model. For more than two decades, researchers have tried to regenerate the injured optic nerve using different growth factors and/or agents that overcome natural growth inhibition. At best, these approaches result in regeneration brain connection of approximately one percent of the injured NFL, while most of the cells eventually die. Zinc concentrations increase dramatically in the amacrine cells and continue to increase over the first day post optic nerve injury, which then transfers slowly to the RGC. Chelating the zinc that is released as a result of the optic nerve injury protects RGC and the NFL, resulting in dramatic levels of axon regeneration in a mouse model. Zinc chelators have been proven in mice, and if proven to work as well in humans, such a treatment could greatly benefit patients with all types of optic neuropathy.<sup>9</sup> Zinc chelators already exist and could potentially be given either systemically or through injection into the eye.

### **A new enzyme DINE was identified as a nerve regeneration-associated molecule.<sup>11</sup>**

Bentowich et al.<sup>4</sup> review article summarized what was known regarding optic nerve regeneration ability. Previous studies showed the combining double-deletion of PTEN and socs3 with CNTF strongly synergistic effects on optic nerve regeneration, though not many axons extend past the optic chiasm.<sup>4</sup> Damage-induced neuronal endopeptidase (DINE)/endothelin-converting enzyme-like 1 (ECE1) is a membrane-bound metalloprotease that was identified as a nerve regeneration-associated molecule.<sup>11</sup> The expression of DINE is upregulated in injured RGCs but not in normal RGCs. DINE is a crucial endopeptidase for injured RGCs to promote axonal regeneration after optic nerve injury.<sup>11</sup>

### **GSK3 activity and axonal regeneration.<sup>12</sup>**

The role of GSK3 in axon regeneration is controversial. Whereas increased GSK3 activity accelerates peripheral nerve regeneration, it shows the opposite effect in the CNS. Moreover, KO/knockdown of GSK3 $\beta$  in growth-stimulated RGCs was disinhibitory and potentiated optic nerve regeneration. This dichotomy was the result of a GSK3-dependent and CNS-specific inhibition of axonal CRMP2, which compromised RGCs' ability for axon growth. As GSK3 inhibition, neuronal expression of constitutively active CRMP2 (CRMP2<sup>T/A</sup>) potentiated optic nerve regeneration and, strikingly, unmasked an axon growth-promoting effect of active GSK3 as in peripheral nerves. CRMP2<sup>T/A</sup> expression and GSK3 activation additively enabled extensive optic nerve regeneration, thereby reconciling conflicting data in GSK3-mediated axon regeneration and opening novel treatment possibilities for CNS repair.<sup>12</sup>

## **STEM CELLS**

### **Mesenchymal stem cell derived exosomes promote survival of RGCs through miRNA-Dependent Mechanisms.**<sup>13</sup>

Mesenchymal derived stem cells (MSC) have a demonstrable neuroprotective effect on RGCs. Exosomes, small extracellular vesicles secreted from MSCs, can be easily purified from the MSCs and when delivered into a rodent model of optic nerve crush, protect RGC from death and preserve function. BMSC-derived exosomes promoted statistically significant survival of RGCs and regeneration of their axons while partially preventing RGCs axonal loss and RGCs dysfunction.<sup>13</sup>

## **THE INFLAMMATORY ENVIRONMENT: A BARRIER TO REGENERATION?**

The unmyelinated segment of the RGC axon is part of a complex microenvironment as it passes through the retina and optic nerve head. This environment includes not only astrocytes, but also a highly mobile population of microglia. In exiting the nerve head, axons become myelinated by oligodendrocyte glia that populate the remainder of the optic projection. These glial groups represent potent sources for interactions with RGCs involving extracellular signals commonly categorized as pro-inflammatory, including cytokines, chemokines, and other soluble signals typically associated with innate immunity (e.g., complement, nitric oxide etc).<sup>4</sup> Inflammation itself is often viewed as pathogenic but under certain circumstances, other immune derived inflammatory signals can be protective of RGCs.<sup>4</sup>

### **Microglia are irrelevant for neuronal degeneration and axon regeneration after acute injury**<sup>14</sup>

Elimination of microglia (using colony stimulating factor 1 inhibitor PLX5622) in the murine retina and optic nerve did not affect the time to RGC degeneration following optic nerve injury. However, repopulation of the optic nerve with astrocytes was slower. Only double deletion of microglia and infiltrated macrophages significantly comprised optic nerve regeneration.<sup>14</sup>

### **The anti-inflammatory Oroxylin A promotes RGC survival in a rat optic nerve crush model.**<sup>15</sup>

Oroxylin A has neuroprotective effects on RGC survival with preserved visual function and a decrease in microglial infiltration in the ONs after ON crush injury. Oroxylin A (5,7-dihydroxy-6-methoxyflavone) is a plant-originated flavonoid isolated from medical herb *Scutellariae baicalensis Georgi*. A previous study demonstrated that oroxylin A suppressed LPS-induced iNOS and cyclooxygenase-2 expression through inhibiting the activation of NF $\kappa$ B-p65 in RAW264.7 macrophages. Oroxylin A was shown to exert anti-inflammatory and neuroprotective effects. Oroxylin A administration enhanced RGC survival following ON crush, reduced apoptosis, reduced ED-1 positive cells in the ONs and reduced the upregulation of GFAP. Oroxylin A attenuates the elevated expression of pro-inflammatory cytokines, iNOS and COX-2 in the retina after ONC injury. Systemic administration of oroxylin A promotes RGCs survival and improves visual function as measured by VEP. The oroxylin A mechanisms of action may include anti-apoptotic effects and modulation of neuro-inflammation by blocking microglia activation, reactive gliosis and the induction of iNOS and COX2 in the damaged tissue.<sup>15</sup>

### **Caspases in RGC death and axon regeneration- a novel non-apoptotic role for caspases**<sup>16</sup>

RGC die by caspase-dependent mechanisms, including apoptosis, during development and following optic nerve injury. Inhibition of caspases through genetic or pharmacological approaches can arrest the apoptotic cascade and protect a proportion of the RGCs. Novel findings have also highlighted a pyroptotic role of inflammatory caspases in RGC death. **Pyroptosis**, a specialized form of inflammatory programmed cell death, **mediated by inflammatory caspases**, can occur in RGCs.

Caspase-3 is activated during RGC developmental, whereas most other apoptotic and inflammatory caspases are active during trauma and disease. **siRNA knockdown of caspase-2 provides the greatest neuroprotection after axotomy**. Non-apoptotic roles for caspases, such as inflammatory pyroptotic death or facilitating formation of necroptotic complexes are also critical in RGC death. Caspases also have a novel role in RGC axon regeneration; in particular, **caspase-6 inhibition mediates regeneration** indirectly through CNTF upregulation in retinal glia.

**Inflammasomes** are large multimeric protein complexes that sense pathogen- and host-derived danger signals. Inflammatory caspases (-1 or -11 in mice and -1, -4 and -5 in humans) can be activated in the inflammasome protein signaling complex. The main functions of the inflammasome are to activate caspase-1 to cleave precursor cytokines IL-1 $\beta$  and IL-18 into their mature active forms and induce pyroptosis (a lytic form of cell death).

Cleaved caspase-2, -8, -9, -3, -6 and -7, as well as inflammatory caspases -11 and -1, have all been detected in RGC after crush or axotomy, highlighting the crucial role played by caspases. Caspase-3 is activated after RGC axotomy and can be blocked directly or indirectly by Rho-associated protein kinase (ROCK) inhibitors or treatment with the broad spectrum histone deacetylase inhibitor, valproic acid.

Recent studies have indicated a pivotal role of caspase-2 in apoptotic RGC injury. After optic nerve axotomy and crush injury, active caspase-2 is exclusively localized to RGCs, and its inhibition using siRNA provides significant neuroprotection. siCASP2 is being developed by Quark Pharmaceuticals Inc. and is currently in Phase III clinical trials for ischemic optic neuropathy and glaucoma.

RGCs are protected by intravitreal caspase-6 and -8 inhibitors and siRNA against caspase-6 and -8 (siCASP6 and siCASP8) after I/R injury. Caspase-6 inhibition may act indirectly by increasing retinal glial CNTF production. Both siCASP8 and siCASP6 administration elevate RGC survival by ~ 60%. siRNA gene knockdown reduces caspase gene expression and could affect non-apoptotic caspase roles, such as caspase-8 in complex IIb, 'FADDosome', 'riposome' and inflammasome formation.

### **Caspases and axonal regeneration**

In addition to promoting RGC survival, caspases promote RGC axon regeneration after ON injury. Pharmacological inhibition of caspases-6 and -8 provides RGC neuroprotection and promotes limited RGC axon regeneration, with few axons extending >1000  $\mu$ m beyond the lesion site. Combined suppression of caspase-2 and -6 promotes significant regeneration. Although caspase-6 is localized to RGCs and some microglia, the neuroprotective and pro-regenerative effects of caspase-6 inhibition are mediated indirectly by CNTF upregulation in retinal glia and are blocked by suppression of gp130 and the JAK/STAT pathway.<sup>16</sup>

### **Intranasal delivery of an anti-inflammatory agent preserved the optic nerve.**<sup>17</sup>

A new therapeutic agent tested in a mouse model of multiple sclerosis produced anti-inflammatory activity and prevented loss of cells in the optic nerve. The therapeutic agent called ST266, is a solution of molecules that stimulates paracrine signaling.

The many factors in ST266 not only bind to cell receptors and cause changes within the cells they bind to, but those cells then alter their own secretions and provide additional signals to other



neighboring cells, thus propagating the effect from a relatively small amount of protein present in the therapy itself. This study demonstrates, for the first time, the ability **to treat the optic nerve via an intranasal route**.

When ST266 was given to MS mice intranasally, it reached the CNS within 30 minutes and was detected at higher concentrations in parts of the eye and optic nerve compared to other areas of the brain. These findings demonstrated that this type of delivery can target tissues of the eye, which is easier, less painful, and less invasive than injecting medications directly into the eye.

In mice with optic neuritis, the team showed that early treatment with ST266 prevented damage and dysfunction, marked by significantly reduced loss of optic nerve cells, and suppression of inflammatory cell infiltration into the optic nerve. This in turn was associated with an attenuated degree of demyelination caused by MS-related optic neuritis. Treatment of later-stage optic neuritis in the MS mice showed similar results, resulting in improved visual function compared to untreated groups. The data suggest that ST266 helps promote optic neuron survival by potentially activating multiple pathways, including those that prevent cell death.

These results are particularly important as the preservation of retinal cells is a significant factor when treating optic neuritis. There is an increased need for combination treatment options that are able to prevent nerve-cell axon loss for patients with optic neuritis. ST266's ability to preserve vision in the preclinical model and reduce neuronal loss would be a huge advance if it translates to human patients.

17

## **NEW INSIGHTS INTO HOW VISUAL THREATS ARE TRANSLATED RAPIDLY INTO DEFENSIVE BEHAVIORAL RESPONSES.**

Animals promote their survival by avoiding rapidly approaching objects that indicate threats. In mice, looming-evoked defensive responses are triggered by the superior colliculus (SC) which receives direct retinal inputs.

A subset of RGCs that control mouse looming-evoked defensive responses through axonal collaterals to the dorsal raphe nucleus (DRN) and SC were identified.<sup>18</sup> Looming signals transmitted by DRN-projecting RGCs activate DRN GABAergic neurons that in turn inhibit serotonergic neurons. A dedicated population of RGCs signals rapidly approaching visual threats and their input to the DRN controls a serotonergic self-gating mechanism that regulates innate defensive responses. The DRN and SC work in concert to extract and translate visual threats into defensive behavioral responses.

## **CME ANSWERS:**

1. (All)
2. D
3. D
4. C
5. D
6. (All)

## **REFERENCES:**

1. Fischer D, Harvey AR, Pernet V, Lemmon VP, Park KK. Optic nerve regeneration in mammals: Regenerated or spared axons? *Exp Neurol*. 2017;296:83-88. doi:10.1016/j.expneurol.2017.07.008.
2. Jorstad NL, Wilken MS, Grimes WN, et al. Stimulation of functional neuronal regeneration from Müller glia in adult mice. *Nature*. 2017;548(7665):103-107. doi:10.1038/nature23283.
3. Norsworthy MW, Bei F, Kawaguchi R, et al. Sox11 Expression Promotes Regeneration of Some

- Retinal Ganglion Cell Types but Kills Others. *Neuron*. 2017;94(6):1112-1120.e4. doi:10.1016/j.neuron.2017.05.035.
4. Benowitz LI, He Z, Goldberg JL. Reaching the brain: Advances in optic nerve regeneration. *Exp Neurol*. 2017;287:365-373. doi:10.1016/j.expneurol.2015.12.015.
  5. Kurimoto T, Yin Y, Omura K, et al. Long-Distance Axon Regeneration in the Mature Optic Nerve: Contributions of Oncomodulin, cAMP, and pten Gene Deletion. *J Neurosci*. 2010;30(46):15654-15663. doi:10.1523/JNEUROSCI.4340-10.2010.
  6. Cartoni R, Norsworthy MW, Bei F, et al. The Mammalian-Specific Protein Armcx1 Regulates Mitochondrial Transport during Axon Regeneration. *Neuron*. 2016;92(6):1294-1307. doi:10.1016/j.neuron.2016.10.060.
  7. Patel AK, Park KK, Hackam AS. Wnt signaling promotes axonal regeneration following optic nerve injury in the mouse. *Neuroscience*. 2017;343:372-383. doi:10.1016/j.neuroscience.2016.12.020.
  8. Weng Y-L, An R, Cassin J, et al. An Intrinsic Epigenetic Barrier for Functional Axon Regeneration. *Neuron*. 2017;94(2):337-346.e6. doi:10.1016/j.neuron.2017.03.034.
  9. Li Y, Andereggen L, Yuki K, et al. Mobile zinc increases rapidly in the retina after optic nerve injury and regulates ganglion cell survival and optic nerve regeneration. *Proc Natl Acad Sci U S A*. 2017;114(2):E209-E218. doi:10.1073/pnas.1616811114.
  10. Li S, He Q, Wang H, et al. Injured adult retinal axons with Pten and Socs3 co-deletion reform active synapses with suprachiasmatic neurons. *Neurobiol Dis*. 2015;73:366-376. doi:10.1016/j.nbd.2014.09.019.
  11. Kaneko A, Kiryu-Seo S, Matsumoto S, Kiyama H. Damage-induced neuronal endopeptidase (DINE) enhances axonal regeneration potential of retinal ganglion cells after optic nerve injury. *Cell Death Dis*. 2017;8(6):e2847. doi:10.1038/cddis.2017.212.
  12. Leibinger M, Andreadaki A, Golla R, et al. Boosting CNS axon regeneration by harnessing antagonistic effects of GSK3 activity. *Proc Natl Acad Sci*. 2017;114(27):E5454-E5463. doi:10.1073/pnas.1621225114.
  13. Mead B, Tomarev S. Bone Marrow-Derived Mesenchymal Stem Cells-Derived Exosomes Promote Survival of Retinal Ganglion Cells Through miRNA-Dependent Mechanisms. *Stem Cells Transl Med*. 2017;6(4):1273-1285. doi:10.1002/sctm.16-0428.
  14. Hilla AM, Diekmann H, Fischer D. Microglia Are Irrelevant for Neuronal Degeneration and Axon Regeneration after Acute Injury. *J Neurosci*. 2017;37(25):6113-6124. doi:10.1523/JNEUROSCI.0584-17.2017.
  15. Lin S-F, Chien J-Y, Kapupara K, Huang C-YF, Huang S-P. Oroxylin A promotes retinal ganglion cell survival in a rat optic nerve crush model. *PLoS One*. 2017;12(6):e0178584. doi:10.1371/journal.pone.0178584.
  16. Thomas CN, Berry M, Logan A, Blanch RJ, Ahmed Z. Caspases in retinal ganglion cell death and axon regeneration. *Cell Death Discov*. 2017;3:17032. doi:10.1038/cddiscovery.2017.32.
  17. Khan RS, Dine K, Bauman B, et al. Intranasal delivery of a novel amnion cell secretome prevents neuronal damage and preserves function in a mouse multiple sclerosis model. *Sci Rep*. 2017;7. doi:10.1038/srep41768.
  18. Huang L, Yuan T, Tan M, Xi Y, Hu Y, Tao Q, Zhao Z, Zheng J, Han Y, Xu F, Luo M, Sollars PJ, Pu M, Pickard GE, So KF, Ren C. A retinoraphe projection regulates serotonergic activity and looming-evoked defensive behaviour. *Nat Commun*. 2017;8:14908.

## LITERATURE REVIEW: DEVELOPMENTS IN DISEASE MECHANISMS AND TREATMENT

Leonard A. Levin, MD, PhD  
McGill University  
Montreal, Canada

### LEARNING OBJECTIVES

1. Understand new mechanisms for how retinal ganglion cells die in disease and how their death can be detected.
2. Learn about new therapies for neuronal disease.
3. Appreciate how axons die is relevant to neuro-ophthalmic diseases.

### CME QUESTIONS (True/False)

1. If axon degenerated but the cell body continues to die, the DARC technique would detect the same number of positive retinal ganglion cells.
2. A therapy based on decrease NAD<sup>+</sup> levels would help preserve axon connectivity between the eye and the brain
3. Improving gap junction connectivity should help improve neuronal survival in the face of injury.

### KEYWORDS (5 Max)

1. Apoptosis
2. Axonal degeneration
3. Wallerian degeneration slow (Wld<sup>S</sup>)
4. Connexins
5. NAD<sup>+</sup>

### Real-time imaging of single neuronal cell apoptosis in patients with glaucoma

Cordeiro MF, Normando EM, Cardoso MJ, Miodragovic S, Jeylani S, Davis BM, Guo L, Ourselin S, A'Hern R, Bloom PA. *Brain*. 2017 Jun 1;140(6):1757-1767.

**ABSTRACT:** Retinal cell apoptosis occurs in many ocular neurodegenerative conditions including glaucoma—the major cause of irreversible blindness worldwide. Using a new imaging technique that we have called DARC (detection of apoptosing retinal cells), which until now has only been demonstrated in animal models, we assessed if annexin 5 labelled with fluorescent dye DY-776 (ANX776) could be used safely in humans to identify retinal cell apoptosis. Eight patients with glaucomatous neurodegeneration and evidence of progressive disease, and eight healthy subjects were randomly assigned to intravenous ANX776 doses of 0.1, 0.2, 0.4 and 0.5 mg in an open-label, phase 1 clinical trial. In addition to assessing the safety, tolerability and pharmacokinetics of ANX776, the study aimed to explore whether DARC could successfully visualize individual retinal cell apoptosis in vivo in humans, with the DARC count defined as the total number of unique ANX776-labelled spots. DARC enabled retinal cell apoptosis to be identified in the human retina using ANX776. Single ANX776-labelled cells were visualized in a dose-dependent pattern ( $P < 0.001$ ) up to 6 h after injection. The DARC count was significantly higher (2.37-fold, 95% confidence interval: 1.4–4.03,  $P = 0.003$ ) in glaucoma patients compared to healthy controls, and was significantly ( $P = 0.045$ ) greater in patients who later showed increasing rates of disease progression, based on either optic disc, retinal nerve fibre layer or visual field parameters. Additionally, the DARC count significantly correlated with decreased central corneal thickness (Spearman's  $R = 0.68$ ,  $P = 0.006$ ) and increased cup-disc ratios (Spearman's  $R = 0.47$ ,  $P = 0.038$ ) in glaucoma patients and with increased age (Spearman's  $R = 0.77$ ,  $P = 0.001$ ) in healthy controls. Finally, ANX776 was found to be safe

and well-tolerated with no serious adverse events, and a short half-life (10–36 min). This proof-of-concept study demonstrates that retinal cell apoptosis can be identified in the human retina with increased levels of activity in glaucomatous neurodegenerative disease. To our knowledge, this is the first time individual neuronal apoptosis has been visualized in vivo in humans and is the first demonstration of detection of individual apoptotic cells in a neurodegenerative disease. Furthermore, our results suggest the level of apoptosis ('DARC count') is predictive of disease activity, indicating the potential of DARC as a surrogate marker. Although further trials are clearly needed, this study validates experimental findings supporting the use of DARC as a method of detection and monitoring of patients with glaucomatous neurodegeneration, where retinal ganglion cell apoptosis is an established process and where there is a real need for tools to non-invasively assess treatment efficacy.

*COMMENT: Although this study was performed in participants with glaucoma, the principal of detecting dying retinal ganglion cells is applicable to any optic neuropathy. The use of a non-toxic fluorescently labeled marker of apoptotic cells allowed Cordeiro and colleagues to quantify the rate of retinal ganglion cell death in glaucomatous optic neuropathy. The exact same principle could be used to quantify the death of retinal ganglion cells as a means to determine how well a therapy works, with a time course much faster and probably less variable than visual acuity, visual fields, retinal nerve fiber layer thickness, or ganglion cell complex thickness.*

#### **JUN is important for ocular hypertension-induced retinal ganglion cell degeneration**

Syc-Mazurek SB, Fernandes KA, Libby RT. Cell Death Dis. 2017 Jul 20;8(7):e2945.

**ABSTRACT:** Ocular hypertension, a major risk factor for glaucoma, is thought to trigger glaucomatous neurodegeneration through injury to retinal ganglion cell (RGC) axons. The molecular signaling pathway leading from ocular hypertension to RGC degeneration, however, is not well defined. JNK signaling, a component of the mitogen-activated protein kinase (MAPK) family, and its canonical target, the transcription factor JUN, have been shown to regulate neurodegeneration in many different systems. JUN is expressed after glaucoma-relevant injuries and Jun deficiency protects RGCs after mechanical injury to the optic nerve. Here, we tested the importance of JNK–JUN signaling for RGC death after ocular hypertensive axonal injury in an age-related, mouse model of ocular hypertension. Immunohistochemistry was performed to evaluate JUN expression in ocular hypertensive DBA/2J mice. JUN was expressed in a temporal and spatial pattern consistent with a role in glaucomatous injury. To determine the importance of JUN in ocular hypertension-induced RGC death, a floxed allele of Jun and a retinal expressed cre recombinase (Six3-cre) were backcrossed onto the DBA/2J background. Intraocular pressure (IOP) and gross morphology of the retina and optic nerve head were assessed to determine whether removing Jun from the developing retina altered IOP elevation or retinal development. Jun deficiency in the retina did not alter DBA/2J IOP elevation or retinal development. Optic nerves and retinas were assessed at ages known to have glaucomatous damage in DBA/2J mice. Jun deficiency protected RGC somas from ocular hypertensive injury, but did not protect RGC axons from glaucomatous neurodegeneration. Jun is a major regulator of RGC somal degeneration after glaucomatous ocular hypertensive injury. These results suggest in glaucomatous neurodegeneration, JNK–JUN signaling has a major role as a pro-death signaling pathway between axonal injury and somal degeneration.

*COMMENT In almost all optic neuropathies, the primary injury occurs at the retinal ganglion cell axon, and is inexorably followed by death of the soma (cell body). Even if the axon could be spared, or even regenerated, the death of the soma essentially makes the visual loss irreversible. Understanding how axon loss causes somal death has been critical neurobiologists, and many have used the optic nerve as a*

*model system for their investigations. This article from Libby's laboratory demonstrated that the transcription factor JUN is a necessary step in somal loss after axonal degeneration in glaucoma. These results are relevant not just to glaucoma, but to any optic neuropathy where the primary injury is the axon. They also raise the attractive possibility that a therapeutic strategy for optic neuropathy is pharmacological interruption of JNK-JUN signaling.*

### **Targeting neuronal gap junctions in mouse retina offers neuroprotection in glaucoma**

Akopian A, Kumar S, Ramakrishnan H, Roy K, Viswanathan S, Bloomfield SA. J Clin Invest. 2017 Jun 30;127(7):2647-2661.

**ABSTRACT:** The progressive death of retinal ganglion cells and resulting visual deficits are hallmarks of glaucoma, but the underlying mechanisms remain unclear. In many neurodegenerative diseases, cell death induced by primary insult is followed by a wave of secondary loss. Gap junctions (GJs), intercellular channels composed of subunit connexins, can play a major role in secondary cell death by forming conduits through which toxic molecules from dying cells pass to and injure coupled neighbors. Here we have shown that pharmacological blockade of GJs or genetic ablation of connexin 36 (Cx36) subunits, which are highly expressed by retinal neurons, markedly reduced loss of neurons and optic nerve axons in a mouse model of glaucoma. Further, functional parameters that are negatively affected in glaucoma, including the electroretinogram, visual evoked potential, visual spatial acuity, and contrast sensitivity, were maintained at control levels when Cx36 was ablated. Neuronal GJs may thus represent potential therapeutic targets to prevent the progressive neurodegeneration and visual impairment associated with glaucoma.

### **Tonabersat prevents inflammatory damage in the central nervous system by blocking connexin43 hemichannels**

Kim Y, Griffin JM, Nor MNM, Zhang J, Freestone PS, Danesh-Meyer HV, Rupenthal ID, Acosta M, Nicholson LFB, O'Carroll SJ, Green CR. Neurotherapeutics. 2017 Oct;14(4):1148-1165.

**ABSTRACT:** The cis benzopyran compound tonabersat (SB-220453) has previously been reported to inhibit connexin26 expression in the brain by attenuating the p38-mitogen-activated protein kinase pathway. We show here that tonabersat directly inhibits connexin43 hemichannel opening. Connexin43 hemichannels have been called "pathological pores" based upon their role in secondary lesion spread, edema, inflammation, and neuronal loss following central nervous system injuries, as well as in chronic inflammatory disease. Both connexin43 hemichannels and pannexin channels released adenosine triphosphate (ATP) during ischemia in an in vitro ischemia model, but only connexin43 hemichannels contributed to ATP release during reperfusion. Tonabersat inhibited connexin43 hemichannel-mediated ATP release during both ischemia and reperfusion phases, with direct channel block confirmed using electrophysiology. Tonabersat also reduced connexin43 gap junction coupling in vitro, but only at higher concentrations, with junctional plaques internalized and degraded via the lysosomal pathway. Systemic delivery of tonabersat in a rat bright-light retinal damage model (a model for dry age-related macular degeneration) resulted in significantly improved functional outcomes assessed using electroretinography. Tonabersat also prevented thinning of the retina, especially the outer nuclear layer and choroid, assessed using optical coherence tomography. We conclude that tonabersat, already given orally to over 1000 humans in clinical trials (as a potential treatment for, and prophylactic treatment of, migraine because it was thought to inhibit cortical spreading depression), is a connexin hemichannel inhibitor and may have the potential to be a novel treatment of central nervous system injury and chronic neuroinflammatory disease.

*COMMENT: These two papers demonstrate that modulation of gap junctions in injury models of optic nerve and retinal diseases is neuroprotective, and therefore may be translated to human disease. Although neither glaucoma or photic injury are the same injuries as what is seen in more typical optic neuropathies, many of the principles for treatment are the same, and are based on lowering the spread of injury from one cell to another via gap junctions.*

### **Vitamin B<sub>3</sub> modulates mitochondrial vulnerability and prevents glaucoma in aged mice**

Williams PA, Harder JM, Foxworth NE, Cochran KE, Philip VM, Porciatti V, Smithies O, John SW. *Science*. 2017 Feb 17;355(6326):756-760.

**ABSTRACT:** Glaucomas are neurodegenerative diseases that cause vision loss, especially in the elderly. The mechanisms initiating glaucoma and driving neuronal vulnerability during normal aging are unknown. Studying glaucoma-prone mice, we show that mitochondrial abnormalities are an early driver of neuronal dysfunction, occurring before detectable degeneration. Retinal levels of nicotinamide adenine dinucleotide (NAD<sup>+</sup>, a key molecule in energy and redox metabolism) decrease with age and render aging neurons vulnerable to disease-related insults. Oral administration of the NAD<sup>+</sup> precursor nicotinamide (vitamin B<sub>3</sub>), and/or gene therapy (driving expression of *Nmnat1*, a key NAD<sup>+</sup>-producing enzyme), was protective both prophylactically and as an intervention. At the highest dose tested, 93% of eyes did not develop glaucoma. This supports therapeutic use of vitamin B<sub>3</sub> in glaucoma and potentially other age-related neurodegenerations.

*COMMENT: This paper demonstrated that nicotinamide lowers the amount of neuronal damage occurring in a mouse model of glaucoma, probably by increasing levels of nicotinamide adenine dinucleotide (NAD). Although the amount of drug would be difficult to achieve in a human (several grams per day), the mechanism suggested by this work could be translated to other human optic neuropathies. It also ties in to the following three papers.*

### **Axonal Degeneration in Retinal Ganglion Cells Is Associated with a Membrane Polarity-Sensitive Redox Process**

Almasieh M, Catrinescu MM, Binan L, Costantino S, Levin LA. *J Neurosci*. 2017 Apr 5;37(14):3824-3839.

**ABSTRACT:** Axonal degeneration is a pathophysiological mechanism common to several neurodegenerative diseases. The slow Wallerian degeneration (*Wld<sup>s</sup>*) mutation, which results in reduced axonal degeneration in the central and peripheral nervous systems, has provided insight into a redox-dependent mechanism by which axons undergo self-destruction. We studied early molecular events in axonal degeneration with single-axon laser axotomy and time-lapse imaging, monitoring the initial changes in transected axons of purified retinal ganglion cells (RGCs) from wild-type and *Wld<sup>s</sup>* rat retinas using a polarity-sensitive annexin-based biosensor (annexin B12-Cys101, Cys260-N,N - dimethyl-N-(iodoacetyl)-N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl) ethylenediamine). Transected axons demonstrated a rapid and progressive change in membrane phospholipid polarity, manifested as phosphatidylserine externalization, which was significantly delayed and propagated more slowly in axotomized *Wld<sup>s</sup>* RGCs compared with wild-type axons. Delivery of bis(3-propionic acid methyl ester)phenylphosphine borane complex, a cell-permeable intracellular disulfide-reducing drug, slowed the onset and velocity of phosphatidylserine externalization in wild-type axons significantly, replicating the *Wld<sup>s</sup>* phenotype, whereas extracellular redox modulation reversed the *Wld<sup>s</sup>* phenotype. These findings are consistent with an intra-axonal redox mechanism for axonal degeneration associated with the initiation and propagation of phosphatidylserine externalization after axotomy.

*COMMENT: This paper studies how axonal degeneration is signaled, using a purified retinal ganglion cell culture where axons are cut with a laser. The finding that slowed axonal degeneration in a naturally occurring mutant (Wld<sup>S</sup>) can be replicated by administration of a redox-active drug is suggestive of a redox-mediated mechanism, and also suggests a therapeutic strategy. Interestingly, the fact that Wld<sup>S</sup> protects axons by increasing NAD<sup>+</sup> levels (Wang et al, PNAS 112:10093, 2015) supports the role for the latter in preventing axon degeneration.*

**Sarm1 Deletion, but Not Wld<sup>S</sup>, Confers Lifelong Rescue in a Mouse Model of Severe Axonopathy**

Gilley J, Ribchester RR, Coleman MP. Cell Rep. 2017 Oct 3;21(1):10-16.

ABSTRACT: Studies with the Wld<sup>S</sup> mutant mouse have shown that axon and synapse pathology in several models of neurodegenerative diseases are mechanistically related to injury-induced axon degeneration (Wallerian degeneration). Crucially, an absence of SARM1 delays Wallerian degeneration as robustly as Wld<sup>S</sup>, but their relative capacities to confer long-term protection against related, non-injury axonopathy and/ or synaptopathy have not been directly compared. While Sarm1 deletion or Wld<sup>S</sup> can rescue perinatal lethality and widespread Wallerian-like axonopathy in young NMNAT2-deficient mice, we report that an absence of SARM1 enables these mice to survive into old age with no overt phenotype, whereas those rescued by Wld<sup>S</sup> invariably develop a progressive neuromuscular defect in their hindlimbs from around 3 months of age. We therefore propose Sarm1 deletion as a more reliable tool than Wld<sup>S</sup> for investigating Wallerian-like mechanisms in disease models and suggest that SARM1 blockade may have greater therapeutic potential than WLDS-related strategies.

**Axon Self-Destruction: New Links among SARM1, MAPKs, and NAD+ Metabolism**

Gerdts J, Summers DW, Milbrandt J, DiAntonio A. Neuron. 2016 Feb 3;89(3):449-60.

ABSTRACT: Wallerian axon degeneration is a form of programmed subcellular death that promotes axon breakdown in disease and injury. Active degeneration requires SARM1 and MAP kinases, including DLK, while the NAD<sup>+</sup> synthetic enzyme NMNAT2 prevents degeneration. New studies reveal that these pathways cooperate in a locally mediated axon destruction program, with NAD<sup>+</sup> metabolism playing a central role. Here, we review the biology of Wallerian-type axon degeneration and discuss the most recent findings, with special emphasis on critical signaling events and their potential as therapeutic targets for axonopathy.

*COMMENT: The above two papers demonstrate and discuss the key role of SARM1 as part of the mechanism by which Wld<sup>S</sup> blocks axonal degeneration. There is excellent evidence for SARM1 metabolizing NAD<sup>+</sup> in response to injury, and if Wld<sup>S</sup> is active, there is a compensatory increase in NAD<sup>+</sup> that prevents axonal degeneration. Although not studied in other optic neuropathies, SARM1 adds to the short list of critical pathways for axonal degeneration that may lead to life-changing therapeutic discoveries.*

**CME ANSWERS**

1. True
2. False
3. False

## REFERENCES

1. Real-time imaging of single neuronal cell apoptosis in patients with glaucoma
2. Cordeiro MF, Normando EM, Cardoso MJ, Miodragovic S, Jeylani S, Davis BM, Guo L, Ourselin S, A'Hern R, Bloom PA. *Brain*. 2017 Jun 1;140(6):1757-1767.
3. JUN is important for ocular hypertension-induced retinal ganglion cell degeneration
4. Syc-Mazurek SB, Fernandes KA, Libby RT. *Cell Death Dis*. 2017 Jul 20;8(7):e2945.
5. Targeting neuronal gap junctions in mouse retina offers neuroprotection in glaucoma
6. Akopian A, Kumar S, Ramakrishnan H, Roy K, Viswanathan S, Bloomfield SA. *J Clin Invest*. 2017 Jun 30;127(7):2647-2661.
7. Tonabersat prevents inflammatory damage in the central nervous system by blocking connexin43 hemichannels
8. Kim Y, Griffin JM, Nor MNM, Zhang J, Freestone PS, Danesh-Meyer HV, Rupenthal ID, Acosta M, Nicholson LFB, O'Carroll SJ, Green CR. *Neurotherapeutics*. 2017 Oct;14(4):1148-1165.
9. Vitamin B<sub>3</sub> modulates mitochondrial vulnerability and prevents glaucoma in aged mice
10. Williams PA, Harder JM, Foxworth NE, Cochran KE, Philip VM, Porciatti V, Smithies O, John SW. *Science*. 2017 Feb 17;355(6326):756-760.
11. Axonal Degeneration in Retinal Ganglion Cells Is Associated with a Membrane Polarity-Sensitive Redox Process
12. Almasieh M, Catrinescu MM, Binan L, Costantino S, Levin LA. *J Neurosci*. 2017 Apr 5;37(14):3824-3839.
13. Sarm1 Deletion, but Not Wld<sup>s</sup>, Confers Lifelong Rescue in a Mouse Model of Severe Axonopathy
14. Gilley J, Ribchester RR, Coleman MP. *Cell Rep*. 2017 Oct 3;21(1):10-16.
15. Axon Self-Destruction: New Links among SARM1, MAPKs, and NAD<sup>+</sup> Metabolism
16. Gerdts J, Summers DW, Milbrandt J, DiAntonio A. *Neuron*. 2016 Feb 3;89(3):449-60.



## LITERATURE REVIEW: HIGHLIGHTS FROM IOVS 2017

Gregory Van Stavern, MD

Department of Ophthalmology and Visual Sciences, Washington University in St. Louis  
St. Louis, MO

### LEARNING OBJECTIVES:

1. The attendee will be aware of relevant research published in IOVS and Journal of Neuroscience
2. The attendee will be able to discuss the application of novel technologies (including OCT angiography, photopic negative response, and driver evaluation software) to neuro-ophthalmic diseases
3. The attendee will be able to discuss the potential role of the glymphatic system in neuro-ophthalmic disorders

### CME QUESTIONS:

1. What is the role of the glymphatic system?
2. The photopic negative response assesses the function of what component of the visual system?
3. T/F: contrast sensitivity in the better eye is associated with a higher rate of crashes

### KEY WORDS:

1. Glymphatic system
2. OCT angiography
3. Photopic negative response
4. Non arteritic anterior ischemic optic neuropathy (NAION)
5. Driving safety

I reviewed articles published in Investigative Ophthalmology and Visual Science and Journal of Neuroscience from 1/17 through 12/17. Articles were selected based upon relevance to clinicians and researchers in the field of Neuro Ophthalmology. Articles of particular interest were chosen for presentation.

### DEFORMATION OF THE LAMINA CRIBROSA AND OPTIC NERVE DUE TO CHANGES IN CEREBROSPINAL FLUID PRESSURE

#### Abstract:

*PURPOSE.* Cerebrospinal fluid pressure (CSFp) changes are involved or implicated in various ocular conditions including glaucoma, idiopathic intracranial hypertension, and visual impairment and intracranial pressure syndrome. However, little is known about the effects of CSFp on lamina cribrosa and retrolaminar neural tissue (RLNT) biomechanics, potentially important in these conditions. Our goal was to use an experimental approach to visualize and quantify the deformation of these tissues as CSFp increased.

*METHODS.* The posterior eye and RLNT of porcine eyes ( $n = 3$ ) were imaged using synchrotron radiation phase-contrast micro-computed tomography (PC ICT) at an intraocular pressure of 15 mm Hg and CSFps of 4, 10, 20, and 30 mm Hg. Scans of each tissue region were acquired at each CSFp step and analyzed using digital volume correlation to determine 3-dimensional tissue deformations.

**RESULTS.** Elevating CSFp increased the strain in the lamina cribrosa and RLNT of all three specimens, with the largest strains occurring in the RLNT. Relative to the baseline CSFp of 4 mm Hg, at 30 mm Hg, the lamina cribrosa experienced a mean first and third principal strain of 4.4% and 3.5%, respectively. The corresponding values for the RLNT were 9.5% and 9.1%.

**CONCLUSIONS.** CSFp has a significant impact on the strain distributions within the lamina cribrosa and, more prominently, within the RLNT. Elevations in CSFp were positively correlated with increasing deformations in each region and may play a role in ocular pathologies linked to changes in CSFp.

### Comments

A wide variety of conditions selectively affect the optic nerve head (glaucoma, papilledema, ischemic optic neuropathy). Mechanical changes at the level of the lamina cribrosa may underlie some of these conditions but the exact mechanism for tissue injury is uncertain. Some of the damage may be related to competing forces, including intraocular pressure and orbital CSF pressure. To help answer this question, this group performed an animal study evaluating the deformation of the lamina cribrosa, using a porcine model. Intraocular pressure was controlled and intraorbital CSF pressure was increased by injected fluid into the subarachnoid space, under the optic nerve sheath. CSF pressure was increased in a stepwise fashion and deformation of lamina cribrosa was assessed using 3D imaging and volume analysis. They specifically measured the degree of mechanical strain and regional distribution of the strain. They found that increased orbital CSF pressure caused mechanical strains on the lamina cribrosa and retrolaminar neural tissue, with the greatest strain on the retrolaminar neural tissue. They also manipulated IOP while keeping CSF pressure constant and found an even greater mechanical strain and deformation. They concluded that orbital CSF pressure causes increased mechanical strain on both the lamina cribrosa and retrolaminar neural tissues.

**Limitations:** These results may not apply to human disease and the sample size was relatively small. They also did not show evidence of neuronal or axonal injury related to the mechanical strain itself.

**Potential clinical relevance:** This study suggests a potential mechanism for optic nerve injury with intracranial hypertension and papilledema as well as glaucoma.

## EVIDENCE FOR CSF ENTRY INTO THE OPTIC NERVE VIA A GLYMPHATIC PATHWAY

### Abstract:

**PURPOSE.** The purpose of this study was to determine whether cerebrospinal fluid (CSF) enters the optic nerve via a glymphatic pathway and whether this entry is size-dependent.

**METHODS.** Fluorescent dextran tracers (fluorescein isothiocyanate [FITC]) of four different sizes (10, 40, 70, and 500 kDa) and FITC-ovalbumin (45 kDa) were injected into the CSF of 15 adult mice. Tracer distribution in the orbital optic nerve at 1 hour after injection was assessed in tissue sections with confocal microscopy. Tracer distribution within the optic nerve was studied in relation to blood vessels and astrocytes identified by isolectin histochemistry and glial fibrillary acidic protein (GFAP) immunofluorescence, respectively. Aquaporin 4 (AQP4) immunostaining was performed to assess astrocytic endfeet in relation to CSF tracer.

**RESULTS.** One hour following tracer injection into CSF, all tracer sizes (10–500 kDa) were noted in the subarachnoid space surrounding the orbital optic nerve. In all cases, 10 kDa ( $n = 4/4$ ) and 40 kDa ( $n = 3/3$ ) tracers were noted within the optic nerve, while 70-kDa tracer was occasionally noted ( $n = 1/4$ ).

*Tracer found within the nerve was specifically localized between isolectin-labeled blood vessels and GFAP-positive astrocytes or AQP4-labeled astrocytic endfeet. The 500-kDa tracer was not detected within the optic nerve.*

*CONCLUSIONS. To our knowledge, this is the first evidence of a glymphatic pathway in the optic nerve. CSF enters the optic nerve via spaces surrounding blood vessels, bordered by astrocytic endfeet. CSF entry into paravascular spaces of the optic nerve is size-dependent, and this pathway may be highly relevant to optic nerve diseases, including glaucoma.*

### **Comments**

There is increasing interest in the “glymphatic” system, a channel of paravascular spaces by which CSF egresses from brain and clears waste products. Evidence is emerging that dysfunction of this system could result in buildup of neurotoxic waste products, resulting in neuronal and axonal injury. Dysregulation of this system has been implicated in several diseases but there is little research regarding optic nerve injury and glymphatic dysfunction. This study attempted to determine whether the glymphatic system played a role in the integrity of the optic nerve. Mice were used, since they share similar CSF drainage pathways and optic nerve anatomy with humans. Labelled tracers were injected into the cisterna magna, and CSF flow into the orbital optic nerve was measured. Animals were euthanized one hour post-injection. Labelled tracer localized to blood vessels, astrocytes, and Aquaporin 4 positive astrocyte end feet. They concluded that a glymphatic pathway exists for the optic nerve, by which CSF enters the optic nerve by paravascular spaces, and that these channels are surrounded by AQP4 + astrocytic endfeet.

Limitations: This study shows that an anatomic pathway exists for glymphatic drainage from the optic nerve but did not examine whether this relates to human disease. Further research could explore experimentally impaired glymphatic drainage, to determine whether neural tissue injury results, or study the glymphatic system in human or animal models of aquaporin 4 related disorders.

Potential clinical relevance: This study provides a possible model for mechanism of injury in NMO related optic neuritis and potentially glaucoma, due to inadequate clearance of neurotoxins.

### **EVALUATION OF PROGRESSIVE VISUAL DYSFUNCTION AND RETINAL DEGENERATION IN PATIENTS WITH PARKINSON’S DISEASE**

#### **Abstract:**

*PURPOSE. To quantify changes in visual function parameters and in the retinal nerve fiber layer and macular thickness over a 5-year period in patients with Parkinson’s disease (PD).*

*METHODS. Thirty patients with PD and 30 healthy subjects underwent a complete ophthalmic evaluation, including assessment of visual acuity, contrast sensitivity vision, color vision, and retinal evaluation with spectral-domain optical coherence tomography (SD-OCT). All subjects were reevaluated after 5 years to quantify changes in visual function parameters, the retinal nerve fiber layer, and macular thickness. Association between progressive ophthalmologic changes and disease progression was analyzed.*

*RESULTS. Changes were detected in visual function parameters and retinal nerve fiber layer thickness in patients compared with controls. Greater changes were found during the followup in the PD group than healthy subjects in visual acuity, contrast sensitivity, Lanthony color test ( $P < 0.016$ ), in superotemporal*

and temporal retinal nerve fiber layer sectors ( $P < 0.001$ ), and in macular thickness (all sectors except inner superior and inner inferior sectors,  $P < 0.001$ ). Progressive changes in the retinal nerve fiber layer were associated with disease progression ( $r = 0.389$ ,  $P = 0.028$ ).

**CONCLUSIONS.** Progressive visual dysfunction, macular thinning, and axonal loss can be detected in PD. Analysis of the macular thickness and the retinal nerve fiber layer by SD-OCT can be useful for evaluating Parkinson's disease progression.

**Comments:**

There is increasing evidence that axonal and neuronal loss in the retina and optic nerve can occur in neurodegenerative conditions such as Alzheimer's disease and Multiple Sclerosis. Most such studies have been cross sectional, with no longitudinal follow up. The evidence for a similar effect in Parkinson's disease has been mixed. This was a 5 year, prospective study of OCT in a cohort of Parkinson's disease (PD). This included 30 subjects and 30 controls. Visual outcomes included Pelli-Robson contrast sensitivity as well as standard visual metrics. At 5 years, all visual outcomes were worse in PD subjects.

Although there was no overall difference in rNFL thickness and macular thickness between PD subjects and controls, the PD group demonstrated a greater rate of change over time compared with controls, albeit only in the temporal rNFL. There was a moderate correlation in the PD group between progression of rNFL thinning and disease progression.

Limitations: There were only two time points assessed and the study used a relatively small sample size. There was overall no significant difference between groups in OCT metrics, despite the rate of change difference.

Potential clinical relevance: This is one of the few prospective assessments of axonal loss in neurodegenerative diseases, and suggests that axonal loss in the retina could serve as a surrogate marker for neurodegeneration, even if the results are underwhelming. If validated with further studies, this could provide more support for use of OCT as a biomarker for neurodegenerative diseases, including PD.

## **QUANTITATIVE ASSOCIATION BETWEEN PERIPAPILLARY BRUCH'S MEMBRANE SHAPE AND INTRACRANIAL PRESSURE**

**Abstract:**

**PURPOSE.** The purpose of this study was to determine if there is a quantitative relationship between chronic intracranial pressure (ICP) and peripapillary Bruch's membrane (pp-BM) shape and to determine whether change in pp-BM shape can be detected within 1 hour after ICP lowering by lumbar puncture (LP).

**METHODS.** In this study, 308 nasal-temporal optical coherence tomography B-scans were obtained within 1 hour before and after LP in 39 eyes from 20 patients (age 23–86 years, 75% female, ICP [opening pressure] 10–55 cm H<sub>2</sub>O). A total of 16 semi-landmarks defined pp-BM on each image. Geometric morphometric analysis identified principal components of shape in the image set. Generalized estimating equation models, accounting for within-subject correlation, were used to identify principal components that were associated with chronic ICP (comparing pre-LP images between eyes) and/or acute ICP changes (comparing pre- and post-LP images within eyes). The pp-BM width and anterior pp-BM location were calculated directly from each image and were studied in the same manner.

*RESULTS. Principal component 1 scalar variable on pre-LP images was associated with ICP ( $P < 0.0005$ ). Principal component 4 magnitude changed within eyes after LP ( $P = 0.003$ ). For both principal components 1 and 4, lower ICP corresponded with a more posterior position of pp-BM. Chronic ICP was associated with both pp-BM width (6.81  $\mu\text{m}/\text{cm H}_2\text{O}$ ;  $P = 0.002$ ) and more anterior location of temporal and nasal pp-BM margins (3.41, 3.49  $\mu\text{m}/\text{cm H}_2\text{O}$ ;  $P < 0.0005, 0.002$ ).*

*CONCLUSIONS. This study demonstrates a quantitative association between pp-BM shape and chronic ICP level. Changes in pp-BM shape are detectable within 1 hour of lowering ICP. pp-BM shape may be a useful marker for chronic ICP level and acute ICP changes. Further study is needed to determine how pp-BM shape changes relate to clinical markers of papilledema.*

**Comments:**

The mechanism of neural injury in papilledema remains unclear, but may be partially related to the forces exerted against the lamina cribrosa by increased orbital CSF pressure. It is also unclear how quickly structural changes in the lamina cribrosa occur when orbital CSF pressure changes. This study was designed to study whether mechanical deformation of the lamina cribrosa occurs in papilledema and how quickly this change develops. They specifically evaluated the relationship between intracranial hypertension and peripapillary Bruch's membrane (ppBM) shape using geographic morphometric shape analysis with OCT. 20 subjects were included, with 39 eyes, 8 with normal ICP and no papilledema. Measurements were made using principal component analysis to detect the shape and configuration of ppBM before and 1 hour after lumbar puncture. Overall, they found that patients with chronically elevated ICP and papilledema had deflection of ppBM toward the vitreous, and this converted to deflection away from the vitreous post-LP. However, this deformation did not occur in eyes without papilledema, suggesting that these mechanical changes might be dependent upon initial load-strain. This deformation only applied to one component of the shape analysis.

Limitations: The study may have been underpowered due to the small sample with papilledema. Further, the measurements may be affected by variations in optic nerve anatomy. Only one time point was measured, so it is possible that further deformation could occur hours/days/week after LP, along with medical treatment of elevated ICP.

Potential clinical relevance: This study demonstrates that there is a rapid anatomic change in response to lowering of ICP in eyes with papilledema, but not in those without. This indicates that the mechanical strain and deformation of neural tissue due to papilledema is rapidly reversible, which has implications for diseases such as Idiopathic Intracranial Hypertension.

**THE PHOTOPIC NEGATIVE RESPONSE: AN OBJECTIVE OF RETINAL GANGLION CELL FUNCTION IN PATIENTS WITH LEBER'S HEREDITARY OPTIC NEUROPATHY**

**Abstract:**

*PURPOSE. The photopic negative response (PhNR) is a slow negative component of a flash photopic full-field ERG that has been shown to be specific for retinal ganglion cell (RGC) activity. Direct evaluation of RGC function is desirable in patients with Leber's hereditary optic neuropathy (LHON) in which the loss of central acuity can make it difficult to monitor patients with standard metrics. The purpose of this study was to evaluate the use of PhNR as an objective noninvasive clinical metric in LHON.*

**METHODS.** Full-field photopic ERG recordings were collected in subjects with the mt.11778G>A/ND4 LHON mutation using a red on blue stimulus. The PhNR was identified using a computer-based automated detection system, and data were manually examined to remove movement artifacts.

**RESULTS.** The PhNR amplitude was compared between controls ( $n = 13$ ), carriers ( $n = 17$ ), and affected ( $n = 6$ ). Mean PhNR amplitude decreased significantly across groups ( $P < 0.0001$ ). Post hoc Tukey's test revealed a significant decrease in PhNR amplitude between carriers and controls ( $P < 0.05$ ) and between carriers and affected ( $P < 0.01$ ).

**CONCLUSIONS.** We are able to demonstrate that the PhNR amplitude is significantly decreased in patients affected by LHON compared to carriers in a well-described pedigree. Surprisingly, there was also a decrease in PhNR in carriers, suggesting potential subclinical RGC dysfunction in some carriers. This is important in patients affected with LHON who typically have a dense central scotoma. The PhNR may be a useful objective outcome measure for future clinical trials.

**Comments:**

Although structural changes in retinal ganglion cells (RGC) can be easily assessed with OCT, functional changes are more challenging to quantify. Pattern ERG is one such modality but suffers from small signal amplitude and heavy reliance upon good visual acuity and fixation. The photopic negative response (PhNR) is a component of the full field ERG that arises from the RGC layer and can quantify RGC function. Since it is a full field response, it is less dependent upon visual acuity and fixation. This study assessed the utility of using the photopic negative response (PnNR) as an outcome marker in Leber's Hereditary Optic Neuropathy (LHON). They included 6 symptomatic LHON subjects, 17 asymptomatic LHON carriers, and 13 normal controls. All LHON subjects (symptomatic and carriers) harbored the 11778 mutation. All subjects underwent standard eye exam, including ETDRS visual acuity, perimetry, and OCT. They found that the PhNR was reduced in LHON symptomatic subjects compared with controls. They also found that PhNR was also significantly reduced in asymptomatic carriers compared with controls. There was a small but statistically significant correlation between PhNR amplitude and OCT.

**Limitation:** It is unclear whether the PhNR provides more clinical information than would be provided by conventional measures, particularly in symptomatic patients. Its value may be greater in the research arena.

**Potential clinical relevance:** PhNR may have utility as a clinical metric for monitoring visual function in LHON and could be used as an objective outcome in clinical trials. The reduction in RGC function in the asymptomatic carriers is interesting and raises the possibility that PhNR may have a predictive or prognostic role.

**FOVEAL AND PERIPAPILLARY VASCULAR DECUREMENT IN MIGRAINE WITH AURA DEMONSTRATED BY OPTICAL COHERENCE TOMOGRAPHY**

**Abstract:**

**PURPOSE.** Migraine, particularly with aura, has been associated with ocular and systemic ischemic complications, but there are limited data on the ocular vasculature in migraine. We used optical coherence tomography angiography (OCTA) to assess perfusion of the macula and optic nerve in migraine patients, with (MA) and without (MO) aura, compared to healthy controls (HC).

*METHODS. We recruited 15 MA (mean age 42 years), 12 MO (mean age 46 years), and 22 HC (mean age 39 years) participants from neurology and neuro-ophthalmology clinics. Participants underwent optical coherence tomography and 3 3 3 mm OCTA of the macula and optic nerve. Foveal avascular zone area was automatically measured using AngioVue software, and vessel density was calculated as blood vessel length divided by scan area (mm<sub>-1</sub>) after skeletonization of OCTA images.*

*RESULTS. On macular OCTA, MA participants had an enlarged foveal avascular zone area when compared with HC (0.300 ± 0.019 vs. 0.220 ± 0.066 mm<sup>2</sup>, P = 0.006). In addition, superficial foveal vessel density was decreased in MA participants when compared with MO participants (7.8 ± 0.31 vs. 9.3 ± 0.44, P = 0.04) and HC (7.8 ± 0.31 vs. 9.4 ± 0.21 mm<sub>-1</sub>, P = 0.002). On optic nerve OCTA, the MA participants had reduced superior peripapillary vessel density when compared with the MO participants (12.0 ± 0.45 vs. 14.0 ± 0.38 mm<sub>-1</sub>, P = 0.031) and HC (12.0 ± 0.45 vs. 14.1 ± 0.53 mm<sub>-1</sub>, P = 0.035). There were no significant differences between the MO and HC groups.*

*CONCLUSIONS. Migraine with, but not without, aura was associated with foveal and peripapillary vascular decrements, which may possibly mediate increased risk of ocular and systemic vascular complications in these patients. OCTA could potentially be useful as a biomarker for migraine with aura.*

**Comments:**

Migraine with aura is a risk factor for ischemic stroke, both in the eye and the brain. The specific mechanisms underlying the increased risk are unclear. This study was designed to evaluate optic nerve and retinal microvasculature and perfusion in migraineurs compared with normal controls. They used OCT Angiography in 3 groups of subjects: migraine with visual aura (n=15); migraine without visual aura (n=12); and healthy controls (n=22). All three groups were characterized by the International Headache Society Revised Criteria and were rigorously defined. All groups were matched for age and appropriate exclusionary criteria were used for OCT. Each subject was evaluated with conventional OCT metrics and OCT angiography-based metrics including vessel density and Foveal Avascular Zone (FAZ). Conventional OCT metrics (rNFL thickness, macular thickness, etc) showed no significant differences between groups. They found a larger FAZ and reduced foveal vessel density in the migraine with aura group. They also found that the superior peripapillary vessel density was reduced in the migraine with aura group. The potential mechanisms for these differences are uncertain, but they raise the possibility that they could be related to the increased risk of ischemic systemic ocular complications in patients with migraine and aura (ischemic optic neuropathy, glaucoma, cerebral ischemic stroke, etc).

Limitations: They used a relatively small sample size. The variability and reproducibility of OCT angiography is still being actively explored, and this was a cross-sectional study- a follow up longitudinal study would provide more support for their results. Finally, there is still some uncertainty regarding OCT-A metrics and relation to pathology.

Clinical relevance: The changes in retinal and optic nerve microvasculature could account for increased risk for ocular ischemic events in patient experiencing migraine with aura

## PLASTICITY BEYOND V1: REINFORCEMENT OF MOTION PERCEPTION UPON BILATERAL CENTRAL RETINAL LESIONS IN ADULTHOOD

### Abstract:

*Induction of a central retinal lesion in both eyes of adult mammals is a model for macular degeneration and leads to retinotopic map reorganization in the primary visual cortex (V1). Here we characterized the spatiotemporal dynamics of molecular activity levels in the central and peripheral representation of five higher-order visual areas, V2/18, V3/19, V4/21a, V5/PMLS, area 7, and V1/17, in adult cats with central 10° retinal lesions (both sexes), by means of real-time PCR for the neuronal activity reporter gene zif268. The lesions elicited a similar, permanent reduction in activity in the center of the lesion projection zone of area V1/17, V2/18, V3/19, and V4/21a, but not in the motion-driven V5/PMLS, which instead displayed an increase in molecular activity at 3 months postlesion, independent of visual field coordinates. Also area 7 only displayed decreased activity in its LPZ in the first weeks postlesion and increased activities in its periphery from 1 month onward. Therefore we examined the impact of central vision loss on motion perception using random dot kinematograms to test the capacity for form from motion detection based on direction and velocity cues. We revealed that the central retinal lesions either do not impair motion detection or even result in better performance, specifically when motion discrimination was based on velocity discrimination. In conclusion, we propose that central retinal damage leads to enhanced peripheral vision by sensitizing the visual system for motion processing relying on feedback from V5/PMLS and area 7.*

### Comments:

There is evidence that visual cortex reorganization occurs after retinal injury, reflecting plasticity of the neuro-visual system. This study assessed visual cortical reorganization after experimentally induced retinal lesions, with the goal of identifying the time course and the role of visual association areas. Adult cats were used as subjects. All cats received training with a series of motion direction and discrimination tasks prior to lesioning. Retinal lesions were induced by photocoagulation with area centralis/fovea and confirmed with fundus photography in vivo and then histopathology in vitro. Animals were then sacrificed and studied with histopathology and PCR for gene expression, targeting genes localizing to cortical visual areas. They specifically studied the “lesion projection zone” (LPZ, V1) and surrounding regions. They found that the lesion projection zone recovers after lesioning, with increased gene expression. The center of the LPZ was permanently abnormal, and peripheral visual field representations showed a time-dependent restoration of pre-lesion activity. Area V5 showed retinotopy-independent hyperactivity (increased gene expression) after induction of retinal lesions- in contrast to other visual cortex areas, which showed downregulation of zif268 mRNA. Overall, they concluded that other visual association areas (outside of the primary visual cortex) play a role in cortical reorganization after retinal lesions, and that central retinal lesions enhance peripheral vision, with major contributions from V5 and area 7.

Limitations: relevance to human neuroplasticity; correlation between structure and function;

Clinical relevance: This suggests that central retinal injury (e.g., age related macular degeneration) can result in enhancement in peripheral vision, which could have implications for rehab and neuroprotective/neurogenerative strategies.



## NEUROPROTECTIVE EFFECTS OF OMEGA-3 POLYUNSATURATED FATTY ACIDS IN A RAT MODEL OF ANTERIOR ISCHEMIC OPTIC NEUROPATHY

### Abstract:

**PURPOSE.** *The purpose of this study was to investigate the therapeutic effect of omega-3 polyunsaturated fatty acid (x-3 PUFA) administration in a rat model of anterior ischemic optic neuropathy (rAION).*

**METHODS.** *The level of blood arachidonic acid/eicosapentaenoic acid (AA/EPA) was measured to determine the suggested dosage. The rAION-induced rats were administered fish oil (1 g/day EPA) or phosphate-buffered saline (PBS) by daily gavage for 10 consecutive days to evaluate the neuroprotective effects.*

**RESULTS.** *Blood fatty acid analysis showed that the AA/EPA ratio was reduced from 17.6 to 1.5 after 10 days of fish oil treatment. The retinal ganglion cell (RGC) densities and the P1-N2 amplitude of flash visual-evoked potentials (FVEP) were significantly higher in the x-3 PUFA-treated group, compared with the PBS-treated group ( $P < 0.05$ ). The number of apoptotic cells in the RGC layer of the x-3 PUFA-treated rats was significantly decreased ( $P < 0.05$ ) compared with that of the PBS-treated rats. Treatment with x-3 PUFAs reduced the macrophage recruitment at the optic nerve (ON) by 3.17-fold in the rAION model. The M2 macrophage markers, which decrease inflammation, were induced in the x-3 PUFA-treated group in contrast to the PBS-treated group. In addition, the mRNA levels of tumor necrosis factor-alpha, interleukin-1 beta, and inducible nitric oxide synthase were significantly reduced in the x-3 PUFA-treated group.*

**CONCLUSIONS.** *The administration of x-3 PUFAs has neuroprotective effects in rAION, possibly through dual actions of the antiapoptosis of RGCs and anti-inflammation via decreasing inflammatory cell infiltration, as well as the regulation of macrophage polarization to decrease the cytokine-induced injury of the ON.*

### Comments:

Non arteritic anterior ischemic optic neuropathy results in permanent visual loss and has no proven treatment. The investigators used a rodent model of non-arteritic anterior ischemic optic neuropathy to study the potential neuroprotective effects of polyunsaturated fatty acids (PUFA). There is evidence that neurogenic inflammation, mediated by macrophages, plays a role in neuronal and axonal injury in NAION. Omega 3 PUFAs have been shown to transition pro-inflammatory macrophages to anti-inflammatory; they can also stabilize damaged blood-brain barrier after ischemic injury. Both of these mechanisms could improve visual outcomes after NAION. They used a standard rodent model of NAION, and used retinal ganglion cell (RGC) density, flash VEP, and arachidonic acid/eicoaspentaenoic acid (AA/EPA) levels as outcome markers. AA/EPA levels are surrogate markers for proinflammatory cytokines, and in humans, high AA/EPA levels shown to be associated with higher rates of cardiovascular disease. There was a treated group and control group (n=6 in each). Treated rodents received PUFAs 3 days prior to induction of NAION and continued administrations for another 6 days. They found increased density of RGCs and a reduced number of apoptotic cells in the treated group. They also found a reduced number of pro-inflammatory cytokines (reduced AA/EPA levels) in treated animals. Flash VEP latencies were similar in each group, although amplitudes were greater in the treated group.

Limitations: The animals were treated 3 days prior to onset of NAION, which is not practical in human NAION. The functional outcomes (FVEP) were similar, so it is questionable whether there is a true clinically relevant functional benefit.

## **VISUAL SENSORY AND VISUAL-COGNITIVE FUNCTION AND RATE OF CRASH AND NEAR-CRASH INVOLVEMENT AMONG OLDER DRIVERS USING NATURALISTIC DRIVER DATA**

### **Abstract:**

*PURPOSE.* An innovative methodology using naturalistic driving data was used to examine the association between visual sensory and visual-cognitive function and rates of future crash or near-crash involvement among older drivers.

*METHODS.* The Strategic Highway Research Program (SHRP2) Naturalistic Driving Study was used for this prospective analysis. The sample consisted of  $N = 659$  drivers aged  $\geq 70$  years and study participation lasted 1 or 2 years for most participants. Distance and near visual acuity, contrast sensitivity, peripheral vision, visual processing speed, and visuospatial skills were assessed at baseline. Crash and near-crash involvement were based on video recordings and vehicle sensors. Poisson regression models were used to generate crude and adjusted rate ratios (RRs) and 95% confidence intervals, while accounting for person-miles of travel.

*RESULTS.* After adjustment, severe impairment of the useful field of view ( $RR = 1.33$ ) was associated with an increased rate of near-crash involvement. Crash, severe crash, and at-fault crash involvement were associated with impaired contrast sensitivity in the worse eye ( $RRs = 1.38, 1.54, \text{ and } 1.44$ , respectively) and far peripheral field loss in both eyes ( $RRs = 1.74, 2.32, \text{ and } 1.73$ , respectively).

*CONCLUSIONS.* Naturalistic driving data suggest that contrast sensitivity in the worse eye and far peripheral field loss in both eyes elevate the rates of crash involvement, and impaired visual processing speed elevates rates of near-crash involvement among older drivers. Naturalistic driving data may ultimately be critical for understanding the relationship between vision and driving safety.

### **Comments:**

Accurate assessment of driving safety is challenging and can have important implications. Previous studies have primarily relied upon crash data (which will miss near-crash events and unreported crashes) and self-reported driver assessment. This study used monitoring equipment to assess driving safety in older drivers. 659 elderly drivers (age  $> 70$  years) were recruited. Their vehicles were equipped with driver monitoring software. All participants completed surveys related to demographics, driving history, and medical conditions. All participants underwent detailed visual testing including high contrast VA (log MAR), contrast sensitivity, perimetry, and a validated Driver Health inventory to assess visual processing speed. Clock drawing test was used to assess cognitive function and visual spatial performance. The main outcomes were crash and near-crash events. Analysts reviewed video data to assess crash and near crash events. Overall, over a 3 year driving period,  $\sim 25\%$  of drivers were involved in a crash related event. There were a total of 251 crashes for a rate of 5.3 crashes per 100,000 miles traveled. They found the following associations:

1. Visual acuity was NOT related to crash events
2. Impaired contrast sensitivity in worse eye was associated with crash events
3. Far peripheral vision impairment was associated with a higher rate of crash events
4. Impaired spatial ability NOT related to crash events

5. Useful field of vision (related to visual processing speed) was related to near crash but not crash events

Limitations: There are potential limitations in software metrics in detecting all crash events. This study involved a mostly Caucasian population, so it is uncertain whether this is generalizable to other ethnic populations.

Clinical relevance: This study demonstrates that naturalistic driving data studies are feasible. This data yields insight into the relationship between visual function and driving safety, which could ultimately be incorporated into driver safety regulations.

### **CORTICAL SPREADING DEPRESSION CLOSES PARAVASCULAR SPACES AND IMPAIRS GLYMPHATIC FLOW: IMPLICATIONS FOR MIGRAINE HEADACHE**

#### **Abstract:**

*Functioning of the glymphatic system, a network of paravascular tunnels through which cortical interstitial solutes are cleared from the brain, has recently been linked to sleep and traumatic brain injury, both of which can affect the progression of migraine. This led us to investigate the connection between migraine and the glymphatic system. Taking advantage of a novel in vivo method we developed using two-photon microscopy to visualize the paravascular space (PVS) in naive uninjected mice, we show that a single wave of cortical spreading depression (CSD), an animal model of migraine aura, induces a rapid and nearly complete closure of the PVS around surface as well as penetrating cortical arteries and veins lasting several minutes, and gradually recovering over 30 min. A temporal mismatch between the constriction or dilation of the blood vessel lumen and the closure of the PVS suggests that this closure is not likely to result from changes in vessel diameter. We also show that CSD impairs glymphatic flow, as indicated by the reduced rate at which intraparenchymally injected dye was cleared from the cortex to the PVS. This is the first observation of a PVS closure in connection with an abnormal cortical event that underlies a neurological disorder. More specifically, the findings demonstrate a link between the glymphatic system and migraine, and suggest a novel mechanism for regulation of glymphatic flow.*

#### **Comments:**

Cortical spreading depression (CSD), which accounts for migraine visual aura, is linked to cerebral ischemic events, and involves an inflammatory cascade involving NO and COX-2. The investigators a functional relationship between CSD and the glymphatic system. The glymphatic system is thought to regulate CSF egress from the brain and is involved in the clearance of intraparenchymal extracellular macromolecules. The function of the glymphatic system seems be removal of neurotoxic waste products from brain into extracellular paravascular compartments. The investigators performed transcranial imaging using 2 photon microscopy to evaluate paravascular spaces in mice. They wanted to determine whether changes in paravascular spaces (and secondary impairment in clearance of waste products) occurred after induction of CSD. They used a validated rodent model of CSD, initiated by craniotomy and pinprick. CSF was labelled to quantify clearance. They found that CSD was followed by arterial constriction, with rapid and complete closure of paravascular spaces (PVS) in surface vessels. Penetrating artery vessels were also affected, although these were harder to quantify. There was impaired clearance of CSF in the mice with induced CSD. They concluded that CSD resulted in structural and functional changes in the glymphatic system, with closure of paravascular spaces on the pial surface and perhaps on deeper arteries. This causes impaired clearance of CSF which may cause accumulation of neurotoxic waste products. The outer wall of PVS consists of astrocytic endfeet and they speculate the

neuronal and astrocytic edema may be the causative mechanism. Aquaporin 4 channels predominate on astrocytic endfeet, which may relate to the pathophysiologic mechanisms of optic nerve injury in NMO spectrum disorders.

Limitations: This may or may not have relevance to human brain and spontaneously generated CSD. The pathologic significance of these findings and their relationship to future ischemic events is highly speculative at this point.

Potential clinical relevance: This may shed light on the pathophysiology of the relationship between migraine aura and cerebrovascular ischemia, as well as the relationship of the glymphatic system to migraine and migraine aura.

#### **CME ANSWERS:**

1. To facilitate egress of CSF through paravascular spaces and potentially clear neurotoxins
2. The PhNR arises from the ganglion cell layer in the retina
3. True

#### **REFERENCES:**

1. Feola AJ, Coudrillier B, Mulvihill J et al. Deformation of the lamina cribrosa and optic nerve due to changes in cerebrospinal fluid pressure. *Invest Ophthalmol Vis Sci* 2017;58:2070-2078
2. Mathieu E, Gupta N, Ahari A et al. Evidence for CSF entry into the optic nerve via a glymphatic pathway. *Invest Ophthalmol Vis Sci* 2017;58:4784-4791
3. Satue M, Rodrigo MJ, Obis J et al. Evaluation of progressive visual dysfunction and retinal degeneration in patients with Parkinson's disease. *Invest Ophthalmol Vis Sci* 2017;58:1151-1157
4. Gampa A, Vangipuram G, Shirazi G et al. Quantitative association between peripapillary Bruch's membrane shape and intracranial pressure. *Invest Ophthalmol Vis Sci* 2017;58:2730-35
5. Karanjia R, Berezovsky A, Sacai PY et al. The photopic negative response: an objective of retinal ganglion cell function in patients with Leber's Hereditary Optic Neuropathy. *Invest Ophthalmol Vis Sci* 2017;58:300-306
6. Chang MY, Phasukijwatana N, Garrity S et al. Foveal and peripapillary vascular decrement in migraine with aura demonstrated by optical coherence tomography. *Invest Ophthalmol Vis Sci* 2017;58:5477-5484
7. Burnat K, Hu T-T, Kossut M et al. Plasticity beyond V1: Reinforcement of motion perception upon bilateral central retinal lesions in adulthood. *J Neurosci* 2017;37:8989-8999
8. Georgiou T, Wen Y-T, Chang C-H et al. Neuroprotective effects of omega-3 polyunsaturated fatty acids in a rat model of anterior ischemic optic neuropathy. *Invest Ophthalmol Vis Sci* 2017;58:1603-1611
9. Huisinigh C, Levitan EB, Irvin MR et al. Visual sensory and visual-cognitive function and rate of crash and near-crash involvement among older drivers using naturalistic driver data. *Invest Ophthalmol Vis Sci* 2017;58:2059-2067
10. Schain AJ, Melo-Carillo A, Strassman AM et al. Cortical spreading depression closes paravascular spaces and impairs glymphatic flow: implications for migraine headache. *J Neurosci* 2017;37:2904-2915

## LITERATURE REVIEW: WILD CARD

Lynn K Gordon, MD, PhD  
Stein Eye Institute, David Geffen School of Medicine at UCLA  
Los Angeles, California

In this section, new and interesting publications from the genetic, basic science, and clinical translational science literature were identified for presentation. A limited selection were judged to have potential relevance to the neuro-ophthalmic community and selected for presentation.

### LEARNING OBJECTIVES

1. The attendee will identify new phenotypes associated with mitochondrial mutations.
2. The attendee will be able to discuss a new *in vivo* model for myasthenia gravis and be able to understand how epitope specificity can aid in developing specific new therapies for antibody mediated disease.
3. The attendee will gain new understanding of ocular dominance plasticity.

### CME QUESTIONS

1. Mutations in OPA10
  - a. are associated with optic atrophy only in the absence of other neurologic findings
  - b. are on the RTN41P1 gene which encodes a non-mitochondrial targeted protein
  - c. have been found only in a single family
  - d. are associated with a spectrum of presentations from optic atrophy alone to encephalopathies
2. In traumatic brain injury, microglial polarization through toll-like receptor signaling through TLR4
  - a. induces microglial polarization toward a proinflammatory phenotype
  - b. limits expression of proinflammatory molecules
  - c. induces neuroprotection
  - d. has no effect on the M2 phenotype
3. Removal of pathologic antibodies in experimental autoimmune myasthenia gravis
  - a. should not be selectively removed as this is ineffective
  - b. can be selectively removed using antigen-specific immunoadsorption
  - c. are not required because immune suppression is effective
  - d. have no theoretical advantage over plasmapheresis

### KEYWORDS

1. Plasticity
2. Neuro-immunology
3. TLR4 signal
4. Dominant optic atrophy
5. Progressive supranuclear palsy

### SUMMARY

### **Genetics and Mitochondria:**

Gerstenecker et al tried to correlate genes (microtubule-associated protein tau, myelin-associated oligodendrocyte basic protein, eukaryotic translation initiation factor 2-alpha kinase 2, syntaxin 6, and apolipoprotein E) previously identified as risk alleles in progressive supranuclear palsy and cognitive dysfunction in progressive supranuclear palsy. They studied 305 participants who underwent a neuropsychological evaluation as well as genetic analysis. They found that: “cognition varied significantly at the subhaplotype level, with carriers of the microtubule-associated protein tau rs242557/A allele, which marks the H1c subhaplotype, performing better than noncarriers on measures of general cognitive function, executive function, and attention.” Larger studies would be required to determine if this relationship, better cognition in PSP patients with this haplotype, is accurate.

Charif et al in JAMA Neurology describe neurologic phenotypes in recessive mutations in the RRTN4lp1 gene that encodes a mitochondrial quinone oxidoreductase. They presented individuals from 11 families 6 of which presented with isolated optic atrophy and 5 which had severe neurologic syndromes with early death. The families with severe neurologic consequences had rare mutations that led to the absence of the protein.

Gerber et al observed dominant mutations in DNM1L in three large families with isolated optic atrophy. DNM1L is expressed in retinal ganglion cells and their axons. There is increased mitochondrial fusion caused by the mutations in contrast to excess mitochondrial fission that is observed in mutations in OPA1, both leading to clinical optic atrophy.

Madsen et al were interested in whether mitochondrial dysfunction in oligodendrocytes could participate in the pathophysiology of demyelinating disease. They employed a genetic mouse model in which double-strand breaks in the mitochondrial DNA were induced in myelinating oligodendrocytes starting at 3 weeks of age. These mice had a more robust demyelinating disease in experimental autoimmune encephalomyelitis and mimicked some of the features of chronic or progressive demyelination.

### **Inflammation and Immunity:**

Yao et al studied the role of the TLR4 signal in the microglial M1/M2 phenotype following a defined cortical brain injury in mice. Mice that lacked the TLR4 receptor had decreased brain injury by quantitation of the infarct volume and improved behavioural outcomes. In the absence of TLR4, there was a greater M2 phenotype of the microglia which may be protective.

Lazaridis et al had two publications that are discussed. The first characterized a rat model of experimental autoimmune myasthenia gravis using specific extracellular domains of the human acetylcholine receptor subunits. These animals developed symptoms of MG and antibodies, however the efficiency of induction of disease varied depending on the inciting antigen. This group continued their studies in the second paper to develop an antigen-specific immunoadsorption to selectively remove antibodies with specificity for the human acetylcholine receptor.

### **Wild Cards:**

Jaepel et al studies experience-dependent plasticity after monocular deprivation in adult mice. In a high profile paper in Nature Neuroscience they presented new evidence for ocular dominance shifts that may reflect plasticity of eye-specific inputs onto the lateral geniculate neurons. This was a novel and unexpected finding but the authors feel that one needs to reconsider using only “cortical interpretations of ocular dominance plasticity”.

In another recent Nature Neuroscience paper, Poletti, Rucci, and Carrasco use precise retinal stimulation within the foveola to identify extremely “precise control of attention and its involvement in fine spatial vision”. In this paper they conclude that shifts in covert attention is a way to improve and enhance processing.

### CME ANSWERS

1. D Mutations in OPA10, encoding a mitochondrial quinone oxidoreductase, are associated with a spectrum of presentations from optic atrophy alone to encephalopathies
2. A Genetic evidence using TLR4 knockout animals suggests that TLR4 signalling in a cortical impact model induces microglial polarization toward a proinflammatory phenotype.
3. B Immunoabsorption in a selective way is effective using antigen-specific immunoabsorption in an experimental model of MG.

### REFERENCES

1. Gerstenecker A, Roberson ED, Schellenberg GD, et al. Genetic influences on cognition in progressive supranuclear palsy. *Mov Disord.* 2017; 32:1764-1771.
2. Charif M, Nasca A, Thompson K, et al. Neurologic Phenotypes Associated With Mutations in RTN4IP1 (OPA10) in Children and Young Adults. *JAMA Neurol.* 2017; Nov 27. Epub ahead of print.
3. Gerber S, Charif M, Chevrollier A, et al. Mutations in DNM1L, as in OPA1, result in dominant optic atrophy despite opposite effects on mitochondrial fusion and fission. *Brain.* 2017; 140:2586-2596.
4. Madsen PM, Pinto M, Patel S, et al. Mitochondrial DNA Double-Strand Breaks in Oligodendrocytes Cause Demyelination, Axonal Injury, and CNS Inflammation. *J Neurosci.* 2017; 37:10185-10199.
5. Yao X, Liu S, Ding W, et al. TLR4 signal ablation attenuated neurological deficits by regulating microglial M1/M2 phenotype after traumatic brain injury in mice. *J Neuroimmunol.* 2017; 310:38-45.
6. Lazaridis K, Baltatzidi V, Trakas N, et al. Characterization of a reproducible rat EAMG model induced with various human acetylcholine receptor domains. *J Neuroimmunol.* 2017; 303:13-21.
7. Lazaridis K, Dalianoudis I, Baltatzidi V, Tzartos SJ. Specific removal of autoantibodies by extracorporeal immunoabsorption ameliorates experimental autoimmune myasthenia gravis. *J Neuroimmunol.* 2017; 312:24-30.
8. Jaepel J, Hübener M, Bonhoeffer T, Rose T. Lateral geniculate neurons projecting to primary visual cortex show ocular dominance plasticity in adult mice. *Nat Neurosci.* 2017; 20:1708-1714.
9. Poletti M, Rucci M, Carrasco M. Selective attention within the foveola. *Nat Neurosci.* 2017; 20:1413-1417.

## NEUROLOGICAL LITERATURE OF NEURO-OPHTHALMOLOGICAL SIGNIFICANCE

Caroline Tilikete, MD-PhD  
Hospices Civils de Lyon, University Lyon I  
Lyon, France

### LEARNING OBJECTIVES

1. The attendee will hear about new possibilities for treating acquired nystagmus.
2. The attendee will understand the vestibulo-ocular deficit associated to internuclear ophthalmoplegia.
3. The attendee will have the newest information about clinical spectrum of MOG associated optic neuritis.
4. The attendee will hear new information about some clinic aspects and therapeutics in NMOSD.
5. The attendee will know the 2017 proposed revisions to the McDonald diagnostic criteria for multiple sclerosis
6. The attendee will get knowledge of the newest neurovisual criteria of posterior cerebral atrophy (PCA).

### CME QUESTIONS

1. Which of the following clinical sign(s) may be helpful in internuclear ophthalmoplegia to exclude a differential diagnosis a pseudo-INO from myasthenia gravis? (there could be more than one)
  - a. Preservation of convergence
  - b. Deficit of contralesional posterior semi-circular function
  - c. Ocular tilt reaction
  - d. Nystagmic abducting eye
2. Which of the following item(s) is(are) true regarding MOG-Ab related optic neuritis? (there could be more than one)
  - a. % of optic neuritis
  - b. Frequently associated to swollen disk
  - c. Good prognosis with rare optic atrophy
  - d. Anterior extensive MRI hypersignal of the optic nerve
3. 2017 proposed revisions to the McDonald diagnostic criteria for multiple sclerosis include the following change(s) (there could be more than one)
  - a. CSF-specific oligoclonal bands can be used for dissemination in time criteria
  - b. Asymptomatic MRI lesion cannot be used for dissemination in space or time
  - c. Optic neuritis can be used for dissemination in space
  - d. Cortical lesions can be used to demonstrate dissemination in space

### KEYWORDS:

1. Eye movements
2. MOG-Ab
3. NMOSD
4. MS criteria
5. Posterior cerebral atrophy



## HIGHLIGHTS

### Nystagmus

One study suggests establishing zebrafish as a pharmacologic animal model for treating infantile nystagmus, in showing that gabapentin/ memantine significantly reduced nystagmus intensity (1). Implantation of a magnetic oculomotor prosthesis can help patients with acquired disabling nystagmus as suggested in a case report in a patient with longstanding upbeat nystagmus due to paraneoplastic syndrome (2). Amantadine as an alternative treatment for periodic alternating nystagmus is suggested by the report of successful treatment in a patient with PAN refractory to baclofen and intolerance to memantine (3).

### Vestibular testing in internuclear ophthalmoplegia

Two studies questioned the vestibulo-ocular deficit associated to internuclear ophthalmoplegia (INO). In unilateral INO, either in MS patients(4) or in stroke patients (5), severe deficit of contralesional posterior semicircular canal (SCC) function was found. In bilateral INO, horizontal, posterior and anterior SCC deficit were found, with the most severe for the posterior SCC. Posterior SCC VOR being invariably impaired is consistent with the concept that all posterior SCC signals are transmitted through the MLF. The formal vestibular testing vertical-canal planes of patients with INO may be helpful to exclude a differential diagnosis of a pseudo-INO from myasthenia gravis which will not show the vertical SCC VOR loss. In the stroke patients, at least one component of the OTR, including head tilt, skew deviation, and ocular tilt, was frequently observed in 90% of patients (5). These signs can also help to distinguish INO from pseudo-INO in myasthenia gravis.

### MOG associated optic neuritis

Demographic and clinical data in a UK cohort of 252 myelin-oligodendrocyte-glycoprotein (MOG-ab) positive patients showed that patients typically presents with isolated optic neuritis (55%, bilateral in almost half), transverse myelitis (18%) or acute disseminated encephalomyelitis-like presentations (18%) (6). On follow up 16% patients had visual acuity 46/36 in at least one eye; EDSS > 4 in 7% and > 6 in 5%; bladder issues, bowel dysfunction and erectile dysfunction in respectively 28, 20% and 21%. The annualized relapse rate was 0.2 and decreased by immunosuppression longer than 3 months.

In an observational French study of 110 patients with optic neuritis (ON), MS related ON was the most frequent (71%), followed by idiopathic (14,5%), MOG-ab related ON (10%) and AQP4 Ab related ON (4.5%) (7). In a cross sectional study performed in UK, MOG-ab were found in 40% of AQP4-ab negative NMOSD patients (8).

A study analyzed the clinical spectrum of a cohort of 47 patients with optic neuritis associated to positive MOG-ab (9). At the onset, ON events were accompanied by optic nerve head swelling in 70% of cases. Disc edema was also found much more frequent in MOG-Ab-ON than in AQP4-ab-ON in a different study (10). Extensive optic nerve T2 hyperintensity with gadolinium enhancement predominant in the anterior part was observed (9). In this study ON was found to occur almost equally in males and females, was initially severe, but generally has a good short term visual prognosis. However, in 1/3 of the cases severe atrophy on RNLF values were reported at 3 months.

A European multicentric study evaluated the retinal atrophy in 13 MOG-ab, 19 AQP4-ab, 13 RRMS patients and 13 healthy controls (11). They found that MOG-ab patients disclosed pRNLF and mGCL atrophy that appear severe in the eyes with clinical episodes of optic neuritis and slighter in the unaffected eye, as compared to health subjects. pRNLF was also significantly more severely atrophied in

MOG-ab patients than MS and NMOSD patients. However the number of optic neuritis per eye may have differed in patient populations which would account for this unexpected result of more severely affected eyes in MOG-ab than in AQP4-ab patients. Indeed, in a similar multicentric study, comparing a group of 10 AQP4-ab-ON and 6 MOG-ab-ON patients, final average RNFL was significantly better in eyes following MOG-ab-ON, compared to AQP4-ab-ON, after adjusting for the number of ON attacks (10).

## **NMOSD**

### *Diagnostic MRI criteria for NMOSD.*

A multicenter European study tested the following criteria of '(1) at least 1 lesion adjacent to the body of the lateral ventricle and in the inferior temporal lobe; or (2) the presence of a subcortical U-fibre lesion or (3) a Dawson's finger-type lesion' in an independent cohort of relapsing-remitting multiple sclerosis (RRMS) and AQP4-ab, MOG-ab positive and ab-negative NMOSD (12). Over the whole NMOSD group vs RRMS group, the sensitivity of these criteria was 90.9% and the specificity was 89.7%.

### *Paraneoplastic NMOSD*

The diagnosis of a possible paraneoplastic etiology for NMOSD is done according to the PNS Euronetwork criteria, when detection of cancer occurs within the first 2 years of diagnosis of NMOSD, without concurrent onconeural antibodies or other antibodies against neuronal surface antigens. AQP4 reactivity has been proven on some tumors. Paraneoplastic NMOSD is rare, found in 3% of 156 NMOSD patients (13). The most common tumors were adenocarcinoma of the lung and breast. In NMOSD, the risk for cancer is higher in (1) patients who present with brainstem involvement, mainly nausea and vomiting, and (2) patients older than 45 years, usually male, presenting with extensive transverse myelitis (LETM). However, optic neuritis can also occur.

### *Treatment of NMOSD*

A very convincing retrospective study evaluated the effect of delay of plasma exchange (PLEX) initiation on severe optic neuritis and spinal cord attacks in NMOSD patients (14). It showed that maximal improvement is achieved when the delay in initiating PLEX treatment is minimized ( $\leq 5$  days), even more improved when PLEX is initiated at day 1. These results should change our way of treating attacks of NMOSD, suggesting starting PLEX before day 2 in addition to steroids, and not considering PLEX as a rescue therapy after steroid failure.

## **2017 proposed revisions to the McDonald diagnostic criteria for multiple sclerosis**

The International Panel on Diagnosis of MS reviewed the McDonald diagnostic criteria for multiple sclerosis (to be published in Lancet Neurol in January 2018). The major changes are the following:

1. In a patient with a typical clinical isolated syndrome (CIS) and fulfilment of clinical or MRI criteria for "dissemination in space" and no better explanation for the clinical presentation, demonstration of CSF-specific oligoclonal bands allows an MS diagnosis to be made without the previously required "dissemination in time."
2. Both symptomatic and asymptomatic MRI lesions can be used for fulfilling MRI criteria for dissemination in space or dissemination in time.
3. In addition to juxtacortical lesions, cortical lesions can also be used to demonstrate dissemination in space requirements.

The group also declined to include the presence of optic neuritis pathology in the revised criteria, but acknowledged that the condition is an "important manifestation of MS" and represents an "area of high priority for research."

### **Posterior cerebral atrophy (PCA)**

In a recent consensus, a new three-level classification framework for PCA has been proposed (15). Classification level 1 (PCA) defines the core clinical, cognitive, and neuroimaging features and exclusion criteria of the clinico-radiological syndrome. Classification level 2 (PCA-pure, PCA-plus) establishes whether, in addition to the core PCA syndrome, the core features of any other neurodegenerative syndromes are present. Classification level 3 (PCA attributable to Alzheimer Disease [PCA-AD], Lewy body disease [PCA-LBD], corticobasal degeneration [PCA-CBD], prion disease [PCA-prion]) provides a more formal determination of the underlying cause of the PCA syndrome, based on available pathophysiological biomarker evidence.

### **SUMMARY**

Significant data of 2017 literature review concern mainly MOG-ab and AQP4-ab associated neurological syndromes and the new MS criteria. We learned that the prognosis of MOG-associated disease is not benign, with 30% of severe optic atrophy following optic neuritis, and 50% of permanent sphincter and erectile functions following myelitis. MOG-ab disease has a moderate relapse risk, which might be mitigated by medium term immunosuppression at onset. Specific MRI criteria may be helpful for NMOSD diagnosis. Paraneoplastic NMOSD should be looked for in male patients with myelitis above 45 year old. Plasma exchange should be started before day 2 in addition to steroids in NMOSD attacks. The 2017 McDonald diagnostic criteria for multiple sclerosis suggest mainly to consider CSF-specific oligoclonal bands equivalent to a "dissemination in time" criteria. This might prompt to perform more systematic lumbar puncture at onset.

### **CME ANSWERS**

1. A, B, C
2. B, D
3. A, D

### **REFERENCES**

1. Bogli SY, Afthinos M, Huang MY. Effect of Gabapentin/Memantine on the Infantile Nystagmus Syndrome in the Zebrafish Model: Implications for the Therapy of Ocular Motor Diseases. *Invest Ophthalmol Vis Sci.* 2017;58(7):3149-57.
2. Nachev P, Rose GE, Verity DH, Manohar SG, MacKenzie K, Adams G, et al. Magnetic Oculomotor Prosthetics for Acquired Nystagmus. *Ophthalmology.* 2017;124(10):1556-64.
3. Lee SH, Lee SY, Choi SM, Kim BC, Kim MK, Kim JS. Resolution of periodic alternating nystagmus with amantadine. *J Neurol Sci.* 2016;364:65-7.
4. Aw ST, Chen L, Todd MJ, Barnett MH, Halmagyi GM. Vestibulo-ocular reflex deficits with medial longitudinal fasciculus lesions. *J Neurol.* 2017;264(10):2119-29.
5. Choi SY, Kim HJ, Kim JS. Impaired vestibular responses in internuclear ophthalmoplegia: Association and dissociation. *Neurology.* 2017.
6. Jurynczyk M, Messina S, Woodhall MR, Raza N, Everett R, Roca-Fernandez A, et al. Clinical presentation and prognosis in MOG-antibody disease: a UK study. *Brain.* 2017;140(12):3128-38.

7. Deschamps R, Lecler A, Lamirel C, Aboab J, Gueguen A, Bensa C, et al. Etiologies of acute demyelinating optic neuritis: an observational study of 110 patients. *Eur J Neurol*. 2017;24(6):875-9.
8. Hamid SHM, Whittam D, Mutch K, Linaker S, Solomon T, Das K, et al. What proportion of AQP4-IgG-negative NMO spectrum disorder patients are MOG-IgG positive? A cross sectional study of 132 patients. *J Neurol*. 2017;264(10):2088-94.
9. Biotti D, Bonneville F, Tournaire E, Ayrignac X, Dalliere CC, Mahieu L, et al. Optic neuritis in patients with anti-MOG antibodies spectrum disorder: MRI and clinical features from a large multicentric cohort in France. *Journal of Neurology*. 2017;264(10):2173-5.
10. Stiebel-Kalish H, Lotan I, Brody J, Chodick G, Bialer O, Marignier R, et al. Retinal Nerve Fiber Layer May Be Better Preserved in MOG-IgG versus AQP4-IgG Optic Neuritis: A Cohort Study. *PLoS One*. 2017;12(1):e0170847.
11. Havla J, Kumpfel T, Schinner R, Spadaro M, Schuh E, Meinl E, et al. Myelin-oligodendrocyte-glycoprotein (MOG) autoantibodies as potential markers of severe optic neuritis and subclinical retinal axonal degeneration. *J Neurol*. 2017;264(1):139-51.
12. Jurynczyk M, Tackley G, Kong Y, Geraldles R, Matthews L, Woodhall M, et al. Brain lesion distribution criteria distinguish MS from AQP4-antibody NMOSD and MOG-antibody disease. *J Neurol Neurosurg Psychiatry*. 2017;88(2):132-6.
13. Sepulveda M, Sola-Valls N, Escudero D, Rojc B, Baron M, Hernandez-Echebarria L, et al. Clinical profile of patients with paraneoplastic neuromyelitis optica spectrum disorder and aquaporin-4 antibodies. *Multiple sclerosis*. 2017:1352458517731914.
14. Bonnan M, Valentino R, Debeugny S, Merle H, Ferge JL, Mehdaoui H, et al. Short delay to initiate plasma exchange is the strongest predictor of outcome in severe attacks of NMO spectrum disorders. *J Neurol Neurosurg Psychiatry*. 2017.
15. Crutch SJ, Schott JM, Rabinovici GD, Murray M, Snowden JS, van der Flier WM, et al. Consensus classification of posterior cortical atrophy. *Alzheimers Dement*. 2017;13(8):870-84.

## NEUROSURGICAL MANUSCRIPTS OF NEURO-OPHTHALMOLOGICAL SIGNIFICANCE

Neil R. Miller, MD FACS  
Johns Hopkins University School of Medicine  
Baltimore, Maryland

### LEARNING OBJECTIVES

1. The attendee will know the latest surgical approaches to lesions that compress the anterior visual pathways.
2. The attendee will understand the effect of venous sinus stenting on intracranial pressure in patients with primary pseudotumor cerebri.
3. The attendee will understand the status of flow diversion devices for ophthalmic segment/paraophthalmic unruptured aneurysms.
4. The attendee will understand the effect of endovascular occlusion of both ruptured and unruptured internal carotid-posterior communicating artery junction aneurysms on pre-existing aneurysm-related third nerve palsies.
5. The attendee will know the results and potential complications of microvascular decompression of the facial nerve in patients with hemifacial spasm.
6. The attendee will know the latest molecular biological findings in skull base meningiomas.

### CME QUESTIONS

1. Venous sinus stenting in patients with primary pseudotumor lowers intracranial pressure:
  - a. Immediately
  - b. 24 hours later
  - c. 1 week later
  - d. 4 weeks later
2. Potential side effects of microvascular decompression include:
  - a. Hearing loss
  - b. Facial nerve palsy
  - c. Sixth nerve palsy
  - d. All of the above
3. In selected patients with skull base lesions, the advantages of an endoscopic approach is preferred over open craniotomy because of:
  - a. Potentially shorter surgical time
  - b. Shorter hospital stays
  - c. Improved quality of life
  - d. All of the above

### KEYWORDS

1. Pseudotumor cerebri
2. Venous sinus stenosis
3. Third nerve palsy
4. Hemifacial spasm
5. Molecular genetics

## HIGHLIGHTS

There is an increasing shift from open craniotomy to endoscopic or keyhole surgical approaches in patients with suprasellar lesions because of shorter operating times, shorter hospital stays and improved quality of life.

Venous sinus stenting in patients with pseudotumor cerebri and venous sinus stenosis lowers intracranial pressure immediately.

Endovascular occlusion of aneurysms using a flow diversion device is a safe and effective approach that commonly results in improvement of associated visual manifestations such as optic neuropathy in patients with paraophthalmic aneurysms and third nerve palsy in patients with internal carotid-posterior communicating artery junction aneurysms.

Microvascular decompression of the seventh nerve in patients with hemifacial spasm is associated with an excellent outcome in most patients; however, there is a definite morbidity associated with the procedure.

The molecular genetic profile of skull base meningiomas is being identified, hopefully leading to targeted therapy in the future.

## SUMMARY

Publications reviewed (January 2017 through January 2018): Acta Neurochirurgica, British Journal of Neurosurgery, Child's Nervous System, Journal of Neurosurgery, Journal of Neurosurgery Pediatrics, Neuroradiology, Neurosurgery, and World Neurosurgery.

### **Surgical Approaches to Lesions Compressing the Anterior Visual Pathway**

The transition from microscopic to endoscopic approaches to lesions that compress the anterior visual pathway continues. Numerous articles, all retrospective studies, suggest that endoscopic techniques provide excellent visual and neurological outcomes while resulting in shorter operative times, shorter hospital stays, and improved quality of life.<sup>1-6</sup> Similarly, the supraorbital "keyhole" approach is being increasingly favored over open craniotomy for suprasellar lesions such as meningiomas and aneurysms.<sup>7,8</sup>

### **Venous Sinus Stenting for Pseudotumor Cerebri**

The treatment of pseudotumor cerebri (PTC, aka idiopathic intracranial hypertension) with venous sinus stenting continues to be a common theme in the neurosurgical literature. Some of the articles on the subject<sup>9</sup> are what I would consider "Me too" publications; i.e., they indicate that in their small series, stenting was effective in reducing symptoms of increased intracranial pressure (ICP) and resolution of papilledema. Two papers, however, are important. Liu et al.<sup>10</sup> described 10 patients with PTC and venous sinus stenosis with an elevated gradient across the region of stenosis ( $30.0 \pm 13.2$  mm Hg) and elevated ICP ( $42.2 \pm 15.9$  mm Hg) for whom medical therapy had failed and who subsequently underwent venous sinus stenting. Following stent placement, all patients had resolution of the stenosis and gradient ( $1 \pm 1$  mm Hg). More importantly, however, the authors monitored ICP throughout the procedure and noted an **immediate decrease in ICP** following placement of the stent ( $17.0 \pm 8.3$  mm Hg) with a further decrease overnight. This publication and another by Matloob et al.<sup>11</sup> confirm the immediate effects of venous sinus stenting on ICP in this group of patients. This obviously is an important consideration for those patients who present with evidence of optic nerve dysfunction and

for whom a decision must be made regarding performing immediate optic nerve sheath decompression, and/or drainage of cerebrospinal fluid.

### **The Effect of Aneurysm Treatment on the Afferent and Efferent Visual Pathways**

Another theme among papers of neuro-ophthalmological interest in neurosurgical journals in 2017 is the effect of aneurysm treatment on the afferent or efferent visual pathways. For the afferent visual system, the issue relates to treatment of ophthalmic segment aneurysms. Griessenauer et al.<sup>12</sup> treated 127 consecutive patients with 160 ophthalmic segment aneurysms using flow diverters. In this cohort, complete occlusion of the aneurysm was observed in 90 of 101 (89%) cases with a mean follow-up of 18 months. Of 10 patients with visual symptoms, one had immediate improvement in visual function. Among 117 patients without visual symptoms, 2 (1.6%) experienced visual impairment following treatment. There was no mortality related to the procedure, but, in addition to the 2 patients who experienced visual impairment post-procedure, 2 developed a permanent neurological deficit (hemiplegia). Based on their experience in this large series, the authors concluded that treatment of ophthalmic segment aneurysms with flow diversion is a safe and effective procedure compared with clipping. Several of the same authors participated in a two-center retrospective cohort study of consecutively treated ophthalmic segment aneurysms that compared stent-assisted coil embolization with flow diversion.<sup>13</sup> A total of 62 aneurysms were treated with stent-coiling and 106 were treated with flow diversion. The authors found that stent-coiling and flow diversion were equally effective in treating these aneurysms and that there were no significant differences in procedural complications or in angiographic, functional, or visual outcomes. In fact, in this series, no patient with stent-coiling had a permanent visual complication whereas only one patient in the flow diversion series had permanent visual loss.

For the efferent visual system, the issue relates to third nerve palsy recovery after treatment of ruptured and unruptured internal carotid-posterior communicating (PCom) aneurysms. Zu et al.<sup>14</sup> described the effect of endovascular treatment of 34 patients with third nerve palsy associated with a **ruptured** PCom aneurysm. At 6-month follow-up, 21 (61.8%) had experienced complete recovery of their palsy whereas 8 (23.5%) had incomplete recovery. The mean time to resolution was 24.5 days. As might be expected, there was a trend toward complete recovery among patients with an initially incomplete palsy. No patient in this series had post-operative worsening of an incomplete palsy.

Hall et al.<sup>15</sup> described the effect of treatment of **unruptured** PCom aneurysms on resolution of third nerve palsy. These authors described their experience with 15 patients and also provided a narrative review of 179 patients from 31 case reports or cohort studies. Based on their experience and literature review, they concluded that surgical clipping was associated with a higher rate of recovery than was endovascular treatment. Again, patients who presented with a complete palsy had a lower rate of recovery than did those with a partial palsy.

### **Surgical Treatment of Hemifacial Spasm**

Although hemifacial spasm (HFS) can be treated with botulinum toxin, the only cure is microvascular decompression (MVD) of the facial nerve that, in experienced hands, cures the condition in over 90% of patients. However, whereas botulinum toxin injections are unassociated with any mortality or permanent morbidity, MVD has the potential for both. Thus, many neuro-ophthalmologists are loathed to recommend the procedure to their patients with HFS. Zhao et al.<sup>16</sup> reviewed their experience with 1548 patients with HFS who were treated with MVD and followed for at least 2 years. They found that 92.5% had complete disappearance of their spasms and another 4.2% had marked improvement in their spasms. Postoperative complications occurred in 16% (n = 249). There was no MVD-related mortality,

but facial nerve palsy occurred in almost 10% of patients and hearing impairment occurred in 3.5%. Other complications included CSF leakage, wound infections and, in 14 patients, ipsilateral sixth nerve palsy. Among the 150 patients with a post-operative facial nerve palsy, 134 (94%) experienced complete recovery in 10-92 days. At the end of a 2-year follow-up 6 patients still had a palsy. Of the 55 patients with postoperative hearing impairment, only one became completely deaf, but 11 had permanent impairment. All 14 patients with a postoperative sixth nerve palsy recovered completely within 2 months. Based on their experience, the authors conclude that MVD is a safe treatment for HFS. I would conclude that one can look at the authors' results as a glass "half full" or "half empty". On the one hand, there is a very high chance that a patient with HFS who undergoes MVD by an experienced neurosurgeon will have an excellent result with no complications. On the other hand, there is a definite risk of a potentially disabling complication. Botulinum toxin, although not a cure, remains a safe and reasonably effective alternative.

### **Molecular Genetics of Anterior Skull Base Meningiomas**

Although anterior basal skull meningiomas can be treated relatively successfully with surgery, radiation, or both, both treatments can be associated with significant morbidity and mortality. Thus, the search continues for medical therapy. To date, drugs such as anti-estrogen and anti-progesterone agents, although impressive in *in vitro* experiments, have not proved clinically useful. Not surprisingly, therefore, attention has turned toward the molecular biology of these tumors. In particular, genomic research has identified oncogenic SMO and AKT1 mutations in some meningiomas.<sup>17</sup> More recently, Strickland et al.<sup>(17)</sup> performed targeting sequencing in a cohort of 62 patients with anterior skull base meningiomas. These investigators found SMO mutations in 7 of 62 (11%) tumors and AKT1 mutations in 12 (19%). Although these percentages are relatively small, targeted therapy for these and other mutations may one day obviate the need for more invasive treatment of these tumors.

### **CME ANSWERS**

1. A
2. D
3. D

### **REFERENCES**

1. Eseonu CI, ReFaey K, Rincon-Torroella J, et al. Endoscopic versus microscopic transsphenoidal approach for pituitary adenomas: Comparison of outcomes during the transition of methods of a single surgeon. *World Neurosurg* 97:317-325, 2017..
2. Kourtourousiou M, Filho FVG, Fernandez-Miranda JC, et al. Endoscopic endonasal surgery for tumors of the cavernous sinus: A series of 234 patients. *World Neurosurg* 103:713-732, 2017.
3. Luomaranta T, Raappana A, Saarela V, Liinamaa MJ. Factors affecting the visual outcome of pituitary adenoma patients treated with endoscopic transsphenoidal surgery. *World Neurosurg* 105:422-431, 2017.
4. Li A, Liu W, Cao P, Zheng Y, et al. Endoscopic versus microscopic transsphenoidal surgery in the treatment of pituitary adenoma: A systematic review and meta-analysis. *World Neurosurg* 101:236-246, 2017.
5. Patel VS, Thamboo A, Quon J, et al. Outcomes after endoscopic endonasal resection of craniopharyngiomas in the pediatric population. *World Neurosurg* 108:6-14, 2017.
6. Wolf A, Coros A, Bierer J, et al. Quantitative evaluation of vision-related and health-related quality of life after endoscopic transsphenoidal surgery for pituitary adenoma. *J Neurosurg* 27:409-416, 2017.



7. Singh H, Essayed WI, Jada A, et al. Contralateral supraorbital keyhole approach to medial optic nerve lesions: an anatomicoclinical study. *J Neurosurg* 126:940-944, 2017.
8. Zumofen DW, Rychen J, Roethlisberger M, et al. A review of the literature on the transciliary supraorbital keyhole approach. *World Neurosurg* 98:614-624, 2017.
9. Lenck S, Vallée F, Labeyrie M-A, et al. Stenting of the lateral sinus in idiopathic intracranial hypertension according to the type of stenosis. *Neurosurgery* 80:393-400, 2017.
10. Liu KC, Starke RM, Durst CR, et al. Venous sinus stenting for reduction of intracranial pressure in IIH: a prospective pilot study. *J Neurosurg* 127:1126-1133, 2017.
11. Matloob SA, Toma AK, Thompson SD, et al. Effect of venous stenting on intracranial pressure in idiopathic intracranial hypertension. *Acta Neurosurg* 159:1429-1437, 2017.
12. Griessenauer CJ, Piske RL, Baccin CE, et al. Flow diverters for treatment of 160 ophthalmic segment aneurysm: Evaluation of safety and efficacy in a multicenter cohort. *Neurosurgery* 80:726-732, 2017.
13. Adeeb N, Griessenauer CJ, Foreman PM, et al. Comparison of stent-assisted coil embolization and the Pipeline embolization device for endovascular treatment of ophthalmic segment aneurysms: A multicenter cohort study. *World Neurosurg* 105:206-212, 2017.
14. Zu Q-Q, Liu X-L, Wang B, et al. Recovery of oculomotor nerve palsy after endovascular treatment of ruptured posterior communicating artery aneurysm. *Neuroradiology* 59:1165-1170, 2017.
15. Hall S, Sadek A-R, Dando A, et al. The resolution of oculomotor nerve palsy caused by unruptured posterior communicating artery aneurysms: A cohort study and narrative review. *World Neurosurg* 107:581-587, 2017.
16. Zhao H, Zhang X, Tang Y-d, et al. Operative complications of microvascular decompression for hemifacial spasm: Experience of 1548 cases. *World Neurosurg* 107:559-564, 2017.
17. Brastianos PK, Horowitz PM, Santagata S, et al. Genomic sequencing of meningiomas identifies oncogenic SMO and AKT1 mutations. *Nat Genet* 45:285-289, 2013.
18. Strickland MR, Gill CM, Nayyar N et al. Targeted sequencing of SMO and AKT1 in anterior skull base meningiomas. *J Neurosurg* 127:438-444, 2017.

## Ophthalmological Literature of Neuro-Ophthalmological Significance

Helen V Danesh-Meyer, MbChB, MD, PhD, FRANZCO  
Department of Ophthalmology, University of Auckland  
Auckland, New Zealand

### LEARNING OBJECTIVES

1. Understand the potential implications of copy number and heteroplasmy in LHON
2. To recognise that LHON is associated with higher risk of other systemic diseases.
3. To appreciate the changes in sub-basal corneal nerves in patients with optic neuritis
4. To discuss the usefulness of different modalities for identifying optic nerve head drusen in a pediatric population
5. To appreciate the emerging role of OCTA in the evaluation of patients with optic neuropathies and neurological diseases.

### CME QUESTIONS (True/False)

1. LHON is associated with increased incidence of cardiovascular, neurological and autoimmune disorders.
2. Corneal confocal microscopy can detect reduction in corneal nerve fiber density in MS but this does not correlate with a clinical measures of MS severity.
3. OCTA had the highest accuracy for classifying an eye correctly with eyes with papilledema demonstrating leakage of the optic nerve vessels

### KEYWORDS

1. Heteroplasmy
2. retinal nerve fiber layer thickness
3. optical coherence tomograph angiography (OCTA)
4. pseudo-papilledema
5. Alzheimers type dementia

**Publications reviewed (January 2017 through January 2018):** Ophthalmology, American Journal of Ophthalmology, British Journal of Ophthalmology, Investigative Ophthalmology and Vision Science, JAMA Ophthalmology, Graefe's Archives of Clinical and Experimental Ophthalmology

### **Leber's Hereditary Optic Neuropathy (LHON)**

Several areas of LHON have been explored in the ophthalmological literature in 2017. Investigators attempted to shed light on the possible reasons for incomplete penetrance in LHON by studying the mitochondrial (mtDNA) copy number in patients who possess heteroplasmic primary mutations.<sup>1</sup>The investigators found higher cellular mtDNA content in peripheral blood cells of unaffected heteroplasmic mutation carriers with respect to the affected persons. They suggest that increase of cellular mtDNA content may prevent loss of vision despite the presence of a heteroplasmic state of LHON primary mutation, suggesting that it is a key factor responsible for penetrance of LHON.

Other investigators explored whether patients LHON are at increased risk of other diseases.<sup>2</sup>They identified that there is an almost two-fold mortality risk with a specific increased incidence of atherosclerosis and stroke (RR=2.38X) for LHON patients. They also found an association between LHON patients and an increased prevalence of neurologic conditions: demyelinating disorders (RR=12.9X), dementia (RR=4X), epilepsy (RR=3X), and alcohol-related disorders.

The natural history of LHON was studied in a prospective observational case study of 285 individuals from the Soave-Brazil pedigree (m.11778G>A/ND4) who were monitored over 15 years.<sup>3</sup> They identified 6 patients who were unaffected mutation carriers who converted to affected status and reviewed the ophthalmological records one year pre-conversion to one year post conversion. They identified that an increase in the RNFL thickness preceded conversion as early as 4 to 6 months, peaked at conversion, and decreased until individual plateaus. This suggests that structural changes precede clinically significant vision loss. Hence, the natural history of LHON is not a subacute process, as previously believed, but progresses more slowly, taking up to 8 months to plateau.

### **Optic Neuritis and Multiple Sclerosis (MS)**

There have been several new insights in the area of optic neuritis and MS. An observational longitudinal study<sup>4</sup> followed 100 patients with relapsing-remitting MS and 50 controls for 5 years. Patients with MS had thinning of the average RNFL thickness and the P100 latency of visual evoked potentials. This suggests that there is progressive axonal loss in the optic nerve which was shown to correlate with increased disability and reduced quality of life.

An important retrospective cross-sectional study considered the diagnostic error rate of optic neuritis.<sup>5</sup> An overdiagnosis rate of nearly 60% was shown for those referred with acute optic neuritis. Overdiagnosis was most commonly caused by errors in taking the history in particular related to eye pain which often was part of a primary headache disorder rather than optic neuritis. Discounting normal examination findings was a common source of diagnostic error identified. Importantly, a RAPD was one of the more consistent examination findings that correlated with a true diagnosis of optic neuritis and its absence should lead to consideration of other diagnosis. Finally, misinterpreting MRI findings also led to diagnostic errors. In particular, making the diagnosis of optic neuritis in the presence of normal imaging should be cautioned.

A further finding of interest is related to the evaluation of corneal nerve fiber density in patients with MS.<sup>6</sup> Corneal confocal microscopy demonstrated significant reduction in corneal nerve fiber density, branch density and length that correlated with a clinical measure of MS severity. The corneal nerve changes were found to be independent of age, MS duration and stage, and RNFL loss. Axonal loss occurring in MS is partially independent of primary demyelination, and is predictive of irreversible neurological disability. This raises the intriguing possibility the corneal subbasal innervation may be a useful biomarker for the detection of neuroaxonal injury.

### **Non-arteritic Anterior Ischemic Optic Neuropathy (NAION)**

Several studies have provided new insights into NAION. The association of NAION with cataract surgery has been challenged by a large retrospective study (148 patients) over a five-year period.<sup>7</sup> While 9.6% had undergone surgery during the year prior to developing NAION, there was no significant temporal relationship between cataract surgery and the subsequent development of NAION using modern (phacoemulsification) techniques. The major limitation of this study is that it is retrospective. With regards to patients with and without NAION who have diabetes, a case-control study of 92 patients demonstrated that patients with diabetes who have an NAION event do not have a worse visual outcome.<sup>8</sup> In nondiabetics the most prevalent risk factor was hyperlipidemia (63%), while for diabetics it was both hypertension (83%) and hyperlipidemia (83%). Diabetes was not correlated with visual outcome, however, ischemic heart disease and older age, independently correlated with worse VA.

A prospective study of 10 patients<sup>9</sup> with acute NAION identified that in aqueous humor samples there was increased levels of vascular endothelial growth factor (VEGF) and lower levels of interleukin-2.

Other interleukins, cytokines and tumor necrosis factor did not show any difference in concentrations. This may have potential implications for therapeutic interventions and is an area worthy of further investigation.

### **Papilledema**

One area of focus has been differentiating papilledema from pseudo-papilledema in a pediatric population.<sup>10</sup> A prospective observational study of 19 children evaluated 5 different modalities: B-scan ultrasonography, fundus photography, autofluorescence, fluorescein angiography, OCT rNFL and volumetric OCT with both spectral domain and enhanced imaging OCT. Fluorescein angiography had the highest accuracy (97%) for classifying an eye correctly with eyes with papilledema demonstrating leakage of the optic nerve vessels. Other modalities had substantial likelihood (30% -70%) of misinterpretation of papilledema as pseudo-papilledema with fundus photography having the lowest rate of misinterpretation of the non-invasive modalities.

### **Optical Coherence Tomograph Angiography (OCTA)**

OCTA has been used to evaluate several different neurological and neuro-ophthalmic disorders in order to detect, quantify and elucidate the vascular changes associated optic nerve damage. OCTA can localize blood vessels in each vascular layer of the retina and choroid by detecting blood flow by decorrelating the motion of red blood cells from the static tissues without the need for contrast injection. While the studies below raise intriguing new possibilities regarding the role of OCTA in neuro-ophthalmic disorders, they are all small studies and limited by our evolving understanding of OCTA. Some of the limitations include that it is difficult to conclude that OCTA signal attenuation is a result of primary ischaemic process or secondary shadowing effect of fluid or haemorrhage creating artefacts. Reduced flow density also may be a result of tissue loss and metabolic need rather than primary vascular abnormal process. Nevertheless, this new technology is allowing visualisation and study of vasculature previously unattainable with OCT.

In a case-control study<sup>11</sup> of 67 patients (123 eyes), peripapillary retinal nerve fibre layer (NFL) thickness, macular ganglion cell complex (GCC) thickness and optic nerve head perfusion were measured. Optic nerve head perfusion was determined by a signal average over the optic disc, ONH-F (Optic Nerve Head Flow Index (ONH-FI)). Compared to patients without MS, patients with MS had both thinner GCC thickness and decreased optic nerve head perfusion. Furthermore, eyes without documented optic neuritis also demonstrated structural loss and decreased optic nerve head perfusion.

OCTA was also used to study non-arteritic anterior ischaemic optic neuropathy (AAION) in the context of giant cell arteritis (GCA).<sup>12</sup> Four patients with AAION were evaluated in an observational study and compared to two healthy control patients. The study found diffusely dilated superficial peripapillary capillaries in combination with focal non-perfusion, which was observed consistently in patients across a wide spectrum of clinical severity. This raises the possibility that OCTA may serve as a useful adjunctive diagnostic tool for AAION.

Another such area has been to evaluate non-arteritic anterior ischemic optic neuropathy (NAION).<sup>13</sup> This small case-control study assessed 5 NAION patients and 19 age-matched controls with OCTA and measured flow densities and blood flow at the retinal and choroidal level. The study determined that in the acute stage there is a global reduction in the mean peripapillary flow density in the retina and choroid. This was followed by partial reperfusion. A further investigation<sup>14</sup> compared NAION to AAION with both fluorescein angiography, indocyanine green angiography and OCTA in 4 patients with NAION and one patient with AAION within 2 weeks of their acute presentation. In two of the 4 NAION and the

AAION, OCTA identified the boundary of the ischemic area at the level of the optic nerve head with corresponded to optic disc filling defects detected by fluorescein angiography. While the other two patients demonstrated generalised leakage with fluorescein angiography but sectorial peripapillary network reduction.

Other neurological diseases have also been explored with OCTA technology. A case control study of 26<sup>15</sup> patients with Alzheimers dementia showed a decrease in retinal vascular density and enlarged foveal avascular zone. Significant correlations were found between the the Mini Mental Status Examination and all vascular density parameters. Given the close association between retinal and cerebral circulations deficits, this raises the interesting question whether microvasculature deficits detected early with OCTA can be used as a new biomarker in the early detection of Alzheimers type dementia or monitoring of its progression and response to therapies.

### CME ANSWERS

1. False- it is not associated with increased autoimmune disorders
2. False- it does correlate with disease severity
3. False- it is FFA

### REFERENCES

1. Bianco A, Bisceglia L, Russo Let al. High Mitochondrial DNA Copy Number Is a Protective Factor From Vision Loss in Heteroplasmic Leber's Hereditary Optic Neuropathy (LHON). *Invest Ophthalmol Vis Sci.* 2017;58:2193–2197.
2. Vestergaard N, Rosenberg T, Torp-Pedersen C, et al. Increased Mortality and Comorbidity Associated With Leber's Hereditary Optic Neuropathy: A Nationwide Cohort Study *Invest Ophthalmol Vis Sci.* 2017;58:4586–4592.
3. Hwang TJ, Karanjia R, Moraes-Filho MN, et al. Natural History of Conversion of Leber's Hereditary Optic Neuropathy. *Ophthalmology* 2017;124:843- 850
4. Garcia-Martin E, Ara JR, Martin J. Retinal and Optic Nerve Degeneration in Patients with Multiple Sclerosis Followed up for 5 Years. *Ophthalmology* 2017;124:688-696
5. Stunkel L, Kung NH, Wilson, MA, McClelland CM, Van Stavern, GP. Incidence and Causes of Overdiagnosis of Optic Neuritis. *JAMA Ophthalmology* 2017 Dec 7. doi: 10.1001/jamaophthalmol.2017.5470. [Epub ahead of print]
6. Petropoulos IP, Kamran S, Li Y, et al. Corneal Confocal Microscopy: An Imaging Endpoint for Axonal Degeneration in Multiple Sclerosis. *Invest Ophthalmol Vis Sci.* 2017;58:3677– 3681.
7. Moradi A, Kanagalingam S, Diener-West, M, Miller NR. Post-Cataract Surgery Optic Neuropathy: Prevalence, Incidence, Temporal Relationship, and Fellow Eye Involvement *Am J Ophthalmol* 2017;175:183–193.
8. Sharma S, Kwan S, Fallano KA, Wang J, Miller NR, Subramanian PS. Comparison of Visual Outcomes of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients with and without Diabetes Mellitus. *Ophthalmology* 2017;124:450-455.
9. Micieli JA, Lam C, Najem K, Margolin EA. Aqueous Humor Cytokines in Patients With Acute Nonarteritic Anterior Ischemic Optic Neuropathy. *Am J Ophthalmol* 2017;177:175–181.
10. Chang MY, Velez FG, Demer JL, et al. Accuracy of Diagnostic Imaging Modalities for Classifying Pediatric Eyes as Papilledema Versus Pseudopapilledema. *Ophthalmology* 2017;124:1839-184
11. Spain RI, Liu L, Zhang X, et al. Optical coherence tomography angiography enhances the detection of optic nerve damage in multiple sclerosis. *Br J Ophthalmol* Published Online First: 16 August 2017. doi: 10.1136/bjophthalmol-2017-310477
12. Gaier ED, Gilbert AL, Cestari DM, et al. Optical coherence tomographic angiography identifies

peripapillary microvascular dilation and focal non-perfusion in giant cell arteritis. *Br J Ophthalmol*. Published Online First: 09 November 2017. doi: 10.1136/bjophthalmol-2017-310718

13. Sharma S, Ang M, Najjar RP, et al. Optical coherence tomography angiography in acute non-arteritic anterior ischaemic optic neuropathy. *Br J Ophthalmol* 2017;101:1045–1051.
14. Balducci N, Morara M, Veronese C, et al. Optical coherence tomography angiography in acute arteritic and non-arteritic anterior ischemic optic neuropathy. *Graefes Arch Clin Exp Ophthalmol* (2017) 255:2255–2261.
15. Bulut M, Kurtuluş F, Gözkaya O, et al. Evaluation of optical coherence tomography angiographic findings in Alzheimer's type dementia. *Br J Ophthalmol* Published Online First: 09 June 2017. doi: 10.1136/bjophthalmol-2017-310476

## WHAT'S NEW IN GRAVES' ORBITOPATHY?

James A. Garrity MD  
Mayo Clinic  
Rochester, MN

### LEARNING OBJECTIVES

1. The attendee will be able to differentiate Graves' orbitopathy (GO) from IgG4-related orbital disease.
2. The attendee will be able to determine the mechanism and effectiveness of various biologic agents used to treat GO.
3. The attendee will be able to identify differences in the two randomized controlled trials of rituximab for GO.

### CME QUESTIONS (True/False)

1. The best blood test to support a diagnosis of GO is which of the following?
  - a. TPO
  - b. TSH receptor antibody
  - c. TSH
  - d. T4
2. Which of the following is most suggestive of IgG4-related orbital disease?
  - a. Enlargement of the extraocular muscles
  - b. An enlarged extraocular muscle plus a soft tissue infiltrate
  - c. An enlarged lacrimal gland plus an enlarged extraocular muscle
  - d. An enlarged infraorbital nerve
3. Which of the following monoclonal antibodies targets the IGF-1 (insulin like growth factor 1)?
  - a. Rituximab
  - b. Tocilizumab
  - c. Adalimumab
  - d. Teprotumumab

### KEYWORDS (5 Max)

1. Graves' orbitopathy
2. Thyroid eye disease
3. Biologic medications
4. TSH-receptor
5. IGF-1 receptor

Graves' orbitopathy (GO) is the most frequent extrathyroidal manifestation of Graves' disease (GD). Depending upon the diagnostic criteria used up to 50% of patients with GD have ophthalmic findings with lid retraction/lid lag being the most common<sup>1-3</sup>. More severe, sight-threatening disease is seen in approximately 5% of hyperthyroid individuals<sup>4</sup>. While most GO requires no eye specific treatment, approximately 15% of GO progress and is of interest to this presentation<sup>5,6</sup>.

Best evidence suggests that activated T-cells interact with an antigen and secrete cytokines/chemokines which influence the local environment to recruit more inflammatory cells and to affect the target cell (orbital fibroblasts) to release glycosaminoglycans leading to muscle enlargement and to progress towards differentiation into adipocytes, overall increasing the volume of the orbital tissues<sup>7</sup>. See figure 1. Understanding the antigens and cytokine/chemokine profile provides an avenue of potential therapeutic agents<sup>4,8</sup>. The TSH receptor has been identified as a potential antigen. While there has not been an in-vivo TSH-receptor antagonist, elevated levels of TSH-receptor antibody assist in the diagnosis of GO<sup>3</sup>, they have been shown to correlate with clinical activity score and offers prognostic information<sup>9-11</sup>. Another important player is the insulin like growth factor-1 (IGF-1) receptor<sup>12,13</sup>. There is evidence of cross-talk between these two antigens leading to a clinical response<sup>14</sup>. A randomized clinical trial with an IGF-1 receptor inhibitor was just completed demonstrating a positive clinical response<sup>15</sup>.

Considering the pathophysiology depicted in figure 1, there are many potential therapeutic targets. We will consider the cytokines (interleukin-6 (IL-6), tumor necrosis factor (TNF- $\alpha$ )), lymphocyte depletion and IGF-1 receptor inhibition. The first cytokine to consider is TNF- $\alpha$ . Anti TNF- $\alpha$  agents (etanercept, infliximab, adalimumab) have been subjects of small case series and case reports. Infliximab as a case report improved steroid toxicity and improved an optic neuropathy in one patient<sup>16</sup>. Etanercept and adalimumab were subjects of small uncontrolled case series. The adalimumab series had concomitant steroid use and mixed results after 3 months of treatment<sup>17</sup>. Etanercept<sup>18</sup> was used in 10 patients (no concomitant steroids). Soft tissue improvement was noted in all patients (clinical activity score (CAS) decreased by 60%), 3/6 patients with diplopia improved and 2 patients with mild optic neuropathy improved. Three patients had recurrent soft tissue changes after cessation of therapy.

Interleukin-6 is a pro-inflammatory cytokine and has been found to be elevated in GO. Tocilizumab is a monoclonal directed against the IL-6 receptor. There were two reports each describing improvement in clinical symptoms following therapy. The first was an uncontrolled trial from Spain<sup>19</sup> which treated 18 patients with "corticosteroid resistant GO". All patients improved and the CAS improved from an initial 6.5 to a final average of 0.61. Proptosis improved from an average of 22.3 mm to 19.8 mm, 9/18 patients improved their visual acuity by one line or more, one patient with an optic neuropathy improved optic nerve function within the first dose and TSH-receptor antibodies decreased by 40%. Minimum follow-up was 9 months. All side effects were mild and did not require any specific treatment or discontinuation of therapy.

Another report of 2 patients treated with tocilizumab who had failed corticosteroid therapy and orbital decompression improved CAS after the first dose and reduced TSH-receptor antibody levels. In one patient a pre-therapy orbital fat biopsy showed inflammatory cells and a post-therapy orbital fat biopsy in the other patient showed absence of inflammatory cells following therapy implying that there are localized treatment effects from the therapy<sup>20</sup>. A randomized clinical trial (NCT01297699) comparing tocilizumab to placebo has been completed but no results published to date.

There has been much interest in rituximab because of its effect in other autoimmune diseases. Rituximab is a monoclonal antibody directed against CD20 on B-lymphocytes and causes lymphocyte depletion. Plasma cells are unaffected by rituximab and therefore would have minimal if any effect on TSH-receptor antibody levels. Its effect on reducing T-cell activation is most likely controlled through cytokine production and inhibition of antigen presentation<sup>21</sup>. Two randomized clinical trial were recently published, with differing conclusions. The study from the US<sup>22</sup> compared rituximab (1000 mg X 2) to placebo and found no difference in CAS (primary endpoint) at 24 weeks. The Italian study<sup>23</sup> showed that rituximab (1000 mg X 2 for 5 patients and 500 mg X 1 for 10 patients) was slightly better



than intravenous methylprednisolone (IVMP) at 24 weeks. At the 52 week examination the rituximab group was better than the IVMP group and there were no disease relapses in the rituximab group versus 5/16 (31%) relapses in the IVMP group. Possible differences between the trials to account for the lack of response in the US trial include the longer duration of disease, older age, male sex, and higher TSH-receptor antibody levels in the US patients<sup>24</sup>. Between the two trials there were a total of 5 cases of dysthyroid optic neuropathy, 2 patients treated with rituximab in the US trial, 2 patients treated with rituximab in the Italian trial and 1 patient treated with IVMP in the Italian trial.

The most recent randomized clinical trial compared teprotumumab to placebo in patients with active moderate to severe GO<sup>15</sup>. Teprotumumab is a monoclonal antibody directed against the IGF-1 receptor and was given every 3 weeks X 8. Eighty eight patients were randomized, 45 (39 completed study) to placebo and 42 (36 completed study) to teprotumumab. Primary endpoints were reduction of CAS by 2 or more points and reduction of proptosis by 2 or more mm at the 24 week exam. The teprotumumab group had 29/42 (69%) and the placebo group had 9/45 (20%) response at 24 weeks. The only drug related adverse event was hyperglycemia in diabetic patients which was controlled with medication. The study was funded by the drug company and there was no orbital imaging done during the study. Unanswered questions include uncertainty about the therapeutic durability or what is the minimal effective dose. The drug is not yet commercially available.

Figure 1 Schematic depiction of pathogenesis of GO (from Wiersinga<sup>4</sup>)

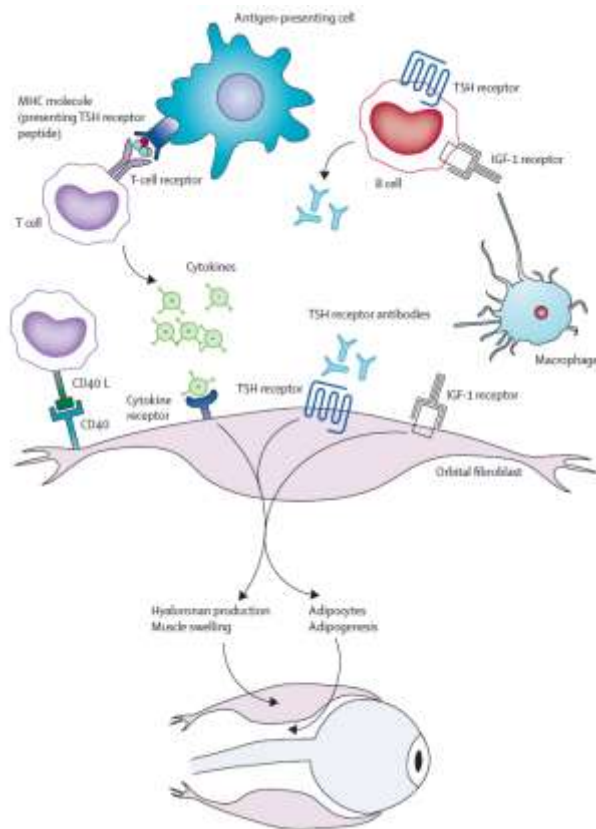


Figure 2 A Characteristics of 2 randomized clinical trials of rituximab (from Stan and Salvi<sup>24</sup>)

**Table 2** Population differences between the two RCTs.

	Italian study (n=15)	US study (n=13)	Comments
Age (mean, years)	51.9	57.6	Possibly different
Gender (% women)	93	69	Possibly different
Smokers (%)	66.7	15.4	Likely to be different
GO duration (months)	Mean: 4.5 ± 2.9	Mean: 30 ± 47.6 Median: 12 (8.2–27.2)	Likely to be different
CAS baseline	Mean: 4.4/10 ± 0.7	Mean: 4.9/7 ± 1.0	Likely to be same
CAS ≥ 4/CAS ≥ 6	14/15 and 2/15	13/13 and 3/13	CAS 7 (US, Italy) and 10 (Italy)
GO severity	Moderate-to-severe	Moderate-to-severe ± progressive	Likely to be same
Previous steroid therapy	3/15 (20%) (≥ 12 weeks prior)	4/13 (31%) (≥ 8 weeks prior)	Likely to be same
TRAb (IU/L)	Mean: 10.7 ± 9.1	Mean: 28.1 ± 23.4 Median: 20 (9–60)	Likely to be different
TRAb > 20	4/15	7/13	Likely to be same

Figure 2 B Characteristics of 2 randomized clinical trials of rituximab (from Wiersinga<sup>4</sup>)

	Stan et al <sup>29</sup>		Salvi et al <sup>30</sup>	
	Rituximab (n=13)	Placebo (n=12)	Rituximab (n=15)	Intravenous corticosteroids (n=16)
Female	9 (69%)	8 (67%)	14 (93%)	12 (75%)
Age, years (SD)	58 (13)	62 (11)	52 (13)	50 (11)
Smoking	2 (15%)	2 (17%)	10 (67%)	9 (56%)
Disease duration	373 days (range 240–1080)	299 days (range 253–595)	4–5 months (SD 2.9)	4–6 months (SD 2.6)
Previous corticosteroids	4 (31%)	6 (50%)	6 (40%)	6 (38%)
Corticosteroid-free period before trial	At least 4 weeks	At least 4 weeks	At least 12 weeks	At least 12 weeks
TSHR antibodies, U/L	20 (range 9–60)	20 (range 2–29)	10.7 (SD 9.1)	18.2 (SD 21.7)
Lid aperture, mm (SD)	11.1 (2.8)	9.8 (2.0)	11.9 (2.3)	11.5 (1.8)
Proptosis, mm (SD)	24.2 (3.3)	23.0 (2.4)	23.5 (3.5)	22.5 (3.7)
Diplopia score (range)	2 (1–2.5)	2 (1–3.75)	1 (0–2.5)	1 (0–2)
Rituximab dosage	2 × 1000 mg	..	2 × 1000 mg (n=5) or 1 × 500 mg (n=10)	..
Baseline clinical activity score (SD)	4.9 (1.0)	5.3 (1.0)	4.4 (0.7)	4.7 (0.7)
Clinical activity score at 24 weeks (SD)	3.7 (1.9)	3.8 (1.4)	0.6 (0.3)	2.3 (0.5)

Data are n (%) unless otherwise specified. In one trial, rituximab was compared with placebo,<sup>29</sup> in the other it was compared with intravenous corticosteroids.<sup>30</sup> TSHR=thyroid-stimulating-hormone receptor.

**Table 1:** Baseline characteristics and primary outcomes (clinical activity score) of two randomised clinical trials of rituximab in patients with active, moderate-to-severe Graves' ophthalmopathy

## CME ANSWERS

1. B
2. D
3. D

## REFERENCES

1. Bartley GB. The epidemiologic characteristics and clinical course of ophthalmopathy associated with autoimmune thyroid disease in Olmsted county, Minnesota. *TransAmOphthalmolSoc* 1994;92:477-588.
2. Bartley GB, Fatourech V, Kadrmas EF, et al. Clinical features of Graves' ophthalmopathy in an incidence cohort. *American Journal of Ophthalmology* 1996;121:284-90.
3. Bartley GB, Gorman CA. Diagnostic criteria for Graves' ophthalmopathy. *American Journal of Ophthalmology* 1995;119:792-5.
4. Wiersinga WM. Advances in treatment of active, moderate-to-severe Graves' ophthalmopathy. *Lancet Diabetes Endocrinol* 2017;5:134-42.
5. Perros P, Crombie AL, Kendall-Taylor P. Natural history of thyroid associated ophthalmopathy. *Clinical Endocrinology* 1995;42:45-50.
6. Perros P, Kendall-Taylor P. Natural history of thyroid eye disease. *Thyroid* 1998;8:423-5.
7. Bahn RS. Current insights into the pathogenesis of Graves' ophthalmopathy. *HormMetabRes* 2015;47:773-8.
8. Garrity JA, Bahn RS. Pathogenesis of Graves ophthalmopathy: Implications for prediction, prevention, and treatment. *AmJOphthalmol* 2006;142:147-53.
9. Eckstein AK, Plicht M, Lax H, et al. Thyrotropin receptor autoantibodies are independent risk factors for Graves' ophthalmopathy and help to predict severity and outcome of the disease. *J Clin Endocrinol Metab* 2006;91:3464-70.
10. Jang SY, Shin DY, Lee EJ, Yoon JS. Relevance of TSH-receptor antibody levels in predicting disease course in Graves' orbitopathy: comparison of the third-generation TBII assay and Mc4-TSI bioassay. *Eye* 2013;27:964-71.
11. Shyamasunder AH, Abraham P. Measuring TSH receptor antibody to influence treatment choices in Graves' disease. *Clin Endocrinol* 2017;86:652-7.
12. Smith TJ, Janssen JAMJL. Building the case for insulin-like growth factor receptor-1 involvement in thyroid-associated ophthalmopathy. *Front Endocrinol* 2017;7:1-8.
13. Wiersinga WM. Autoimmunity in Graves' ophthalmopathy: The result of an unfortunate marriage between TSH receptors and IGF-1 receptors? *J Clin Endocrinol Metab* 2011;96:2386-94.
14. Krieger CC, Neuman S, Marcus-Samuels B, Gershengorn MC. TSHR/IGF-1R cross-talk, not IGF-1R stimulating antibodies, mediate Graves' ophthalmopathy pathogenesis. *Thyroid* 2017;27:746-7.
15. Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *NEngJ Med* 2017;376:1748-61.
16. Durrani OM, Reuser TQ, Murray PI. Infliximab: A novel treatment for sight-threatening thyroid associated ophthalmopathy. *Orbit* 2005;24:117-9.
17. Ayabe R, Rootman DB, Hwang CJ, Ben-Artzi A, Goldberg R. Adalimumab as steroid-sparing treatment of inflammatory-stage thyroid eye disease. *OphthalPlastReconstrSurg* 2014;30:415-9.
18. Paridaens D, van den Bosch WA, van der Loos TL, van Hagen PM. The effect of etanercept on Graves' ophthalmopathy: a pilot study. *Eye* 2005;19:1286-9.
19. Perez-Moreiras JV, Alvarez-Lopez A, Gomez EC. Treatment of active corticosteroid-resistant Graves' orbitopathy. *OphthalPlastReconstrSurg* 2014;30:162-7.

20. Sy A, Eliasieh K, Silkis RZ. Clinical response to tocilizumab in severe thyroid eye disease. *OphthalPlastReconstrSurg* 2017;33:e55-e7.
21. Salvi M, Vannucchi G, Beck-Peccoz P. Potential utility of rituximab for Graves' orbitopathy. *J Clin Endocrinol Metab* 2013;98:4291-9.
22. Stan MN, Garrity JA, Carranza Leon BG, Prabin T, Bradley EA, Bahn RS. Randomized controlled trial of rituximab in patients with Graves' orbitopathy. *J Clin Endocrinol Metab* 2015;100:432-41.
23. Salvi M, Vannucchi G, Curro N, et al. Efficacy of B-cell targeted therapy with rituximab in patients with active moderate to severe Graves' orbitopathy: a randomized controlled study. *J Clin Endocrinol Metab* 2015;100:422-31.
24. Stan MN, Salvi M. Rituximab therapy for Graves' orbitopathy-lessons from randomized control trials. *Eur J Endocrinol* 2017;176:R101-R9.

## RARE CAUSES OF ORBITAL INFLAMMATORY DISEASE

Steven E. Feldon, MD, MBA  
Flaum Eye Institute / University of Rochester Medical Center  
Rochester, NY

### LEARNING OBJECTIVES

1. The attendee will be able to identify rare systemic inflammatory diseases that are associated with orbital symptoms and signs
2. The attendee will be able to differentiate among rare systemic causes of orbital inflammation by presence or absence of key clinical symptoms or signs
3. The attendee will be able to determine which diagnostic tests are indicated to definitively diagnose the specific systemic cause of an orbital inflammatory process

### CME QUESTIONS

1. Granulomatosis with polyangiitis (GPA) is usually diagnosed by:
  - a. biopsy demonstrating vasculitis in large vessels
  - b. biopsy notable for absence of necrosis
  - c. Antibodies present to neutrophil cytoplasmic antibodies
  - d. All of the above
  - e. None of the above
2. Rosai-Dorfman Disease characteristics include
  - a. Being more common in adults
  - b. Overproduction of non Langerhans histiocytes
  - c. Rarely involves lymph nodes
  - d. All of the above
  - e. None of the above
3. Erdheim-Chester
  - a. Is primarily seen in adults
  - b. Often spare long bones
  - c. May result in death due to organ involvement
  - d. Is easily distinguished from Langerhans cell histiocytosis
  - e. A and C
  - f. B and D

### KEY WORDS

1. Orbital inflammation
2. Histiocytosis
3. Proptosis
4. Vasculitis
5. Granuloma

## INTRODUCTION

The vast majority of orbital inflammations are related to thyroid eye disease or idiopathic orbital inflammation. However, the differential diagnosis includes a number of relatively rare systemic diseases that may manifest primarily or solely in the orbit with unique or characteristic imaging and histopathology. The purpose of this review is to point out the systemic, ocular, and orbital manifestations that aid in the differential diagnosis. Based upon these observations, appropriate diagnostic testing and treatment options can be defined.

## SARCOIDOSIS

**Demographics:** Observed in both genders with peak in 3<sup>rd</sup> decade; a possible secondary peak occurs in women over 50. There is a pediatric presentation with rare orbital involvement often confused with sarcoid, now recognized as Blau Syndrome, which is a separate entity with de novo genetic mutations. Worldwide the incidence is highest in Scandinavian counties with incidence of 60/100,000. In the US the incidence in African Americans is 35.5/100,000 and for Caucasians, the incidence is 10.9/100,000. Occupations with exposures to toxins may have a higher incidence (spike in NYC post-911 to 86/100,000).

**Systemic, Ocular, and Orbital manifestations:** 5% of cases are asymptomatic but fatigue and weight loss with arthralgias are common. Pulmonary disease affects up to 90% of patients (hilar adenopathy, infiltrates, and fibrosis). Skin is the second most effected organ system, presenting as rashes, nodules, erythema nodosum, granulomas or lupus pernio. Neurosarcoid is present in 10-25% of sarcoidosis, most commonly affecting the facial nerves. Uveitis, as the most frequent manifestation of systemic sarcoid may be granulomatous or non-granulomatous, and present as anterior, intermediate, posterior or panuveitis. Optic neuropathy and eyelid granulomas may occur as do asymptomatic conjunctival lesions that may progress to symblepheron. Lacrimal manifestations may include dry eye due to lacrimal gland inflammation or the presence of a palpable mass in the lacrimal fossa. According to several published retrospective series, bilateral disease occurs in 50% and systemic manifestations in 70% (half prior to orbital disease). On orbital imaging lacrimal gland infiltration in 55%, discrete orbital mass in 20%, and optic nerve sheath infiltration in 20% were encountered most frequently.

**Radiation and Pathology:** Imaging demonstrates enhancing well-circumscribed masses most commonly involving lacrimal gland, occasionally eyelid, deep orbit and rarely lacrimal sac. The characteristic orbital pathology includes noncaseating granulomas with some giant cells and often Schumann body inclusions along with background fibrosis. On MRI, the lacrimal glands may be enlarged and hypointense on both T1 and T2 weighted images that enhance with contrast. Infiltrative lesions demonstrate mixed signal on T2 weighted imaging and enhance on T1, post-contrast.

**Diagnostic Testing and Treatment:** A definitive diagnosis of sarcoid is by biopsy of affected tissue. Supportive laboratory investigation includes chest x-ray or CT scan, gallium scintigraphy or other nuclear imaging such as PET studies, elevated serum calcium, angiotensin converting enzyme (ACE), and/or lysozyme. The KVEIM adjuvant test using tissue of a sarcoid patient is of historical interest, but is not utilized clinically to to lack of obtaining reagent and possibility of transmission. Common initial treatment is oral corticosteroids with cyclosporine or azathioprine used as adjunctive therapy. Some patients benefit from direct injection of corticosteroids into the lesion.

## CHURG-STRAUSS SYNDROME

**Demographics:** The mean age of onset is in fifth decade of life and it is rarely seen in children.

**Systemic, Ocular and Orbital manifestations:** Asthma is the most common manifestation. Skin, heart, and GI tract are occasionally involved with symptoms including hay fever, rash, pain and numbness in hands and feet, loss of appetite, weight loss, night sweats, joint pain, fatigue, cough, abdominal pain and GI bleeding. Neuro-ophthalmic presentation may reflect either an ischemic or a granulomatous

pathological mechanism. Ischemic vasculitis may present with amaurosis fugax, ischemic optic neuropathy, central or branch retinal artery occlusion. With the infiltrative process, lid swelling and exophthalmos, palpable lacrimal gland enlargement can occur. Orbital inflammation may include dacryoadenitis, myositis, periscleritis, conjunctival granulomas and episcleritis.

**Radiology and Pathology:** B-scan ultrasonography demonstrates choroidal thickening in the macula and MRI may show thickened optic nerve sheaths, enlarged lacrimal glands, and myositis. Orbital biopsy shows evidence of granulomatous inflammation with marked eosinophil infiltration and vasculitis changes.

**Diagnostic Testing and Treatment:** Weakly positive ANCA is often seen in diagnostic testing. A biopsy should be conducted. Corticosteroids, methotrexate, cytotoxic drugs are prescribed for refractory cases.

### **WEGENER'S GRANULOMATOSIS: GRANULOMATOSIS WITH POLYANGIITIS (GPA)**

**Demographics:** There is an equal incidence in both genders. Peak ages 40-70 years, but may occur at any age, including in children. It is more common in Caucasians with annual incidence of .4-.8/100,000; orbital involvement is present in about half of patients.

**Systemic, Ocular, and Orbital manifestations:** Common presentations include weight loss, fever, fatigue, arthralgia and myalgia. Upper airway involvement is present in 90% of patients along with sinus involvement, tracheal stenosis resulting in epistaxis or sinusitis as well as deafness, hoarseness and respiratory stridor. Classical findings are nasal septal perforation and saddle nose deformity and granulomatous involvement of lungs and kidneys are common. Ocular Manifestations include episcleritis, scleritis, keratitis (interstitial or peripheral ulcerative), retinal vasculitis (occlusion may occur). Uveitis is rare, but dacryoadenitis is common. Orbital manifestations may result from a primary inflammatory process or extension from adjacent sinuses. The disease is often bilateral. Proptosis with or without pain, diplopia, optic nerve compression and exophthalmos may occur. There may be late onset of fibrosis.

**Radiology and Pathology:** Radiologic findings are infiltration and obliteration of fat. CT shows bone thinning and sinus inflammation, lacrimal drainage involvement, thinning/obliteration of nasal septum. MRI may show low signal intensity lesions on non-fat suppressed T1 and T2 weighting involving nasal cavity, sinuses and orbit. Traditional triad is parenchymal necrosis, vasculitis and granulomatous inflammation. The characteristics are orbital fat necrosis with giant cells and free vacuoles as well as fibrosis.

**Diagnostic Testing and Treatment:** cANCA is positive in >90% of cases. Treating disease with corticosteroids alone is rarely sufficient, usually requiring the addition of cyclophosphamide with methotrexate or azathioprine useful in chronic management. Various monoclonal antibody therapies (anti-TNF and anti CD20+) have variable efficacy.

### **GIANT CELL ARTERITIS**

**Demographics:** GCA occurs most commonly in Caucasians and the women- to- men ratio is (2:1). Mean age at onset is 72 years, with diagnosis unlikely under 50 years. There is some familial clustering.

**Systemic, Ocular and Orbital manifestations:** The common manifestations are headache, neck pain, weight loss, jaw claudication, polymyalgia rheumatica, scalp tenderness. Severe systemic manifestations include aortic aneurysms, stroke and myocardial infarction. Up to 20% suffer permanent visual loss in one or both eyes from anterior or posterior ischemic optic neuropathy. Amaurosis fugax may precede vision loss in 30% of patients with permanent visual loss. Diplopia may occur from ocular myopathy or cranial neuropathy; rare ocular ischemic syndrome. Orbital infarction with ophthalmoplegia and visual

loss may rarely occur. It rarely may cause orbital inflammatory syndrome with proptosis, chemosis, and conjunctival injection with diplopia or vision loss.

**Radiology and Pathology:** Orbital MRI shows poorly defined infiltrative process on fat-suppressed, enhanced sequences with thickening and enhancement of extraocular muscles and optic nerve sheath. The pathology is characterized by epithelioid cells, giant cells, round cell infiltration.

**Diagnostic Testing and Treatment:** Elevated Westergren sedimentation rate, C-reactive protein tests are characteristic but not diagnostic. The diagnosis is confirmed by positive temporal artery biopsy and/or orbital biopsy. GCA is treated by high dose corticosteroids with adjunct use of steroid-sparing agents such as methotrexate, azathioprine, or cyclosporine.

#### **ADULT XANTHOGRANULOMATOUS DISEASES**

**Demographics:** This rare disease peaks in sixth decade with no gender predominance.

**Systemic, Ocular and Orbital manifestations:** **AOX (adult onset)** has no systemic involvement and no immune dysfunction. **AAPOX (adult onset asthma and periocular)** is associated with asthma and lymphadenopathy. **NBX (necrobiotic)** is associated with paraproteinemia from monogammopathy or multiple myeloma. **ECD (Erdheim-Chester)** is characterized by fibrosclerosis of lungs, heart, and retroperitoneal space with bone involvement common. Some ocular manifestations are eyelid lesions in all types, rare scleritis and uveitis in NBX. Orbital manifestations include preseptal yellowish lesions and lacrimal gland enlargement for all but ECD. Intraconal diffuse infiltration is seen in almost all ECD patients, but is rare for others.

**Radiology and Pathology:** Discrete preseptal and eyelid masses as well as lacrimal enlargement on CT scan and diffuse orbital infiltration may be seen. All types of xanthogranulomatous diseases are characterized pathologically with foamy histiocytes (CD 68+) and Touton giant cells along with spindle shaped monocular cells, foreign body giant cells, eosinophils and lymphocytes. NBX demonstrates necrosis, ulceration, and scarring.

**Diagnostic Testing and Treatment:** Some findings are paraproteinemia and lymphadenopathy. Treatment includes management of the primary paraproteinemia, and potential local excision of anterior and lid masses. There have been poor results with systemic therapy, primarily multi-agent chemotherapy with or without radiation. There is a possible benefit of cyclosporine in combination with cyclophosphamide.

#### **ROSAI-DORFMAN**

**Demographics:** This is a male predominant disease. 80% are <21 years of age, but onset may occur at any age.

**Systemic, Ocular and Orbital Manifestations:** The principal systemic manifestation is lymphadenopathy with predilection for head and neck. Extranodal manifestation may include respiratory tract, salivary glands, skin, bone, meninges, CNS, testes and orbit. Ocular manifestations include rare scleritis, uveitis, marginal corneal infiltration, and choroidal mass. Examples of orbital manifestations are painless proptosis due to intraconal involvement with concurrent paranasal sinus involvement, Periorbital and eyelid masses as well as lacrimal gland enlargement are usually bilateral.

**Radiology and Pathology:** CT shows a homogeneous mass with rare evidence of bony destruction. MRI on T1 with gadolinium shows homogenous enhancement. Emperipolesis wherein lymphocytes are found phagocytized with large histiocytes is diagnostic. Extranodal sites have lymph node architecture without true sinuses. Scattered mixed inflammatory cell infiltration and epithelioid cells are seen as well.

**Diagnostic Testing and Treatment:** CBC test may show anemia. Other results include polyclonal hypergammaglobulinemia. Biopsy is often diagnostic. It can be treated by excision or debulking of masses. Spontaneous remissions may occur. Radiation, steroids and chemotherapy for recurrent or unresponsive cases are used for treatment.



## CME ANSWERS

1. C
2. B
3. E

## REFERENCES

### SARCOIDOSIS

1. Demirci H and Christianson MD. Orbital and adnexal involvement in sarcoidosis: analysis of clinical features and systemic disease in 30 cases. *Am J Ophthalmol.* 2011;151(6):1074-1080
2. Mavrikakis I, and Rootman J. Diverse clinical presentations of orbital sarcoid. *Am J Ophthalmol.* 2008; 144(5):769-775.
3. Prabhakaran VC, Saeed P, Esmaeli B, et al.: Orbital and adnexal sarcoidosis. *Arch Ophthalmol* 2007; 125(12):1657-1662.

### CHURG STRAUSS SYNDROME

4. Ghosh S, Bhattacharya M, and Dhar S. Churg-Strauss Syndrome. *Indian J Dermatol.* 2011 Nov-Dec; 56(6): 718–721.
5. Pradeep TG<sup>1</sup>, Prabhakaran VC, McNab A, et al.: Diffuse bilateral orbital inflammation in Churg- Strauss syndrome. *Ophthal Plast Reconstr Surg.* 2010 Jan-Feb;26(1):57-9
6. Takanashi T, Uchida S, Arita M, et al.: Orbital Inflammatory Pseudotumor and Ischemic Vasculitis in Churg-Strauss Syndrome. Report of Two Cases and Review of the Literature. *Ophthalmology* 2001;108:1129–1133

### WEGENER'S GRANULOMATOSIS: GRANULOMATOSIS WITH POLYANGIITIS (GPA)

7. Pakrou N, Selva D, and Leibovitch I. Wegener's Granulomatosis: Ophthalmic Manifestations and Management *Semin Arthritis Rheum* 2006, 35:284-292
8. Seo P, and Stone JH. The antineutrophil cytoplasmic antibody-associated vasculitides. *Am J Med* 2004;117:39-50.
9. Tarzi RM, and Pusey CD, Current and future prospects in the management of granulomatosis with polyangiitis (Wegener's granulomatosis). *Therapeutics and Clinical Risk Management* 2014 10:279-293.

### GIANT CELL ARTERITIS

10. Chertok P, Leroux JL, Le Marchand M, et al.: Orbital pseudo-tumor in temporal arteritis revealed by computerized tomography. *Clin Exp Rheumatol* 1990 8: 587-589.
11. Lee AG, Tang RA, Feldon SE, et al.: Orbital presentations of giant cell arteritis. *Graefe's Arch Clin Exp Ophthalmol* 2001 239:509-513.
12. Nassani S, Cocito L, Arcuri T, et al.:Orbital pseudotumor as a presenting sign of temporal arteritis.*Clin Exp Rheumatol.* 1995 May-Jun;13(3):367-9.

### ADULT XANTHOGRANULOMATOUS DISEASES

13. Gonzales JA, Haemel A, Gross AJ, et al.: Management of Uveitis and Scleritis in Necrobiotic Xanthogranuloma.*Journal of Ocular Pharmacology and Therapeutics.* Volume 33, Number 4, 2017
14. Kerstetter J<sup>1</sup>, Wang J<sup>2</sup>. Adult Orbital Xanthogranulomatous Disease: A Review with Emphasis on Etiology, Systemic Associations, Diagnostic Tools, and Treatment. *Dermatol Clin.* 2015 Jul;33(3):457-63.
15. Sivak-Callcott JA, Rootman J, Rasmussen SL, et al.: Adult xanthogranulomatous disease of the orbit and ocular adnexa: new immunohistochemical findings and clinical review. *Br J Ophthalmol* 2006;90:602–608. doi: 10.1136/bjo.2005.085894

## ROSAI-DORFMAN

16. Kala C, Agarwal A, and Kala S. Extranodal manifestation of Rosai-Dorfman disease with bilateral ocular involvement. *Journal of Cytology / Indian Academy of Cytologists*. 2011; 28(3), 131–133.
17. Tan JJ, Narang S, Purewal B, et al.: Extranodal Rosai-Dorfman Disease of the Orbit: Clinical features of 8 cases. *Ophthal Plast Reconstr Surg*, 32(6):458-461, 2016.
18. Vemuganti G K, Naik MN, and Honavar SG. Rosai dorfman disease of the orbit. *Journal of Hematology and Oncology*.2008. 1, 7. Available at : <http://doi.org/10.1186/1756-8722-1-7>

## **NONSPECIFIC ORBITAL INFLAMMATION (NSOI)**

**Howard R Krauss, MD**

**Professor of Ophthalmology and Neurosurgery Pacific Neuroscience Institute  
Santa Monica, CA**

### **LEARNING OBJECTIVES**

1. The attendee will be able to classify non-specific orbital inflammation (NSOI) in accordance with the likely orbital tissue or origin and potential underlying auto-immune disorder.
2. The attendee will be able to order an appropriate comprehensive blood panel in a case of NSOI.
3. The attendee will know the role of various imaging modalities in the evaluation and ongoing management of NSOI.

### **CME QUESTIONS (True/False)**

1. Orbital pseudotumor may be associated with pseudotumor cerebri.
2. Radiation therapy is an acceptable therapeutic modality in the treatment of NSOI.
3. Infliximab may be a useful therapeutic option in NSOI.

### **KEYWORDS (5 Max)**

1. Non-specific orbital inflammation (NSOI)
2. Pseudotumor
3. posterior scleritis
4. orbital myositis
5. perioptic neuritis

Nonspecific orbital inflammation (NSOI) was first described in 1905 by Birch-Hirschfeld. It is, as stated, nonspecific; thus it does not include Thyroid Eye Disease (TED), lymphoma, sarcoid, Churg-Strauss, Wegener's, GCA, xanthogranulomatous disease, Rosai-Dorfman, or any other specific inflammatory disorder. As our diagnostic acumen improves, there may one day be no NSOI.

It was named as inflammatory pseudotumor in 1954 by Umiker et al. because of its propensity to mimic a malignant process. Today "orbital pseudotumor" is a pseudodiagnosis which should be relegated to the trash heap, as it includes all orbital inflammatory diseases and lymphoid processes which present with orbital mass effect, compounded by confusion produced in the continued use of the similar sounding but unrelated diagnostic term, pseudotumor cerebri, which would best be known as Idiopathic Intracranial Hypertension (IIH); let's agree to expunge the word pseudotumor from our modern lexicon, although it will remain in the old literature.

Although NSOI may include contiguous structures, in many cases it appears to arise within a specific orbital tissue or organ, and when it does it is best connoted as such, e.g., posterior scleritis, myositis, dacryoadenitis, perioptic neuritis.

The histopathology is, of course, nonspecific, including diffuse polymorphous infiltration, lymphoid, granulomatous, sclerosing, eosinophilic or vasculitic inflammation.

The etiology and pathogenesis of NSOI is unknown. Both infectious and immune-mediate etiologies have been implicated. NSOI has also been observed in association with a variety of rheumatologic conditions including Crohn's disease, systemic lupus erythematosus, rheumatoid arthritis, myasthenia gravis, and ankylosing spondylitis.

NSOI is typically characterized by the abrupt onset of pain, proptosis and other inflammatory signs such as edema and erythema. Unilateral presentation is more typical but bilateral presentations are not uncommon. Pediatric NSOI is more commonly bilateral and accompanied by uveitis, disc edema or eosinophilia. Pain is the most common symptom in adult NSOI, followed by diplopia. Periorbital edema is the most common sign, followed by proptosis, restricted eye movement, ocular injection, chemosis, decreased vision and ptosis. Examination of patients with suspected NSOI involves lid assessment, orbital assessment, extraocular muscles, anterior segment, vitreous, retina and optic nerve. Because of the association between rheumatologic disease and NSOI the typical laboratory work-up for suspected NSOI should include a complete blood count, basic metabolic panel, thyroid function studies, erythrocyte sedimentation rate, antinuclear antibodies, antineutrophil cytoplasmic antibodies, angiotensin-converting enzyme level, rapid plasma reagin test, and rheumatoid factor.

Evaluation of NSOI will frequently involve imaging, which may include echography, high-resolution computed tomography (CT) or magnetic resonance imaging (MRI), with or without contrast. Echography is a readily available chairside tool, which may reveal findings characteristic of posterior scleritis (T sign), myositis or dacryoadenitis, with typical thickening and low internal reflectivity, characteristic of edema and/or inflammatory infiltrative disease. CT or MRI will reveal thickened, enlarged or infiltrated structures; contrast enhancement will provide evidence of vascular permeability, as seen in most non-infectious inflammatory disease. Echography is a useful clinical tool to easily monitor clinical response to treatment, in that signs and symptoms will typically resolve before echographic abnormalities, allowing avoidance of a premature cessation of treatment which all too often produces a difficult-to-manage rebound.

While observation and/or non-steroidal anti-inflammatory drugs (NSAIDs) may be considered for mild cases, most are treated with corticosteroids. Systemic corticosteroids are generally considered mainstay therapy for NSOI. Typically, response to steroids is rapid with a dramatic improvement in all symptoms and findings. Treatment doses can differ in range but are generally 1.0-1.5 mg/kg or 50-100 mg/day for 1-2 weeks followed by slow taper for 5-8 weeks.

Radiation therapy is an acceptable therapeutic modality in the treatment of NSOI. It has generally been used when NSOI is found to be resistant to corticosteroid therapy, or for patients intolerant of corticosteroids. Hopefully, access to an increasing armamentarium of immunologic agents may reduce the frequency of radiotherapy.

What's new? Anecdotal reports and limited case series of treatment with:

A calcineurin inhibitor, cyclosporine-A, an immunosuppressant that acts on T-lymphocytes inhibits synthesis T-cell growth cytokines, IL-2 and IFN- $\gamma$ . A few studies have shown that cyclosporine can be efficacious in diabetic NSOI patients who cannot tolerate steroids. Diaz-Llopis and Menezo recommend treating NSOI with 5mg/kg/day then tapering to 2mg/kg/day over ten months. Zacharopoulos et al. treated a patient using 4mg/kg/day for 6 weeks and this patient remained symptom free for 5 years without any medication.

Several cytotoxic antiproliferative drugs have anecdotally been applied to NSOI, including azathioprine, cyclophosphamide and methotrexate. Regarding methotrexate for ocular immunosuppression Hemady et al recommend 10 to 25 mg divided over 36 to 48 hours every 1 to 4 weeks. Smith and Rosenbaum reported treating seven NSOI patients with methotrexate ranging from 15 to 25 mg/week for periods of 4 weeks to 34 months. Of those seven patients, four demonstrated clinical benefit; in one patient methotrexate was stopped due to side effects; in one there was no response, and 2 patients did not complete the 4 months trial for undisclosed reasons. Shah et al. evaluated methotrexate use in NSOI at low doses of 12.5 mg/wk and reported 16 out of 22 patients had a reduction of inflammatory activity. Fourteen of the 16 patients were able to taper or discontinue corticosteroid therapy and 5 patients had complete remission. Six patients did not respond to methotrexate.

It's a mab mab world:

Infliximab may be a useful therapeutic option in NSOI. Garrity et al. reported the treatment of 7 patients with chronic and refractory orbital myositis. Patients received a dosing schedule of 3 to 5 mg/kg (up to 10 mg/kg) given at weeks 0,2,and 6 with treatments every 4 to 8 weeks afterwards. It was noted that all 7 patients had a favorable response to treatment with no untoward effects after a mean follow-up of 15.7 months (range, 4 to 31 months). Miguel et al. has reported two cases of steroid dependent NSOI who developed adverse effects from conventional steroid-sparing agents, in both cases symptoms had disappeared with infliximab with follow-up of at least 20 months. Sahlin et al. described successful treatment of 1 patient with sclerosing NSOI with combination infliximab and methotrexate therapy. Wilson et al. has reported success in the treatment in a pediatric patient with refractory bilateral NSOI and has remained symptom free and off corticosteroids 2 years since initial diagnosis.

Undoubtedly, other mabs will be offered and reported.

Other immunotherapies: IVIG and plasmapheresis have not been employed with adequate frequency in NSOI to offer comment.

#### **CME ANSWERS**

1. False
2. True
3. True

## REFERENCES

1. Lee AG, Burkat CN, Jirawuthiworavong GV, Chundury RV, Espinoza G: Nonspecific Orbital Inflammation (Idiopathic orbital inflammation, Orbital inflammatory syndrome, Orbital pseudotumor), EyeWiki, American Academy of Ophthalmology, 2017.
2. Birch-Hirschfeld A. Zur Diagnostic and Pathologic der Orbital Tumoren. Bericht uber die Zusammenkunft der Deutschen Ophthalmologischen Gesellschaft 1905;32:127e35.
3. Umiker WO, Iverson LC. Post inflammatory tumor of the lung: report of four cases simulating xanthoma, fibroma, or plasma cell granuloma. *J. Thorac Surg* 1954;28:55-62.
4. Ahn Yuen SJ, Rubin PAD. Idiopathic Orbital Inflammation Distribution, Clinical Features, and Treatment Outcome. *Arch Ophthalmol*. 2003;121:491-499.
5. Espinoza GM. Orbital Inflammatory Pseudotumors: Etiology, Differential, Diagnosis, and Management. *Curr Rheumatol Rep* 2010;12:443-447.
6. Swamy BN, McCluskey P, Nemet A, Crouch R, Martin P, Bengner R, Ghabriel R, Wakefield D. Idiopathic orbital inflammatory syndrome: Clinical features and treatment outcomes. *Br J Ophthalmol* 2007;91:1667-1670.
7. Carruth BP, Wladis EJ. Inflammatory modulators and biologic agents in the treatment of idiopathic orbital inflammation. *Curr Opin Ophthalmol* 2012;23:420-426.
8. Narla LD, Newman B, Spottswood SS, Narla S, Kolli R: Inflammatory Pseudotumor. *Radiographics*, online publication 2003;23:719-720.
9. Hemady R, Tauber J, Foster CS. Immunosuppressive drugs in immune and inflammatory ocular disease. *Surv Ophthalmol*. 1991;35:369-385.
10. Smith JR, Rosenbaum JT. A role for methotrexate in the management of non-infectious orbital inflammatory disease. *Br J Ophthalmol* 2001;85:1220-1224.
11. Shah SS, Lowder CY, Schmitt MA, et al. Low-dose methotrexate therapy for ocular inflammatory disease. *Ophthalmology* 1992;99:1419-1423.
12. Diaz-Lopez M, Menezo JL. Idiopathic inflammatory orbital pseudotumor and low-dose cyclosporine. *Am J Ophthalmol* 1989;107:547-548.
13. Zacharopoulos IP, Papadaki T, Manor RS, Briscoe D. Treatment of idiopathic orbital inflammatory disease with cyclosporine-A: a case presentation. *Semin Ophthalmol* 2009;24:260-261.
14. Winn BJ, Rootman J. Sclerosing Orbital Inflammation and Systemic Disease. *Ophthal Plast Reconstr Surg* 2012;28(2):107-118.
15. Garrity JA, Coleman AW, Matteson EL, et al. Treatment of Recalcitrant Idiopathic Orbital Inflammation (Chronic Orbital Myositis) With Infliximab. *Am J Ophthalmol* 2004;138:925-930.
16. Miguel T, Abad S, Badelon I, Vignal C, et al. Successful treatment of idiopathic orbital inflammation with infliximab: An alternative to conventional steroid-sparing agents. *Ophthal Plast Reconstr Surg* 2008;24(5):415-417.
17. Sahlin S, Lignell B, Williams M, et al. Treatment of idiopathic sclerosing inflammation of the orbit (myositis) with infliximab. *Acta Ophthalmol* 2009;87:906-908.
18. Wilson MW, Shergy WJ, Haik BG. Infliximab in the Treatment of Recalcitrant Idiopathic Orbital Inflammation. 2004;20(5):381-399.

19. Pemberton JD, Fay A. Idiopathic Sclerosing Orbital Inflammation: A Review of Demographics, Clinical Presentation, Imaging, Pathology, Treatment, and Outcome. *Ophthal Plast Reconstr Surg* 2012;28:79-83.

## A RATIONAL APPROACH TO TREATING INFLAMMATORY OPTIC NEUROPATHIES: WHICH TREATMENT AND WHY

Jeffrey L. Bennett, M.D., Ph.D.

Departments of Neurology and Ophthalmology, Program in Neuroscience  
University of Colorado School of Medicine

### LEARNING OBJECTIVES

1. Enumerate immune and infectious causes of inflammatory optic neuropathy.
2. Describe data supporting various treatments of acute inflammatory optic neuropathy.
3. List inflammatory optic neuropathies with high risk of poor visual recovery or recurrent disease.

### CME QUESTIONS

1. All of the following findings suggest an infectious cause of inflammatory optic neuropathy except:
  - a. Vitritis
  - b. Severe disc edema
  - c. Macular star
  - d. Long enhancing optic nerve lesion on orbital MRI
2. Therapeutic options for acute treatment of steroid refractory optic neuritis include all of the following except:
  - a. Plasma exchange
  - b. Rituximab
  - c. Tryptophan immunoadsorption
  - d. Intravenous immunoglobulin
3. Inflammatory optic neuropathies with a high risk of recurrence include:
  - a. MOG-IgG seropositive optic neuritis
  - b. GFAP-IgG seropositive papillitis
  - c. AQP4-IgG seropositive neuromyelitis optica
  - d. AQP4-IgG seronegative neuromyelitis optica
  - e. A and C

### KEYWORDS

1. Optic neuritis
2. Intravenous methylprednisolone
3. Plasma exchange
4. Immunosuppression

### HIGHLIGHTS

Inflammatory optic neuropathy, or optic neuritis (ON), is the most common cause of optic nerve injury in young adults. Although high contrast visual recovery after idiopathic ON is generally considered to be good,<sup>1</sup> poor visual outcomes are commonly observed in association with disorders such as neuromyelitis optica spectrum disease (NMOSD), and many patients complain of persistent visual problems after recovery.<sup>2</sup> Acute ON therapies are needed to minimize injury and optimize recovery.

Optimal treatment of AON is ultimately dependent on the mechanism underlying the inflammatory injury. While ON is typically synonymous with autoimmunity, infectious, and non-infectious causes of optic nerve inflammation should always be considered in the differential diagnosis. Diagnosis of an infectious agent may direct therapies, inform on visual prognosis, and mitigate the use of immunosuppression.<sup>3,4</sup> Based on suspicion for autoimmune or paraneoplastic disorders, additional serologic studies may be performed.



Since the Optic Neuritis Treatment Trial (ONTT), high dose intravenous methylprednisolone (IVMP) has been the treatment of choice for immediate therapy of acute ON.<sup>1</sup> While accelerating recovery, IVMP has failed to improve long-term function or prevent optic nerve atrophy.<sup>5,6</sup> Intramuscular or subcutaneous adrenocorticotropic hormone (ACTH) is also approved for the treatment of ON and MS-related relapses.<sup>7</sup> Orally-administered corticosteroids at bioequivalent doses to IVMP add therapeutic flexibility.<sup>8</sup> Intravenous immunoglobulin (IVIg) and plasma exchange (PLEX) have been studied for the treatment of acute ON and ON refractory to IVMP. IVIg showed no effect on visual recovery after acute ON.<sup>9</sup> Conversely, PLEX has been used successfully in the treatment of steroid refractory ON and NMO/OSD ON;<sup>10</sup> however, the use or timing of PLEX remain ill-defined.<sup>11</sup> Male sex, lower baseline disability, rapid initiation of treatment, and shorter relapse duration have been associated with greater response.<sup>12</sup> Therapeutic apheresis (IA) offers the potential advantage of removing pathogenic autoantibodies while sparing other plasma proteins and has been reported to benefit steroid refractory ON and NMO/OSD ON.<sup>13</sup>

In certain situations, treatment of acute ON should be tailored. Cases of recurrent optic neuritis may demand more immediate, aggressive treatment as the prognosis for visual recovery may not be as good. Unless otherwise contraindicated, antibiotic therapy should be initiated with symptomatic therapy if suspicion for infection is high. The exception may be Bartonella infection, where the benefit of antibiotic therapy remains unclear.<sup>14</sup> For paraneoplastic ON, anecdotal success has been reported with the use of intravitreal triamcinolone in the treatment of CRMP-5 autoimmunity.<sup>15</sup> Steroid responsive recurrent optic neuropathies include autoimmune optic neuropathy,<sup>16</sup> chronic relapsing inflammatory optic neuropathy (CRION),<sup>17</sup> and ON associated with serum autoantibodies against myelin oligodendrocyte glycoprotein (MOG-IgG).<sup>18</sup> An inflammatory meningoencephalitis associated with optic disc edema, vision loss, perivascular inflammation, and GFAP autoantibodies (GFAP-IgG) was recently reported and may also benefit from corticosteroids.<sup>19</sup>

## SUMMARY

ON treatment should be based on the underlying diagnosis. High dose IVMP should be instituted first for most conditions with strong consideration for escalating therapy in cases of poor recovery, recurrent disease, and NMO/OSD.

## CME ANSWERS

1. D
2. B
3. E

## REFERENCES

1. Beck, R.W., et al., A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. The Optic Neuritis Study Group. *N Engl J Med*, 1992. 326(9): 581-8.
2. Galetta, S.L., et al., Acute optic neuritis: Unmet clinical needs and model for new therapies. *Neurol Neuroimmunol Neuroinflamm*, 2015. 2(4): e135.
3. Boudreault, K., M.L. Durand, and J.F. Rizzo, 3rd, Investigation-Directed Approach to Inflammatory Optic Neuropathies. *Semin Ophthalmol*, 2016. 31(1-2): 117-30.
4. Bennett, J.L., et al., Re-evaluating the treatment of acute optic neuritis. *J Neurol Neurosurg Psychiatry*, 2015. 86(7): 799-808.
5. Beck, R.W. and P.A. Cleary, Optic neuritis treatment trial. One-year follow-up results. *Arch Ophthalmol*, 1993. 111(6): 773-5.
6. Hickman, S.J., et al., Corticosteroids do not prevent optic nerve atrophy following optic neuritis. *J Neurol Neurosurg Psychiatry*, 2003. 74(8): 1139-41.
7. Filippini, G., et al., Corticosteroids or ACTH for acute exacerbations in multiple sclerosis. *Cochrane Database Syst Rev*, 2000.
8. Alam, S.M., et al., Methylprednisolone in multiple sclerosis: a comparison of oral with intravenous therapy at equivalent high dose. *J Neurol Neurosurg Psychiatry*, 1993. 56(11): 1219-20.

9. Roed, H.G., et al., A double-blind, randomized trial of IV immunoglobulin treatment in acute optic neuritis. *Neurology*, 2005. 64(5): 804-10.
10. Deschamps, R., et al., Plasma exchange response in 34 patients with severe optic neuritis. *J Neurol*, 2016.
11. Pula, J.H. and C.C. Glisson, Should plasma exchange be offered to patients with multiple sclerosis-associated optic neuritis? *J Neuroophthalmol*, 2015. 35(1): p. 86-89.
12. Kleiter, I., et al., Neuromyelitis optica: Evaluation of 871 attacks and 1,153 treatment courses. *Ann Neurol*, 2016. 79(2): 206-16.
13. Koziolok, M.J., et al., Immunoabsorption therapy in patients with multiple sclerosis with steroid-refractory optical neuritis. *J Neuroinflammation*, 2012. 9(1): 80.
14. Bhatti, M.T. and M.S. Lee, Should patients with bartonella neuroretinitis receive treatment? *J Neuroophthalmol*, 2014. 34(4): 412-416.
15. Pulido, J., et al., Bilateral autoimmune optic neuritis and vitreitis related to CRMP-5-IgG: intravitreal triamcinolone acetate therapy of four eyes. *Eye*, 2008. 22(9): 1191-1193.
16. Frohman, L., et al., Clinical characteristics, diagnostic criteria and therapeutic outcomes in autoimmune optic neuropathy. *Br J Ophthalmol*, 2009. 93(12): 1660-6.
17. Petzold, A. and G.T. Plant, Chronic relapsing inflammatory optic neuropathy: a systematic review of 122 cases reported. *J Neurol*, 2014. 261(1): 17-26.
18. Pache, F., et al., MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 4: Afferent visual system damage after optic neuritis in MOG-IgG-seropositive versus AQP4-IgG-seropositive patients. *J Neuroinflammation*, 2016. 13(1): 282.
19. Flanagan, E.P., et al., Glial fibrillary acidic protein immunoglobulin G as biomarker of autoimmune astrocytopathy: Analysis of 102 patients. *Ann Neurol*, 2017. 81(2): 298-309.

## DO THE EXTRAOCULAR MUSCLES CAUSE GLAUCOMA AND ANTERIOR ISCHEMIC OPTIC NEUROPATHY?

Joseph L. Demer, M.D., Ph.D.  
Stein Eye Institute and Department of Neurology  
University of California, Los Angeles

### LEARNING OBJECTIVES

1. The attendee will be able to describe how extraocular muscle counterforce influences the optic nerve in adduction.
2. The attendee will be able to describe the relationship between adduction tethering of the optic nerve and common, progressive patterns of temporal optic disc tilting, peripapillary atrophy, acquired optic pits, and nerve fiber bundle defects.
3. The attendee will be able to describe a plausible, non-vascular mechanism for normal tension glaucoma and non-arteritic anterior ischemic optic neuropathy.

### CME QUESTIONS

1. Is it normal for the optic nerve to become stretched in adduction?
2. Which ocular tissue is stiffest?
  - a. Posterior sclera
  - b. Optic nerve sheath outer layer
  - c. Optic nerve sheath inner layer
  - d. Optic nerve
3. What changes in posterior ocular tissues are associated with normal tension glaucoma?  
(There may be more than one answer.)
  - a. Softening of the posterior sclera
  - b. Sclerosis of the optic nerve sheath
  - c. Sclerosis of the optic nerve
  - d. Softening of the optic nerve
  - e. Softening of the limbal sclera

### KEYWORDS (5 Max)

1. Anterior ischemic optic neuropathy
2. Magnetic resonance imaging
3. Normal tension glaucoma
4. Optic nerve sheath

### HIGHLIGHTS

The pathophysiology of most common forms of acquired optic neuropathy is mysterious, and even increasingly so. For example, elevated IOP is no longer part of the definition of primary open angle glaucoma (POAG). Most cases of normal tension glaucoma (NTG) worldwide are not associated with elevated intraocular pressure (IOP), and progressive vision loss often continues during therapy despite normal or subnormal IOP. But IOP is considered the only modifiable “risk factor” for POAG, so patients are aggressively treated medically and surgically to reduce IOP. The strong association with advancing age, axial myopia, and peripapillary atrophy is unexplained.

Non-arteritic anterior ischemic optic neuropathy (NA-AION) is a disease of middle age associated with the “disc at risk” whose appearance is opposite that of POAG. Vasculopathic associations exist, but are relatively weak. Apoplectic onset and progression, usually during sleep.

It is now proposed that repetitive strain to the optic nerve (ON) caused by eye movements may be a major of NTG and NA-AION. The normal ON is insufficiently long to avoid tethering in adduction and supraduction. Normal eye movements are frequent intense, and relentless during saccades, vestibular quick phases coordinated with eye movements, convergence, Bell's phenomenon, and REM sleep. Magnetic resonance imaging (MRI) demonstrates ON tethering in adduction and supraduction in most healthy people, leading to globe retraction that is significantly greater in NTG. Optical coherence tomography (OCT) shows deformation of the optic disc and peripapillary tissues with optic cup changes.

Finite element biomechanical analysis suggests that adduction tethering concentrates medial rectus counterforce at the temporal edge of the lamina cribrosa. Typical pattern of temporal peripapillary atrophy that is progressive from childhood, especially in myopes. Strain is concentrated at the typical location of early glaucomatous nerve fiber and visual field loss in NTG. The predicted strains from adduction tethering are many-fold larger than with extreme IOP elevation.

The ON contains abundant internal collagenous connective tissue: its entire substance is like the lamina cribrosa, differing only that the lamina also contains elastin. It is proposed that progressive, age-related thickening and mechanical stiffening of the ON and its sheath are responsible for pathological repetitive strain injury in NTG. Average scleral mechanics vary regionally, with limbal and circumpapillary sclera stiffest, followed by equatorial sclera; peripapillary sclera is softest. However, there is marked interindividual variation in biomechanical tissue properties and anatomical risk factors. Axial myopia causes more ON severe tethering (but might also be caused in part by tethering since predicted strain matches patterns typical of myopic staphylomata). Likely pathological factors include progressive stiffening of the ON and its sheath, relative to soft posterior sclera, larger adducting eye movements, and stiffer orbital tissues resisting normal globe translation during eye movements

Young and middle aged people retain large range of supraduction and Bell's phenomenon, while elderly people lose supraduction which protect them from supraduction tethering. Maybe the crowded optic disc develops vascular occlusion due to prolonged supraduction tethering during sleep?

## SUMMARY

Repetitive strain injury to the globe-ON junction may underlie many cases of NTG and NA-AION.

## CME ANSWERS

1. Yes
2. C
3. B and C

## REFERENCES

1. Chang, M. Y., Shin, A., Park, J. Nagiel, A., *et al.* Deformation of optic nerve head and peripapillary tissues by horizontal duction. *Am. J. Ophthalmol.* 174: 85-94, 2017.
2. Demer, J. L., Clark, R. A., Suh, S. Y., *et al.* Magnetic resonance imaging of optic nerve traction during adduction in primary open angle glaucoma with normal intraocular pressure. *Invest. Ophthalmol. Vis. Sci. (IOVS)* 58: 4114-4125, 2017.
3. Shin, A., Yoo, L. Park, J., and Demer, J. L. Finite element biomechanics of optic nerve sheath traction in adduction. *J. Biomech. Eng.* 139: 2017. doi: 10.1115/1.4037562.
4. Sibony, P. A. Gaze-evoked deformations of the peripapillary retina and papilledema and ischemic optic neuropathy. *Invest. Ophthalmol. Vis. Sci.* 57:4979-87, 2016.
5. Suh, S. Y., Le, Alan, Shin, A., Park, J., and Demer, J. L. Progressive deformation of the optic nerve head and peripapillary structures by graded horizontal duction. *IOVS.* 58:5015-5021, 2017.
6. Wang, X., Beotra, M.R., Tun, TA, *et al.* In vivo 3-dimensional strain mapping confirms large optic nerve head deformations following horizontal eye movements. *IOVS.* 2016;57:5825-33.
7. Wang, X., Fisher, L. K., Milea, D., *et al.* Predictions of optic nerve traction forces and peripapillary tissue stresses following horizontal eye movements. *IOVS.* 58:2044-53, 2017.



North American Neuro-Ophthalmology Society

# 44th Annual Meeting

March 3– March 8, 2018

The Hilton Waikoloa Village • The Big Island of Hawaii

## PLATFORM SESSION I

Monday, April 3, 2017 • 5:00 pm - 7:00 pm

**Moderators: Marc Dinkin, MD, Billi Wallace, MD J. Thurtell**

- 5:00 pm - 5:15 pm      Jonathan A. Micieli, MD  
Does Optic Nerve Appearance Predict Visual Outcome in Patients with Idiopathic Intracranial Hypertension (IIH)?
- 5:15 pm - 5:30 pm      Keira A. Markey, MD  
Safety and Efficacy of an 11 $\beta$ -Hydroxysteroid Dehydrogenase Type-1 Inhibitor (AZD4017) in Idiopathic Intracranial Hypertension
- 5:30 pm - 5:45 pm      Chiara La Morgia, MD, PhD  
Next Generation Sequencing Results in an Italian Cohort of Hereditary Optic Neuropathies Patients
- 5:45 pm - 6:00 pm      Eric D. Gaier, MD, PhD  
Interocular Phase Delay Shifts Visual Cortical Dominance: a Potential New Therapeutic Approach for Amblyopia
- 6:00 pm - 6:15 pm      Hamish P. Dunn, MD  
eFOCUS Phase 2: Comparative Clinical Performance of Smartphone & Traditional Funduscopy
- 6:15 pm - 6:30 pm      Lael J. Stander, MD  
Assessment of a Fully-Automated RAPD Test as a Routine Screening Tool
- 6:30 pm - 6:45 pm      Angela J. Oh  
Ocular Motor Abnormalities During Saccadic Reading in Different Neuro-Ophthalmic Diseases
- 6:45 pm - 7:00 pm      General Q&A
- 7:00 pm - 7:15 pm      Barrett Katz, MD, MBA  
Safety/Acuity Outcomes 96-Weeks Post-Treatment with rAAV2/2-ND4; Gene Therapy for ND4 LHON: a Phase I/II Trial.

*\*Please note that all abstracts are published as submitted.*

**Monday, March 5th from 5:00 pm - 5:15 pm**

**Does optic nerve appearance predict visual outcome in patients with idiopathic intracranial hypertension (IIH)?**

Jonathan Micieli<sup>1</sup>, Beau Bruce<sup>2</sup>, Caroline Vasseneix<sup>1</sup>, Richard Blanch<sup>1</sup>, Damian Berezovsky<sup>3</sup>, Jason Peragallo<sup>4</sup>, Nancy Newman<sup>5</sup>, Valérie Biousse<sup>6</sup>

<sup>1</sup>Department of Ophthalmology, Emory University, Atlanta, Georgia, USA, <sup>2</sup>Departments of Ophthalmology, Neurology and Epidemiology, Emory University, Atlanta, Georgia, USA, <sup>3</sup>Barrow Neurological Institute, Phoenix, Arizona, USA, <sup>4</sup>Departments of Ophthalmology and Pediatrics, Emory University, Atlanta, Georgia, USA, <sup>5</sup>Departments of Ophthalmology, Neurology and Neurological Surgery, Emory University, Atlanta, Georgia, USA, <sup>6</sup>Departments of Ophthalmology and Neurology, Emory University, Atlanta, Georgia, USA

**Introduction:**

Stratification of IIH patients allows aggressive treatment to prevent vision loss in high-risk patients. We assessed whether Frisén grade, optic disc hemorrhages (ODH) and cotton wool spots (CWS) predict outcome in IIH.

**Methods:**

389/1244 consecutive IIH patients (773 eyes) were seen before/within 30 days of diagnostic lumbar puncture/medical treatment, with fundus photographs at presentation. Patients' characteristics, visual acuity (VA) and visual field (VF) grade[1] were recorded. Fundus photographs graded by 3 independent reviewers used a standardized protocol for presence, type, and severity of ODH and CWS,[2] and papilledema grade.[3] Multivariable linear and logistic mixed models evaluated the association between Frisén grade, ODH, CWS and visual outcomes controlling for confounding variables.

**Results:**

205/773 (26.5%) eyes had  $\geq 1$  ODH, 99/773 (12.8%) eyes had  $\geq 1$  CWS, 86/773 (11.1%) had both ODH and CWS. Controlling for Frisén grade,[3] BMI, black race, and gender, the presence of ODH/CWS was associated with worse VA and VF grade at initial presentation ( $p < 0.03$ ), but not at final follow-up. Results were the same when limiting the analysis to the 223 patients (352 eyes) who would have qualified for the IIHTT[2] by VF criteria (HVF-MD, -2 to -7dB). More patients with  $\geq 1$  ODH (21.5% vs 6.7%) or CWS (31.3% vs 4.7%) underwent surgical treatment compared to those without ODH/CWS, but ODH/CWS were not independent predictors of surgery. The presence of ODH/CWS was associated with higher Frisén grade ( $p < 0.001$ ). Frisén grade correlated with worse mean deviation and VF grade at final follow-up ( $p < 0.001$ ).

**Conclusions:**

While the IIHTT associated ODH with both worse Frisén grade and treatment failures,[2,4] they did not examine whether ODH was a risk factor independent of papilledema severity (likely due to the low frequency of treatment failures in a population with mild disease). In our study, neither ODH nor CWS were independently associated with poorer visual function at last follow-up.

**References:** 1. Bruce BB, Preechawat P, Newman NJ, Lynn MJ, Biousse V. Racial differences in idiopathic intracranial hypertension. *Neurology* 2008;70:861-867. 2. Wall M, Thurtell MJ, NORDIC IIH Study Group. Optic disc haemorrhages at baseline as a risk factor for poor outcome in the Idiopathic Intracranial Hypertension Treatment Trial. *Br J Ophthalmol* 2017;101:1256-60. 3. Scott CJ, Kardon RH, Lee AG, Frisen L, Wall M. Diagnosis and grading of papilledema in patients with raised intracranial pressure using optical coherence tomography vs clinical expert assessment using a clinical staging scale. *Arch Ophthalmol* 2010;128:705-11. 4. Wall M, Falardeau J, Fletcher WA, et al. Risk factors for poor visual outcome in patients with idiopathic intracranial hypertension. *Neurology* 2015;85:799-805.

**Keywords:** Pseudotumor Cerebri, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Supported by Research to Prevent Blindness

**Monday, March 5th from 5:15 pm - 5:30 pm**

**Safety and Efficacy of an 11 $\beta$ -Hydroxysteroid Dehydrogenase Type-1 Inhibitor (AZD4017) in Idiopathic Intracranial Hypertension.**

Keira Markey<sup>1</sup>, Ryan Ottridge<sup>2</sup>, James Mitchell<sup>1</sup>, Caroline Rick<sup>2</sup>, Rebecca Woolley<sup>2</sup>, Natalie Ives<sup>2</sup>, Tim Matthews<sup>3</sup>, Anita Krishnan<sup>4</sup>, Pushkar Shah<sup>5</sup>, William Scotton<sup>1</sup>, Susan Mollan<sup>3</sup>, Alex Sinclair<sup>1</sup>

<sup>1</sup>Institute of Metabolism and Systems Research, Edgbaston, United Kingdom, <sup>2</sup>Birmingham Clinical Trials Unit, University of Birmingham, Edgbaston, United Kingdom, <sup>3</sup>University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom, <sup>4</sup>The Walton Centre Nhs Foundation Trust, Liverpool, United Kingdom, <sup>5</sup>NHS Glasgow and Greater Clyde, Glasgow, United Kingdom

**Introduction:**

Pharmacological therapy in IIH is limited. We investigated the safety, tolerability and efficacy of a novel drug, an 11 $\beta$ -hydroxysteroid dehydrogenase type-1 inhibitor (AZ4017).

**Methods:**

IIH:DT was a phase 2 multicentre randomised, double-blind, placebo-controlled trial. Thirty-one females aged between 18-55 years with active IIH (lumbar puncture (LP) pressure >25cmCSF and papilloedema (Frisen grade>1)) were block randomised 1:1 by centre to receive either 400mg twice daily oral AZ4017 (n=17) or matching placebo for 12 weeks (n=14). The primary outcome was the difference in LP pressure at week 12; analysed by intention to treat using linear regression models adjusting for baseline.

**Results:**

At baseline, the mean (SD) age was 31.2 years (6.9) and BMI of 39.2kg/m<sup>2</sup> (12.6). LP pressure decreased from 33.7 (6.3) at baseline to 29.7 (5.2) cmCSF at 12 weeks in the AZ4017 group and from 32.7 (4.8) to 31.3 (6.7) cmCSF in the placebo group (diff:-2.8, 95%CI:-7.1-1.5; p=0.2). The Humphrey Field Analyser perimetric mean deviation (PMD) (worst eye) changed from -6.1 dB (5.4) at baseline to -3.4 dB (3.2) at 12 weeks in the AZ4017 group and from -3.4 dB (6.8) to -2.2 dB (3.1) in the placebo group (diff=0.3, 95%CI:-2.0-2.7, p=0.8). There were 47 adverse events in the placebo group vs. 114 (47 in same patient) in the AZ4017 group, of which 9/114 were deemed to be drug-related and no patients withdrew due to side effects. There was one serious adverse event in the placebo group (unrelated to study drug).

**Conclusions:**

This is the first phase 2 trial in IIH and assesses a novel agent, AZD4017. Treatment was safe and tolerable. We noted a trend for improvement which would be interesting to evaluate in a larger phase 3 randomised controlled trial.

**References:** None.

**Keywords:** High intracranial pressure/headache, Pseudotumor Cerebri, Perimetry

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Monday, March 5th from 5:30 pm - 5:45 pm**

**Next Generation Sequencing results in an Italian cohort of hereditary optic neuropathies patients**

Chiara La Morgia<sup>1</sup>, Francesca Tagliavini<sup>2</sup>, Leonardo Caporali<sup>2</sup>, Michele Carbonelli<sup>2</sup>, Lidia Di Vito<sup>2</sup>, Piero Barboni<sup>3</sup>, Maria Lucia Cascavilla<sup>4</sup>, Arturo Carta<sup>5</sup>, Alessandra Rufa<sup>6</sup>, Stefania Bianchi Marzoli<sup>7</sup>, Francesco Mari<sup>8</sup>, Michelangelo Mancuso<sup>9</sup>, Maria Alice Donati<sup>10</sup>, Anna Maria De Negri<sup>11</sup>, Federico Sadun<sup>12</sup>, Maria Lucia Valentino<sup>1</sup>, Rocco Liguori<sup>1</sup>, Valerio Carelli<sup>1</sup>

<sup>1</sup>IRCCS Institute of Neurological Sciences of Bologna; DIBINEM, University of Bologna, Bologna, Italy, <sup>2</sup>IRCCS Institute of Neurological Sciences of Bologna, Bologna, Italy, <sup>3</sup>IRCCS San Raffaele Institute, Milan; Studio Oculistico D'Azeglio, Bologna, Italy, Milan; Bologna, Italy, <sup>4</sup>IRCCS San Raffaele Institute, Milan, Milan, Italy, <sup>5</sup>Department of Ophthalmology, University of Parma, Parma, Italy, <sup>6</sup>Department of Medical Sciences, Surgery and Neuroscience, University of Siena, Siena, Italy, <sup>7</sup>IRCCS Auxologic Institute, Department of Ophthalmology, Milan, Italy, <sup>8</sup>Meyer Children's Hospital, University of Florence, Florence, Italy, Florence, Italy, <sup>9</sup>Neuroscience Department, University of Pisa, Pisa, Italy, <sup>10</sup>Neuroscience Department, Meyer Children's Hospital, Florence, Italy, Florence, Italy, <sup>11</sup>San Camillo-Forlanini Hospital, Department of Ophthalmology, Rome, Italy, <sup>12</sup>Department of Ophthalmology, Ospedale Parodi Delfino, Colferro, Rome, Italy

**Introduction:**

Hereditary optic neuropathies (HON) have common pathophysiologic mechanisms involving mitochondrial dysfunction. Known causative mutations are reported in mitochondrial DNA genes (i.e. LHON) but also in nuclear-encoded genes with mitochondrial functions such as mitochondrial dynamics (i.e. OPA1). Next Generation Sequencing (NGS), by screening simultaneously several candidate genes, has become the main gold standard to discover molecular defects in rare hereditary diseases. We aimed at genetically screening consecutive HON patients negative for LHON and OPA1 mutations.

**Methods:**

Using the Illumina sequencing platform, we designed a custom panel of 35 targeted nuclear genes already described or suspected to be causative for HON, syndromic or non syndromic. So far, we investigated 99 unrelated HON probands.

**Results:**

Mutations in HON related genes were identified in 35/99 cases (35%), even if in 16/35 cases these variants must be further validated (segregation analysis, in vitro studies). Among the 19 consolidated positive results, we found mutations in AFG3L2 (5) (AD); WFS1 (4) (AR); ACO2 (4) (3 AD + 1 AR); SDHA (2) (AD); SPG7 (2) (AR); RTN4IP1 (1) (AR); TMEM126A (1) (AR) AFG3L2, WFS1 and ACO2 were the most frequent genes responsible of isolated optic neuropathy in our cohort and mutations in WFS1 were identified also in cases without diabetes. Interestingly, AFG3L2 gene mutations, previously described only in a single non-syndromic HON family, were found in additional five families. Also its paralogous gene, SPG7, has been found mutated in two additional recessive cases with isolated ON. We also found both recessive (1) and autosomal dominant (3) cases harboring ACO2 mutations.

**Conclusions:**

In conclusion, NGS-based diagnostic improves the rate of successful identification of unsolved cases, enlarging the landscape of genetic causes for hereditary optic neuropathies. Moreover, this approach allowed expanding the clinical spectrum of HON caused by mutations in genes involving mitochondrial functions.

**References:** None.

**Keywords:** Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Monday, March 5th from 5:45 pm - 6:00 pm**

**Interocular Phase Delay Shifts Visual Cortical Dominance: a Potential New Therapeutic Approach for Amblyopia**

Eric Gaijer<sup>1</sup>, Daniel Montgomery<sup>2</sup>, Arnold Heynen<sup>2</sup>, Mark Bear<sup>2</sup>

<sup>1</sup>Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, USA, <sup>2</sup>Picower Institute for Learning and Memory, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA

**Introduction:**

Amblyopia imparts a delay in visually evoked response (VEP) latency (~5 ms/2 Snellen lines) through the affected eye that neutralizes with successful treatment [1, 2]. The delay in signals reaching the visual cortex may actively preclude visual recovery of the affected eye since delay of synaptic activation tends to weaken visual cortical synapses [3]. Along this line, manipulation of interocular stimulus phase could strengthen the amblyopic eye. To this goal, we hypothesized that introduction of an interocular phase delay would induce plasticity in the visual cortex to shift ocular dominance.

**Methods:**

We employed an established model of visual cortical plasticity termed stimulus-selective response plasticity (SRP), in which exposure to inverting sinusoidal grating stimuli presented to a head-fixed mouse on repeated days induces long-term plasticity in binocular V1 [4]. This potentiation is sinusoidal orientation-specific, and multiple orientations can be tested in parallel. We induced SRP over 6 days of conditioning for 3 orientations (10 min each; 10 Hz inversions) run with no interocular delay, a contralateral eye-leading delay (17 ms), and an ipsilateral eye-leading delay.

**Results:**

In adolescent mice (P32, N=3), SRP training with no interocular offset induced significant potentiation of contralateral and ipsilateral VEPs (p values<0.042) with no change in ocular dominance. A similar pattern and magnitude of potentiation was observed in the contralateral-leading condition (p values<0.041) without a change in ocular dominance. In the ipsilateral-leading condition, significant potentiation was specific to the ipsilateral eye (p=0.022) with a significant shift in ocular dominance favoring the ipsilateral eye compared to all other conditions (p values<0.023). We found similar results in older animals (P60, N=7).

**Conclusions:**

In the current study, interocular phase delay induced cortical plasticity in an eye-specific manner and was sufficient to shift ocular dominance. Future experiments may further support the potential role for manipulation of interocular stimulus phase to treat amblyopia.

**References:** 1. Parisi, V., et al., Electrophysiological detection of delayed postretinal neural conduction in human amblyopia. *Invest Ophthalmol Vis Sci*, 2010. 51(10): p. 5041-8. 2. Kelly, J.P., et al., Occlusion therapy improves phase-alignment of the cortical response in amblyopia. *Vision Res*, 2015. 114: p. 142-50. 3. Smith, G.B., A.J. Heynen, and M.F. Bear, Bidirectional synaptic mechanisms of ocular dominance plasticity in visual cortex. *Philos Trans R Soc Lond B Biol Sci*, 2009. 364(1515): p. 357-67. 4. Cooke, S.F. and M.F. Bear, Stimulus-selective response plasticity in the visual cortex: an assay for the assessment of pathophysiology and treatment of cognitive impairment associated with psychiatric disorders. *Biol Psychiatry*, 2012. 71(6): p. 487-95.

**Keywords:** Pediatric neuro-ophthalmology, Miscellaneous

**Financial Disclosures:** It should be noted that the current work applies to a provisional patent, of which EDG is the sole inventor. Plans are in place to execute a limited, exclusive license based on this patent for Luminopia (a virtual reality start-up company in Cambridge, MA)

**Grant Support:** There is no direct grant support for this project

**Monday, March 5th from 6:00 pm - 6:15 pm**

**eFOCUS Phase 2: Comparative Clinical Performance of Smartphone & Traditional Funduscopy**

Hamish Dunn<sup>1</sup>, Samuel Marks<sup>2</sup>, Kai Teo<sup>2</sup>, Christine Kang<sup>3</sup>, Stewart Dunn<sup>4</sup>, Paul Healey<sup>2</sup>, Andrew White<sup>5</sup>

<sup>1</sup>University of Sydney, Westmead Hospital, Sydney, Australia, <sup>2</sup>University of Sydney, Sydney, Australia, <sup>3</sup>Westmead Hospital, Sydney, Australia, <sup>4</sup>University of Sydney, Pam McClean Centre, Sydney, Australia, <sup>5</sup>University of Sydney, Westmead Institute of Medical Research, Sydney, Australia

**Introduction:**

Funduscopy is performed infrequently and poorly outside of ophthalmology and neurology (1, 2). Decline in use has been ascribed to technical examination challenges and interpretation difficulty (3). We hypothesise that capturing fundus images using smartphones would minimise these challenges, thereby increasing clinical usability.

**Methods:**

103 second and final-year medical students participated in this randomised cross-over trial. An eLearning course in optic disc interpretation was provided. Participants were randomly allocated to one of two smartphone funduscopy adaptors (SF): the PanOptic-iExaminer (Welsch Allyn), and D-eye. A 20-minute practical training session on SF and direct ophthalmoscopy (DO) was conducted. Participants then examined 4 patients and 8 simulators with pathological and normal optic discs, with a crossover between SF and DO. Optic discs were graded independently by three masked ophthalmologists. A final survey assessed preferred technique, confidence, and ease of funduscopy.

**Results:**

Students' interpretation of abnormal or normal discs showed fair agreement between ophthalmologists and students using SP (Kappa = 0.250, p = 0.005), but insignificant agreement when students used DO (Kappa = 0.084, p = 0.353). The post-workshop questionnaire found 74% of students preferred SF over DO for clinical use (p < 0.001). Confidence in ability to view the fundus on a 1-5 Likert scale was significantly greater for SF (3.42, SD 1.02) than DO (2.60, SD 1.09) p<0.001. Ease of viewing the fundus was likewise significantly greater using SF (3.40, SD 0.91) than DO (2.43, SD 1.08) p<0.001.

**Conclusions:**

Smartphone funduscopy by medical students has somewhat better clinical sensitivity than direct ophthalmoscopy for determining disc pathology after a 20-minute tutorial and eLearning. Significantly, student-reported ease and confidence in funduscopy was greater for SF over DO, with a strong preference for smartphone use in clinical practice. This suggests that smartphone funduscopy may help overcome the technical barriers to the examination.

**References:** 1. Roberts E, Morgan R, King D, Clerkin L. Funduscopy: a forgotten art? *Postgrad Med J.* 1999;75(883):282-4. 2. Bruce BB, Lamirel C, Biousse V, Ward A, Heilpern KL, Newman NJ, et al. Feasibility of nonmydriatic ocular fundus photography in the emergency department: Phase I of the FOTO-ED study. *Acad Emerg Med.* 2011;18(9):928-33. 3. Mackay DD GP, Bruce BB, Newman NJ, Biousse V. The demise of direct ophthalmoscopy: A modern clinical challenge. *Neurol Clin Pract.* 2015;5(2):150-7.

**Keywords:** Neuroimaging, Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Pupils Retina, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Monday, March 5th from 6:15 pm - 6:30 pm**  
**Assessment of a Fully-Automated RAPD Test as a Routine Screening Tool**

Lael Stander<sup>1</sup>, Shira Simon<sup>1</sup>, Matthew Thurtell<sup>2</sup>, Michael Wall<sup>2</sup>, Randy Kardon<sup>1</sup>

<sup>1</sup>University of Iowa, Iowa City, Iowa, USA, <sup>2</sup>University of Iowa Hospitals and Clinics, Iowa City, Iowa, USA

**Introduction:**

The clinical log-unit relative afferent pupillary defect (RAPD)[1] has inherent variability and bias among examiners, and can be imprecise, especially with darkly-pigmented irides, anisocoria, and with small or poorly-reactive pupils. Studies have demonstrated the effectiveness of automated, infrared pupillography for measuring the RAPD[2,3,4,5,6,7] but not as a standard clinical screening tool. We compared the clinically-measured RAPD with an automated RAPIDo™ pupillometer test (Neuroptics Inc; Irvine, CA), and correlated these measurements to asymmetry of OCT retinal nerve fiber layer (RNFL) and retinal ganglion cell-inner plexiform layer (GCL) thickness.

**Methods:**

Consecutive patients were tested at intake by a technician with a 30 second RAPIDo™ test (each eye is dimmed by one log-unit to derive the log-unit RAPD). The clinical log-unit RAPD was assessed using neutral density filters by faculty and resident/fellow. The average RNFL and GCL thickness was obtained with a Cirrus 5 OCT (Zeiss-Meditec; Dublin, CA). Statistical analysis was then performed to evaluate the correlation between each method of RAPD testing, and between RAPD and OCT-derived RNFL and GCL inter-eye asymmetry.

**Results:**

Of 108 patients tested, the correlations ( $p=0.001$ ) between the clinical and automated RAPD were 0.67 for trainee and 0.58 for faculty RAPD measurement. Correlation coefficient ( $r$ ) of trainee RAPD was 0.48 for RNFL and 0.49 for GCL. Faculty RAPD was 0.67 for RNFL and 0.59 for GCL. RAPIDo RAPD was 0.55 for RNFL and 0.42 for GCL.

**Conclusions:**

Based on initial data, RAPIDo automated log-unit RAPD significantly correlates with the clinically-measured log-unit RAPD. Both automated and clinical log-unit RAPD correlate similarly with inner retinal layer asymmetry, providing a means for comparing and validating the RAPD measurements against an independent measure of retinal structural asymmetry.

**References:** [1] Thompson et al. How to measure the relative afferent pupillary defect. *Surv Ophthalmol.* 1981 Jul-Aug;26(1):39-42. [2] Miki et al. Pupillography of automated swinging flashlight test in amblyopia. *Clin Ophthalmol.* 2008 Dec;2(4):781-6 [3] Sarezky, Volpe, Park, Tanna. Correlation Between Inter-Eye Difference in Average Retinal Nerve Fiber Layer Thickness and Afferent Pupillary Response as Measured by an Automated Pupillometer in Glaucoma. *J Glaucoma.* 2016 Mar;25(3):312-6 [4] Johnson, Hill, Bartholomew. Correlation of afferent pupillary defect with visual field loss on automated perimetry. *Ophthalmology.* 1988 Dec;95(12):1649-55 [5] Waisbourd et al. Detection of asymmetric glaucomatous damage using automated pupillography, the swinging flashlight method and the magnified-assisted swinging flashlight method. *Eye (Lond).* 2015 Oct;29(10):1321-8 [6] Cayless, Bende. First results of automated RAPD-SWIFT method in dynamic pupillometry. *Z Med Phys.* 2016 Jun;26(2):143-9 [7] Wilhelm et al. Automated swinging flashlight test in patients with optic nerve diseases. *Klin Monbl Augenheilkd.* 2001 Jan;218(1):21-5

**Keywords:** Pupils Retina, Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Monday, March 5th from 6:30 pm - 6:45 pm**

**Ocular Motor Abnormalities during Saccadic Reading in Different Neuro-Ophthalmic Diseases**

Angela Oh<sup>1</sup>, Tiffany Chen<sup>2</sup>, Mohammad Shariati<sup>1</sup>, Naz Jehangir<sup>1</sup>, Caroline Yu<sup>1</sup>, Carmel Mercado<sup>1</sup>, Rosa Yu<sup>1</sup>, Joyce Liao<sup>1</sup>

<sup>1</sup>Stanford Department of Ophthalmology, Redwood City, California, USA, <sup>2</sup>Stanford Department of Ophthalmology University of California Berkeley, Palo Alto, USA

**Introduction:**

Neuro-ophthalmic conditions like stroke, cancer, trauma, and neurodegeneration often lead to visual field loss, eye movement abnormality, or both, resulting in difficulties with common daily visual functions including saccadic reading. In this study, we investigate reading difficulties using a simple rapid number reading test and infrared oculography.

**Methods:**

We performed a case control study to assess reading and visual disability at a single institution in controls and patients with different neuro-ophthalmic diseases. Subjects read 120 regularly-spaced single digit numbers to assess basic ocular motor abilities necessarily for left-to-right saccadic reading without semantic context. Some underwent 500-Hz binocular 2D infrared oculography (SMI) in order to quantify their saccade and fixation parameters during reading.

**Results:**

Among 5 groups of 195 subjects (controls, hemianopia, cerebellar ataxia, down-beating nystagmus, Parkinson's disease), patients with cerebellar ataxia read the slowest, about 35% slower than controls ( $p=0.003$ ), followed by Parkinson's disease (25%,  $p0.05$ ). Infrared oculography of 72 subjects revealed different patterns of impaired saccadic reading. Patients with hemianopia exhibited striking spatial bias toward their visual field defect, which was present during saccadic reading but was more prominent while watching a video. In contrast, patients with eye movement abnormality due to cerebellar ataxia and down-beating nystagmus exhibited no spatial bias but made significantly greater number of saccades and fixations ( $p\leq0.006$ ), smaller saccade amplitudes and slower velocities ( $p\leq0.01$ ), and greater fixation dispersion ( $p<0.05$ ). Patients with Parkinson's disease also exhibited no spatial bias and had significantly increased number of saccades and fixations ( $p<0.004$ ). However, they had normal saccade amplitudes, velocities, and fixation dispersion.

**Conclusions:**

Single digit number reading test is an easy way to assess reading difficulties in the clinical setting, and eye movement recording reveals a variety of ways that saccadic reading can be slowed in different neurological conditions.

**References:** Leigh RJ, Kennard C. Using saccades as a research tool in the clinical neurosciences. *Brain*, 127(Pt 3), 460-77, 2004. Lin TP, Adler CH, Hentz JG, Balcer LJ, Galetta SL, et al. Slowing of Number Naming Speed by King-Devick Test in Parkinson's Disease. *Parkinsonism & related disorders*, 20(2), 226-229, 2014. Rizzo J-R, Hudson TE, Dai W, et al. Objectifying eye movements during rapid number naming: Methodology for assessment of normative data for the King-Devick test. *Journal of the neurological sciences*, 362, 232-239, 2016. Starr MS, Rayner K. Eye movements during reading: some current controversies. *Trends Cogn Sci*, 5, 156-163, 2001. Thurtell MJ. Treatment of Nystagmus. *Semin Neurol*. 35(5), 522-6, 2015.

**Keywords:** Ocular Motility, Ocular manifestations of vestibular disorders, Nystagmus, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** NANOS Pilot Grant, Weston Havens Foundation grant, and Bonderman Gift Grant

**Monday, March 5th from 7:00 pm - 7:15 pm**

**Safety/Acuity Outcomes 96-Weeks Post-Treatment with rAAV2/2-ND4; Gene Therapy for ND4 LHON: a Phase I/II Trial.**

Barrett Katz<sup>1,3</sup>, Catherine Vignal<sup>2</sup>, Celine Bouquet<sup>3</sup>, Nitza Thomasson<sup>3</sup>, Ann Galy<sup>3</sup>, Serge Fitoussi<sup>3</sup>, Jose Sahel<sup>4</sup>

<sup>1</sup>Albert Einstein College of Medicine and the Montefiore Medical Center, New YORK, New York, USA, <sup>2</sup>Centre Hospitalier National d'Ophthalmologie des Quinze-Vingts, Paris, France, <sup>3</sup>GenSight Biologics, Paris, France, <sup>4</sup>Sorbonne Universités, UPMC Univ Paris 06, Paris, France

**Introduction:**

rAAV2/2-ND4 is an investigational gene therapy enabling allotropic transgene expression. We report safety and visual acuity outcomes 96 weeks post-treatment in a Phase I/II open-label dose escalation trial.

**Methods:**

Fifteen LHON subjects with G11778A ND4 mutation received a single intravitreal injection of rAAV2/2-ND4 in their worse-seeing eye. Three subjects were included in each dose escalation cohort (9E9, 3E10, 9E10, 1.8E11 vg/eye) and 3 in the extension cohort (9E10 vg/eye).

**Results:**

At study entry, mean logMAR visual acuity in treated eyes was + 2.29. Mean duration of vision loss was 72.3 months. No unexpected adverse events (AE) were noted. No systemic AE or any serious AE were related to study drug or procedures. Most frequently reported ocular AEs included anterior and intermediate uveitis and transient IOP elevation, mild and all responsive to treatment. In subjects with  $\leq 2$ -years vision loss and logMAR visual acuity  $< 2.79$  at baseline (N=5), mean logMAR acuity changes from baseline to Week 96 were: - 0.574 in treated eyes vs. - 0.296 in untreated eyes. Mean differences in LogMAR acuities in treated vs. untreated eyes, from baseline to weeks 24, 36, 48, and 78 and 96, were respectively: + 0.136, - 0.218, - 0.338, - 0.398, - 0.278. Three out of 5 of treated eyes - 60% - gained  $\geq 15$  ETDRS letters by Week 96.

**Conclusions:**

Intravitreal rAAV2/2-ND4 was safe and well-tolerated. At 96 weeks, in subjects with  $\leq 2$  years vision loss, 60% of treated eyes had a clinically meaningful gain in vision ( $\geq 15$  ETDRS letters). In those subjects, better acuity was seen in treated vs. untreated eyes after Week 36. Pre-conversion changes of the RNFL in LHON subjects may afford predictable and recognizable bio-anatomic markers that signal impending loss of vision. This may suggest an ideal window of opportunity for pre-conversion therapeutic intervention that could offer enhanced prospects for improved clinical outcomes.

**Keywords:** Optic Neuropathy, Genetic Disease, LHON, Gene Therapy

**Financial Disclosures:**

Barrett Katz, (GenSight-Biologics employee)  
Catherine Vignal (GenSight-Biologics consultant)  
Celine Bouquet, (GenSight Biologics employee)  
Nitza Thomasson, (GenSight-Biologics employee)  
Anne Galy (GenSight-Biologics employee)  
Serge Fitoussi (GenSight-Biologics employee)  
Jose Alain Sahel (GenSight-Biologics co-founder, shareholder and consultant)

GenSight - Biologics is the sponsor of the CLIN 01 study and the developer of Recombinant AAV2 Containing the ND4 Gene (rAAV2/2-ND4).

**Grant Support:** None.

## TUESDAY, MARCH 6

6:00 am - 6:45 am	Yoga Class (Pre-registration required, SOLD OUT) .....	Ocean View Terrace
6:30 am - 7:30 am	Breakfast.....	Grand Promenade
6:30 am - 7:30 am	JNO Editorial Board Meeting .....	Kona 1
6:30 am - 12:00 pm	Registration/Help Desk .....	Grand Promenade
6:30 am - 10:30 am	Exhibits .....	Grand Promenade
7:30 am - 9:30 am	Scientific Platform Presentations: Session II .....	Grand Ballroom
	<i>Moderators: Marie Acierno, MD, Kevin Lai, MD</i>	
7:30 am - 7:45 am	<b>Clinical Outcomes of Myelin Oligodendrocyte Glycoprotein Autoantibody (MOG-IgG)-Related Optic Neuritis</b> , <i>John J. Chen, MD, PhD</i>	
7:45 am - 8:00 am	<b>Combinations of Polymorphic Mitochondrial DNA Variants Cause Leber's Hereditary Optic Neuropathy</b> , <i>Valerio Carelli, MD, PhD</i>	
8:00 am - 8:15 am	<b>Increase ER Stress in Ischemic Optic Neuropathy: Implications in Diabetes and Effects of Insulin Treatment</b> , <i>Y. Joyce Liao, MD, PhD</i>	
8:15 am - 8:30 am	<b>In Vivo Evaluation of Drugs Used to Treat Idiopathic Intracranial Hypertension</b> , <i>James L. Mitchell, MD</i>	
8:30 am - 8:45 am	<b>Prospective Evaluation of the Effect of Lumbar Puncture on Headaches in Idiopathic Intracranial Hypertension</b> , <i>Tim D. Matthews, DO, FRCS, FRCOphth</i>	
8:45 am - 9:00 am	<b>Optical Coherence Tomography Angiography Findings in Pre-Clinical, Biomarker Positive Alzheimer's Disease</b> , <i>Bliss Elizabeth O'Bryhim, MD, PhD</i>	
9:00 am - 9:15 am	<b>Objectively Assessing Concussion Using Steady-State Visual Evoked Potentials</b> , <i>Clare L. Fraser, MD</i>	
9:15 am - 9:30 am	<b>Improving Prosopagnosia: Rehabilitative Studies with Perceptual Learning</b> , <i>Jason J. Barton, MD, PhD, FRCPC</i>	
9:30 am - 10:00 am	Coffee Break with Exhibitors .....	Grand Promenade
10:00 am - 12:00 pm	Scientific Platform Presentations: Session III .....	Grand Ballroom
	<i>Moderators: Kaushal Kulkarni, MD, Valérie Biousse, MD</i>	
10:00 am - 10:15 am	<b>Social Deprivation, Rising Incidence and Increased Economic Burden in Idiopathic Intracranial Hypertension in England</b> , <i>Susan P. Mollan, MB, ChB, FRCOphth</i>	
10:15 am - 10:30 am	<b>Characterizing Structural Optic Nerve Head Changes in High ICP and Strategies to Address Image Uncertainty</b> , <i>Megh D. Patel, BS</i>	
10:30 am - 10:45 am	<b>Assessment of Cyclotorsion Using SLO Fundus Imaging in Patients With and Without Forth Nerve Palsy</b> , <i>Ghislaine L. Traber, MD</i>	
10:45 am - 11:00 am	<b>Diagnostic Evaluation of Pediatric Horner Syndrome</b> , <i>Mary-Magdalene U. Dodd, MD</i>	
11:00 am - 11:15 am	<b>Buzzing Sympathetic Nerves: A New Test to Enhance Reflex Pupil Dilation in Suspected Horner Syndrome</b> , <i>Rawan Omary, MD</i>	
11:15 am - 11:30 am	<b>Repetitive Ocular Vestibular Evoked Myogenic Potentials (oVEMP) Stimulation for Myasthenia Gravis: Comparison Of Stimulation Paradigms</b> , <i>Magdalena A. Wirth, MD</i>	
11:30 am - 11:45 am	<b>A Prospective Study of Neuro-Ophthalmic Abnormalities in Children with Neonatal Abstinence Syndrome</b> , <i>Jennifer E. Lambert, CO</i>	
11:45 am - 12:00 pm	<b>Normal Topography and Binocularity of the Superior Colliculus in Strabismus</b> , <i>Jonathan C. Horton, MD, PhD</i>	
12:00 pm - 6:00 pm	Free Afternoon	
12:30 pm - 4:30 pm	Optional Excursions (pre-registration required)	
6:00 pm - 9:30 pm	Poster Session II: Scientific Advancements in Neuro-Ophthalmology.....	Kohala Ballroom
	<i>Event is complimentary for attendees and a dinner buffet is included. Guests are welcome. Guest tickets are available for \$50 per person.</i>	
	<b>Authors will be standing by their posters during the following hours:</b>	
	<b>Odd-Numbered Posters:</b> 6:45 pm - 7:30 pm	
	<b>Even-Numbered Posters:</b> 7:30 pm - 8:15 pm	
9:00 pm - 10:00 pm	Abstract Committee Meeting .....	Kona 1



North American Neuro-Ophthalmology Society

# 44th Annual Meeting

March 3– March 8, 2018

The Hilton Waikoloa Village • The Big Island of Hawaii

## PLATFORM SESSION II

Tuesday, March 6, 2018 • 7:30 am - 9:30 am

**Moderators: Marie Acierno, MD, Kevin Lai, MD**

- 7:30 am - 7:45 am      John J. Chen, MD, PhD  
Clinical Outcomes of Myelin Oligodendrocyte Glycoprotein Autoantibody (MOG-IgG)-  
Related Optic Neuritis
- 7:45 am - 8:00 am      Valerio Carelli, MD, PhD  
Combinations of Polymorphic Mitochondrial DNA Variants Cause Leber's Hereditary  
Optic Neuropathy
- 8:00 am - 8:15 am      Y. Joyce Liao, MD, PhD  
Increase ER Stress in Ischemic Optic Neuropathy: Implications in Diabetes and Effects of  
Insulin Treatment
- 8:15 am - 8:30 am      James L. Mitchell, MD  
In Vivo Evaluation of Drugs Used to Treat Idiopathic Intracranial Hypertension
- 8:30 am - 8:45 am      Tim D. Matthews, DO, FRCS, FRCOphth  
Prospective Evaluation of the Effect of Lumbar Puncture on Headaches in Idiopathic  
Intracranial Hypertension
- 8:45 am - 9:00 am      Bliss Elizabeth O'Bryhim, MD, PhD  
Optical Coherence Tomography Angiography Findings in Pre-Clinical, Biomarker Positive  
Alzheimer's Disease
- 9:00 am - 9:15 am      Clare L. Fraser, MD  
Objectively Assessing Concussion Using Steady-State Visual Evoked Potentials
- 9:15 am – 9:30 am      Jason J. Barton, MD, PhD, FRCPC  
Improving Prosopagnosia: Rehabilitative Studies with Perceptual Learning

*\*Please note that all abstracts are published as submitted.*

**Tuesday, March 6th from 7:30 am - 7:45 am**

**Clinical Outcomes of Myelin oligodendrocyte glycoprotein autoantibody (MOG-IgG)-related optic neuritis**

John Chen<sup>1</sup>, Eoin Flanagan<sup>1</sup>, Alfonso Lopez Chiriboga<sup>1</sup>, Jim Fryer<sup>1</sup>, Jiraporn Jitprapaikulsan<sup>1</sup>, Jacqueline Leavitt<sup>1</sup>, Jeffrey Bennett<sup>2</sup>, Victoria Pelak<sup>2</sup>, Collin McClelland<sup>3</sup>, Michael Lee<sup>3</sup>, Ore-ofe Adesina<sup>4</sup>, Yanjun Chen<sup>5</sup>, Gregory Van Stavern<sup>6</sup>, Eric Eggenberger<sup>7</sup>, Paul Brazis<sup>7</sup>, Dean Wingerchuk<sup>8</sup>, Marie Acierno<sup>8</sup>, Sean Pittock<sup>1</sup>

<sup>1</sup>Mayo Clinic, Rochester, Minnesota, USA, <sup>2</sup>University of Colorado, Denver, Colorado, USA, <sup>3</sup>University of Minnesota, Minneapolis, Minnesota, USA, <sup>4</sup>Cizik Eye Clinic, Houston, Texas, USA, <sup>5</sup>University of Wisconsin, Madison, Wisconsin, USA, <sup>6</sup>Washington University, St. Louis, Missouri, USA, <sup>7</sup>Mayo Clinic, Jacksonville, Florida, USA, <sup>8</sup>Mayo Clinic, Scottsdale, Arizona, USA

**Introduction:**

Myelin oligodendrocyte glycoprotein autoantibody (MOG-IgG) is a biomarker of optic neuritis whose phenotype is still being characterized. We report the largest cohort to date of MOG-IgG seropositive optic neuritis patients.

**Methods:**

We reviewed the visual outcomes and clinical characteristics of patients with optic neuritis positive for MOG-IgG1. MOG-IgG1 was detected using a validated flow cytometry assay utilizing full length MOG-transfected HEK293 cells.

**Results:**

76 patients with optic neuritis, seropositive for MOG-IgG1 were seen within a single medical enterprise and 10 were seen by outside neuro-ophthalmologists. Among the 86 patients, the median age of onset of neurologic symptoms was 30.3 years, range 2-79 (58% female). The median number of optic neuritis attacks was 3 (range 1 to 8) with an average follow-up of 4.7 years (0.7 optic neuritis attacks per year). The average BCVA at the nadir of the worst attack was HM with average final BCVA at last follow-up of 20/30. Only 5 patients had a final BCVA of 20/200 or worse in either eye. Optic disc edema was present in 85% at onset and described as moderate/severe in 55%. Pain with eye movements occurred in 85%. MRI showed 79% had optic nerve sheath involvement and 82% had >50% length of the nerve affected. 26 patients had recurrent optic neuritis, 8 had single optic neuritis, 15 had CRION, and 36 had optic neuritis with other neurologic symptoms (most NMOSD or ADEM). One patient with low MOG-IgG1 titer (2.8; normal range, 0-2.5) had an MRI compatible with multiple sclerosis. Approximately 70% received chronic immunosuppression to prevent recurrent attacks.

**Conclusions:**

MOG-IgG-related optic neuritis is diverse, but is overall associated with a relapsing course that can present with severe visual deficits. Despite recurrent attacks with severe vision loss, long term visual outcomes were good, although the majority of patients required chronic immunosuppression due to recurrent disease.

**References:** None.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Optic neuropathy, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Tuesday, March 6th from 7:45 am - 8:00 am**

**Combinations of polymorphic mitochondrial DNA variants cause Leber's hereditary optic neuropathy**

Valerio Carelli<sup>1</sup>, Leonardo Caporali<sup>2</sup>, Luisa Iommarini<sup>3</sup>, Chiara La Morgia<sup>1</sup>, Anna Olivieri<sup>4</sup>, Alessandro Achilli<sup>4</sup>, Alessandra Maresca<sup>5</sup>, Mariantonietta Capristo<sup>5</sup>, Francesca Tagliavini<sup>5</sup>, Valentina Del Dotto<sup>5</sup>, Piero Barboni<sup>6</sup>, Michele Carbonelli<sup>5</sup>, Antonio Torroni<sup>3</sup>

<sup>1</sup>*IRCCS Institute of Neurological Sciences of Bologna; DIBINEM, University of Bologna, Bologna, Italy*, <sup>2</sup>*IRCCS Institute of Neurological Sciences of Bologna, Bologna, Italy*, <sup>3</sup>*Department of Pharmacy and Biotechnology (FABIT), University of Bologna, Bologna, Italy*, <sup>4</sup>*Department of Biology and Biotechnology, "L. Spallanzani", University of Pavia, Pavia, Italy*, <sup>5</sup>*IRCCS Institute of Neurological Sciences of Bologna, Bologna, Italy*, <sup>6</sup>*IRCCS San Raffaele Institute; Studio Oculistico D'Azeglio, Milan; Bologna, Italy*

**Introduction:**

Leber's hereditary optic neuropathy (LHON) is traditionally associated with primary mitochondrial DNA (mtDNA) mutations exerting the role of a necessary but not sufficient genetic factor for disease. A few families segregating LHON along the maternal line lack a primary mtDNA pathogenic mutation, posing the question if some mtDNA haplotypes with peculiar combinations of missense polymorphic variants may predispose to LHON.

**Methods:**

Complete mtDNA sequence has been performed in 2 LHON Italian families with the recurrence of LHON along the maternal line. Functional significance of the mtDNA variants found has been investigated in cybrids and modelled in complex I (CI) crystal structure.

**Results:**

We here report on the existence of LHON associated with peculiar combinations of individually non-pathogenic missense mitochondrial DNA (mtDNA) variants affecting the MT-ND1, MT-ND4L and MT-ND6 subunit genes of CI. The pathogenic potential of these mtDNA haplotypes is supported by multiple evidences: first, the LHON phenotype is strictly inherited along the maternal line in one very large family; second, the combinations of mtDNA variants are unique to the two maternal lineages that are characterized by recurrence of LHON; third, the CI-dependent respiratory and oxidative phosphorylation defect is co-transferred from the proband's fibroblasts into the cybrid cell model. Finally, all but one of these missense mtDNA variants cluster along the same predicted pathway, contributed by the ND1, ND4L and ND6 subunits, in the CI crystal structure deputed to proton translocation (E-channel).

**Conclusions:**

The definition of the pathogenic role of a specific mtDNA mutation becomes blurrier than ever, and only an accurate evaluation of mitogenome sequence variation data from the general population, combined with functional analyses using the cybrid cell model, may lead to its final validation. We introduce a new diagnostic perspective that implies, as mandatory gold standard diagnostic approach, the complete sequence analysis of mitogenomes in LHON.

**References:** None.

**Keywords:** Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** This study received support from "Programma di ricerca Regione-Università 2010-2012" (PRUa1RI-2012-008 to V.C.), Telethon – Italy (Grant no. GGP06233 to V.C.), the Italian Ministry of Health (Ricerca Corrente 2016), the Italian Ministry of Education, Univ

**Tuesday, March 6th from 8:00 am - 8:15 am**

**Increase ER Stress in Ischemic Optic Neuropathy: Implications in Diabetes and Effects of Insulin Treatment**

Yaping Joyce Liao<sup>1</sup>, Varun Kumar<sup>1</sup>, Louise Mesentier Louro<sup>1</sup>, Kathleen Heng<sup>1</sup>, Mohammed Shariati<sup>1</sup>, Angela Oh<sup>1</sup>

<sup>1</sup>Stanford University, Stanford, California, USA

**Introduction:**

Non-arteritic anterior ischemic optic neuropathy (NAION) is due to loss of oxygen to the anterior optic nerve, a watershed area (1-2) and leads to degeneration of retinal ganglion cell (RGC) body and axons as well as loss of optic nerve oligodendrocytes and demyelination (3-6). NAION in animals with diabetes mellitus (DM) leads to significant increase in retinal edema, VEGF levels, and greater loss of RGCs (7). Diabetes is also associated with increased risk of metabolic stress, which is particularly prominent in cells with high metabolic activity such as RGCs and oligodendrocytes and may contribute to the development of NAION and bilateral involvement. In this study, we investigated endoplasmic reticulum (ER) stress responses after experimental NAION.

**Methods:**

We induced NAION and streptozotocin-induced diabetic NAION in over 80 adult C57BL/6 mice using photochemical thrombosis and performed morphometric analyses of horizontal frozen sections or whole mount preparations of the retinae and optic nerves. Immunohistochemistry was performed using antibodies against CHOP (marker of proapoptotic ER pathway activation), olig2 (marker of oligodendrocytes), Brn3A (marker of RGCs), and others.

**Results:**

After 3 weeks of diabetes, there was little expression of C/EBP homologous protein (CHOP) in the retina or optic nerve; after 2 months, there was near confluent expression of CHOP in optic nerve oligodendrocytes but not in Brn3A+ RGCs. One day after NAION, there was significant increase in expression of CHOP in Brn3A+ RGCs and in optic nerve olig2+ oligodendrocytes ( $p < 0.001$ ). Animals with diabetic NAION developed significantly greater CHOP upregulation compared with those with NAION ( $p = 0.02$ ) or diabetes ( $p = 0.02$ ). Treatment with insulin significantly reduced CHOP expression ( $p = 0.001$ ).

**Conclusions:**

In diabetic NAION, significant activation of the proapoptotic PERK-eIF2 $\alpha$ -CHOP pathway occurred by day 1 in retinal ganglion cells and in optic nerve oligodendrocytes. This ER stress was significantly reduced by treatment with insulin, indicating reversible metabolic derangement with glycemic control alone.

**References:** 1. Arnold AC. *J Neuroophthalmol* 2003;23:157-163. 2. Biousse V and Newman NJ. *N Engl J Med* 2015;372:2428-36. 3. Bernstein SL, Guo Y, Kelman SE, Flower RW, Johnson MA. *Invest Ophthalmol Vis Sci* 2003;44:4153-4162. 4. Goldenberg-Cohen N, Guo Y, Margolis F, Cohen Y, Miller NR, Bernstein SL. *Invest Ophthalmol Vis Sci* 2005;46:2716-2725. 5. Bernstein SL, Johnson MA, Miller NR. *Prog Retin Eye Res* 2011;30:167-187. 6. Ho JK, Stanford M, Shariati MA, Dalal R, Liao YJ. *Invest Ophthalmol Vis Sci* 2013;54:5981-5988. 7. Sun MH, Shariati MA, Liao YJ. *Invest Ophthalmol Vis Sci* 2017;58:2296-2305.

**Keywords:** Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** NANOS Pilot Grant, Bonderman Gift Grant, McCormick Grant

**Tuesday, March 6th from 8:15 am - 8:30 am**

**In Vivo Evaluation of Drugs Used to Treat Idiopathic Intracranial Hypertension**

James Mitchell<sup>1</sup>, William Scotton<sup>1</sup>, Hannah Botfield<sup>1</sup>, Connor Westgate<sup>1</sup>, Andreas Yiangou<sup>2</sup>, Maria Uldall<sup>3</sup>, Rigmor Jensen<sup>3</sup>, Alex Sinclair<sup>1</sup>

<sup>1</sup>*Institute of Metabolism and Systems Research University of Birmingham, Birmingham, United Kingdom*, <sup>2</sup>*Institute of Metabolism and Systems Research, Edgbaston, Birmingham, United Kingdom*, <sup>3</sup>*Danish Headache Centre, Rigshospitalet-Glostrup, University of Copenhagen, Glostrup, Denmark*

**Introduction:**

The management of idiopathic intracranial hypertension (IIH) is focused on reducing ICP to try to both preserve visual function, as well as reduce chronic headaches. There is sparse evidence to support the use of some of the drugs commonly used to manage IIH, therefore we propose to evaluate the efficacy of acetazolamide, topiramate, furosemide, amiloride and octreotide at lowering ICP in healthy rats.

**Methods:**

Using a validated epidural ICP recording method, we measured ICP over two hours in female rats, after subcutaneous administration of acetazolamide, topiramate, furosemide, amiloride and octreotide at clinically relevant doses and high doses. In addition, we measured ICP over 12 hours, after oral administration of high doses of acetazolamide and topiramate.

**Results:**

At clinical doses, subcutaneous administration of topiramate lowered ICP by 32% ( $p=0.0009$ ). There was no significant reduction in ICP noted with acetazolamide, furosemide, amiloride or octreotide. At high doses, subcutaneous topiramate lowered ICP by 21% ( $p=0.015$ ) whilst there was no significant reduction in ICP noted with the other drugs. Oral administration of high dose topiramate significantly lowered ICP by 22% ( $p=0.018$ ), compared to 5% reduction with acetazolamide ( $p=>0.999$ ).

**Conclusions:**

Our in vivo studies have demonstrated that both subcutaneous and oral administration of topiramate significantly lowers ICP. Other drugs tested, including acetazolamide, the current first line oral therapy in IIH, did not significantly reduce ICP. Future clinical trials evaluating efficacy and side effects of topiramate in IIH would be of interest.

**References:** None.

**Keywords:** High intracranial pressure/headache, Pseudotumor Cerebri

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Tuesday, March 6th from 8:30 am - 8:45 am**

**Prospective evaluation of the effect of lumbar puncture on headaches in idiopathic intracranial hypertension**

Tim Matthews<sup>1</sup>, Andreas Yiangou<sup>2</sup>, James Mitchell<sup>2</sup>, Keira Markey<sup>2</sup>, William Scotton<sup>2</sup>, Peter Nightingale<sup>3</sup>, Hannah Botfield<sup>2</sup>, Ryan Ottridge<sup>4</sup>, Susan Mollan<sup>5</sup>, Alexandra Sinclair<sup>2</sup>

<sup>1</sup>Birmingham Neuro-Ophthalmology Unit, Birmingham, United Kingdom, <sup>2</sup>Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom, <sup>3</sup>NIHR/Wellcome Trust Clinical Research Facility, Queen Elizabeth Hospital, Birmingham, United Kingdom, <sup>4</sup>Birmingham Clinical Trials Unit, University of Birmingham, Birmingham, United Kingdom, <sup>5</sup>Birmingham Neuro-Ophthalmology Unit, University Hospitals Birmingham, Birmingham, United Kingdom

**Introduction:**

Lumbar puncture (LP) may be considered to evaluate disease status and for therapeutic relief in Idiopathic Intracranial Hypertension (IIH). The aim was to characterise the effect of LP on IIH headache severity in the week post-LP.

**Methods:**

Headache severity was recorded using a numeric rating scale (NRS) (range:0, no pain – 10, most severe pain) prior and following a standardised LP at 1, 4 and 6 hours and daily to 7 days. Pre-LP headache severity was categorised as mild (1-3) moderate (4-6) and severe (7-10). Demographics, LP opening pressure and papilloedema grade were recorded.

**Results:**

52 IIH patients were prospectively recruited with a median BMI 39 kg/m<sup>2</sup> (interquartile range (IQR) 35-47) an LP opening pressure of 32 cmCSF (IQR 28–37) and a mean baseline headache score of 3.6 (SD: 2.8). 64% of patients experienced an exacerbation in headache severity at some point in the week after LP, with 30% experiencing an exacerbation  $\geq 4$  NRS. Improvement in headache severity was most marked at 1 hour post LP, with 58% improving although the reduction in headache severity was small (mean NRS reduction 1.1 (SD: 2.6),  $p < 0.001$ ), this reduction was maintained at 7 days. In those with severe headache pre-LP the chance of improvement or deterioration at any point during the week following LP were 92% and 33% respectively and by day 7 headache severity was reduced (mean NRS 3.0 (SD:2.8),  $p = 0.012$ ). There was no relationship between the post-LP headache and LP opening pressure, papilloedema or BMI.

**Conclusions:**

Many IIH patients will experience exacerbation of headache in the week post dural-puncture. IIH patients with severe headaches may benefit from a therapeutic LP. For those with less severe baseline headaches, the risk of headache exacerbation rises and the therapeutic benefit falls.

**References:** None.

**Keywords:** High intracranial pressure/headache, Pseudotumor Cerebri, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** This work was supported by the Medical Research Council (MR/K015184/1) and the National Institute for Health Research (NIHR-CS-011-028). AS is funded by an NIHR Clinician Scientist Fellowship (NIHR-CS-011-028). The views expressed in this publication are

**Tuesday, March 6th from 8:45 am - 9:00 am**

**Optical Coherence Tomography Angiography Findings in Pre-Clinical, Biomarker Positive Alzheimer's Disease**

Bliss Elizabeth O'Bryhim<sup>1</sup>, Nathan Kung<sup>2</sup>, Rajendra Apte<sup>1</sup>, Gregory Van Stavern<sup>1</sup>

<sup>1</sup>Washington University in St. Louis, St. Louis, Missouri, USA, <sup>2</sup>Blue Sky Neurology, Denver, Colorado, USA

**Introduction:**

Alzheimer's disease (AD) is marked by slowly progressive memory loss, behavioral changes, and deterioration of executive function. Approved treatments prevent further neurodegeneration, but symptoms of AD only become apparent after irreversible loss has already occurred. Optical coherence tomography (OCT) and OCT angiography (OCTA) are noninvasive imaging techniques that allow analysis of retinal and microvascular anatomy. Here, we use OCT and OCTA technology to compare retinal architecture and vascularization between individuals with pre-clinical, biomarker positive AD and biomarker-negative age-matched controls.

**Methods:**

Patients were recruited from Washington University Alzheimer's Disease Research Center (ADRC). All subjects were cognitively normal and had either positron emission tomography or cerebrospinal fluid analysis for known biomarkers of AD, and separated into either biomarker positive or biomarker negative groups. OCTA was performed using an AngioVueHD (OptoVue, California); retinal nerve fiber layer thickness, ganglion cell layer thickness, inner and outer foveal thickness, vascular density, macular volume, and foveal avascular zone (FAZ) data were collected. A model III analysis of covariance was used to analyze data.

**Results:**

Fifty-seven eyes from 30 patients were included in the analysis; 16 biomarker negative, 14 biomarker positive. The FAZ was significantly increased in biomarker positive patients (0.30mm<sup>2</sup> vs. 0.40mm<sup>2</sup>, n = 0.002). Inner foveal thickness was found to be thinner in biomarker positive patients (75.4µm vs. 66µm, p = 0.0278).

**Conclusions:**

These data suggest that patients with biomarker positive, pre-clinical AD have retinal microvascular abnormalities in addition to foveal thinning. Furthermore, patients with pre-clinical AD may be identifiable by OCTA characteristics prior to the onset of cognitive dysfunction, which would allow for early therapeutic intervention to prevent neuronal loss.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Educational grant from OptoVue

**Tuesday, March 6th from 9:00 am - 9:15 am**

## **Objectively Assessing Concussion Using steady-state Visual Evoked Potentials**

Clare Fraser<sup>1</sup>, Daryl Fong<sup>2</sup>, Adrian Cohen<sup>1</sup>, Phillip Broughton<sup>2</sup>

<sup>1</sup>Save Sight Institute, Sydney, Australia, <sup>2</sup>University of Sydney, Dept of Biomedical Engineering, Sydney, Australia

### **Introduction:**

Concussion assessment tools are symptom, balance and vision assessments, which are hindered by their subjectivity and lack of practicality. There is currently no objective, reliable and portable sideline assessment tool available.

### **Methods:**

A portable, steady-state visual-evoked potential (ssVEP) system was developed for sideline use and for return to play (RTP) determination. A 15Hz flicker visual stimulus was delivered with a smartphone in a head-mounted Google Cardboard VR headset. The signals were recorded cortically with a commercially available EEG headset. All results were analysed across the frequency spectrum from 5Hz to 30Hz. Subjects were tested for 30 seconds for the presence of a 15Hz flicker response to the stimulus. This response was quantified into a signal-to-noise ratio (SNR), comparing the response strength relative to background EEG activity. Recordings were done during a rugby football season and were stratified into 3 groups: control, concussed and recovered. Concussed subjects recently been diagnosed with concussion by an experienced doctor. Recovered subjects were previously concussed, but had been clinically cleared for RTP.

### **Results:**

60 controls and 10 concussed subjects were evaluated. Of the 10 concussed subjects, 4 recovered in the study period. Controls had a mean SNR of  $5.1 \pm 1.8$ , indicating a normal response. Concussed subjects had a significant reduction of mean SNR of  $2.2 \pm 0.7$  ( $p < 0.05$ ). A reduction in alpha and increase in theta rhythms was also observed in concussed subjects. Recovered subjects were found to have a mean SNR of  $4.8 \pm 0.8$ , similar to their pre-concussion mean SNR  $4.9 \pm 1.0$ . Recovered subjects also had their alpha rhythm and theta rhythm return to pre-concussion levels.

### **Conclusions:**

The system was able to detect a consistent response in healthy control subjects, which changed in concussed subjects, but returned to pre-concussion levels upon clinical recovery which were similar to healthy control subjects.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Higher Visual Cortical functions, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Optic nerve trauma and treatment, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Tuesday, March 6th from 9:15 am - 9:30 am**

**Improving prosopagnosia: rehabilitative studies with perceptual learning**

Jason Barton<sup>1</sup>, Sherryse Corrow<sup>1</sup>, Kimberley Fletcher<sup>2</sup>, Jodie Davies-Thompson<sup>3</sup>

<sup>1</sup>University of British Columbia, Vancouver, Canada, <sup>2</sup>University of Nottingham, Nottingham, United Kingdom, <sup>3</sup>University of Swansea, Swansea, United Kingdom

**Introduction:**

Whether acquired or developmental prosopagnosia can be improved is uncertain. There are a few attempts in single-case of acquired prosopagnosia, using a variety of mnemonic or perceptual approaches, with mixed results, as well as some recent promising perceptual approaches in developmental prosopagnosia. Our goal was to create and evaluate a perceptual learning program that incorporated variations in view and expression, to emphasize ecological validity.

**Methods:**

We recruited ten patients with acquired prosopagnosia and ten patients with developmental prosopagnosia: results for the acquired cohort have recently been published (1). Subjects undertook an 11-week face training program and an 11-week control task. Training required shape discrimination between morphed facial images, whose similarity was manipulated by a staircase procedure to keep training near a perceptual threshold. Training progressed from blocks of neutral faces in frontal view through increasing variations in view and expression.

**Results:**

While the control task did not change perception, training improved perceptual sensitivity for the trained faces and generalized to new untrained expressions and views of these faces. There was also a significant transfer to new faces, and benefits were maintained over a 3-month period. In acquired prosopagnosia training benefit was slightly greater for those with unilateral than for those with bilateral lesions. Effects were similar but more modest in developmental prosopagnosia.

**Conclusions:**

Perceptual learning can lead to persistent improvements in face discrimination in both acquired or developmental prosopagnosia. This reflects both acquisition of new skills that can be applied to new faces, as well as a degree of over-learning of the stimulus set at the level of three-dimensional expression-invariant representations.

**References:** 1. Davies-Thompson J, Fletcher K, Hills C, Pancaroglu R, Corrow SL, Barton JJS. Perceptual learning of faces: A rehabilitative study in acquired prosopagnosia. *J Cogn Neurosci* 29, 573-91, 2017.

**Keywords:** Higher Visual Cortical functions, Higher visual functions

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** This study was supported by grant MOP-102567 from the Canadian Institutes of Health Research and grant 228984 from the Canadian Foundation for Innovation. JB was supported by a Canada Research Chair 950-228984 and the Marianne Koerner Chair in Brain Diseases. SC was supported by National Eye Institute award F32 EY023479-02. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.



North American Neuro-Ophthalmology Society

# 44th Annual Meeting

March 3– March 8, 2018

The Hilton Waikoloa Village • The Big Island of Hawaii

## PLATFORM SESSION III

Tuesday, March 6, 2018 • 10:00 am - 12:00 pm

**Moderators: Kaushal Kulkarni, MD, Valérie Biousse, MD**

- 10:00 am - 10:15 am      Susan P. Mollan, MB, ChB, FRCOphth  
Social Deprivation, Rising Incidence and Increased Economic Burden in Idiopathic Intracranial Hypertension in England
- 10:15 am - 10:30 am      Megh D. Patel, BS  
Characterizing Structural Optic Nerve Head Changes in High ICP and Strategies to Address Image Uncertainty
- 10:30 am - 10:45 am      Ghislaine L. Traber, MD  
Assessment of Cyclotorsion Using SLO Fundus Imaging in Patients With and Without Forth Nerve Palsy
- 10:45 am - 11:00 am      Mary-Magdalene U. Dodd, MD  
Diagnostic Evaluation of Pediatric Horner Syndrome
- 11:00 am - 11:15 am      Rawan Omary, MD  
Buzzing Sympathetic Nerves: A New Test to Enhance Reflex Pupil Dilatation in Suspected Horner Syndrome
- 11:15 am - 11:30 am      Magdalena A. Wirth, MD  
Repetitive Ocular Vestibular Evoked Myogenic Potentials (oVEMP) Stimulation for Myasthenia Gravis: Comparison Of Stimulation Paradigms
- 11:30 am - 11:45 am      Jennifer E. Lambert, CO  
A Prospective Study of Neuro-Ophthalmic Abnormalities in Children with Neonatal Abstinence Syndrome
- 11:45 am - 12:00 pm      Jonathan C. Horton, MD, PhD  
Normal Topography and Binocularity of the Superior Colliculus in Strabismus

*\*Please note that all abstracts are published as submitted.*



**Tuesday, March 6th from 10:00 am - 10:15 am**

**Social Deprivation, Rising Incidence and Increased Economic Burden in Idiopathic Intracranial Hypertension in England.**

Susan Mollan<sup>1</sup>, Magda Aguiar<sup>2</sup>, Felicity Evison<sup>3</sup>, Emma Frew<sup>2</sup>, Alexandra Sinclair<sup>4</sup>

<sup>1</sup>Birmingham Neuro-Ophthalmology, University Hospitals Birmingham, Birmingham, United Kingdom, <sup>2</sup>Health Economics Unit, Institute of Applied Health Research, University of Birmingham, Birmingham, United Kingdom, <sup>3</sup>Department of Informatics, University Hospitals Birmingham NHS Trust, Birmingham, United Kingdom, <sup>4</sup>Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom

**Introduction:**

The incidence [1] and economic burden [2,3] of Idiopathic Intracranial Hypertension (IIH) is rising. This observational study aimed to investigate the magnitude of IIH related hospital care in England.

**Methods:**

Registered national data sets were used, and included all patients with IIH admitted between January 2002 and December 2016. Patient demographics including socio-economic deprivation (Index of Multiple Deprivation (IMD) 2010) were extracted. National rates of obesity were correlated with IIH rates, by region. A patient pathway was constructed based on the data and an economic model conservatively estimated direct annual costs [4,5] of each new IIH case utilising hospital care.

**Results:**

Of the 23,182 new IIH cases diagnosed, 82.4% were female and 17.6% were male (median age at diagnosis of 28 years (range:21-40 years)). The majority of the cohort resided in the most deprived IMD areas, with 30% in the most deprived area (IMD 1); and 12.6% in the least deprived (IMD 5). The incidence in the general population was 2.26 per 100,000 in 2002; rising to 4.69 per 100,000 in 2016. The highest recorded incidence in women of any age was 8.16 per 100,000 and the peak incidence was seen in women aged 25 years (15.2 per 100,000). There were 47,982 hospital admissions, a 442% increase between 2002 and 2016. 1.92% had visual loss; 12.2% had CSF diversion procedures; 1.1% underwent bariatric surgery and 0.1% had optic nerve sheath fenestration. Women with IIH were significantly more likely to undergo caesarean sections than in the general population (p<0.005). The total estimated cost for IIH was £8.8million in 2002, which has increased by £38.9 million to £47.7 million in 2016.

**Conclusions:**

This is the first study reporting social deprivation in association with IIH. Increasing incidence and multiple hospital admissions per patient is causing the rise in the economic burden of the disease.

**References:** 1 Kilgore KP, Lee MS, Leavitt JA, Mokri B, Hodge DO, et al.. Re-evaluating the Incidence of Idiopathic Intracranial Hypertension in an Era of Increasing Obesity. *Ophthalmology* S0161-6420(16)30874-0, 2017 2 Friesner D, Rosenman R, Lobb BM, Tanne E Idiopathic intracranial hypertension in the USA: the role of obesity in establishing prevalence and healthcare costs. *Obes Rev*, 12:e372-80, 2011 3 Kalyvas AV, Hughes M, Koutsarnakis C, Moris D, Liakos F, Sakas DE, Stranjalis G, Fouyas I. Efficacy, complications and cost of surgical interventions for idiopathic intracranial hypertension: a systematic review of the literature. *Acta Neurochir (Wien)*, 159, 33-49, 2017 4 Department of Health. National Health Service reference costs 2015 to 2016: National schedule of reference costs. 2016. (last accessed 30th October, 2017) 5 Richards H, Seeley H, Fernandez Mendez R, Joannides A, Pickard J. UK Shunt Registry Draft Report. 2017

**Keywords:** Pseudotumor Cerebri

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** AS is funded by an NIHR Clinician Scientist Fellowship (NIHR-CS-011-028). The views expressed in this publication are those of the authors and not necessarily those of the NIHR, National Health Service or the Department of Health, UK.

**Tuesday, March 6th from 10:15 am - 10:30 am**

## **Characterizing Structural Optic Nerve Head Changes in High ICP and Strategies to Address Image Uncertainty**

Megh Patel<sup>1</sup>, Kiran Malhotra<sup>2</sup>, Zainab Shirazi<sup>2</sup>, Heather Moss<sup>1</sup>

<sup>1</sup>Stanford University, Palo Alto, California, USA, <sup>2</sup>University of Illinois at Chicago, Chicago, Illinois, USA

### **Introduction:**

Candidate OCT based markers of high intracranial pressure(ICP) include optic nerve head volume(ONHV) and Bruch's membrane(BM) displacement into the eye. Both require identifying BM margins, but uncertainty is caused when swollen ONH reduce central BM image quality. The objectives of this study were to (1)determine the quantitative relationship between ONHV and Bruch's membrane displacement volume(BMDV) with ICP and (2)compare three strategies of addressing segmentation uncertainty.

### **Methods:**

Radial OCT B-scans centered over the ONH(Heidelberg Spectralis, 6-scans, 30°-spacing) were acquired in 17 human subjects immediately prior to lumbar puncture(LP) for clinical indications. ICP was determined by the LP opening pressure(range 10-55cm H2O). Two raters independently segmented the internal limiting membrane(ILM) and BM. Customized MATLAB software was used to calculate two volumes in a 5.59mm circle centered on the ONH based on interpolation between adjacent B-scans of the two segments. ONHV was defined as the tissue volume between ILM and BM. BMDV was defined as the volume between BM and a surface intersecting BM points in a 2.795mm radius around the ONH center. BM beneath the ONH was represented using three strategies: (1)connecting rater identified BM margins(traditional) (2)excluding a 1.61mm radius cylinder from volume calculations(excluding) (3)defining BM margins at 1.61mm radius from ONH center and connecting these(estimated). Generalized estimating equations(GEE) were used to model ONVH and BMDV as a function of ICP for each BM representation.

### **Results:**

ONHV showed a positive correlation with ICP for traditional( $0.021\text{mm}^3/\text{cmH}_2\text{O}$ [ $0.006,0.037$ ]p=0.006) and estimated( $0.023\text{mm}^3/\text{cmH}_2\text{O}$ [ $0.008,0.038$ ]p=0.003) strategies. The excluding strategy generated borderline association for ONHV( $0.007\text{mm}^3/\text{cmH}_2\text{O}$ [ $6.382 \cdot 10^{-7},0.014$ ]p=0.05). BMDV showed a negative correlation with ICP for traditional( $-0.006\text{mm}^3/\text{cmH}_2\text{O}$ [-0.009,-0.004]p<0.0005), excluding( $-0.002\text{mm}^3/\text{cmH}_2\text{O}$ [-0.003,-0.001]p=0.001), and estimated( $-0.005\text{mm}^3/\text{cmH}_2\text{O}$ [-0.007,-0.002]p<0.0005) strategies.

### **Conclusions:**

ONHV increases while BMDV decreases as ICP increases. These relationships hold using either manually identified or distance defined BM margins. Excluding the uncertain region from image analysis did not alter BMDV vs ICP but reduced the precision of the ONHV vs ICP relationship.

**References:** Kaufhold et al, Optic nerve head quantification in idiopathic intracranial hypertension by spectral domain OCT, PLoS One, 7.5, 2012. Gampa et al, Quantitative Association Between Peripapillary Bruch's Membrane Shape and Intracranial Pressure ICP and Peripapillary Bruch's Membrane Shape, Investigative Ophthalmology & Visual Science 58.5, 2739-2745, 2017.

**Keywords:** High intracranial pressure/headache, Pseudotumor Cerebri, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** NIH, K23 024345, Research to Prevent Blindness

**Tuesday, March 6th from 10:30 am - 10:45 am**

**Assessment of cyclotorsion using SLO fundus imaging in patients with and without fourth nerve palsy**

Ghislaine Traber<sup>1</sup>, Madeleine Kanku<sup>1</sup>, Gregor Jaggi<sup>1</sup>, Klara Landau<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology, University Hospital Zurich, University of Zurich, 8091 Zurich, Switzerland*

**Introduction:**

Scanning Laser Ophthalmoscopy (SLO) imaging is a new method of foveo-papillary angle (FPA) measurement for objective assessment of cyclotorsion. This case-control study assesses the SLO-based FPA in patients with fourth nerve palsy and in healthy controls.

**Methods:**

25 patients with fourth nerve palsy and 25 matched controls were recruited at the University Hospital Zürich. The FPA measurements in both eyes were performed on SLO fundus imaging using the integrated algorithm by Heidelberg Spectralis. In addition, the FPA was measured on conventional fundus photographs.

**Results:**

Using SLO imaging, the mean FPA in the patient group (18 congenital, 7 acquired; 11 men, 14 women; mean age 45.5, range 24 – 80 years) was  $-11.3^\circ$  compared with  $-6.3^\circ$  in the controls (mean age 46.9, range 25 – 79 years). There was a statistically significant difference between these two groups ( $p < 0.0001$ ). The discrimination between patients and controls by the foveo-papillary angle is very good with an AUC=0.92 [95% CI ranging from 0.84 to 0.98]. The mean FPA measured manually on fundus photographs was  $-11.4^\circ$  in patients with fourth nerve palsy and  $-5.8^\circ$  in healthy controls ( $p < 0.0001$ ). Comparing the FPA on SLO imaging with the FPA on photographs, the differences showed limits of agreement of  $-6.13^\circ$  and  $+6.59^\circ$  in the Bland Altman Plot.

**Conclusions:**

Semi-automated measurement of the FPA with SLO imaging is a convenient and reliable method for objective assessment of cyclotorsion. The FPA obtained with this method showed very good discrimination between patients and controls. Patients with fourth nerve palsy had significantly higher FPAs both on SLO imaging and on fundus photographs. The Bland Altman Plot did not show any systematic bias in the difference between SLO- and photograph-based FPAs. However, differences in FPA obtained with these two methods could reach up to  $7.6^\circ$  in an individual patient.

**References:** None.

**Keywords:** Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** GLT: 'Filling the Gap', University of Zurich, Zurich, Switzerland

**Tuesday, March 6th from 10:45 am - 11:00 am**  
**Diagnostic Evaluation of Pediatric Horner Syndrome**

Mary-Magdalene Dodd<sup>1</sup>, Sule Gurbuz<sup>1</sup>, Sanjay Prabhu<sup>1</sup>, Gena Heidary<sup>1</sup>

<sup>1</sup>*Boston Children's Hospital, Boston, Massachusetts, USA*

**Introduction:**

Although pediatric Horner syndrome may be associated with potentially fatal mass lesions, there is no uniform protocol for best practice in evaluating these patients. Recommendations for the diagnostic evaluation in children have been mixed with respect to the choice of which neuroimaging should be performed and the relevance of urine catecholamine testing. The purpose of this study was to review a recently developed protocol to determine which diagnostic studies were of the highest yield in the evaluation of pediatric Horner syndrome.

**Methods:**

Retrospective chart review of all patients diagnosed with Horner syndrome and/or anisocoria seen by pediatric ophthalmology at a tertiary care center over a 5 year study period were reviewed. Inclusion criteria were: 1. Clinically diagnosed Horner syndrome, 2. No prior surgery that would explain the presence of Horner syndrome, 3. Neuroimaging performed as per current hospital protocol. 589 charts were reviewed, 61 patients were identified with Horner syndrome of whom 28 patients fulfilled the strict inclusion criteria.

**Results:**

Of the 28 patients, 60% were male and the median age was 0.42 years (IQR: 0.31, 0.83). All patients had anisocoria; additional clinical findings: ptosis (46.4%), anhidrosis (7.1%), and iris heterochromia (17.9%). Neuroimaging included MRI with and without contrast of the brain, neck and chest. In addition, MRA of the brain was performed in 50% and MRA neck in 71% of patients. The MRI was normal in 89%, however 11% (n=3) of children were diagnosed with neuroblastoma. MRA was normal in all patients. The urine catecholamines were normal in the 3 diagnosed with neuroblastoma.

**Conclusions:**

Neuroimaging of the brain, neck and upper chest successfully identified a mass lesion in pediatric Horner syndrome. Although MRA has been recommended, this modality did not yield further diagnostic information, and urine catecholamine testing was of low yield in this patient cohort.

**References:** Mahoney, N.R., Liu, G.T., Menacker, S.J., Wilson, M.C., Hogarty, M.D. and Maris, J.M. (2006) Pediatric Horner Syndrome: Etiologies and Roles of Imaging and Urine Studies to Detect Neuroblastoma and Other Responsible Mass Lesions. *American Journal of Ophthalmology*, 142, 651-659. Smith, S. J., Diehl, N. N., Smith, B. D., & Mohny, B. G. (2010). Urine catecholamine levels as diagnostic markers for neuroblastoma in a defined population: Implications for ophthalmic practice. *Eye*, 24(12), 1792-1796.

**Keywords:** Neuroimaging, Pediatric neuro-ophthalmology, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Paraneoplastic syndromes, Pupils Retina

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Tuesday, March 6th from 11:00 am - 11:15 am**

**Buzzing Sympathetic Nerves: A New Test to Enhance Reflex Pupil Dilation in Suspected Horner Syndrome**

Rawan Omary<sup>1</sup>, Randy Kardon<sup>2</sup>, Christopher Bockisch<sup>3</sup>, Klara Landau<sup>1</sup>, Konrad Weber<sup>4</sup>

<sup>1</sup>Department of Ophthalmology, University Hospital Zurich, Zurich, Switzerland, <sup>2</sup>Department of Ophthalmology, University of Iowa and Veteran Medical Center, Iowa, Iowa, USA, <sup>3</sup>Departments of Ophthalmology, Neurology and ENT, University Hospital Zurich, Zurich, Switzerland, <sup>4</sup>Departments of Ophthalmology and Neurology, University Hospital Zurich, Zurich, Switzerland

**Introduction:**

Patients with suspected Horner syndrome and equivocal pupil dilation lag and pharmacologic testing might undergo unnecessary MR imaging. Our purpose was to increase the diagnostic sensitivity of pupillometry by accentuating sympathetic innervation to the iris dilator by surface electrical stimulation of the median nerve using a standard electromyography machine. We hypothesized that any difference in sympathetic innervation to the right and left eye would be accentuated.

**Methods:**

Seven healthy volunteers tested before and after monocular instillation of brimonidine 0.2% to induce pharmacological Horner syndrome were compared to two patients with proven Horner syndrome. Pupillary responses were measured with binocular pupillometry (DP-2000, Neuroptics; Irvine, CA) in response to sympathetic activation by electrical stimulation (0.2ms, 50mA) of the median nerve in darkness and at various times after extinction of a 3log lux light stimulus (1 vs. 4 seconds). Sudomotor sympathetic responses from the palm were recorded simultaneously.

**Results:**

In subjects with Horner syndrome or pharmacologically induced unilateral sympathetic deficit, electrical stimulation in combination with the extinction of light greatly enhanced the anisocoria during the evoked pupil dilation and was well tolerated. The asymmetric sympathetic response was greatest when the electrical stimulus was given 1-2s after termination of the light. Two discernible reflex dilation responses appeared; an initial symmetric dilation due to central inhibition of the Edinger-Westphal nucleus followed by an accentuated asymmetric dilation due to enhanced peripheral sympathetic stimulation.

**Conclusions:**

Electrical sympathetic stimulation given at the termination of a short light stimulus appears to greatly enhance the sensitivity for diagnosing asymmetric pupil dilation due to Horner syndrome. This strategy may improve upon the ability to rule in or rule out a unilateral oculosympathetic deficit, especially if the results of topical pharmacological testing are inconclusive.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuro-opth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Cattaruzza-Foundation, University of Zurich, Switzerland.

**Tuesday, March 6th from 11:15 am - 11:30 am**

**Repetitive Ocular Vestibular Evoked Myogenic Potentials (oVEMP) Stimulation For Myasthenia Gravis: Comparison Of Stimulation Paradigms**

Magdalena Wirth<sup>1</sup>, Yulia Valko<sup>2</sup>, Sally Rosengren<sup>3</sup>, Tanja Schmueckle-Meier<sup>2</sup>, Christopher Bockisch<sup>4</sup>, Dominik Straumann<sup>2</sup>, Klara Landau<sup>1</sup>, Konrad Weber<sup>85</sup>

<sup>1</sup>Department of Ophthalmology, University Hospital Zurich, Zurich, Switzerland, <sup>2</sup>Department of Neurology, University Hospital Zurich, Zurich, Switzerland, <sup>3</sup>Department of Neurology, Royal Prince Alfred Hospital, Camperdown, Australia, <sup>4</sup>Departments of Neurology and Otorhinolaryngology, University Hospital Zurich, Zurich, Switzerland, <sup>5</sup>Departments of Neurology and Ophthalmology, University Hospital Zurich, Zurich, Switzerland

**Introduction:**

Early and accurate diagnosis is of utmost importance for the course and outcome of myasthenia gravis (MG). Recently, repetitive ocular vestibular evoked myogenic potential (oVEMP) stimulation has been developed as a novel diagnostic tool for MG. Quantification of extraocular muscle response decrement after repetitive stimulation facilitates the often challenging diagnosis of MG. Comparison of different stimulation paradigms is needed to determine the most sensitive and specific parameters for detecting the characteristic oVEMP decrement.

**Methods:**

Repetitive bone-conducted oVEMPs were elicited in 18 MG patients and 17 healthy subjects. We compared four different repetition rates (20Hz, 30Hz, 40Hz, 50Hz) to determine the most sensitive and specific oVEMP paradigm for decrement detection.

**Results:**

Mean age of MG patients and healthy subjects was 62±18 and 30±6 years, respectively. Mean duration of MG amounted to 42±70 months. The majority (89%) of MG patients had ocular symptoms at time of measurement, including ptosis (n=14) and diplopia (n=12). Eight patients (44%) had isolated ocular symptoms, 4 (22%) had additional bulbar weakness and 9 (50%) generalized muscle weakness. Repetitive stimulation at 30Hz yielded the best differentiation between MG patients and healthy subjects, with a sensitivity of 82% and a specificity of 83% (area under the curve (AUC) 0.84) when using an overall decrement of ≥9% as cutoff. 20Hz stimulation allowed differentiation of MG from healthy subjects with 68% sensitivity and 69% specificity (cutoff≥17%, AUC 0.75), 40Hz with 81% sensitivity and 61% specificity (cutoff≥8%, AUC 0.73), and 50 Hz with 69% sensitivity and 72% specificity (cutoff≥14%, AUC 0.76), respectively.

**Conclusions:**

Preliminary data of our study suggest 30Hz repetitive oVEMP stimulation from the inferior oblique muscles as the most effective stimulation paradigm. Repetitive oVEMP stimulation with optimal parameters facilitates early and accurate diagnosis of ocular MG.

**References:** Valko Y, Rosengren SM, Jung HH, Straumann D, Landau K, Weber KP. Ocular vestibular evoked myogenic potentials as a test for myasthenia gravis, *Neurology*, 2016 Feb 16;86(7):660-8.

**Keywords:** Myasthenia, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Swiss National Science Foundation (SNSF, 320030\_166346) and Uniscientia Stiftung Vaduz, Liechtenstein

Tuesday, March 6th from 11:30 am - 11:45 am

## A Prospective Study of Neuro-Ophthalmic Abnormalities in Children with Neonatal Abstinence Syndrome

Jennifer Lambert<sup>1</sup>, Kate McConnell<sup>2</sup>, Stephen Christiansen<sup>1</sup>

<sup>1</sup>Boston University School of Medicine, Boston, Massachusetts, USA, <sup>2</sup>University of Washington School of Public Health, Seattle, Washington, USA

### Introduction:

Previous studies suggest that children diagnosed with neonatal abstinence syndrome (NAS) have a higher rate of congenital ocular anomalies than the general population. This study prospectively assesses the risk of neuro-ophthalmic abnormalities in NAS babies.

### Methods:

Over a two-year period, all infants exposed to maternal drugs of abuse were referred for ophthalmological examination as part of the NAS screening protocol at our institution. Demographic data, exposures, and eye exam findings were recorded.

### Results:

A total of 91 babies diagnosed with NAS were examined - 54% were male, 84% were white. The mean gestational age was 38.2 weeks and mean birth weight was 3.0 kg. Mean age at examination was 6.9 months. All 91 children were exposed to at least one opiate substance in utero, including methadone (65%), buprenorphine (35%), heroin (32%), and prescription opioid analgesic (15%); 75 children (82%) required pharmacologic treatment for symptoms of withdrawal. Twenty-nine children (32%) had abnormal ocular findings - six (7%) had strabismus, four (4%) had nystagmus, and ten (11%) had optic nerve anomalies including hypoplasia and morning glory disc.

### Conclusions:

This study reveals an increased incidence of strabismus, nystagmus, and optic nerve anomalies in children with NAS. Our rate of strabismus (7%) is three times higher than that reported in the general population. There also appears to be a much greater risk of nystagmus and optic nerve hypoplasia in NAS children (4% and 5%, respectively) compared to whole population congenital estimates (0.0012% and 0.0024%, respectively). Further study is warranted to identify infants at highest risk for poor visual outcomes and to clarify the etiology of these anomalies.

**References:** Garcia-Fillion P, Fink C, Geffner ME, Borchert M. Optic nerve hypoplasia in North America: a re-appraisal of perinatal risk factors. *Acta Ophthalmol.* 2010; 88: 527-534. Gill AC, Oei J, Lewis NL, Younan N, Kennedy I, Lui K. Strabismus in infants of opiate-dependent mothers. *Acta Paediatr Oslo Nor* 1992. 2003;92(3):379-385. McGlone L, Mactier H, Hamilton R, et al. Visual evoked potentials in infants exposed to methadone in utero. *Arch Dis Child.* 2008;93(9):784-786. Kocherlakota P. Neonatal abstinence syndrome. *Pediatrics.* 2014;134(2):e547-e561.

**Keywords:** Pediatric neuro-ophthalmology, Nystagmus, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Tuesday, March 6th from 11:45 am - 12:00 pm**

**Normal Topography and Binocularity of the Superior Colliculus in Strabismus**

Jonathan Horton<sup>1</sup>, Brittany Rapone<sup>1</sup>, Daniel Adams<sup>1</sup>, John Economides<sup>1</sup>

<sup>1</sup>UCSF, San Francisco, California, USA

**Introduction:**

In subjects with alternating strabismus, either eye is used to saccade to visual targets. The brain must calculate the correct vector for the saccade, which will depend on which eye is chosen to make it. To learn how accurate eye movements are made in strabismus, topographic maps were examined in the superior colliculus, a major midbrain center for saccade generation.

**Methods:**

Alternating exotropia was induced in macaques at age one month by sectioning the medial recti. Once the animals grew to maturity, they were trained to fixate targets with either eye. Receptive fields were mapped in the superior colliculus using a sparse-noise stimulus, while the monkeys alternated fixation. In some instances, sparse-noise was presented dichoptically, to probe for anomalous retinal correspondence. After some recordings, microstimulation was applied to compare sensory and motor maps.

**Results:**

Receptive fields were offset in position by the ocular deviation, but otherwise remained aligned in the right eye and the left eye. In one animal, the left eye's coordinates were rotated approximately 20° clockwise with respect to those of the right eye. This was accounted for by a corresponding cyclorotation of the ocular fundi, which also produced an A-pattern deviation. Microstimulation drove the eyes accurately to the site of receptive fields, as in normal animals. Single cell recordings uncovered no evidence for anomalous retinal correspondence. Despite strabismus, neurons remained responsive to stimulation of either eye.

**Conclusions:**

Strabismus might corrupt the topography of the superior colliculus in two ways: by disturbing the alignment between the sensory and motor maps or by shifting the relationship between the maps serving each eye. The main conclusion from this study is that neither phenomenon occurs: the registration of maps in the superior colliculus remains unaltered by strabismus. Moreover, neurons remain responsive to stimulation of either eye, despite loss of binocular function in striate cortex.

**References:** None.

**Keywords:** Ocular Motility, Pediatric neuro-ophthalmology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** EY10217, EY02162, Physician Scientist Award from Research to Prevent Blindness.





North American Neuro-Ophthalmology Society

# 44th Annual Meeting

March 3 – March 8, 2018

The Hilton Waikoloa Village • The Big Island of Hawaii

## Poster Session II: Scientific Advancements in Neuro-Ophthalmology

Tuesday, March 6, 2018 6:00 pm – 9:30 pm

*Authors will be standing by their posters during the following times:*

*Odd-Numbered Posters: 6:45 pm - 7:30 pm*

*Even-Numbered Posters: 7:30 pm - 8:15 pm*

Poster #		Presenting Author
<b>Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)</b>		
144	Clinical Features of Pediatric Monophasic and Recurrent Idiopathic Optic Neuritis	Soren Jonzson
145	Risk Factors for Fellow Eye Involvement in NAION: Optic Disc Drusen (ODD) and CPAP Non-compliance	Melinda Chang
146	Ophthalmic Manifestations of Biopsy Proven Giant Cell Arteritis in Chinese Patients	Carmen Chan
147	Safety and Efficacy of RPh201 in Patients with Previous Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)	Leonard A Levin
148	The spectrum of Pauci-Symptomatic Isolated Unilateral Optic Nerve Head Edema (IUONHE)	Eman E Hawy
149	Mitochondrial Haplogroup V/HV is Associated with Sequential NAION	Marisa G Tieger
150	Are the 2016 Guidelines on the Neuro-ophthalmic Evaluation of Pituitary Adenomas Already Obsolete?	Jonathan A Micieli
151	Retinal Ganglion Cell and Nerve Fiber Loss in Autosomal Dominant Optic Atrophy:Correlations with Visual Functions	Jin Choi MD
152	Long Term Treatment with Idebenone in Leber's Hereditary Optic Neuropathy (LHON): Real World Clinical Practice	Xavier Llòria
153	Color Contrast Sensitivity in Age-Related Macular Degeneration	Danielle Leong
154	Analysis of Nonarteritic Anterior ischemic Optic Neuropathy demography in Mexico	Graciela Garcia Briones
155	The Epidemiology of Pediatric Visual Pathway Injuries – Analysis of the National Trauma Data Bank	Ryan A Gise
156	A Patient Questionnaire to Assess the Psychosocial Impact of Visual Loss in Optic Nerve Disorders	Rebecca J Kay
159	Correlation of Visual Field Loss with MRI Findings in Patients with Pituitary Tumours	Christian J Lueck
160	Misdiagnosis of Optic Nerve Sheath Meningiomas (ONSM): A Serious Problem	Pinar K Koytak
161	Baseline Characteristics of LHON Subjects in the RESCUE and REVERSE Phase III Gene Therapy Trials	Mark L Moster
162	The Epidemiology and Clinical Characteristics of Leber Hereditary Optic Neuropathy (LHON) in a Canadian Province.	Colten Wendel
163	Unilateral Pigmentary Retinopathy Associated with Multiple Sclerosis	Eric D Gaier
164	Validation of a Symptom-Based Questionnaire for Pediatric CNS Neuroinflammatory Diseases	Amy Waldman
165	Inter-ocular Difference in Retinal Nerve Fiber Layer Thickness Predicts Optic Neuritis in Pediatric-onset Multiple Sclerosis	Amy T Waldman

166	Visual Function in Wolfram Syndrome	An-Guor Wang
167	Ischemic Optic Neuropathy and Renal Failure: Our Casuistry	Mariana De Virgiliis
168	Antibodies to Myelin Oligodendrocyte Glycoprotein in Patients with Chronic Relapsing Inflammatory Optic Neuropathy	Haeng-Jin Lee
169	Afferent System Disparity When Anatomy (OCT) and Psychophysics( Acuity and Perimetry) Fail to Meet	Steven A Newman
170	Baseline OCT Findings in Phase 3 RESCUE and REVERSE Trials	Robert C Sergott
171	Retinal Structural and Metabolic Alterations in Parkinson's Disease	Satya Karna
172	Study of Morphological, Retinal Nerve Fibre Layer and Blood Flow Changes on FD-OCT in NA-AION	Vivekanand U Warkad
173	Inter-Eye Difference Thresholds for Predicting an Optic Nerve Lesion in in MS: An International Study	Rachel Nolan
174	The influence of Volume and Anatomic Location of Optic Disc Drusen on sensitivity of Autofluorescence	Frederik C Loft
175	Optic Nerve Head Parameters in Patients with Non-Arteritic Ischemic Optic Neuropathy	Hwan Heo
<b>Disorders of the Posterior Visual Pathway and Visual Processing</b>		
176	Correlation Between Stereopsis and Reverse Stereopsis in Homonymous and Bitemporal Hemianopias	Michael Dattilo
177	Transcranial Magnetic Stimulation, a New Hope for Treatment of Post-Concussion Syndrome: A Randomized Double-Blind Study	Behzad Mansouri
178	Dichoptic Treatment of Amblyopia in a Clinical Setting – a Retrospective Study	Giovanni M Travi
179	Visual Function after Cerebral Hemispherectomy	Shauna E Berry
180	Faces, Music and Voices: Evidence for a Right-dominant Anterior Temporal Agnosia Syndrome	Jason J Barton
181	Headache and Intrinsic Brain Network Improvement in Chronic Migraine Following Onabotulinumtoxin-A Treatment: a Resting-State-Functional-MRI Study	Behzad Mansouri
182	Do Children with Homonymous Field Defects Benefit from Visual Search Training?	Susanne Trauzettel-Klosinski
<b>IIH</b>		
183	Endovascular Venous Sinus Stenting for Idiopathic Intracranial Hypertension: A Systematic Review of the Literature	Brandon J Bond
184	Lumbar Puncture For Diagnosis Of Pseudotumor Cerebri Syndrome In Typical Patients	Mathew S Margolis
185	United Kingdom Consensus Guidance for Adult Idiopathic Intracranial Hypertension	Susan P Mollan
186	A Multidisciplinary Intracranial Hypertension Clinic - the University of Washington Experience	Courtney E Francis
187	Idiopathic Intracranial Hypertension: Update of a 12-Year Retrospective Evaluation at One Large Tertiary Care Center	Bart K Chwalisz
188	Genetics of Idiopathic Intracranial Hypertension	DonRaphael Wynn
189	Retrospective Evaluation of Resource Utilization by Patients with IIH in a University Health System	Zainab Shirazi
190	Idiopathic Intracranial Hypertension and Levonorgestrel Intrauterine Device Use	Lindsey B De Lott
191	Venous Sinus Stenting Improves Visual Fields and Cerebrospinal Fluid Opening Pressures in Idiopathic Intracranial Hypertension	Evan R Schloss
192	Prevalence of Peripapillary and Retinal Folds in Pseudopapilledema and Mild Papilledema	Sara N Reggie
193	A comparison of UK and USA idiopathic intracranial hypertension (IIH) patient populations	Richard J Blanch
194	Optic Disc Drusen (ODD) in the Setting of Idiopathic Intracranial Hypertension (IIH)	Andrew J Sumnicht
195	Direct Retrograde IJ Access for DVSS	Lakshmi Leishangthem
196	Predictive Value of International Classification of Disease Code for IIH in a University Health System	Irma Muminovic

197	Retrospective Analysis of the Effect of Acetazolamide on Anthropometrics in Pediatric Pseudotumor Cerebri Syndrome (PTCS)	Claire A Sheldon
198	Correlation of Opening Pressure with Unilateral Versus Bilateral Venous Sinus Stenosis in Pseudotumor Cerebri	Padmaja Sudhakar
199	"Real World" MRI Findings in Idiopathic Intracranial Hypertension	Philip S Garza
200	The Persistence of MRI Findings in Pediatric Pseudotumor Cerebri Syndrome	Anita A Kohli
<b>Miscellaneous</b>		
202	Comparison of a Smartphone Application with Ishihara Pseudoisochromatic Plate for Testing Color Vision	Jiawei Zhao
203	Development of Nanocarbon Antioxidants for Oxidative Stress Related Injury of the Retina	William K Sikkema
205	Inhibitory Deficits in Visual Snow	Melissa C Tien
206	Glial Changes In An Animal Model Of Ethambutol-Related Optic Neuropathy	Hui-Chen Cheng
207	Smartphone Tests of Visual Acuity, Hyper-acuity, Contrast Sensitivity and Critical Flicker Fusion	Jane A Bailey
208	Assessment of Neurocognitive Consequences of Call Duty in Residents Using Saccadic Eye Movements	Michael E Ding
<b>Neuro-Imaging</b>		
209	Clival Mass: An Under Recognized Cause of Sixth Cranial Nerve Palsy	Talal M Derani
210	Swept Source OCT Angiography Quantification in Optic Nerve Edema: Preliminary Results	Marie-Benedicte Rougier
211	Correlative Image Enhancement: Using Image Processing to Improve Visualization of Optic Neuritis on MRI	Leanne Stunkel
212	Optical Coherence Tomography (OCT) Findings in Rat Model of Anterior Ischemic Optic Neuropathy (rAION)	Tzulun Huang
213	Neuro-ophthalmic Conditions with Discrepancies Between OCT Findings & Visual Function	Noel Chan
214	MRI Features of Demyelinating Diseases Associated with Anti-MOG Antibodies	Damien Biotti
215	Role of Early Neuroimaging in the Management of Acute Isolated Ocular Motor Nerve Palsy	Daniel Rappoport
<b>Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases</b>		
216	Health-Related Quality of Life in Patients With Giant Cell Arteritis Treated With Tocilizumab	Vibeke Strand
217	Retina Nerve Fiber Layer Segmentation with OCT in Patients with Neurodegenerative Diseases	Marcia L Marques
218	Non-arteritic Anterior Ischemic Optic Neuropathy and its Association with Obstructive Sleep Apnea	Ming-Hui Sun
219	Cabin Pressures on Commercial Aircraft and Non-Arteritic Ischemic Optic Neuropathy	Terry D Wood
220	Longitudinal Analysis of Contrast Acuity in Friedreich Ataxia	Ali G Hamedani
221	Ocular Bartonellosis (Cat Scratch Disease): A Case Series	Lakana Kumar Thavaratnam
222	Nasopharyngeal Carcinoma, A Masquerade: A Case Series	Lakana Kumar Thavaratnam
224	Ocular Motor Abnormalities in Autoimmune Ataxias	Xiaojun Zhang
225	Evaluation And Correlation Between Neurophysiological And Visual Functional Tests In Multiple Sclerosis	Elena Garcia-Martin
226	Eyetracking in Pediatric Multiple Sclerosis	Andrew D Yousef
227	Abnormal Chewing Gum Test Results in Patients with Giant Cell Arteritis: A Case Series	Clare Fraser
228	Characteristics and Prognosis of Patients with Ocular Myasthenia Gravis (OMG) and Thymoma.	Su Ann Lim
229	Remote Ischemia Conditioning Protects Retinal Ganglion Cells in Streptozotocin Induced Diabetic Rats	Xuxiang Zhang
230	Visual Sequelae in Children with Primary CNS Tumors	Yin Allison Liu

231	The Relationship of Retinal Nerve Fiber Layer Thickness to Alzheimer's Disease Biomarkers	Victoria S Pelak
232	Asynchronous onset in Leber's Hereditary Optic Neuropathy	Rustum Karanjia
233	Physiologic Dysfunction Precedes Retinal Ganglion Cell Loss in Mice with Neurofibromatosis and Optic Pathway Gliomas	Steven F Stasheff
235	Epidemic Bhutanese Optic Atrophy	Philip M Skidd
236	The Utility of Nomograms for Suspected Giant Cell Arteritis	Nurhan Torun
237	Cognitive Functions in Multiple Sclerosis Patients Presenting with Optic Neuritis Compared to Other First Presentations	Ruth Huna-Baron
238	Reduction of Photopic Negative Response(PhNR) in Optic Neuropathies Obtained Using a Handheld Electroretinogram Device	Fareshta Khushzad
239	Spinocerebellar Ataxia Type 7: A Case Series and Review	DonRaphael P Wynn
240	The Great Imitator on the Rise: Optic Disc Involvement in Syphilis Patients	Dvir Koenigstein
241	Pediatric Research Collaboration ExPLoring Tests In Ocular Neuroimmunology (PERCEPTION)	Jennifer Graves
242	Neuro-ophthalmic Consequences of Firearms-Related Trauma in the United States	Jimmy Y Hu
243	IVIG Treatment in the Management of Corticosteroid Unresponsive Optic Neuritis: Case Series of 15 Cases	Yu Zhao
244	The Heidenhain Variant of Creutzfeldt-Jakob Disease: The New Zealand Experience 1997-2016	Benson S Chen
245	Failure to Find Evidence for a Strong Association Between Herpes Zoster and Giant Cell Arteritis.	Professor CharlesGrose
246	Retinal And Optic Nerve Degeneration In Patients With Multiple Sclerosis Followed Up For 10 Years.	Elena Garcia-Martin
247	The Spectrum of Anti-GAD Antibody Associated Neuro-Ophthalmological and Neurological Conditions	Thirugnanam Umapathi
248	Temporal Artery Ultrasound in Suspected Giant Cell Arteritis	Suellen Li
249	Mobile Universal Lexicon Evaluation System in MS: A New Visual Test of Rapid Picture Naming	Meagan Seay
250	Differential Visual Acuity Data When Utilizing 2 Versus 4 Meter ETDRS Charts in Pediatric Patients	Darrel Conger
252	Are Video-oculography Findings Linked to Specific Clinical Features in Parkinson's Disease?	Woong-Woo Lee
253	Neurophthalmic Manifestations of ZIKA Patients in Venezuela	Emely Z Karam
254	Optic Meningitis	Jean-Philippe G Woillez
255	Saccadic Intrusions Are Rare in Multiple Sclerosis	Lisa N DePledge
256	The Role of Neuro-Ophthalmology in Atypical Parkinsonism: Clinical Findings on a Standardized Ocular Motor Exam	Meagan Seay
258	Internuclear Ophthalmoplegia in Pediatric Patients	Emely Z Karam
259	Focal Thickness Alterations in the Intraretinal Layers in Patients Multiple Sclerosis	Hong Jiang
260	Comparing the Smooth Pursuit and Saccadic Eye Movements in Rugby Players to a Normative Database	Clare Fraser
261	Peripapillary Vessel Density Changes in Alzheimer's Type Dementia; A Pilot Study.	Pareena Chaitanuwong
262	Kayser-Fleischer Ring Detection and Quantification in Wilson's disease using Optical Coherence Tomography	Ruchika Batra
263	Surgical Anatomy of the Superficial Temporal Artery to Prevent Facial Nerve Injury During Arterial Biopsy	Hyun Jin Shin
<b>Ocular Motility Disorders and Nystagmus</b>		
264	Relation of Quantitative Eye Movements with Cognitive Dysfunction in Patients with Concussion	Doria M Gold MD
265	The Effect of Horizontal Rectus Muscle Surgery on Distance-Near Incomitance	Paul H Phillips
266	Molecular Findings Among Patients with Nystagmus Referred for Targeted Next-Generation Sequencing	Jinu Han

267	Clinical Significance of Perverted Head-Shaking Nystagmus	Professor Sun-Young Oh
268	Clinical and Molecular Genetic Features of Congenital Nystagmus with FRMD7 mutations	Jae-Hwan Choi
269	Modulation of Vertical Nystagmus by Convergence: Correlation with Positional Nystagmus	Sun-Uk Lee
270	The New MULES: A Sideline-Friendly Test of Rapid Picture Naming for Concussion	Omar Akhand
271	Long-term Memory Of Object Locations And Strabismus Angle Requires Oculomotor Proprioception	Linus D Sun PhD
272	Association Between Convergence Insufficiency and EVestG Extracted Features in Post-Concussion Syndrome	Behzad Mansouri
273	Evaluation of a Novel Smartphone App For the Automated Evaluation of Strabismus Measurements	Dean M Cestari
274	Magnetic Resonance Imaging (MRI) Reveals Compartmental Violations of Sherrington's Law in Horizontal Fusional Vergence	Joseph L Demer
275	Quantitative Relationship Between Ocular Motility and Superior Oblique Muscle Hypoplasia in Unilateral Superior Oblique Palsy	Ji Eun Lee
276	Clinical Characteristics of Neuro-Ophthalmology Patients Seen by One Orthoptist at a Large Urban Academic Institution	Alex Christoff
277	Improvement of Interictal Ocular Motor Abnormalities in Vestibular Migraine following Migraine Preventive Therapy.	Stacy V Smith
278	'Sandbagging' a Vision Test for Concussion-based Sideline Assessment: An Eye Movement Investigation Reveals the Strategies	John-Ross Rizzo
279	Misdiagnosis of Third Nerve Palsy	Richard M Schroeder
280	New Onset Binocular Diplopia in Patients Over 65 Years	Daniel Rappoport
281	Ocular Myasthenia Gravis Thymectomy Cohort Study	Ali G Hamedani
282	Tonic vs. Phasic Fiber Dysfunction in Isolated, Unilateral Sixth Cranial Nerve Palsy	Elizabeth Fortin
<b>Ocular-Imaging</b>		
283	Role of OCT in Monitoring for Ethambutol Induced Optic Neuropathy	Sona Chaudhry
284	Nonmydriatic Fundus Photography in the Emergency Department for Patients Presenting with Acute Vision Loss.	Caroline Vasseneix
285	Episcleral Delivery System for Neuroprotection in Optic Neuropathy	Kimberly P Cockerham
286	Microvascular changes in macula and optic nerve head in Non-Arteritic Anterior Ischemic Optic Neuropathy	Satya Karna
288	Optical Coherence Tomographic Angiography in Non-arteritic Anterior Ischemic Optic Neuropathy Reveals Biphasic Microvascular Changes	Eric D Gaier
289	Comparison of Peripapillary Retinal Vessel Density of Optic Atrophy after Optic Neuritis and NAION	Parima Hirunwiwatkul
290	Retinal Amyloid Imaging in Patients with Alzheimer's Disease	Oana M Dumitrascu
291	Is Pink the New Black? Comparison of OCT –GCL Mapping to Humphrey Perimetry in Hemianopia	Oded Hauptman
292	Pseudo-papilledema Detection and Prevalence	Richard J Blanch
293	Optical Coherence Tomography Findings in Papilledema Versus Optic Disc Drusen	Laura Dell'Arti
<b>Pupil</b>		
295	Study of Age Correlation of the Intrinsically-photosensitive Retinal Ganglion Cell (ipRGC)-Medicated Pupil Light Reflex (PLR)	YanJun Chen

**Poster 144****Clinical Features of Pediatric Monophasic and Recurrent Idiopathic Optic Neuritis**

Soren Jonzson<sup>1</sup>, Brenda Young<sup>1</sup>, Janace Hart<sup>1</sup>, Andrew Yousef<sup>1</sup>, Leena Suleiman<sup>1</sup>, Emmanuelle Waubant<sup>1</sup>, Jennifer Graves<sup>1</sup>

<sup>1</sup>UCSF, San Francisco, California, USA

**Introduction:**

There is little data available on the characteristics and treatment approaches in pediatric idiopathic optic neuritis (ON). It is unknown if recurrent optic neuritis is a life-long condition or a self-limited illness. We sought to report the clinical features, outcomes, and treatment experience of pediatric subjects with both monophasic and recurrent idiopathic optic neuritis (RION).

**Methods:**

We performed a retrospective cohort study of ON evaluated over a 10 year-period at a pediatric MS center. Subjects were included if they met the criteria of the presence of clinical ON without evidence of an underlying autoimmune, infectious, or neoplastic disease.

**Results:**

In 17 idiopathic cases of ON, 10 were monophasic and 7 were recurrent. The mean age of onset for RION ( $9.86 \pm 3.63$ ) was younger than that of monophasic ON ( $13.3 \pm 4.22$ ). While 50% of monophasic cases were female, 85.7% (6/7) of RION cases were female. Patients with RION were more likely to have had a bilateral first event (57.1% vs. 40%). Of 11 idiopathic ON cases with oligoclonal band results available for review, only 1 participant with monophasic ON had bands present in the CSF. Treatments for the RION cases included use of IV steroid regimens and different formulations of mycophenolate. After 2-3 years of mycophenolate use, treatment was stopped in one child with RION with no further relapses over an additional 3 years of follow-up.

**Conclusions:**

We observed demographic differences between recurrent and monophasic forms of idiopathic ON. Acute events were largely responsive to steroid treatments and mycophenolate appeared to control RION well in the children studied. It may be possible to wean immunosuppressants after several years of quiescence in RION, but larger prospective studies are needed to determine best management strategies in these patients.

**References:** None.

**Keywords:** Pediatric neuro-ophthalmology, Optic nerve trauma and treatment, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** School of Medicine Dean's Summer Research Fellowship

**Poster 145****Risk Factors for Fellow Eye Involvement in NAION: Optic Disc Drusen (ODD) and CPAP Non-compliance**

Melinda Chang<sup>1</sup>

<sup>1</sup>University of California, Davis, Sacramento, California, USA

**Introduction:**

Although several risk factors for developing NAION have been identified, many have not been studied as potential contributors to NAION in the fellow eye. The Ischemic Optic Neuropathy Decompression Trial (IONDT) found that diabetes and poor visual acuity (study eye) were associated with fellow eye NAION. We sought to identify other ocular and systemic risk factors.

**Methods:**

A retrospective chart review of patients seen at a single university between 2007 and 2017 with a diagnosis of ischemic optic neuropathy based on ICD codes was performed. Patients were included if clinical data supported the diagnosis of NAION. Exclusion criteria were fellow eye optic atrophy or bilateral NAION at time of diagnosis. The following data were collected: age, sex, and presence of systemic vascular risk factors and ophthalmic comorbidities. Kaplan Meier analysis was used to calculate 5-year risk of fellow eye NAION. Cox proportional hazard regression was used to calculate hazard ratios for fellow eye involvement.

**Results:**

119 patients met study criteria. Fellow eye NAION occurred in 29 (24%) patients. 5-year risk of fellow eye involvement was 27% (95% CI 19 to 38%). On univariate analysis, significant risk factors for fellow eye NAION included bilateral ODD (HR 2.8, 95% CI 1.12 to 6.90,  $p=0.02$ ) and non-compliance with CPAP (HR 4.50, 95% CI 1.79 to 11.3,  $p=0.0058$ ) in patients with moderate-to-severe OSA. Both remained significant on multivariate analysis. Systemic risk factors such as diabetes, hypertension, hyperlipidemia, and cardiovascular and cerebrovascular disease, and ocular comorbidities including macular degeneration and glaucoma were not associated with fellow eye NAION.

**Conclusions:**

ODD and non-compliance with CPAP are associated with increased risk of NAION in the fellow eye. Possible explanations include structural (ODD) or metabolic (untreated OSA) compromise of optic nerve head vasculature. Compliance with CPAP in patients with unilateral NAION should be stressed to avoid potentially devastating bilateral optic neuropathy.

**References:** Newman NJ, Scherer R, Langenberg P, Kelman S, Feldon S, Kaufman D, Dickersin K; Ischemic Optic Neuropathy Decompression Trial Research Group. The fellow eye in NAION: report from the ischemic optic neuropathy decompression trial follow-up study. *Am J Ophthalmol.* 2002 Sep;134(3):317-28. Purvin V, King R, Kawasaki A, Yee R. Anterior ischemic optic neuropathy in eyes with optic disc drusen. *Arch Ophthalmol.* 2004 Jan;122(1):48-53. Aptel F, Khayi H, Pépin JL, Tamisier R, Levy P, Romanet JP, Chiquet C. Association of Nonarteritic Ischemic Optic Neuropathy With Obstructive Sleep Apnea Syndrome: Consequences for Obstructive Sleep Apnea Screening and Treatment. *JAMA Ophthalmol.* 2015 Jul;133(7):797-804.

**Keywords:** Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 146**

**Ophthalmic Manifestations of Biopsy Proven Giant Cell Arteritis in Chinese Patients**

Carmen Chan<sup>1</sup>, Noel Chan<sup>1</sup>, Charlene Yim<sup>1</sup>, Jerry Lok<sup>1</sup>

<sup>1</sup>Hong Kong Eye Hospital, Kowloon, Hong Kong

**Introduction:**

Compared with Caucasians, giant cell arteritis (GCA) is less common in Asians[1,2] with an estimated annual incidence of 0.34 per 100,000 people aged ≥ 50 per year in Hong Kong[3]. In this study, we aim to evaluate the clinical features of biopsy proven GCA in Hong Kong Chinese patients.

**Methods:**

This is a retrospective case-notes review study of patients with biopsy proven GCA who attended a tertiary referral eye hospital between 1998 & 2017.

**Results:**

A total of 6 patients were identified. The median age at presentation was 77 (range 59-89) with a male predominance (Ratio of 2:1). Two had bilateral involvement. Ophthalmic presentations varied and included visual blurring (50%), transient visual obscuration (16.7%), visual field defect (16.7%), transient diplopia (16.7%) and eye pain associated with uveitis (16.7%). Arteritic anterior ischemic optic neuropathy (AAION) was only found in 3 patients; other ophthalmic diagnoses included anterior uveitis and impending central retinal artery occlusion. Non-ocular symptoms included headache (4 patients) and jaw claudication (2 patients), but only 1 patient reported scalp tenderness; while temporal pulse remained palpable in all patients. All patients had abnormal laboratory parameters at presentation including raised erythrocyte sedimentation rate (100%), raised C-reactive protein level (83.3%), thrombocytosis (50%), anemia (83.3%) and leukocytosis (16.7%). Among the 4 patients with comprehensive ophthalmic record, all were commenced on steroid treatment on the day of ophthalmic presentation (mean steroid treatment duration: 222.17±139.24 weeks), while 3 required additional immunosuppressants. Permanent visual impairment persisted in all eyes presented with AAION.

**Conclusions:**

GCA is a rare disorder amongst Hong Kong Chinese, with heterogenous and somewhat atypical ophthalmic and systemic manifestations. For those with visual symptoms as initial presentation, early diagnosis relied on a high index of clinical suspicion and abnormal laboratory tests, in the absence of systemic symptoms.

**References:** 1. Pereira LS, Yoon MK, Hwang TN, et al. Giant cell arteritis in Asians: a comparative study. Br J Ophthalmol. 2011 Feb;95(2):214-6. 2. Liu NH, LaBree LD, Feldon SE, et al. The epidemiology of giant cell arteritis : a 12-year retrospective study. Ophthalmology. 2001 Jun;108(6):1145-9 3. S Tam, TC Wong. Temporal arteritis in Hong Kong. International Journal of Rheumatic Diseases 2008; 11:163-169.

**Keywords:** Optic neuropathy, Neuro-opth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 147****Safety and Efficacy of RPh201 in Patients with Previous Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)**

Leonard Levin<sup>1</sup>, Eitan Rath<sup>2</sup>, Zvi Segal<sup>2</sup>, Konstantin Adamsky<sup>3</sup>, Zadik Hazan<sup>3</sup>

<sup>1</sup>McGill University, Montreal, QC, Canada, <sup>2</sup>Galilee Medical Center, Nahariya, Israel, <sup>3</sup>Regenera Pharma, Ness Ziona, Israel

**Introduction:**

No proven treatment for nonarteritic anterior ischemic optic neuropathy (NAION) exists, in the acute or late phase. Preclinical data with RPh201, a novel botanical drug, suggest it may have neuroprotective and neuroenhancing effects.

**Methods:**

A Phase 2a, randomized, placebo-controlled, double-masked study in patients with previous NAION (diagnosed  $\geq 6$  months previously) was conducted. Participants were dosed twice weekly by subcutaneous injection with either 20 mg RPh201 or placebo for up to 26 weeks. The primary efficacy analysis of change best-corrected visual acuity (BCVA) measured using ETDRS was performed on the 20 participants. The trial was not powered for efficacy.

**Results:**

Out of the 20 participants, 19 completed 26 weeks of treatment (11 on RPh201). The mean ( $\pm$  SEM) improvement in BCVA was 15 letters ( $\pm 4.6$ ) in the RPh201 group and 7 letters ( $\pm 5.5$ ) in the placebo group. In the RPh201 arm 36.4% (4/11) of the study eyes had an improved BCVA of  $\geq 15$  letters compared to 12.5% (1/8) eyes receiving placebo. Following 13 weeks off-drug period, improvement in BCVA ( $\geq 15$  letters) was maintained, with 25% (3/12 eyes) of the RPh201 group compared to 12.5% (1/8 eyes) of placebo. Overall, 64% of participants treated with RPh201 showed some level of improvement in BCVA from baseline, compared to 38% from the placebo group. Of 154 adverse events (AEs) reported, 52 were related to the study procedures/treatment. The most frequently reported were local injection site pain (23 events in 5 participants) and pruritus (8 events in 4 participants). There were no clinically significant changes in vital signs or laboratory values. None of the participants that received RPh201 had worsening of visual acuity and/or visual field in the fellow eye.

**Conclusions:**

Safety of RPh201 was demonstrated, and the encouraging efficacy results support a larger clinical trial in patients with previous NAION.

**References:** None.

**Keywords:** Optic neuropathy

**Financial Disclosures:** Consultant to Regenera, as well as to Aerie, Inotek, Quark, and Teva

**Grant Support:** None.

**Poster 148**

**The Spectrum of Pauci-Symptomatic Isolated Unilateral Optic Nerve Head Edema (IUONHE)**

Eman Hawy<sup>1</sup>, Jason Peragallo<sup>1</sup>, Beau Bruce<sup>1</sup>, Michael Dattilo<sup>1</sup>, Nancy Newman<sup>1</sup>, Valerie Biousse<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology, Emory University School of Medicine, Atlanta, Georgia, USA*

**Introduction:**

Isolated unilateral optic nerve head edema (IUONHE) with normal visual function is relatively rare, often prompting numerous investigations. Negative workup frequently presumes a diagnosis of “papillophlebitis.” We report 28 patients with IUONHE, describing the natural history and final diagnoses.

**Methods:**

28 IUONHE patients with detailed systematic workup and ≥1 year of followup were identified. Demographics, details of workup, final diagnosis, duration of IUONHE prior to resolution or visual loss, and visual outcome were recorded.

**Results:**

9/28 patients had intracranial hypertension with unilateral papilledema related to idiopathic intracranial hypertension (IIH). All IIH patients were obese and had signs of intracranial hypertension on MRI/MRV. Diagnosis of IIH was made 1-32 months after presentation. 5/28 patients had an optic nerve sheath meningioma (ONSM) with evidence of IUONHE for 1-240 months before diagnosis of ONSM, with poor visual outcomes in patients with delayed diagnosis (lack of appropriate imaging at presentation). 2/28 patients had an orbital mass (one vascular malformation, one orbital extension of an intracranial mass). 3/28 patients had vitreo-papillary traction (VPT), diagnosed 1 week-7 months after presentation. 4/28 patients had incipient nonarteritic anterior ischemic optic neuropathy (NAION); all were >60 yo with discs-at-risk. IUONHE spontaneously resolved within 3-11 months in 3/4 patients; one developed visual loss from NAION 4 months after presentation. 1 patient had a peripapillary choroidal neovascular membrane (CNV) diagnosed 6 weeks after presentation. 4/28 patients (age 21-37yo, 4 women) remained without definite diagnosis and were classified as presumed “papillophlebitis”. All had persistent IUONHE with normal visual function up to 42 months after presentation.

**Conclusions:**

A systematic approach to the evaluation of IUONHE led to a definite diagnosis in 24/28 patients. The diagnosis of “papillophlebitis” remains controversial and poorly defined. The good visual prognosis of patients with unexplained IUONHE remains reassuring. A systematic diagnostic approach should result in earlier diagnosis and improved outcomes.

**References:** None.

**Keywords:** Orbit, Pseudotumor Cerebri, Neuroimaging, Optic neuropathy, Tumors

**Financial Disclosures:** No conflict of interest Supported by Research to Prevent Blindness

**Grant Support:** Supported by Research to Prevent Blindness

**Poster 149****Mitochondrial Haplogroup V/HV is Associated with Sequential NAION**

Marisa Tieger<sup>1</sup>, Eric Gaier<sup>1</sup>, Joseph Rizzo III<sup>1</sup>, Janey Wiggs<sup>1</sup>, Dean Cestari<sup>1</sup>

<sup>1</sup>*Massachusetts Eye and Ear, Boston, Massachusetts, USA*

**Introduction:**

Non-arteritic anterior ischemic optic neuropathy (NAION) is associated with vascular risk factors and a small cup to disc ratio, but the underlying etiology of NAION remains unclear. Molecular defects in mitochondrial function are associated with several heritable optic neuropathies, and we hypothesized that one or more particular mitochondrial haplogroups may be associated with and/or influence the clinical course of NAION.

**Methods:**

We retrospectively identified patients diagnosed with NAION between 2006 and 2016 and prospectively enrolled newly diagnosed patients for mitochondrial genome sequencing. Two control groups were used for comparison of haplogroup distribution: 1. Whole exome database (1283 patients), Ocular Genomics Institute; 2. POAG control group (1886 patients). We separately made clinical comparisons with the NAION group across haplogroups.

**Results:**

Seventy-nine Caucasian patients were genotyped. On retrospective review of the medical records, 3 patients were excluded from the analysis: 1 for highly atypical disease, 2 had taken amiodarone. Haplogroup V/HV was over-represented among patients with NAION compared to each control group (9/76 NAION; 56/1253 and 59/1886 controls; p values < 0.009). Haplogroup V/HV was overrepresented among patients with sequential NAION compared to those with unilateral disease (7/25 bilateral, 1/50 unilateral; p = 0.0015) (one patient was excluded due to optic atrophy of unknown etiology in one eye). Systemic hypertension and diabetes was reported by 37/76 (48%) and 18/76 (23.7%) patients, respectively, and haplogroup V/HV was not associated with systemic hypertension or diabetes individually or when combining these risk factors, arguing that the association of haplogroup V/HV is not secondary to a relationship with vascular risk factors.

**Conclusions:**

We provide preliminary evidence that mitochondrial haplogroup V/HV is associated with sequential NAION. If supported with larger numbers of patients, these results may represent a molecular risk factor for NAION that could provide new insight into the pathogenesis of NAION and valuable prognostic information for patients.

**References:** None.

**Keywords:** Optic neuropathy, Genetic Disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 150**

**Are the 2016 Guidelines on the Neuro-ophthalmic Evaluation of Pituitary Adenomas Already Obsolete?**

Jonathan Micieli<sup>1</sup>, Richard Blanch<sup>1</sup>, Eman Hawy<sup>1</sup>, Jason Peragallo<sup>1</sup>, Kannan Narayana<sup>1</sup>, Nancy Newman<sup>1</sup>, Valerie Biousse<sup>1</sup>

<sup>1</sup>Emory Eye Center, Emory University, Atlanta, Georgia, USA

**Introduction:**

The 2016 neurosurgical guidelines on pretreatment ophthalmology evaluation in patients with pituitary adenomas recommend pre-operative, “optical coherence tomography (OCT) to measure both retinal nerve fiber layer (RNFL) thickness and the presence of damage to the ganglion cell layer (GCL) on algorithms that segment the macular cube,” to assess prognosis for visual recovery[1]. Although RNFL and GCL thickness are routinely used to predict recovery of visual function after treatment[2-4], the importance of OCT for compressive optic neuropathy/chiasmopathy diagnosis is less well recognized. We report a patient series with sellar masses causing mass effect on the anterior visual pathways, normal visual fields (VF) but binasal decreased GCL thickness, suggesting preclinical evidence of compression.

**Methods:**

12 patients seen for assessment and monitoring of sellar lesions causing mass effect on the optic chiasm without definite VF defect, but abnormal GLC were included. VFs were classified as suspicious or not for chiasmal compression. GCL/RNFL analyses using Cirrus-OCT were classified into percentiles based on the manufacturer’s reference range.

**Results:**

In 6/12 cases, VFs were completely normal. GCL analysis was less than 1% in all cases. RNFL analysis was in the reference range in 2/6 cases and less than 5%/greater than 1% in 2/6 and less than 1% in 2/6. In 6/12 cases, VFs were suspicious for, but not diagnostic of, chiasmal compression. All had GCL less than 1% or clear binasal loss. RNFL was normal in 2/6, less than 5%/greater than 1% in 3/6, and less than 1% in 1/6.

**Conclusions:**

In our patients, macular GCL analysis was more sensitive than VFs in detecting chronic chiasmal compression, suggesting that GCL analysis is an essential test in the diagnosis of compressive optic neuropathy, even before VFs become abnormal. Macular GCL analysis should be obtained in all patients with radiologic evidence of anterior visual pathway compression even when VFs appear normal.

**References:** 1. Newman SA, Turbin RE, Bodach ME, et al. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guideline on Pretreatment Ophthalmology Evaluation in Patients With Suspected Nonfunctioning Pituitary Adenomas. *Neurosurgery* 2016;79(4):E530-2. 2. Danesh-Meyer HV, Wong A, Papchenko T, et al. Optical coherence tomography predicts visual outcome for pituitary tumors. *J Clin Neurosci* 2015;22(7):1098-104. 3. Horton JC. Invited Commentary: Ganglion Cell Complex Measurement in Compressive Optic Neuropathy. *J Neuroophthalmol* 2017;37(1):13-5. 4. Vuong LN, Hedges TR, 3rd. Ganglion cell layer complex measurements in compressive optic neuropathy. *Curr Opin Ophthalmol* 2017;28(6):573-8.

**Keywords:** Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Skull Base, Tumors, Visual fields

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 151**

**Retinal Ganglion Cell and Nerve Fiber Loss in Autosomal Dominant Optic Atrophy:Correlations with Visual Functions**

Jin Choi<sup>1</sup>, Jae Yong Park<sup>1</sup>, Won Hyuk Oh<sup>1</sup>

<sup>1</sup>*Inje University Sanggye Paik Hospital, Seoul, Korea, Republic of*

**Introduction:**

To investigate the peripapillary retinal nerve fiber layer (RNFL) thickness and macular retinal ganglion cell layer (RGC) thickness of the autosomal dominant optic atrophy (ADOA) patients and correlate them with visual acuity and visual field parameters.

**Methods:**

34 eyes from 17 patients diagnosed as ADOA and 34 eyes from 17 age-matched healthy subjects were included in the study. Peripapillary RNFL scan and posterior pole scan was conducted with optical coherence tomography (OCT). Early Treatment of Diabetic Retinopathy Study (ETDRS) macular grid was applied on the segmented posterior pole scan to measure the RGC thickness of the 9 sectors. Correlations between RNFL thickness, RGC thickness and the best corrected visual acuity (BCVA), mean deviation (MD) of Humphrey visual field 30-2 test were studied.

**Results:**

Mean visual acuity of patients with ADOA was  $0.33 \pm 0.27$  in logMAR. RNFL thickness of general, temporal, inferotemporal and nasal sectors, and the RGC thickness of all 9 sectors was thinner in patients with ADOA than in healthy subjects ( $p < 0.001$ ). Temporal RNFL thickness showed significant correlation with BCVA ( $r = -0.434$ ,  $p < 0.05$ ). RGC thickness of the inner superior, inner temporal, inner inferior, inner nasal sector correlated with BCVA ( $r = -0.583$ ,  $r = -0.581$ ,  $r = -0.507$ ,  $r = -0.538$ , respectively.  $p < 0.05$ ), whereas RGC thickness of the outer superior, outer temporal, outer inferior, outer nasal sector correlated with MD ( $r = 0.466$ ,  $r = 0.349$ ,  $r = 0.483$ ,  $r = 0.470$ , respectively.  $p < 0.05$ ).

**Conclusions:**

Damage of the RGC in inner sectors influences the visual acuity, whereas the loss of RGC in outer sectors affects the visual field in ADOA. The decrease of the temporal RNFL thickness correlated with the BCVA as well. OCT may therefore be useful in predicting the visual functions of the ADOA patients.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Genetic Disease, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 152

### Long Term Treatment with Idebenone in Leber's Hereditary Optic Neuropathy (LHON): Real World Clinical Practice

Xavier Llòria<sup>1</sup>, Claudia Catarino<sup>2</sup>, Magda Silva<sup>1</sup>, Bettina von Livonius<sup>3</sup>, Constanze Gallenmüller<sup>2</sup>, Felice Lob<sup>3</sup>, Günther Rudolph<sup>3</sup>, Oskars Mikazans<sup>2</sup>, Thomas Klopstock<sup>2</sup>

<sup>1</sup>Santhera Pharmaceuticals, Liestal, Switzerland, <sup>2</sup>Friedrich-Baur-Institute, Department of Neurology, Munich, Germany, <sup>3</sup>Department of Ophthalmology, University Hospital of the Ludwig-Maximilian University, Munich, Germany

#### Introduction:

LHON is caused by mitochondrial DNA (mtDNA) mutations, resulting in progressive bilateral, severe central blindness. Idebenone (900 mg/day) is approved for use in LHON in the EU. We report long-term treatment outcomes in real-world clinical practice from a multicenter Expanded Access Program.

#### Methods:

LHON patients with a confirmed mtDNA mutation, symptom onset <1 year (most recent eye), were treated with idebenone and monitored per normal clinical practice. Efficacy was assessed as clinically-relevant recovery (CRR; from off-[EDTRS] chart to reading 5 letters, or 10 letters' on-chart improvement) or clinically-relevant stabilization (CRS; maintenance of VA <1.0 logMAR (20/200)).

#### Results:

87 patients provided efficacy data. Initial CRR was achieved in 47.1% (41/87) patients, between 2.5 and 26.5 months post-baseline; magnitude of response increased with maintained treatment. Demographic/ baseline characteristics were similar in responders vs non-responders. In eyes without CRR, the time to nadir from BL was longer (~35 months) vs eyes with CRR responders (~14 months). In non-CRR eyes, 24% stopped treatment before 12 months. CRS was observed in 50.0% (12/24) of patients after mean treatment duration of 28.2 months. CRR was achieved by 5/7 eyes where onset was >1 year. No new safety signals were observed.

#### Conclusions:

Idebenone was well tolerated and was associated with both significant recovery of lost vision, and stabilization of good residual VA. Treatment of at least 18-24 months maximised the probability of observing initial CRR. Continued treatment resulted in improved CRR response. Early interruption could be a factor in lack of response.

**References:** [1] Carelli V et al. J Neuroophthalmol. 2017 Dec;37(4) 371-381. doi:10.1097/wno.0000000000000570. PMID: 28991104. [2] Newman, N. J. Nat. Rev. Neurol. 2012; doi:10.1038/nrneurol.2012.167. [3] Raxone® Summary of Product Characteristics (SmPC). European Medicines Agency, 2015. Available at: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Product\\_Information/human/003834/WC500193836.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003834/WC500193836.pdf); Raxone is NOT approved for use in LHON in the US and Canada.

**Keywords:** Optic neuropathy

**Financial Disclosures:** Dr X. Llòria is a full time employee at Santhera Pharmaceuticals

**Grant Support:** None.

## Poster 153

### Color Contrast Sensitivity in Age-Related Macular Degeneration

Danielle Leong<sup>1</sup>, Heather McLeod<sup>1</sup>, Anya Hariprasad<sup>2</sup>, Leonard Messner<sup>1</sup>

<sup>1</sup>Illinois Eye Institute, Illinois College of Optometry, Chicago, Illinois, USA, <sup>3</sup>University of Chicago Laboratory Schools, Chicago, USA

#### Introduction:

As the global population ages, prevalence of age-related macular degeneration (AMD) is rapidly increasing. Sensitive methods to detect early disease progression can improve outcomes. Contrast sensitivity has been shown to be a sensitive measure of visual function.<sup>1</sup> Similarly, color vision loss is one of the earliest manifestations of retinal disease.<sup>2</sup> Previously studied in Parkinson's Disease<sup>3</sup> and amyotrophic lateral sclerosis,<sup>4</sup> the King-Devick Variable Color Contrast Sensitivity Chart (VCCSC) iPad application offers portable availability and variable illumination compared to retro-illuminated chart-types. This pilot study aimed to determine which color contrast sensitivity differences exist in non-exudative AMD (NE-AMD) to develop a baseline for a larger study utilizing this technology in detecting AMD conversion particularly in high risk patients.

#### Methods:

Monocular best corrected visual acuity (BCVA) at 40cm with 100% black contrast was determined for NE-AMD patients (n=13) and controls (n=31). Utilizing the BCVA line, the number of letters correctly identified (out of 5) was recorded for various color presentations (red, green, blue, yellow) and at decreasing contrast levels (75%, 50%, 25%).

#### Results:

NE-AMD patients demonstrated approximately 2 lines worse visual acuity under 100% black letter presentation (median: 0.5 LogMAR [range: 0.09-1.4] vs. 0.3 [0-0.7], p=0.0028). At BCVA, there was no significant difference between controls and NE-AMD patients in the number of letters identified at various contrast and color settings, however blue at various contrast trended toward worsening in NE-AMD.

#### Conclusions:

In this cohort, no color contrast differences were demonstrated between controls and NE-AMD patients. This pilot study supports our desire to perform a larger study to use the King-Devick Variable Color Contrast Sensitivity Chart (VCCSC) iPad application to compare color contrast sensitivity between controls, NE-AMD, and Exudative AMD (E-AMD) patients. Given the results of the current study, we are hopeful that E-AMD patients will have decreased contrast sensitivity compared to both normal controls and NE-AMD patients supporting the widespread use of the VCCSC to detect early conversion to E-AMD in all elderly individuals.

**References:** 1. Balcer L, Raynowska J, Nolan R, et al. Validity of low-contrast letter acuity as a visual performance outcome measure for multiple sclerosis. *Mult Scler J*. 2017; In Press. 2. Arden GB, Wolf JE. Colour vision testing as an aid to diagnosis and management of age related maculopathy. *Br J Ophthalmol*. 2004;88(9):1180-1185. doi:10.1136/bjo.2003.033480. 3. Lin TP, Rigby H, Adler JS, et al. Abnormal visual contrast acuity in Parkinson's disease. *J Parkinsons Dis*. 2015;5(1):125-130. doi:10.3233/JPD-140470. 4. Boven L, Jiang Q, H M. Validation of Strategies to Streamline High and Low Contrast Acuity testing in ALS Subjects. Poster Presentation American Academy of Neurology 2015 Annual Meeting. 2015.

**Keywords:** Higher visual functions, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** Dr. Leong is employed by King-Devick technologies as a Director of Research. She did not participate in data collection and all data was made available to all authors.

**Grant Support:** We would like to acknowledge the generous research grant support from the Illinois Society for the Prevention of Blindness.

**Poster 154**

**Analysis of Nonarteritic Anterior ischemic Optic Neuropathy demography in Mexico**

Graciela Garcia Briones<sup>1</sup>

<sup>1</sup>*hospital de Nuestra Señora de la Luz, Ciudad de Mexico, Mexico*

**Introduction:**

Background: Anterior ischemic Optic Neuropathy is commonly seen in a Neuroophthalmology practice. Two intriguing aspects are its relation to cataract surgery and the time or risk of second eye involvement.

**Methods:**

Methods: We performed a cross sectional study of 174 non arteritis Anterior ischemic Optic Neuropathy eyes in 164 patients to assess clinical outcome.

**Results:**

Results: The average age of NAION was 59 years. Kaplan Mayer survival curve showed that age >50 years at NOION onset was associated with greater risk of second eye involvement. The most common eye involved is the left eye with a visual field characterized by a nasal inferior loss. We also found 24 to 48 hours after cataract surgery (phacoemulsification) even without complications to be the time to present NAION in the operated eye. This are preliminary results

**Conclusions:**

Conclusions: We Showed that NAION onset at age >59 years had greater risk of second eye involvement. And the short period of time after cataract surgery to develop NAION.

**References:** Sun and Liao J Neuro-ophthalmology 2017; 37:258-264

**Keywords:** Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



## Poster 155

### The Epidemiology of Pediatric Visual Pathway Injuries – Analysis of the National Trauma Data Bank

Ryan Gise<sup>1</sup>, Timothy Truong<sup>1</sup>, Afshin Parsikia<sup>2</sup>, Joyce Mbekeani<sup>3</sup>

<sup>1</sup>Montefiore Medical Center/ Albert Einstein College of Medicine, Bronx, New York, USA, <sup>2</sup>Department of Surgery, Jacobi Medical Center, Bronx, New York, USA, <sup>3</sup>Department of Surgery (Ophthalmology), Jacobi Medical Center and Albert Einstein COM, Bronx, New York, USA

#### Introduction:

Traumatic visual pathway injuries (VPI) often are associated with severe head trauma can have profound and deleterious effects on developing children. We sought to elucidate the epidemiology of pediatric VPI in the US.

#### Methods:

A retrospective evaluation of pediatric patients (<21years) with VPI, submitted to the NTDB (2008-2014), was conducted using ICD-9 codes. Statistical analysis was performed with SPSS software. Variables were correlated using students' t and Chi-squared tests and logistic regression analyses. Statistical significance was set at p<0.05.

#### Results:

970 (1.7%) of 58,765 pediatric patients admitted with ocular injuries had VPI. The majority were male (69.2%) and the average age (SD) was 11.6(7.2) years. 55.4% were White, 20.5%, Black and 17.7, Hispanics. The mean injury severity score (ISS) was "severe" at 21 (SD=13). The mean GCS was 9.6 (SD 5.4). Traumatic optic neuropathy (TON) was the most common (86.1%) VPI, followed by visual cortex (3.3%). Of all intracranial nerves, TON had the greatest odds of occurring with oculomotor nerve injury (OR=3.84, 95%CI=2.18-6.74; p<0.001). Associated ocular injuries were open adnexa wounds (87.4%), orbital fractures (23%) and contusions (22.8%). Common mechanisms were motor vehicle-occupant (MVTO) (21.5%), firearms (15.6%) and struck by/against (11.6). MVTO were most likely in Whites (OR=1.48, 95%CI=1.08-2.03; p<0.015) and firearms in Blacks (OR=4.86, 95%CI=3.34-7.07; p<0.001). In the 0-3year age group, VPI were mostly due to falls (OR=2.88, 95%CI=1.77-4.69) and home location (OR=11.84, 95%CI 8.3-16.9); p<0.001 while the 19-21year group had the greatest association with firearms (OR=2.65, 95%CI=1.79-3.93) and street location (OR=2.52, 95%CI=1.82-3.5); p<0.001. Overall mortality was 17.6%.

#### Conclusions:

VPI occurred in both major and minor ocular injuries. The clear majority were TON that mostly were associated with oculomotor neuropathy. The common mechanisms, MVTO and firearms, revealed age and race disparity. Although infrequent, VPI may have devastating sequelae and should be considered in pediatric ocular injuries.

**References:** Ford RL, Lee V, Xing W, Brunce C. A 2 Year Prospective Surveillance of Pediatric Traumatic Optic Neuropathy in the United Kingdom. J AAPOS; 16: 413-417, 2012. Garcia TA, McGetrick BS, Janik JS, Spectrum of Ocular Injuries in Children with Major Trauma. J Trauma; 59:169-174, 2005 Goldenberg-Cohen N, Miller NR, Repka MX. Traumatic Optic Neuropathy in Children and Adolescents. J AAPOS ;8: 20-27, 2004. Shokunbi T and Agbeja A. Ocular Complications of Head Injury in Children. Child's Nerv Syst; 7: 147-149, 1991. Ventura RE, Balcer LJ, Galetta SL. The Neuro-Ophthalmology of Head Trauma. Lancet Neurol; 13:1006-1016, 2014.

**Keywords:** Optic nerve trauma and treatment, Optic neuropathy, Pediatric neuro-ophthalmology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 156**

**A Patient Questionnaire to Assess the Psychosocial Impact of Visual Loss in Optic Nerve Disorders**

Rebecca Kay<sup>1</sup>, Matthew Kay<sup>2</sup>

<sup>1</sup>*Pine Crest School, Fort Lauderdale, Florida, USA*, <sup>2</sup>*Larkin Community Hospital, Miami, Florida, USA*

**Introduction:**

Although a significant literature exists describing the impact upon quality of life (QOL) related to visual loss from multiple sclerosis/optic neuritis and other optic neuropathies including glaucoma, there is a paucity of publications addressing the psychological impact of visual loss secondary to optic nerve disorders. The existing reports generally employ the NEI Visual Functioning Questionnaire-25 (VFQ-25) when assessing the effect of visual deficits on QOL. However, the VFQ-25 predominantly addresses the effect of visual loss on functionality in terms of performing common visually-guided tasks (e.g. picking and matching clothes, viewing live sporting events, navigating curbs in dim illumination). We have designed a novel self-administered patient questionnaire focusing upon the psychosocial ramifications of visual loss in contrast to the VFQ-25's emphasis on visual function.

**Methods:**

We designed a self-administered 23 item questionnaire addressing premorbid psychological history and subsequent psychosocial impact of visual loss. Inquiry includes symptoms of hostility, anxiety, and depression and whether counselling or treatment for these symptoms was sought. Additional questions address impact upon sleep, fear when performing daily activities, loss of self-esteem, social withdrawal, suicidal ideation, and denial, anger, and acceptance of visual loss.

**Results:**

Use of this form, which takes 5-10 minutes to complete, has identified numerous patients with depression, suicidal ideation, and other impairments facilitating prompt initiation of psychiatric evaluations and referrals for physical and occupational therapy and social services.

**Conclusions:**

Whereas the VFQ-25 focuses on visual functionality, our questionnaire emphasizes the psychosocial ramifications of visual loss and can be utilized when conducting studies investigating the psychological impact of visual loss as stratified by diagnosis, ethnicity, level of education, antecedent psychological disorders, visual acuity, and age at onset of visual loss among other parameters. Although our questionnaire was developed for use in evaluating patients with optic neuropathies, it can be utilized in patients with visual loss from any etiology.

**References:** 1. Moschos, M, Physiology and Psychology of Vision and Its Disorders: A Review, Med Hypothesis Discov Innov Ophthalmol, 3(3): 83-90, 2014 2. Jasse, L et al, Persistent Visual Impairment in Multiple Sclerosis: prevalence, mechanisms, and resulting disability, Mult Scler, 19(12), 1618-26, 2013 3. Bailie, M, et al, Visual and Psychological Morbidity Among Patients with Autosomal Dominant Optic Atrophy, Acta Ophthalmol, 91(5), e413-e414, 2013

**Keywords:** Optic neuropathy, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 159**

**Correlation of Visual Field Loss with MRI Findings in Patients with Pituitary Tumours**

Christian Lueck<sup>1</sup>, Emily Kane<sup>2</sup>, Kate Reid<sup>3</sup>, David Ashton<sup>4</sup>

<sup>1</sup>Department of Neurology, The Canberra Hospital, Canberra, Australia, <sup>2</sup>Australian National University Medical School, Canberra, Australia, <sup>3</sup>Department of Ophthalmology, The Canberra Hospital, Canberra, Australia, <sup>4</sup>Department of Radiology, The Canberra Hospital, Canberra, Australia

**Introduction:**

The exact mechanism which gives rise to bitemporal hemianopia in chiasmal compression by pituitary tumors is currently unknown. One theory suggests that it is simply the fact that crossing fibres cross each other, resulting in less surface area of contact and, in turn, greater stress from compressive forces than are experienced by uncrossed fibres. Finite element modelling has been used to investigate this in silico but the hypothesis needs testing in vivo. This study aimed to determine whether extrinsic chiasmal compression was associated with patterns of visual field loss which supported the 'crossing hypothesis' or predictions based on the anatomy.

**Methods:**

Subjects with chiasmal compression secondary to pituitary tumours who also had clear visual field abnormalities were identified from the Canberra Hospital database. Visual fields were analysed to derive 'temporality' and 'bitemporality' indices. MRI scans were analysed to determine the relative elevations of centre and peripheral portions of the optic chiasm and, in turn, the eccentricity of compression. Temporality indices were plotted against central chiasmal elevation, and both temporal and nasal hemifield abnormalities were plotted against eccentricity.

**Results:**

In total, 122 patients were identified, but only 12 were suitable for analysis. Both temporality and bitemporality indices were significantly correlated with central chiasmal elevation. Hemifield studies demonstrated patterns of visual loss with increasing eccentricity which were more consistent with the 'crossing hypothesis', though the correlations failed to reach significance.

**Conclusions:**

This study provides tentative support for the 'crossing hypothesis'. The information will be used to inform further finite element models of chiasmal compression. A larger, prospective study is warranted.

**References:** None.

**Keywords:** Neuroimaging, Visual fields, Tumors, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 160

### Misdiagnosis of Optic Nerve Sheath Meningiomas (ONSM): A Serious Problem

Pinar Koysak<sup>1</sup>, Caroline Vasseneix<sup>2</sup>, Jason Peragallo<sup>2</sup>, Beau Bruce<sup>2</sup>, Nancy Newman<sup>2</sup>, Valérie Biousse<sup>2</sup>

<sup>1</sup>Marmara University School of Medicine, Istanbul, Turkey, <sup>2</sup>Emory University School of Medicine, Atlanta, Georgia, USA

#### Introduction:

The diagnosis of ONSM is often delayed, potentially resulting in worse visual outcomes. The aim of our study was to identify factors contributing to missed or delayed diagnosis of ONSM.

#### Methods:

Retrospective review of >15yo patients with ONSM seen between 2002-2017. The Diagnosis Error Evaluation and Research (DEER) taxonomy tool was applied to cases with missed/delayed diagnoses.

#### Results:

We included 35 unilateral ONSM patients (30W, mean age 45yo [range 16-72yo]): 25/35 (71%) had diagnosis delayed by diagnostic errors for an average of 64 months [range 1 month-29years]. Patients with misdiagnosis saw more providers (2.9 [1-6]) and attended more office visits (4.31 [1-11]) than patients correctly diagnosed with ONSM initially (1.2 [1-2] for both). The most common diagnostic error (19/25,76%) was clinician assessment failure (errors in hypothesis generation and weighing), followed by errors in diagnostic testing (15/25,60%). The most common misdiagnosis was optic neuritis (12/25,48%), followed by failure to recognize optic neuropathy in patients with ocular disorders. Five misdiagnosed patients (20%) underwent unnecessary LP, 12 patients (48%) unnecessary laboratory tests, 6 patients (24%) unnecessary steroids. Among the 16 misdiagnosed patients later correctly diagnosed at our institution, 12 had prior MRIs read as normal: 5 showed the ONSM but were misread by a non-neuroradiologist and 7 were performed incorrectly (no orbital sequence or no contrast). 16/25 (64%) of the misdiagnosed patients had poor visual outcome compared with 3/10 (30%) without diagnostic delay.

#### Conclusions:

Biased pre-established diagnoses, failure to order the correct test (MRI brain/orbits with contrast), and failure to correctly interpret MRIs were the most common sources of diagnostic error and contributed to a major delay in correct diagnosis with worse visual outcomes and increased cost (greater number of office visits and ancillary tests). Easier access to neuro-ophthalmologists, improved diagnostic strategies, and education regarding orbital imaging should help prevent diagnostic errors and improve visual outcomes.

**References:** 1) Fisayo A, Bruce BB, Newman NJ, Biousse V. Overdiagnosis of idiopathic intracranial hypertension. *Neurology* 2016; 86: 341-50. 2) Shapey J, Sabin HI, Danesh-Meyer HV, Kaye AH. Diagnosis and management of optic nerve sheath meningiomas. *J Clin Neurosci* 2013; 20: 1045-56. 3) Schick U, Jung C, Hassler W. Primary optic nerve sheath meningiomas: a follow-up study. *Cen Eur Neurosurg* 2010; 71: 126-33. 4) Schiff GD, Kim S, Abrams R, Cosby K, Lambert B, et al. Diagnosing diagnosis errors: lessons from a multi-institutional collaborative project. In: Henriksen K, Battles JB, Marks ES, Lewin DI, editors. *Advances in Patient Safety: From Research to Implementation (Volume 2: Concepts and Methodology)*. Rockville, MD: Agency for Healthcare Research and Quality (US); 2005: 255-78. 5) Schiff GD, Hasan O, Kim S, Abrams R, Cosby K, et al. Diagnostic error in medicine: Analysis of 583 physician-reported errors. *Arch Intern Med* 2009; 169: 1881-87.

**Keywords:** Optic neuropathy, Neuroimaging

**Financial Disclosures:** Study supported by a department grant from Research to Prevent Blindness

**Grant Support:** Study supported by a department grant from Research to Prevent Blindness.

## Poster 161

### Baseline Characteristics of LHON Subjects in the RESCUE and REVERSE Phase III Gene Therapy Trials

Mark Moster<sup>1</sup>, Catherine Vignal<sup>2</sup>, Nancy Newman<sup>3</sup>, Alfredo Sadun<sup>4</sup>, Patrick Yu-Wai-Man<sup>5</sup>, Valerio Carelli<sup>6</sup>, Thomas Klopstock<sup>7</sup>, Adam Debusk<sup>8</sup>, Robert Sergott<sup>9</sup>, Molly Scannel Bryan<sup>10</sup>, Jose-Alain Sahel<sup>11</sup>, Barrett Katz<sup>12</sup>, Scott Uretsky<sup>13</sup>

<sup>1</sup>Wills Eye Hospital and Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, Pennsylvania, USA, <sup>2</sup>Fondation A de Rothschild, Paris, France, <sup>3</sup>Emory, Atlanta, Georgia, USA, <sup>4</sup>Doheny Eye Institute and UCLA, Los Angeles, California, USA, <sup>5</sup>Wellcome Trust Centre and Moorfields Eye Hospital, London, United Kingdom, <sup>6</sup>University of Bologna, Bologna, Italy, <sup>7</sup>Friedrich-Baur-Institute, University Hospital of LMU, Munich, Germany, <sup>8</sup>Wills Eye Hospital, Philadelphia, Pennsylvania, USA, <sup>9</sup>Wills Eye Hospital and Optic Nerve Research Center, Philadelphia, Pennsylvania, USA, <sup>10</sup>University of Illinois, Chicago, Illinois, USA, <sup>11</sup>Sorbonne Universites and University of Pittsburgh, Paris and Pittsburgh, France, <sup>12</sup>Albert Einstein College of Medicine, New York, New York, USA, <sup>13</sup>Gensight Biologics, Paris, France

#### Introduction:

RESCUE and REVERSE are Phase-III, randomized, multicenter, double-masked, sham-controlled trials of rAAV2/2-ND4, an intravitreally injected gene therapy for treatment of ND4-LHON. RESCUE subjects had vision loss for  $\leq 6$  months and REVERSE subjects from  $>6$  months up to 1 year.

#### Methods:

Inclusion criteria included age  $\geq 15$  years, G11778A-ND4 mutation, and CF vision or better. Concurrent idebenone was prohibited. We describe herein baseline characteristics of 64 subjects.

#### Results:

Of the first 64 subjects enrolled, eighty-three percent were male (RESCUE 24 of 27, REVERSE 29 of 37). Mean age (years): RESCUE 35.7; REVERSE 34.2. Mean duration of vision loss (days) for all eyes: RESCUE 119; REVERSE 271. Thirty-one percent of subjects had simultaneous bilateral onset. Mean LogMAR acuity at baseline for all eyes was: RESCUE 1.3; REVERSE 1.6. Mean LogMAR acuity for best-seeing eyes was: 1.1 in RESCUE and 1.5 in REVERSE. For worst-seeing eyes: 1.5 in RESCUE and 1.7 in REVERSE. For all eyes of all subjects, there was a significant positive correlation ( $r^2=0.238$ ) between duration of vision loss and baseline LogMAR acuity. Of reliable baseline HVFs, mean MD was  $-22.7$  (RESCUE) and  $-28.8$  (REVERSE). Mean of total macular volume (mm<sup>3</sup>) was smaller in REVERSE subjects (8.34 vs. 7.82) with significant thinning of the retinal nerve fiber and ganglion cell layers. Identifiable retinal structural anatomy correlated with acuity - with decreased RNFL and GCL associated with worse vision.

#### Conclusions:

Subjects were enrolled at expected gender prevalence. Acuities, fields, OCT, and HVF findings at study entry were consistent with previously defined LHON populations. The expected positive correlation between duration of vision loss and acuity, RNFL volume, GCL and macular volumes suggest our cohorts approximate real-world LHON patients; forthcoming study results should be applicable to a wider LHON population.

**References:** None.

**Keywords:** Genetic Disease, Optic neuropathy

**Financial Disclosures:** Research support from Gensight

**Grant Support:** Study Sponsored and Funded by Gensight Biologics

**Poster 162****The Epidemiology and Clinical Characteristics of Leber Hereditary Optic Neuropathy (LHON) in a Canadian Province.**

Colten Wendel<sup>1</sup>, Jiyoung Hwang<sup>1</sup>, Andre Mattman<sup>1</sup>, Hilary Vallance<sup>1</sup>, Claire Sheldon<sup>1</sup>

<sup>1</sup>University of British Columbia, Vancouver, BC, Canada

**Introduction:**

With promising clinical trials, there is a need for an accurate understanding of the epidemiology of LHON. This study aims to estimate the prevalence and describe the clinical presentation of LHON in a Canadian Province.

**Methods:**

In this province, all molecular testing for mitochondrial disorders is co-ordinated and documented through the Provincial Biochemical Genetics Laboratory. In a retrospective study, all subjects diagnosed with LHON between 1996-2016 were collated and clinical information was gathered.

**Results:**

We identified 44 subjects with genetically-confirmed LHON. In the mid-year point of the study, there were 3,444,285 people <65 years old. The minimum point prevalence for LHON within this population was 1.28 per 100,000 (95% CI 1.12-1.73 per 100,000). This is lower than seen in England and comparable to prevalence rates in Finland and Denmark. Heteroplasmy was present in 9% of cases. Of the 44 cases, 41 were LHON primary mutations (11778G>A, 14484T>C, and 3460G>A). Overall, subjects were 55% male, with an average age of symptom onset at 27.4 +/- 4.8 years. For those with symptomatic vision loss, the average time between fellow eye involvement was 2.7 +/- 0.9 months. The average wait time from initial onset of visual loss to diagnostic testing was 1.3 +/- 0.7 years. One patient was treated with idebenone. Clinical phenotype varied: there were 3 patients with MS-like illness with symptomatic white matter lesions, 2 with dystonia and 1 with a cardiac conduction abnormality. Finally, seven subjects experienced partial recovery of visual loss.

**Conclusions:**

Epidemiological information can help inform the patient population that may benefit from new treatments. In this province, nearly 2 in 50,000 people possess LHON mt DNA mutations, although there is a significant delay in diagnosis. Mechanisms to improve access to mitochondrial DNA testing is an important consideration in future healthcare policies given the emerging therapies for LHON.

**References:** 1. Chinnery et al., "The Epidemiology of Leber Hereditary Optic Neuropathy in the North East of England." *Am. J. Human Genetics*, 98, Page 1271, 2016. 2. Man, Turnbull, Chinnery., "Leber hereditary optic neuropathy." *J. Med Genetics*, 53, 493, 2016. 3. Nikoskelainen et al., "Epidemiology and penetrance of Leber hereditary optic neuropathy in Finland." *Eur. J. Human Genetics*, 15, 1079-1089, 2007. 4. Norby et al., "Primary pathogenic mtDNA mutations in multigeneration pedigrees with Leber hereditary optic neuropathy." *Am. J. Human Genetics*, 59, 481-5, 1996.

**Keywords:** Genetic Disease, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy, Neuroophth & systemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 163**

**Unilateral Pigmentary Retinopathy Associated with Multiple Sclerosis**

Eric Gaier<sup>1</sup>, Karen Jeng-Miller<sup>1</sup>, Rachel Huckfeldt<sup>1</sup>, Jason Comander<sup>1</sup>

<sup>1</sup>Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, USA

**Introduction:**

Unilateral retinitis pigmentosa (RP) is an incompletely characterized entity that can be mimicked by non-genetic disease processes including uveitis [1]. Although patients with uveitis have an approximately 10-fold elevated risk of developing multiple sclerosis (MS) [2], an association between MS and pigmentary retinopathy has not been described. Herein we report 5 cases of patients presenting with clinical diagnoses of unilateral RP and a history of MS.

**Description of Case(s):**

We describe 5 patients (ages 30-79, 2 men and 3 women) with unilateral pigmentary retinopathy who also reported a history of MS. Visual symptoms related to pigmentary retinopathy or uveitis predated the diagnosis of MS in 2/4 cases for whom details were available. None of the patients reported a family history of retinal degeneration, but one did have a family history of MS. Two patients reported a history of uveitis (pars planitis and presumed Eales disease), and 3 denied any history of ocular inflammation. Overall, patients exhibited relatively preserved visual acuity (range 20/20-20/30 Snellen) but constricted visual fields with some instances of far peripheral islands of sparing (Goldmann). No patients exhibited dyschromatopsia or relative afferent pupillary defects. Full-field electroretinography (ERG) showed reduced amplitudes and delayed implicit times in the affected eyes and normal responses in the contralateral eyes in all cases. Macular optical coherence tomography (OCT) showed peripheral loss of the ellipsoid zone line and associated photoreceptor bands in the affected eye only. Follow up evaluations with repeat testing on 3/5 patients (3, 4, 15 years) showed little or no change in visual function.

**Conclusions, including unique features of the case(s):**

The affected eyes in these cases mimic genetic RP. These cases of unilateral pigmentary retinopathy presenting with histories of MS may represent a previously unrecognized clinical association. If substantiated with further study, these results might suggest patients with unilateral RP would benefit from neurologic evaluation and screening for MS.

**References:** 1. Sevgi, D.D., et al., Retinal pigmentary changes in chronic uveitis mimicking retinitis pigmentosa. *Graefes Arch Clin Exp Ophthalmol*, [Epub ahead of print] 2017. 2. Cunningham, E.T., Jr., et al., Multiple Sclerosis-Associated Uveitis. *Ocul Immunol Inflamm*, 2017. 25(3): p. 299-301.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Demyelinating disease, Pupils Retina, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 164****Validation of a Symptom-Based Questionnaire for Pediatric CNS Neuroinflammatory Diseases**

Amy Waldman<sup>1</sup>, Anusha Yeshokumar<sup>2</sup>, Amy Lavery<sup>3</sup>, Geraldine Liu<sup>1</sup>, Stacy Pineles<sup>4</sup>, Michael Repka<sup>5</sup>, Laura Adang<sup>1</sup>, Sona Narula<sup>1</sup>, Grant Liu<sup>1</sup>

<sup>1</sup>Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA, <sup>2</sup>Icahn School of Medicine at Mt. Sinai, New York, New York, American Samoa, <sup>3</sup>Centers for Disease Control, Atlanta, Georgia, USA, <sup>4</sup>University of California-Los Angeles, Los Angeles, California, USA, <sup>5</sup>Johns Hopkins Medicine, Baltimore, Maryland, USA

**Introduction:**

Optic neuritis (ON) may be an isolated disorder or a symptom of neuroinflammatory disease. An accurate diagnosis requires recognition of symptoms and examination abnormalities indicative of a multifocal neurologic disease or relapsing disorder. We sought to determine the ability of a symptom-based questionnaire to differentiate children with and without neuroinflammatory disease.

**Methods:**

Patients with isolated ophthalmologic symptoms and a normal brain MRI were compared to patients with confirmed pediatric-onset multiple sclerosis (MS) or neuromyelitis optica (NMO) according to consensus criteria. Participants completed a 21-item questionnaire to capture their recent ( $\leq 30$  days) and remote ( $> 30$  days) symptoms of neurologic dysfunction (maximum score 21 points). Responses were compared using t-tests, and only the 8 questions with significantly different responses between groups were retained in the modified questionnaire. Non-overlapping 95% confidence intervals [CI] between groups were used to determine a threshold score indicating neuroinflammatory disease. The sensitivity and specificity were calculated for both questionnaires.

**Results:**

We enrolled 51 subjects (ages 4 to 21 years; 30 [59%] were female): 25 with visual complaints and a normal brain MRI and 26 with MS or NMO. The mean total score for the MS/NMO group was 9.4 points (SD 5.0, 95% CI 7.4-11.4) compared to a total score of 5 points (SD 4.3, 95% CI 3.3-6.9) for the ophthalmology group ( $p=0.0017$ ). Using a score of 7 on the initial questionnaire as the cut-off to predict neuroinflammatory disease in a patient presenting with visual complaints, the sensitivity was 69%, and the specificity was 72%. The modified questionnaire had a sensitivity of 65% and a specificity of 92%.

**Conclusions:**

A symptom-based questionnaire can aid the clinician in identifying children with CNS neuroinflammatory disease. This questionnaire has been proposed as a screening tool to identify children with possible demyelination associated with ON for the Pediatric ON Prospective Outcomes Study.

**References:** None.

**Keywords:** Demyelinating disease, Pediatric neuro-ophthalmology

**Financial Disclosures:** I have received support from the NIH (K23NS069806).

**Grant Support:** NIH K23NS069806



**Poster 165****Inter-ocular Difference in Retinal Nerve Fiber Layer Thickness Predicts Optic Neuritis in Pediatric-onset Multiple Sclerosis**

Amy Waldman<sup>1</sup>, Leslie Benson<sup>2</sup>, John Sollee<sup>1</sup>, Amy Lavery<sup>3</sup>, Geraldine Liu<sup>1</sup>, Ari Green<sup>4</sup>, Gena Heidary<sup>2</sup>, Darrel Conger<sup>5</sup>, Jennifer Graves<sup>4</sup>, Benjamin Greenberg<sup>5</sup>

<sup>1</sup>Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA, <sup>2</sup>Boston Children's Hospital, Boston, Massachusetts, USA, <sup>3</sup>Center for Disease Control, Atlanta, Georgia, USA, <sup>4</sup>University of California San Francisco, San Francisco, California, USA, <sup>5</sup>UT Southwestern Medical Center, Dallas, Texas, USA

**Introduction:**

Optical coherence tomography (OCT) is a useful tool in determining retinal insult. Thinning of the retinal nerve fiber layer (RNFL) is typically defined as 2 standard deviations (SD) below a control population mean. We recently demonstrated in a single-center cohort of 24 pediatric-onset multiple sclerosis (POMS) participants using Cirrus OCT that this definition may miss pathology. Through our PERCEPTION collaboration, we explored whether the inter-ocular difference (IOD) in RNFL thickness informs on remote optic neuritis (ON) in a multi-center cohort.

**Methods:**

POMS (defined using consensus criteria and first attack <18 years) participants were recruited from 4 academic centers. A history of ON (>6 months prior to OCT scan) was confirmed by medical record review. RNFL was measured on Spectralis machines (Heidelberg, Germany). Absolute RNFL thinning was defined as RNFL thickness <86 microns based on a healthy control (HC) cohort also tested on Spectralis. An IOD  $\geq 8$  microns was defined as abnormal (exceeded 2 SD greater than the HC mean IOD). The proportions of POMS with monocular RNFL thinning (<86 microns) and those with an IOD  $\geq 8$  microns were calculated. Logistic regression was used to determine whether IOD predicted remote ON.

**Results:**

148 subjects with POMS (mean 15.5 years; 57 [39%] with remote ON) were enrolled. Absolute RNFL thinning occurred in 37 of 79 (46.8%) ON eyes and 34 of 217 (15.7%) non-ON eyes. An IOD  $\geq 8$  microns occurred in 41 participants, 26 (63%) with remote ON. An additional 15.6% of patients with normal RNFL values (>86 microns in both eyes) were confirmed to have ON by IOD criteria. An IOD  $\geq 8$  microns predicted remote ON using logistic regression ( $p=0.007$ ).

**Conclusions:**

The IOD in RNFL thickness should be considered when interpreting OCT results. For patients with RNFL thickness for each eye in the normal range, an IOD  $\geq 8$  microns may indicate remote ON.

**References:** Waldman AT, Liu GT, Lavery AM, Liu G, Gaetz W, et al. Optical coherence tomography and visual evoked potentials in pediatric MS. *Neurology, Neuroimmunology, and Neuroinflammation*. Volume 4(4). Page: e356. 2017.

**Keywords:** Demyelinating disease, Pediatric neuro-ophthalmology

**Financial Disclosures:** I was supported by a K23 award from the NIH (K23NS069806)

**Grant Support:** Dr. Waldman was supported by a career training award from the NIH (K23NS069806)

**Poster 166**

**Visual Function in Wolfram Syndrome**

An-Guor Wang<sup>1</sup>, Hui-Chen Cheng<sup>2</sup>

<sup>1</sup>Taipei Veterans General Hospital, National Yang-Ming University, Taipei, Taiwan, <sup>2</sup>Taipei Veterans General Hospital, Taipei, Taiwan

**Introduction:**

To characterize the visual function in Wolfram syndrome and literature review

**Methods:**

Retrospective review of the clinical records of Wolfram syndrome in the neuro-ophthalmic clinics of our hospital from 2005 to 2017.

**Results:**

A total of 5 cases were found with genetic confirmation of WFS1 gene mutations. Four males and one female patient were found, with an average age of 18.1 years. Case 1 and case 2 are siblings and have WFS1 gene mutations of c.1811G>A/c.2070\_2079delCAGCCACCTG. Case 3 has gene mutations of c.683G>C/c.683G>C. Case 4 and Case 5 were siblings with mutations of c.1546\_1548delTTC/c.2534\_T>G. For those three patients who have been observed over 1 year, they have onset of optic nerve involvement at 9.3 years of age. Their visions had a mean logMAR of 0.43 at onset, which deteriorated to logMAR 1.11 within of 7.3 years.

**Conclusions:**

Visual impairment typically onsets at 10 years of age in Wolfram syndrome. It commonly progressed gradually, and the patients will become legally blind in a few years.

**References:** None.

**Keywords:** Genetic Disease, Optic neuropathy, Pediatric neuro-ophthalmology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 167****Ischemic Optic Neuropathy and Renal Failure: Our Casuistry**

Mariana De Virgiliis<sup>1</sup>, Luciana Iacono<sup>1</sup>, M. Laura Braccia Gancedo<sup>1</sup>, Pablo Perez Vega<sup>1</sup>, Haydée Martínez<sup>2</sup>, Luciana Lagos<sup>1</sup>, Lidia Sarotto<sup>2</sup>, Dolores Riberó<sup>3</sup>

<sup>1</sup>Hospital Oftalmológico Dr. Pedro Lagleyze, Buenos Aires, Argentina, <sup>2</sup>Hospital de Clínicas José de San Martín, Buenos Aires, Argentina, <sup>3</sup>Hospital Británico de Buenos Aires, Buenos Aires, Argentina

**Introduction:**

The pathogenesis of Nonoarteric Anterior Ischemic Optic Neuropathy (NAION) primarily involves interference with the posterior ciliary artery blood supply to the prelaminar optic nerve. Patients with chronic renal failure often have coexisting pathology such as hypotension (decreased blood delivery), or hypertension, atherosclerosis (increased resistance to blood supply), and anemia (low blood oxygen carrying capacity), predisposing them to ischemic optic neuropathy. The purpose of this study is to describe a case series of patients with NAION and medical history of chronic renal failure and haemodialysis.

**Methods:**

Observational, retrospective and descriptive (case series) of medical records of patients with diagnosis of AION treated at the Neuro-Ophthalmology Section of a Public Hospital between January 2015 and October 2017.

**Results:**

6 patients between 26 and 70 years old with unilateral AION and chronic renal failure were diagnosed. All of them were under haemodialysis treatment. They underwent a complete neuroophthalmologic examination, complementary studies and received corticoid therapy.

**Conclusions:**

Chronic haemodialysis can be considered as a risk factor for ischemic optic neuropathy. ION related to hypotension most often presents in patients with chronic renal failure and dialysis. The accelerated diffuse vasculopathy that occurs in this disease may predispose to the development of ION, as may previous chronic hypertension, with possible arteriosclerosis and impaired autoregulation of the optic disc vascular supply.

**References:** None.

**Keywords:** Optic neuropathy, Vascular disorders, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 168**

**Antibodies to Myelin Oligodendrocyte Glycoprotein in Patients with Chronic Relapsing Inflammatory Optic Neuropathy**

Haeng-Jin Lee<sup>1</sup>, Boram Kim<sup>2</sup>, Patrick Waters<sup>3</sup>, Sung-Min Kim<sup>2</sup>, Seong-Joon Kim<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, Seoul National University College of Medicine, Seoul, Korea, Republic of, <sup>2</sup>Department of Neurology, Seoul National University, College of Medicine, Seoul, Korea, Republic of, <sup>3</sup>Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, Oxford, United Kingdom

**Introduction:**

We investigated the presence of myelin oligodendrocyte glycoprotein antibodies (MOG-Ab) in patients with isolated optic neuritis (ON) and evaluated the features in chronic relapsing inflammatory optic neuropathy (CRION) patients with MOG-Ab.

**Methods:**

The study population consisted of 45 patients with isolated ON, and 94 controls with multiple sclerosis (n=26), neuromyelitis optica spectrum disease with aquaporin-4 antibody (AQP4-Ab) (n=39), and neurological disease without inflammatory demyelinating disease (n=29) as controls. Both MOG-Ab and AQP4-Ab were tested using cell-based assay.

**Results:**

Of 12 patients fulfilled diagnostic criteria for CRION, 8 patients were positive for MOG-Ab. Mean age at first ON onset was  $49.5 \pm 7.6$  years and total number of attacks was  $4.4 \pm 2.1$  during total follow-up period of  $34.8 \pm 11.5$  months. Time interval among attacks was  $4.8 \pm 3.1$  months. Perineural enhancement of optic nerve was found in 85.7% patients. Good steroid responsiveness was found in 75.8% of patients and 87.5% of patients presented visual acuity more than 20/40 at final follow-up.

**Conclusions:**

The majority of CRION patients were positive for MOG-Ab presenting frequent attacks within short interval, rapid recovery after steroid treatment with dependency. The detection of MOG-Ab is important to diagnose the CRION.

**References:** None.

**Keywords:** Optic neuropathy, Demyelinating disease, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 169**

**Afferent System Disparity When Anatomy (OCT) and Psychophysics( Acuity and Perimetry) Fail to Meet**

Steven Newman<sup>1</sup>

<sup>1</sup>*University of Virginia, Charlottesville, Virginia, USA*

**Introduction:**

OCT has been a great advance in ophthalmology. In most cases, anatomic measurements parallel psychophysical findings (acuity and VF), but there are several reasons for disparity.

**Methods:**

Retrospective review of 59 patients coded as disparity.

**Results:**

In spite of 4th generation OCT, artifact still exists (usually anterior segment pathology). A second disparity arises from machine differences in algorithm. One commonly seen disparity where psychophysics looks better than OCT can be seen in patients with recovered optic neuritis. This phenomenon can be seen following optic nerve decompression. The most common (expected) disparity relates to delay in onset of anatomic changes following optic nerve pathology (acute optic neuritis, compressive optic neuropathy). A more interesting disparity can occur when NFL dropout may be obscured by disc edema due to compression at the orbital apex. This has traditionally been seen with nerve sheath meningiomas, but also may occur with other pathology in the orbital apex (tumors, other lesions, vascular malformations, and even thyroid orbitopathy). We call this “green disease” (OCT looks normal although the psychophysics are clearly affected). Ganglion cell segmentation algorithm seems to be less sensitive and may be abnormal, even when the NFL looks normal. A much less common anomaly is due to retinal disease. This may cause anomalies in the anatomy, although psychophysics continue to look relatively normal. Even the most common optic neuropathy (glaucoma) may occasionally demonstrate disparity between the anatomy and psychophysics. Transynaptic changes are much more obvious with ganglion cell analysis than NFL assessment and may not occur in all circumstances.

**Conclusions:**

OCT provides a quantitative reproducible assessment of anatomy of the retina and anterior visual pathways. Although in most cases this parallels psychophysical abnormalities (acuity and VF) cases with disparity can be very instructive. The increasing use of ganglion cell analysis may short out some of the previous abnormalities.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Visual fields, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 170**

**Baseline OCT Findings in Phase 3 RESCUE and REVERSE Trials**

Robert Sergott<sup>1</sup>, Barrett Katz<sup>2</sup>

<sup>1</sup>Wills Eye and Thomas Jefferson University, Philadelphia, Pennsylvania, USA, <sup>2</sup>Montefiore Medical Center, New York, New York, USA

**Introduction:**

rAAV2/2-ND4 is an investigational gene therapy facilitating allotopic transgene expression. We report baseline spectral domain OCT of the RNFL and GCL in two Phase 3 trials.

**Methods:**

39 subjects [RESCUE] and 37 [REVERSE] all with G11778A ND4 genotypes had qualitative and quantitative OCT of RNFL and retina with segmentation of all retinal layers, and topographic mapping at baseline. Analysis was masked to acuity, HVF results, fundus findings, and duration of visual loss. OCT data were analyzed by a central reading center.

**Results:**

RESCUE subjects' [visual loss 6 and <12 months] OCT patterns were more homogeneous with 73/74 eyes with thinning of PMB in all 4 quadrants and diffuse macular thinning. Macular thinning showed absolute loss in 44 eyes and relative loss in 30 eyes compared to a normative data base. All subjects had symmetric macula RNFL loss between the two eyes except for 14 with relative loss. Examples of representative OCT patterns will be shown.

**Conclusions:**

This is the first report of OCT findings in a Phase 3 gene therapy trial for LHON. Subjects with shorter duration of visual loss [RESCUE] demonstrated more heterogeneous patterns of RNFL and GCL changes. Forthcoming results will allow for correlations with acuity, field and duration of visual loss. OCT findings should be a meaningful biomarker to include in analyzing treatment effects of LHON gene therapy.

**References:** None.

**Keywords:** Genetic Disease, Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** GenSight Biologicals, Consultant and Optical Coherence Tomography Reading Center Heidelberg Engineering, Consultant

**Grant Support:** None.

## Poster 171

### Retinal Structural and Metabolic Alterations in Parkinson's Disease

Satya Karna<sup>1</sup>, Karen Sharma<sup>1</sup>, Ashwin Mohan<sup>1</sup>, Rohit Shetty<sup>1</sup>, Abhishek Lenka<sup>2</sup>, Pramod Kumar Pal<sup>2</sup>

<sup>1</sup>Narayana Nethralaya, Bangalore, Bangalore, India, <sup>2</sup>NIMHANS, Bangalore, India

#### Introduction:

Experimental evidence in humans, using OCT, shows retinal ganglion cell changes in Parkinson's disease.

#### Methods:

A cross sectional observational study of 22 eyes of 11 MRI confirmed patients with Parkinson's Disease on treatment was undertaken. Patients with corrected distance visual acuity less than 6/9, any co-existing eye disease were excluded. OCT to measure PRNFL and macular thickness (Spectralis, Heidelberg, Germany) and retinal oximetry (Oxymap T1, Oxymap HF, Reykjavik Iceland) were done. Their RNFL thickness, arteriolar and venous saturations and diameter; and arterio-venous saturation difference (AVSD) were recorded.

#### Results:

The average age of the patients was 56.2 years (95% CI – 53.4-59.0), age of onset of disease was 50.8 years (95% CI – 47.7-53.9), duration of disease was 5.1 years (95% CI – 3.7-6.5), UPDRS III score was 27.9 (95% CI – 25.1-30.7), H&Y score was 2.2 (95% CI – 2.1-2.4) and Levodopa equivalent dosage per day was 626(95% CI - 532.8-719.2). The PRNFL thickness was 103.8  $\mu$ m (95% CI – 100.3-107.3) and macular thickness was 274.1  $\mu$ m (95% CI – 263.8-284.4). The arterial saturation was 97.5% (95% CI – 94.3-100.9), venous saturation 60.1% (95% CI – 58.2-61.9), AVSD was 37.5% (95% CI – 34.4-40.6). The H&Y score correlated negatively with the age of onset ( $r=-0.459$ ,  $p=0.048$ ), positively with the UPDRS score ( $r=0.623$ ,  $p=0.002$ ), and Levodopa dosage ( $r=0.671$ ,  $p=0.001$ ). The arteriolar saturation correlated inversely with Levodopa dosage ( $r=0.554$ ,  $p=0.011$ ) while positively with AVSD ( $r=0.840$ ,  $p<0.001$ ). The RNFL thickness did not show any significant associations with any of the other parameters.

#### Conclusions:

Retinal metabolic parameters like arteriolar saturation and AVSD showed a significant correlation with Levodopa dosage. This may imply that retinal oximetry changes occur in association with underlying CNS derangements. Further studies with larger sample sizes may help to establish retinal oximetry as an indirect biomarker for neurodegenerative diseases.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Pupils Retina, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 172****Study of Morphological, Retinal Nerve Fibre Layer and Blood Flow Changes on FD-OCT in NA-AION**

Vivekanand<sup>1</sup>, Sumit Manthanwar<sup>1</sup>, Aniruddha Banerjee<sup>1</sup>, Suchismita Mishra<sup>2</sup>

<sup>1</sup>L V Prasad Eye Institute, Bhubaneswar, India, <sup>2</sup>IMS & SUM Hospital, Bhubaneswar, India

**Introduction:**

The purpose is to observe the morphological changes, RNFL, Blood flow and Ganglion cell loss (GCL) of optic nerve head at presentation and follow up visit at 1 and 3 month in patients of NA-AION on FD-OCT (Angio) examination

**Methods:**

In this prospective observational study 33 eyes of 33 patients who underwent screening and clinically diagnosed as NA-AION were undergone the FD-OCT(Angio) examination at presentation, 1 month and 3 month at our Neuro-ophthalmology clinic between July-2016 and March 2017. The examination data record consisted of 1) Demographic data record 2) Ocular examination record and 3) FD- OCT (Angio) examination of the patient using TOPCON (DRT Triton Plus) OCT machine and following parameters were analyzed - 1) RNFL thickness 2) GCL (Ganglion cell layer) thickness 3) Angio Changes (Blood Flow dynamics) 4) Optic disc changes were performed.

**Results:**

33 eyes of 33 patients were analysed. Mean age was 53.33 yr (SD  $\pm$  9.76 yr). Male (n=20 out of 33) were predominant 60.6%. Total RNFL changes at presentation was 227.39 $\pm$ 74.84  $\mu$ m, which reduced to 100.9 $\pm$  35.76  $\mu$ m and 80.53 $\pm$ 23.91  $\mu$ m at follow up visit 1 and 3 month respectively. It was found to be statistically significant (<0.0001) when compared with superior RNFL at 1 month and 3 month visit .The affected eye mean GCL thickness was 104.24  $\pm$ 38.55  $\mu$ m, 74 $\pm$ 19.19  $\mu$ m and 64.17 $\pm$ 13.6  $\mu$ m at presentation,1month and 3month respectively. The blood flow changes revealed that the affected eye showed diminished blood supply (Hypo intense images) of the optic nerve head at all visit and it was stable throughout the visits.

**Conclusions:**

FD OCT Angio has a major role in understanding NA-AION progression characterized by gradual decrease in RNFL and GCL thickness over time with no recovery. It also depicts diminished blood supply of the optic nerve head in early stage of NA-AION.

**References:** None.

**Keywords:** Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 173****Inter-Eye Difference Thresholds for Predicting an Optic Nerve Lesion in MS: An International Study**

Rachel Nolan<sup>1</sup>, Omar Akhand<sup>1</sup>, Peter Calabresi<sup>2</sup>, Friedemann Paul<sup>3</sup>, Elena Martinez-Lapiscina<sup>4</sup>, Axel Petzold<sup>5</sup>, Alexander Brandt<sup>3</sup>, Shiv Saidha<sup>2</sup>, Raed Behbehani<sup>6</sup>, Elliot Frohman<sup>7</sup>, Joachim Havla<sup>8</sup>, Bernhard Hemmer<sup>9</sup>, Hong Jiang<sup>10</sup>, Thomas Korn<sup>9</sup>, Letizia Leocani<sup>11</sup>, Athina Papadopoulou<sup>12</sup>, Steven Galetta<sup>1</sup>, Laura Balcer<sup>1</sup>

<sup>1</sup>New York University School of Medicine, New York, New York, USA, <sup>2</sup>Johns Hopkins School of Medicine, Baltimore, Maryland, USA, <sup>3</sup>Charité – Universitätsmedizin Berlin, Berlin, Germany, <sup>4</sup>IDIBAPS, Barcelona, Spain, <sup>5</sup>UCL Institute of Neurology, Queen Square, London, United Kingdom, <sup>6</sup>Dasman Institute, Kuwait City, Kuwait, <sup>7</sup>University of Texas Austin, Austin, Texas, USA, <sup>8</sup>Klinikum der LMU München, München, Germany, <sup>9</sup>Technical University of Munich, Munich, Germany, <sup>10</sup>Bascom Palmer Eye Institute/ University of Miami, Miami, Florida, USA, <sup>11</sup>Ospedale San Raffaele, Milan, Italy, <sup>12</sup>University Hospital of Basel in Switzerland, Basel, Switzerland

**Introduction:**

The optic nerve is a frequent site for involvement in multiple sclerosis (MS). Current international diagnostic criteria for MS do not include the optic nerve as a lesion site despite the high prevalence of acute optic neuritis (ON). Spectral-domain optical coherence tomography (SD-OCT) detects thinning of RNFL and GCIP in MS. We sought to determine optimal thresholds for inter-eye differences in retinal nerve fiber (RNFL) and ganglion cell+inner plexiform (GCIP) layer thicknesses that are predictive of a unilateral optic nerve lesion.

**Methods:**

In this multi-center international study at 9 sites, SD-OCT, high-contrast visual acuity (VA), low-contrast letter acuity (LCLA), and vision-specific quality of life (QOL) were measured for MS patients and healthy controls as part of the International Multiple Sclerosis Visual System Consortium (IMSVISUAL). QOL was measured using the NEI-VFQ-25 and 10-item Neuro-Ophthalmic Supplement (NOS). Presence of an optic nerve lesion was defined as history of acute unilateral ON.

**Results:**

Among healthy controls (n=348), the 95th percentile value for inter-eye difference (upper boundary of expected) was 7.0 microns; for GCIP, the 95th percentile was 3.0 microns. These values were applied to the MS cohort (n=1,346), and were associated with worse vision-specific QOL for inter-eye differences above the threshold values ( $P \leq 0.04$ , linear regression, accounting for age). Greater inter-eye differences in VA and LCLA were associated with greater inter-eye RNFL differences ( $P < 0.001$ ) and GCIP ( $P \leq 0.002$ ). Receiver operating characteristic (ROC) curve analysis demonstrated an optimal RNFL inter-eye difference threshold of 5 microns for identifying patients with unilateral ON (n=404) in the MS cohort (point on ROC curve where sensitivity and specificity are both optimized). For GCIP, the threshold was 4 microns.

**Conclusions:**

Optimal inter-eye differences of 5 microns for peripapillary RNFL and 4 microns for macular GCIP thickness are robust thresholds for identifying unilateral optic nerve lesions based on analyses of an international MS cohort.

**References:** 1. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, Correale J, Fazekas F, Filippi M, Freedman MS, Fujihara K, Galetta SL, Hartung HP, Kappos L, Lublin FD, Marrie RA, Miller AE, Miller DH, Montalban X, Mowry EM, Soelberg-Sorensen P, Tintoré M, Traboulsee AL, Trojano M, Uitdehaag BMJ, Vukusic S, Waubant E, Weinschenker BG, Reingold SC, Cohen JA. Diagnosis of Multiple Sclerosis: 2017 Revisions of the “McDonald” Criteria. *Lancet Neurol* 2017, in press. 2. Galetta SL, Balcer LJ. The optic nerve should be included as one of the typical CNS regions for establishing dissemination in space when diagnosing MS—Yes. *Mult Scler* 2017;1-2 [epub ahead of print].

**Keywords:** Demyelinating disease, Optic neuropathy, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** National Multiple Sclerosis Society

**Poster 174****The Influence of Volume and Anatomic Location of Optic Disc Drusen on Sensitivity of Autofluorescence**

Frederik Loft<sup>1</sup>, Lasse Malmqvist<sup>1</sup>, Anne-Sofie Lindberg<sup>2</sup>, Steffen Hamann<sup>1</sup>

<sup>1</sup>Rigshospitalet, University of Copenhagen, 2600 Glostrup, Denmark, <sup>2</sup>Technical University of Denmark, Copenhagen, Denmark

**Introduction:**

Optic disc drusen are acellular deposits in the optic nerve head. Optic disc drusen can be diagnosed using different imaging modalities such as enhanced depth imaging optical coherence tomography and autofluorescence. It is unknown which factors determine the sensitivity of autofluorescence. The aim of this study was to investigate the effect of volume and anatomic location of optic disc drusen on the sensitivity of autofluorescence.

**Methods:**

Cross sectional study

**Results:**

A total of 38 optic disc drusen patients (75 eyes) were included. In 12/75 (16%) eyes and in 11/ 38 patients (29%) enhanced depth imaging optical coherence tomography detected optic disc drusen that were not detected by autofluorescence. In 24 distinctly solitary optic disc drusen, both larger ODD volume ( $P=0.039$ ) and more superficial ODD location ( $P<0.0001$ ) showed to increase the possibility of autofluorescence detection of ODD, when performing a multivariate analysis. The estimated effect of anatomic location on autofluorescence was more than twice the effect of the volume (semipartial Eta-square of 0.52 and 0.23 respectively. Model descriptors accounted for 0.76 of total variance).

**Conclusions:**

Enhanced depth imaging optical coherence tomography is superior to autofluorescence in the diagnosis of optic disc drusen. Volume and anatomic location of optic disc drusen have a significant impact on the sensitivity of autofluorescence.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 175**

**Optic Nerve Head Parameters in Patients with Non-Arteritic Ischemic Optic Neuropathy**

Hwan Heo<sup>1</sup>, Yung Hui Kim<sup>1</sup>, Sang Woo Park<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of*

**Introduction:**

To investigate early and late visual functions according to optic nerve head (ONH) parameters in patients with non-arteritic ischemic optic neuropathy (NAION).

**Methods:**

Forty patients with NAION and 55 normal controls were included. We compared the age, sex, and spherical equivalent (SE) between the NAION and control groups. At the initial visit, disc area, rim area, cup-to-disc area ratio, cup volume, peripapillary retinal nerve fiber layer (pRNFL) and ganglion cell-inner plexiform layer (GCIPL) thickness were compared between the contralateral eyes of patients with NAION and normal controls. The correlations between ONH parameters of the contralateral eyes and the pRNFL thicknesses and visual functions of eyes with NAION were evaluated. The correlations between ONH parameters of the contralateral eyes at the initial visit and ONH parameters and visual functions of eyes with NAION at the final visit were evaluated.

**Results:**

Age, sex, and SE showed no significant differences between the NAION and control groups. The contralateral eyes of patients with NAION had significantly smaller cup-to-disc area ratios ( $p=0.028$ ) and cup volumes ( $p=0.036$ ) than did the eyes of normal controls. Moreover, in patients with NAION who visited the hospital within 7 days after symptom onset ( $n=21$ ), the larger rim area in the contralateral eyes showed worse VFDs ( $p=0.025$ ). In patients with NAION who had a follow-up period of at least 6 months ( $n=19$ ), the rim area and cup-to-disc area ratio in the contralateral eyes at the initial visit significantly correlated with BCVA ( $p=0.015$  and  $p=0.01$ , respectively) and VFD ( $p=0.017$  and  $p=0.031$ , respectively) at the final visit.

**Conclusions:**

Patients with NAION had smaller cup-to-disc area ratios and cup volumes than did the normal controls. The smaller cup-to-disc area ratios and larger rim areas were associated with early or late visual functions. In patients with NAION, contralateral ONH parameters can be prognostic factors of late visual functions.

**References:** 1. Contreras I, Rebolledo G, Noval S, et al. Optic disc evaluation by optical coherence tomography in nonarteritic anterior ischemic optic neuropathy. *Invest Ophthalmol Vis Sci* 2007;4087-92. 2. Saito H, Tomidokoro A, Tomita G, Araie M, Wakakura M. Optic disc and peripapillary morphology in unilateral nonarteritic anterior ischemic optic neuropathy and age- and refraction-matched normals. *Ophthalmology* 2008;1585-90. 3. Chan CK, Cheng AC, Leung CK, et al. Quantitative assessment of optic nerve head morphology and retinal nerve fibre layer in non-arteritic anterior ischaemic optic neuropathy with optical coherence tomography and confocal scanning laser ophthalmoscopy. *Br J Ophthalmol* 2009;731-5.

**Keywords:** Optic neuropathy, Visual fields, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 176

### Correlation Between Stereopsis and Reverse Stereopsis in Homonymous and Bitemporal Hemianopias

Michael Dattilo<sup>1</sup>, Beau Bruce<sup>1</sup>, Caroline Vasseneix<sup>1</sup>, Valerie Biousse<sup>1</sup>, Nancy Newman<sup>1</sup>, Jason Peragallo<sup>1</sup>

<sup>1</sup>Emory University, Atlanta, Georgia, USA

#### Introduction:

Stereopsis, a binocular phenomenon dependent on higher order visual processing, can reliably suggest a range of visual acuity (VA) in patients with no history of strabismus. Michael Brodsky, M.D. suggested that patients with bitemporal hemianopias may demonstrate absence of stereopsis on reverse stereovision testing. Prior to testing Dr. Brodsky's hypothesis, we showed that there was no difference between traditional stereoacuity (stereoacuity book upright, "TS") and reverse stereoacuity (stereoacuity book rotated 180 degrees, "RS") in patients without visual field defects. Here we report the results of TS and RS testing in patients with homonymous hemianopias (HH) and bitemporal hemianopias (BTH).

#### Methods:

Patients with HH or BTH and good VA (>20/50) seen in a neuro-ophthalmic service over a 2.5-year period underwent a detailed examination, including polarized vectogram stereoacuity measurements (Titmus). Patients were first tested with TS and then RS. Patients with strabismus were excluded.

#### Results:

Of 74 patients with HH or BTH, we included 61 who had no ocular misalignment and >0 circles on TS. 34/61 had HH (56%; median age, 52 years [19-77]) and 27/61 had BTH (44%, median age, 51 years [21-70]). Mean score for HH was 7.3/9 circles correct on TS and 6.9/9 on RS [p=0.34]. Mean score for BTH was 5.3/9 on TS and 5.0/9 on RS [p=0.63]. Patients with HH scored better than patients with BTH on both TS (7.3/9 vs 5.3/9, respectively [p=0.003]) and RS testing (6.9/9 vs 5.0/9, respectively [p=0.02]). The mean difference between TS and RS (TS-RS) was 0.35 circles for HH and 0.26 circles for BTH [p=0.89].

#### Conclusions:

Patients with HH scored significantly better than patients with BTH on both TS and RS. However, there was no significant difference between TS and RS for HH or for BTH patients and there was no significant TS-RS difference between HH and BTH patients.

**References:** 1. Sitko KR, Peragallo JH, Bidot SS, Biousse V, Newman NJ, Bruce BB. Pitfalls in the use of stereopsis for the diagnosis of non-organic visual loss. *Ophthalmology* 2016; 123(1): 198-202 2. Brodsky M. Personal communication at the 2015 NANOS Meeting during the discussion session of our communication1 3. Dattilo M, Vasseneix C, Bruce BB, Sitko KR, Biousse V, Newman NJ, Peragallo JH. Correlation between stereopsis and reverse stereopsis. *Ophthalmology* 2017; 124(3): 411-413 4. Levy NS, Glick EB. Stereoscopic perception and Snellen VA. *Am J Ophthalmol* 1974; 78: 722-724 5. Donzis PB, Rappazzo A, Burde RM, Gordon M. Effect of binocular variations of Snellen's VA on Titmus stereoacuity. *Arch Ophthalmol* 1983; 101: 930-932

**Keywords:** Higher visual functions, Visual fields

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** 1. Departmental grant (Department of Ophthalmology, Emory University) from Research to Prevent Blindness, Inc., New York, 2. NIH/NEI core grant P30-EY006360 (Department of Ophthalmology, Emory University)

**Poster 177****Transcranial Magnetic Stimulation, a New Hope for Treatment of Post-Concussion Syndrome: A Randomized Double-Blind Study**

Behzad Mansouri<sup>1</sup>, Abdelbaset Suleiman<sup>1</sup>, Grant Rutherford<sup>1</sup>, Omid Pouya<sup>1</sup>, Zeinab Dastgheib<sup>1</sup>, Wejia Zhang<sup>1</sup>, Jennifer Salter<sup>1</sup>, Xikui Wang<sup>1</sup>, Brian Lithgow<sup>1</sup>, Zahra Moussavi<sup>1</sup>

<sup>1</sup>*University of Manitoba, Winnipeg, Canada*

**Introduction:**

Here we report the results of a randomized, placebo controlled, double-blind study on eighteen patients where we investigated the effect of Repetitive Transcranial Magnetic Stimulation (rTMS) on patients with post-concussion syndrome (PCS).

**Methods:**

Half the patients were randomly assigned to treatment group. rTMS was given to the left dorsolateral prefrontal cortex. Primary outcome was improvement in patients' symptoms those were measured using the Rivermead Post Concussion Symptoms Questionnaire (RPQ). The secondary outcome was Electrovestibulography (EVestG) improvement, which is an objective physiological measure of cortical, brainstem and vestibular periphery abnormality. Furthermore, the Montgomery-Åsberg Depression Rating Scale (MADRS) was also used to investigate the plausible confounding effect of depression treatment.

**Results:**

Our results showed that participants with more recent injuries (1 year) who received active rTMS. This improvement continued in the follow up assessment and persisted for at least two months after the intervention was completed. No improvement was found in the group with long-term PCS. A plausible confounding effect due to improvement of depression after rTMS treatment was tested, which showed that the improvement in PCS did not correlate with improvement in depression.

**Conclusions:**

We reported here that rTMS treatment might potentially be a plausible treatment for early PCS. This finding brings a new hope to concussed patients who has not had any effective treatment that aims the so far understood pathophysiology of the disease.

**References:** None.

**Keywords:** Vestibular

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** This study was supported by a Manitoba Public Insurance and MITACS Canada to ZKM.

**Poster 178****Dichoptic Treatment of Amblyopia in a Clinical Setting – a Retrospective Study**

Giovanni Travi<sup>1</sup>, Behzad Mansouri<sup>1</sup>

<sup>1</sup>*University of Manitoba, Winnipeg, Canada*

**Introduction:**

Dichoptic Amblyopia Treatment (DAT) is a novel modality for Amblyopia treatment. This study aimed to assess the visual outcome of DAT in a neuro-ophthalmology clinical setting for children and adults who completed all conventional amblyopia treatments and did not have any other treatment options. The primary outcome was the improvement of visual acuity (VA). The secondary outcomes were improvement in stereo acuity (SA) and reduction of suppression.

**Methods:**

We performed a retrospective chart review of amblyopic patients who received DAT from 2014 to 2016. DAT consisted of playing “Falling Cubes” game on an Ipad, using anaglyph glasses for 1 hour per day for 6 weeks. We evaluated the improvement of VA, SA and suppression using HOTV logMAR scale at 9 feet, Stereo Fly Test and Worth-4-Dot test, respectively. We investigated whether other variables, such as age, past treatments, presence of SA at baseline, amblyopia type and severity, correlated with better treatment outcomes.

**Results:**

23 patients with a median age of 12 years-old (IQR=9-30) met the inclusion criteria. Three were excluded because they did not complete the treatment. The median for pre-treatment and post-treatment VA was 0.54 (IQR=0.41-0.84) logMAR and 0.19 (IQR=0.09-0.28) logMAR, respectively. Mean improvement in VA was  $0.33 \pm 0.18$  logMAR (IQR=0.25-0.41) ( $p < 0.001$ ). Patients showed an improvement in SA ( $p = 0.002$ ) and a decrease in suppression ( $p = 0.003$ ). Age, presence of SA at baseline, previous treatment, amblyopia type and severity did not correlate with VA improvement. There was no adverse effect such as double vision or VA reduction in the fellow fixing eye.

**Conclusions:**

The results demonstrate that DAT is effective in improving VA and SA, and reducing suppression in amblyopia in a clinical setting. Diplopia or reverse amblyopia did not occur in any of the treated patients. These results are promising and show that DAT is a feasible treatment in a clinical environment.

**References:** None.

**Keywords:** Higher Visual Cortical functions, Pediatric neuro-ophthalmology, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 179****Visual Function after Cerebral Hemispherectomy**

Shauna Berry<sup>1</sup>, Monica Chen<sup>2</sup>, Federico Velez<sup>1</sup>, Gary Mathern<sup>2</sup>, Stacy Pineles<sup>1</sup>

<sup>1</sup>*UCLA Stein Eye Institute, Los Angeles, California, USA*, <sup>2</sup>*UCLA, Los Angeles, California, USA*

**Introduction:**

Cerebral Hemispherectomy is an effective surgical treatment for children with intractable seizures. However surgery may result in coping strategies to improve vision, including changes in head position and eye alignment [1]. Previous studies are limited by the number of patients and focus mainly on post-hemispherectomy homonymous hemianopia [1,2]. The purpose of this study was to determine and characterize visual function changes in a large population of patients following hemispherectomy.

**Methods:**

Observational study was conducted on a cohort of children with seizure disorder treated with cerebral hemispherectomy. An online survey sent to the parents included demographic and clinical questions. Visual function was assessed by the presence of peripheral field defects, ocular misalignment and anomalous head posture.

**Results:**

A total of 196 participants responded (12.5% of surveys emailed out). Postoperative follow up was 92+/-78 months (range 1-382). An acquired peripheral vision defect was reported in 181 patients (93%). Persistent torticollis was noted in 122 patients (62%). Strabismus was noted in 93 patients (49%). Both torticollis and strabismus were most frequently seen immediately after surgery. Sixty-six patients (34%) underwent strabismus treatment including monocular patching, extraocular muscle, chemodectomectomy, and surgery.

**Conclusions:**

Compensatory mechanisms to improve visual function are common in patients with seizure disorders undergoing cerebral hemispherectomy. Preoperative discussion with parents and patients regarding those compensatory mechanisms is recommended.

**References:** 1. Y Koenraads, DCP Van Der Linden, MMJ Van Schooneveld, et al. Visual function and compensatory mechanisms for hemianopia after hemispherectomy in children. *Epilepsia* 2014;55(6):909–917 2. S Handley, F Vargha-Khadem, R Bowman, and Alki Liasis. Visual function 20 years after Childhood Hemispherectomy for Intractable Epilepsy. *AJO* 2017;177(2) 81-89.

**Keywords:** Pediatric neuro-ophthalmology, Visual fields

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 180****Faces, Music and Voices: Evidence for a Right-dominant Anterior Temporal Agnosia Syndrome**

Jason Barton<sup>1</sup>, Jacob Stubbs<sup>1</sup>, Sebastien Paquette<sup>2</sup>, Gottfried Schlaug<sup>2</sup>, Sherryse Corrow<sup>3</sup>

<sup>1</sup>University of British Columbia, Vancouver, Canada, <sup>2</sup>Harvard Medical School, Boston, Massachusetts, USA, <sup>3</sup>Bethel University, Minneapolis, Minnesota, USA

**Introduction:**

Acquired prosopagnosia is often associated with other deficits, such as dyschromatopsia and topographagnosia, from damage to adjacent perceptual networks. Our recent study showed that some subjects with developmental prosopagnosia also have congenital amusia, but it is not known whether those with the acquired variant have similar problems with music perception. Our goal was to determine if any subjects with acquired prosopagnosia also have acquired amusia, and if so, whether the presence of amusia was linked to a specific functional or anatomical variant of prosopagnosia.

**Methods:**

We studied eight subjects with acquired prosopagnosia from a comprehensively documented cohort, all of whom had extensive neuropsychological and neuroimaging testing. They performed a battery of tests evaluating pitch and rhythm processing, including the Montreal Battery for the Evaluation of Amusia.

**Results:**

Three of eight subjects with acquired prosopagnosia had impaired musical pitch perception, and two were impaired in recognition memory for music, while rhythm perception was spared. One subject reported loss of enjoyment of music, while paradoxically two of the three impaired subjects reported enhanced appreciation of music. The lesions of these three subjects affected the right or bilateral temporal poles as well as the right amygdala and insula: two had an amnesic variant of prosopagnosia. None of the three subjects with apperceptive prosopagnosia from lesions limited to the inferior occipitotemporal cortex had impaired pitch perception or recognition memory for music.

**Conclusions:**

While the apperceptive variant of prosopagnosia from fusiform lesions is associated with dyschromatopsia and topographagnosia as part of a 'ventral visual syndrome', the current findings and the results of our previous study of voice recognition (1) indicate that the amnesic variant of prosopagnosia can be associated with amusia and phonagnosia, as part of a right-dominant 'anterior temporal agnosia syndrome'.

**References:** 1. Liu R, Pancaroglu R, Hills CS, Duchaine B, Barton JJS. Voice recognition in face-blind patients. *Cerebral Cortex* 26, 1473-87, 2016.

**Keywords:** Higher Visual Cortical functions, Higher visual functions

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** CIHR operating grant (MOP-102567) to JB. JB was supported by a Canada Research Chair and the Marianne Koerner Chair in Brain Diseases. G. S. acknowledges support from NIH (DC009823, DC008796). S.P. is supported by a Postdoctoral Fellowship from the Canada



**Poster 181**

**Headache and Intrinsic Brain Network Improvement in Chronic Migraine Following Onabotulinumtoxin-A Treatment: a Resting-State-Functional-MRI Study**

Behzad Mansouri<sup>1</sup>, Anish Kanungo<sup>1</sup>, Tiffany Kolesar<sup>1</sup>, Jennifer Kornelsen<sup>1</sup>, Nicholas Rusnick<sup>1</sup>, Dana Turcotte<sup>1</sup>

<sup>1</sup>*University of Manitoba, Winnipeg, Canada*

**Introduction:**

Here we report the effect of Onabotulinumtoxin-A (Onabot-A) in twelve patients with chronic migraine (CM=15 or more headaches/months), behaviourally, i.e. improvement in the headaches quantity/severity, and functionally, i.e. changes in brain functional connectivity (FC) patterns using resting-state-functional magnetic resonance imaging (rsfMRI).

**Methods:**

Two rounds of Onabot-A injections (Day 0 and 84) were performed. Patients had regular follow-ups after treatment with migraine assessment inventories. rsfMRI was performed at baseline, Days 56, and 140, and analyzed by Independent Component Analysis (ICA).

**Results:**

The results showed significant improvement in headaches (quantity/severity) after treatment. rsfMRI demonstrated significant FC reduction within the lateral pain network and FC enhancement in visual association areas after the first treatment, which were mostly reversed after the second treatment. However, the FCs for some brain networks over the visual association areas were significantly enhanced after the completion of the treatment.

**Conclusions:**

Our data shows that Onabot-A is an effective treatment for CM and correlates with brain FC changes. Most FCs showed biphasic changes after two sets of treatments, the cause of which is likely multifactorial (e.g. headache improvement, discontinuation of prophylactic medication and analgesics). More interestingly, the persistence in some of the enhanced visual association areas FC may correlate with the wave of cortical spreading depression that purported to be connected to visual aura and propagate from visual cortex. Here we showed for the first time: (A) FC changes following Onabot-A treatment in CM along with significant headache improvement and (B) a potential connection between clinical improvement following Onabot-A injections, with FC changes in brain areas relevant to the established migraine pathophysiology.

**References:** None.

**Keywords:** Higher Visual Cortical functions, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** The study was funded by Allergan plc, Markham, Canada at the request of the investigator. All authors met the ICMJE authorship criteria. Neither honoraria nor payments were made for authorship.

**Poster 182****Do Children With Homonymous Field Defects Benefit from Visual Search Training?**

Susanne Trauzettel-Klosinski<sup>1</sup>, Stephan Kuester<sup>1</sup>, Iliya Ivanov<sup>2</sup>, Manfred MacKeben<sup>3</sup>, Martin Staudt<sup>4</sup>

<sup>1</sup>Center for Ophthalmology, University of Tuebingen, 72076 Tübingen, Germany, <sup>2</sup>Institute for Ophthalmic Research, University of Tuebingen, Tuebingen, Germany, <sup>3</sup>The Smith Kettlewell Eye Research Institute, San Francisco, California, USA, <sup>4</sup>University Children's Hospital, Tuebingen, Tuebingen, Germany

**Introduction:**

Homonymous field defects (HFD) lead to difficulties in spatial orientation with limitations of activities in daily life. In a previous RCT we showed the effectiveness of explorative saccadic training based on a search task in adult hemianopic patients (1). The present study investigates, if children with HFD benefit from a visual search training.

**Methods:**

22 children with HFD (median age 11 years, 8 months (6-19y) and 16 healthy normally-sighted age-matched children (median 11y6m, 7-17y) participated. Visual fields were examined by different techniques, dependent on cooperation: by Manual Perimetry, Tangent Screen or a custom gaze field campimeter. A computer-based visual search training was developed for children. The HFD-children trained independently at home 15 minutes/day, 5 days/week, for 6 weeks at 3 different difficulty levels. Search times (STs) were assessed during the complete training period. Eye movements were recorded by eye tracker during a visual search task before training (T1), directly after training (T2) and 6 weeks after end of training (T3). Control subjects performed the task at T1 and T2 (without training) to evaluate any effect by just repeating the search task.

**Results:**

In patients, STs during training and eye tracking decreased significantly from T1 to T2 and were sustained at T3. Eye movement strategy became more effective. No changes occurred in the control Group.

**Conclusions:**

Our results show that children with HFD benefited from the visual search training, indicated by the shorter STs after training, maintained at T3, which shows that they could apply the newly learnt gaze strategy to everyday life. The control children's performance did not change by just repeating the search task.

**References:** 1: Roth T et al. Comparing explorative saccade and flicker training in hemianopia: a randomized controlled study. *Neurology* 72(4): 324-331, 2009

**Keywords:** Pediatric neuro-ophthalmology, Stroke Trauma, Visual fields, Stroke Trauma

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** This study was supported by Brunenbusch-Stein Foundation, Herbert Funke Foundation, Kerstan Foundation, Kossmann Foundation and Niethammer Foundation

**Poster 183**

**Endovascular Venous Sinus Stenting for Idiopathic Intracranial Hypertension: A Systematic Review of the Literature**

Brandon Bond<sup>1</sup>, Kamila Bond<sup>2</sup>, Chike Illorah<sup>1</sup>, Jorge Kattah<sup>1</sup>

<sup>1</sup>University of Illinois College of Medicine, Peoria, Illinois, USA, <sup>2</sup>Mayo Clinic School of Medicine, Rochester, Minnesota, USA

**Introduction:**

Idiopathic intracranial hypertension (IIH) is characterized by raised intracranial pressure outside the context of space-occupying or obstructive lesions. It is well accepted that most IIH patients have transverse sinus stenosis impairing cerebral venous outflow. Untreated, this may cause optic nerve damage and permanent visual loss. The reported annual incidence is 0.9-1.07/100,000 but may reach 15-19/100,000 in subpopulations of overweight women aged 20-44. Medically refractory IIH has historically been treated by therapeutic lumbar punctures, cerebrospinal fluid (CSF) diversion, and optic nerve sheath fenestration (ONSF). Recurrence rates with medication have reached 40%. Shunt failure and revision rates are as high as 60% with infection-related complications reaching 10%. ONSF carries significant risks with failure rates and concomitant recurrence of visual symptoms up to 32%. Since 2002, venous sinus stenting (VSS) has emerged as an alternative treatment option for refractory IIH.

**Methods:**

A systematic literature review was performed to identify all patients with IIH who underwent treatment with VSS. Relevant data on demographics, clinical course, and outcomes were extracted.

**Results:**

A total of 518 subjects were identified (89% female, mean age 34.6+/-7.4y, mean body mass index 34.9+/-6.3kg/m<sup>2</sup>). Initial symptoms included headache (92%), resolved/improved in 76% post-stenting; papilledema (82%), resolved/improved in 88%; visual defects (63%), resolved/improved in 73%; and pulse-synchronous tinnitus (34%), resolved in 82%. Mean follow-up was 16.8+/-11.2m clinically and 16.9+/-19.3m radiologically. Mean stenotic pressure gradient improved from 18.4+/-7.6mmHg to 3.2+/-3.0mmHg after stenting. The complication rate was 18.9% with an 8.9% re-stenting rate and a 3.4% post-stent surgical re-treatment rate.

**Conclusions:**

Venous sinus stenting is a safe and effective alternative to invasive treatments, such as CSF diversion and ONSF, in patients with IIH. Given the excellent clinical outcomes documented in the literature, further investigation with a multi-center randomized clinical trial would be beneficial.

**References:** None.

**Keywords:** Interventional neuroradiology, Pseudotumor Cerebri, Neuroimaging, Optic nerve trauma and treatment, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 184**

**Lumbar Puncture For Diagnosis Of Pseudotumor Cerebri Syndrome In Typical Patients**

Mathew Margolis<sup>1</sup>, Adam DeBusk<sup>2</sup>, Mark Moster<sup>2</sup>, James Ebbot<sup>3</sup>, Eric Eggenberger<sup>3</sup>, Harrison Bennett<sup>2</sup>, Robert Sergott<sup>2</sup>, Gregory Van Stavern<sup>1</sup>

<sup>1</sup>Washington University School of Medicine, St Louis, Missouri, USA, <sup>2</sup>Wills Eye Hospital, Philadelphia, Pennsylvania, USA, <sup>3</sup>Mayo Clinic, Jacksonville, Florida, USA

**Introduction:**

Criteria for the diagnosis of Pseudotumor Cerebri Syndrome (PTCS) are based on clinical exam findings, neuroimaging features [1,2], and lumbar puncture (LP) with elevated opening pressure (OP) without alternative etiology. However, recent evidence suggests the range of “normal” OP is much wider than previously thought [3], and LPs are often performed in variable positions undermining pressure measurement validity [4]. Thus, the newest criteria allow for diagnosis of “Probable PTCS” with normal OP [5]. As LPs are associated with complications including low pressure syndromes [4,6] and radiation exposure if performed under fluoroscopy, this study aims to build upon current work [7] in determining necessity of LP in diagnosis of typical PTCS patients.

**Methods:**

Retrospective chart review was conducted at three university-based neuro-ophthalmology practices. Included were females (BMI >25) of reproductive age (18-45) with papilledema. Patients with atypical presentation or history, neurologic findings, abnormal neuroimaging, or no LP were excluded. All patients included met criteria for PTCS [5]. Further parameters collected included demographics, clinical signs and symptoms, MRI, LP, and CSF results.

**Results:**

A total of 303 patients were identified as potentially eligible, of which 111 (36.6%) met study criteria. Of eligible patients, 9 (8.1%) were found to have CSF abnormalities. Elevated WBC were seen in 7 (6.3%) patients, 4 (3.6%) had elevated protein, 1 (0.9%) had oligoclonal bands, and 1 atypical lymphocytes (0.9%). However, no patients had changes in diagnosis or management based on LP results. No patients with CSF abnormalities required surgical treatment or had significant visual loss.

**Conclusions:**

This study suggests it may not be necessary for PTCS patients with typical demographics, clinical exam, and radiologic findings to undergo LP. These results do not apply to atypical patients; alternative etiologies may be present. Patients who respond atypically to treatment, or present with new onset atypical findings should undergo LP for diagnostic purposes.

**References:** 1. Agid R, et. Al. Idiopathic intracranial hypertension: the validity of cross-sectional neuroimaging signs, *Neuroradiology*, 48:521–527, 2006. 2. Viets R, Parsons M, Van Stavern G, et. Al. Hyperintense optic nerve heads on diffusion-weighted imaging: a potential imaging sign of papilledema, *AJNR Am J Neuroradiol*, 34: 1438–1442, 2013. 3. Lee SC, Lueck CJ. Cerebrospinal fluid pressure in adults. *J Neuroophthalmol. Sep*;34(3):278-83. 2014. 4. Williams, J., Lye, D. C. B. & Umaphathi, T. Diagnostic lumbar puncture: minimizing complications, *Intern. Med. J.* 38, 587–591, 2008. 5. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children, *Neurology*, 81(13):1159-1165, 2013. 6. Basurto Ona, X., Osorio, D. & Bonfill Cosp, X. *Cochrane Database of Systematic Reviews*, John Wiley & Sons, Ltd, 2015. 7. Adam DeBusk, DO; Mark L. Moster, MD; et. Al. Lumbar Puncture for Diagnosis of Idiopathic Intracranial Hypertension, Poster presented at: NANOS 43rd annual meeting.

**Keywords:** Pseudotumor Cerebri, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 185

### United Kingdom Consensus Guidance for Adult Idiopathic Intracranial Hypertension

Susan Mollan<sup>1</sup>, Brendan Davis<sup>2</sup>, Nick Silver<sup>3</sup>, Simon Shaw<sup>2</sup>, Conor Malluci<sup>4</sup>, Ben Wakerley<sup>5</sup>, Anita Krishnan<sup>3</sup>, Swarupsinh Chavda<sup>6</sup>, Satheesh Ramalingam<sup>7</sup>, Julie Edwards<sup>8</sup>, Krsytal Hemmings<sup>9</sup>, Williamson Michelle<sup>9</sup>, Michael Burdon<sup>1</sup>, Ghaniah Hassan-Smith<sup>10</sup>, Kathleen Digre<sup>11</sup>, Grant Liu<sup>12</sup>, Rigmor Jensen<sup>13</sup>, Alexandra Sinclair<sup>14</sup>

<sup>1</sup>Birmingham Neuro-Ophthalmology, University Hospitals Birmingham, Birmingham, United Kingdom, <sup>2</sup>University Hospital North Midlands NHS Trust, Stoke, United Kingdom, <sup>3</sup>The Walton Centre NHS Foundation Trust, Liverpool, United Kingdom, <sup>4</sup>Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom, <sup>5</sup>Nuffield Department of Clinical Neurosciences, Oxford, United Kingdom, <sup>6</sup>University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom, <sup>7</sup>Swarupsinh.Chavda@uhb.nhs.uk, Birmingham, United Kingdom, <sup>8</sup>Sandwell and West Birmingham NHS Trust, Birmingham, United Kingdom, <sup>9</sup>IIH UK, Tyne & Wear, United Kingdom, <sup>10</sup>University Hospitals Birmingham, Birmingham, United Kingdom, <sup>11</sup>University of Utah, Salt Lake City, USA, <sup>12</sup>Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA, <sup>13</sup>Danish Headache Center, Copenhagen, Denmark, <sup>14</sup>University of Birmingham, Birmingham, United Kingdom

#### Introduction:

Patients with IIH face multiple unsolicited hospital attendances in the UK. The aim was to capture interdisciplinary expertise from a large group of clinicians, reflecting practice from across the UK, to inform subsequent development of a national consensus guidance for optimal management of IIH in the UK.

#### Methods:

Between September 2015 and October 2017 a specialist interest group including neurology, neurosurgery, neuro-radiology, neuro-ophthalmology, primary care physician, nurse and patient representatives met. An initial UK survey of attitudes and practice in IIH was sent to a wide group of physicians and surgeons who investigate and manage IIH regularly. A comprehensive systemic literature review was performed to assemble the foundations of the statements. An anonymous modified Delphi process was used to obtain consensus on guidance statements. An international panel (KBD, GTL, RHJ), along with three national professional bodies, namely the Association of British Neurologists, the Royal College of Ophthalmologists and the Society of British Neurological Surgeons, critically reviewed the statements.

#### Results:

Over twenty questions were constructed: One based on the diagnostic principles for optimal investigation of papilloedema and twenty for the management of IIH. 3 main principles were identified: 1, to treat the underlying disease; 2, to protect the vision and 3, to minimise the headache morbidity. Statements presented provide insight to uncertainties in IIH where research opportunities exist. Consensus was provided for intervals of long-term follow-up care based on papilloedema grade and visual field status. Aide memoires for investigation of papilloedema, management of IIH and management of acute exacerbation of headache were drawn.

#### Conclusions:

In collaboration with many different specialists, professions and patient representatives we have developed guidance statements for the investigation and management of adult IIH. Despite the limitations of consensus-based methods these statements reflect an up-to-date expert consensus to guide the clinician and serve our patients.

**References:** 1. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology*, 81, 1159-65, 2013.

**Keywords:** Pseudotumor Cerebri, High intracranial pressure/headache, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 186**

**A Multidisciplinary Intracranial Hypertension Clinic - the University of Washington Experience**

Courtney Francis<sup>1</sup>

<sup>1</sup>*University of Washington, Seattle, Washington, USA*

**Introduction:**

Patients with intracranial hypertension often have complex complaints requiring a multidisciplinary approach with input from ophthalmology, neurology and neurosurgery. With the assistance of a generous gift from a grateful patient and her family, we established a multidisciplinary intracranial hypertension clinic at the University of Washington in March 2017.

**Methods:**

The clinic meets 1/2 day per month in the ophthalmology clinic at the UW Eye Institute. Patients can see a neuro-ophthalmologist, headache specialist, CSF neurologist and vascular neurosurgeon during the same clinic visit.

**Results:**

I will discuss the challenges and successes of setting up a multidisciplinary clinic. I will also provide data for our first 12 months of clinics, including: average unique patients per clinic, average # of MDs/patient, total # of visits/MD, total visits completed, total # of unique patients served. I will also review the number of tests and procedures performed from the clinic including: MRI/MRVs, lumbar punctures, VP shunts/revisions, optic nerve sheath fenestrations, venograms and venous sinus stenting.

**Conclusions:**

A multidisciplinary clinic can provide care to complex patients in an efficient fashion, but logistically has challenges.

**References:** None.

**Keywords:** High intracranial pressure/headache, Pseudotumor Cerebri

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** An unrestricted departmental grant from Research to Prevent Blindness. The clinic is supported by a generous gift from the Catchot Family.

**Poster 187****Idiopathic Intracranial Hypertension: Update of a 12-Year Retrospective Evaluation at One Large Tertiary Care Center**

Bart Chwalisz<sup>1</sup>, Nicholas Koen<sup>2</sup>, Judith Kempfle<sup>3</sup>, Cinthi Pillai<sup>4</sup>, Joseph Rizzo III<sup>5</sup>

<sup>1</sup>Massachusetts General Hospital Neurology, Boston, Massachusetts, USA, <sup>2</sup>Warren Alpert Medical School of Brown University, Providence, Rhode Island, USA, <sup>3</sup>Massachusetts Eye & Ear Infirmary Otolaryngology, Boston, Massachusetts, USA, <sup>4</sup>NYU Langone Medical Center, New York, New York, USA, <sup>5</sup>Massachusetts Eye & Ear Neuro-ophthalmology, Boston, Massachusetts, USA

**Introduction:**

Idiopathic intracranial hypertension (IIH) is a potentially blinding disorder that typically affects young overweight women. The NORDIC IIH treatment trial established new standards regarding the dosing of acetazolamide in the management of IIH. The goal of this study was to reflect upon our own outcomes using a traditional style of intervention in IIH.

**Methods:**

Retrospective data acquisition from patients 14 years and older of 970 patients with IIH at our center between 2004 and 2016, analyzed over the first 10 clinic visits with respect to demographics, history, clinical and radiological signs, results of lumbar puncture, and whether surgery was performed.

**Results:**

Our preliminary data on 100 patients (8% M; 92% F) show presenting symptoms of headache (83%), pulsatile tinnitus (43%), transient visual obscurations (40%), and diplopia (9%). The average perimetric mean deviation score was -2.14 ( $\pm$  3.70) dB in the right and -2.77 ( $\pm$  4.07) dB in the left eye. Average LP opening pressure was 32.99 cmH<sub>2</sub>O. With 81% of our patients prescribed 1500 mg of acetazolamide or less, the average mean deviation score after one year of treatment was -1.50 ( $\pm$ 2.03) dB in the right and -2.5 ( $\pm$ 3.56) dB in the left eye. Headache prevalence improved from 83% to 58% of patients. High-dose acetazolamide (2000-3000 mg/day) was used in 19 patients (19%). Higher doses were not used. Only 5 (5%) of these patients required surgical interventions aimed at alleviating intracranial hypertension. An additional 5 (5%) patient had bariatric surgery.

**Conclusions:**

Our more traditional treatment approach employed acetazolamide at doses that were generally lower than what was used in the NORDIC trial but nevertheless produced chronically stable visual acuities and fields, with generally tolerable side effects and uncommon use of surgery. Our results raise a question about the lowest efficacious dose of acetazolamide to manage the majority of patients with IIH.

**References:** 1. The NORDIC Idiopathic Intracranial Hypertension Study Group Writing Committee. Effects of acetazolamide on visual function in patients with idiopathic intracranial hypertension and mild visual loss. *JAMA*. 2014;311(16):1641-1651. 2. Corbett JJ, Savino PJ, Thompson HS, et al. Visual loss in pseudotumor cerebri. Follow-up of 57 patients from 5 to 41 years and a profile of 14 patients with permanent severe visual loss. *Arch Neurol*. 1982 Aug;39(8):461-74 3. Szewka AJ, Bruce BB, Newman NJ, Biousse V. Idiopathic intracranial hypertension: Relation between obesity and visual outcomes. *J Neuroophthalmol*. 2012 Jan 3.

**Keywords:** Pseudotumor Cerebri, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 188****Genetics of Idiopathic Intracranial Hypertension**

DonRaphael Wynn<sup>1</sup>, Judith Warner<sup>1</sup>, Kathleen Digre<sup>1</sup>, Bradley Katz<sup>1</sup>, Alison Crum<sup>1</sup>, Margaret DeAngelis<sup>1</sup>

<sup>1</sup>John A Moran Eye Center, University of Utah, Salt Lake City, Utah, USA

**Introduction:**

Evidence suggests a genetic predisposition for idiopathic intracranial hypertension. Corbett et. al. described 27 patients with either definitive or probable IIH from eleven ascertained families. This demonstrates that IIH clusters in families. Additionally the IIH treatment trial (IIHTT) reported that 5% of the 165 patients studied had a family member with IIH. To date, no one has performed a rigorous genetic analysis of family members with IIH to better identify IIH-related genes and the potential contribution of genetics to the pathogenesis of this disease. We are conducting whole exome sequencing (WES) on DNA from the members of a large family with IIH in order to elucidate a potential genetic cause.

**Methods:**

Members of a three-generation Utah pedigree were characterized by clinical exam, optical coherence tomography, brain imaging, and lumbar puncture to determine disease status. Affection status was determined by at least three neuro-ophthalmologists. The three affected family members in this pedigree are: the proband and two of her sisters. As we do not know a priori the mode of transmission, whole exome sequencing (Illumina HiSeq2500) is being performed on all definitively affected individuals (proband and sister) and from the following definitively unaffected individuals: both parents of the proband, an older male sibling and an older female sibling. In addition, epidemiological information including body mass index, hypertension, and other known IIH comorbidities were collected from each family member. The goal of our WES experiment is to have greater than 40X read coverage at 95% or greater target basepairs.

**Results:**

Once the data is available, appropriate statistical methods and programs will be applied to clean the data, analyze it, and prioritize variants for segregation analysis on additional family members.

**Conclusions:**

Utilizing the approach of a large clinically well characterized IIH family and whole exome sequencing we hope to pinpoint a genetic component to IIH.

**References:** NORDIC idiopathic intracranial hypertension study group writing committee, Wall M, McDermott MP, Kieburtz KD, Corbett JJ, et. al. Effect of acetazolamide on visual function in patients with idiopathic intracranial hypertension and mild visual loss: the idiopathic intracranial hypertension treatment trial. JAMA. 2014 311:1641-1651. Corbett JJ. The first Jacobson Lecture. Familial idiopathic intracranial hypertension. J neuroophthalmol 2008 28:337-347.

**Keywords:** Pseudotumor Cerebri, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Supported in part by an Unrestricted Grant from Research to Prevent Blindness, Inc., New York, NY, to the Department of Ophthalmology & Visual Sciences, University of Utah



**Poster 189****Retrospective Evaluation of Resource Utilization by Patients with IIH in a University Health System**

Zainab Shirazi<sup>1</sup>, Heather Moss<sup>2</sup>, Megh Patel<sup>2</sup>

<sup>1</sup>University of Illinois at Chicago College of Medicine, Chicago, Illinois, USA, <sup>2</sup>Stanford University, Palo Alto, California, USA

**Introduction:**

The IIH Treatment Trial demonstrated associations between treatment, vision and quality of life. Continuity of care is essential to provide and monitor treatment. Our goal was to characterize resource utilization by patients diagnosed with IIH and to explore factors associated with duration of care.

**Methods:**

Subjects with ICD-9 code 348.2 between Jan 2010-Jun 2015 were identified using a Clinical Research Data Warehouse of a health system. Demographics, number and types of visits with 348.2 code, and relevant testing were extracted. Spearman's rho assessed correlation between duration of care, demographic factors and visit types, and between testing amount and visit types.

**Results:**

384 subjects had 1241 visits (1-41/subject) with ICD9 code 348.2 (age 36+/-15 years, 85.7% (n=329) female, 48.2% (n=185) black non-hispanic, 28.6% (n=110) white non-hispanic, 4.4% (n=17) Hispanic, and 18.5% (n=71) other). Residential distance from the hospital was 22.7+/-3.4 miles. Time followed ranged from 1-1872 days, with 179 (53%) subjects followed for a single day. There were 69 (5.6%) ER visits (47 subjects), 203 (16.4%) inpatient visits (183 subjects), and 969 (78.1%) outpatient visits (284 subjects). 100/177 (56%) subjects with ER or inpatient visits had no outpatient visits. There was no association between time followed or total number of visits and age, gender or race. Time followed correlated strongly with number of outpatient visits ( $\rho=0.76$ ,  $p<0.01$ ), weakly with number of ER visits ( $\rho=0.23$ ,  $p<0.01$ ), and not with number of inpatient visits ( $\rho=-0.06$ ,  $p=0.28$ ). Subjects with at least one outpatient visit had longer time followed than those with no outpatient visits (median 161d vs. 1d,  $p<0.0005$ , Mann-Whitney). Number of CTs and MRIs correlated with number of emergency and inpatient visits but not with number of outpatient visits. Number of visual fields correlated with number of outpatient visits but not with number of emergency or inpatient visits.

**Conclusions:**

In this single center retrospective review of follow up duration for patients with IIH, outpatient visits were associated with longer follow up and more visual field testing. Inpatient and ER visits were associated with more neuro-imaging.

**References:** Koerner JC, Friedman DI (2014). "Inpatient and emergency service utilization in patients with idiopathic intracranial hypertension." *J Neuroophthalmol.* 34(3): 229-32. Wall M, Kupersmith MJ, et al. (2014). "The Idiopathic Intracranial Hypertension Treatment Trial." *JAMA Neurol.* 71(6): 693-701.

**Keywords:** Pseudotumor Cerebri

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** NEI K23-024345 and unrestricted grant from Research to Prevent Blindness

**Poster 190****Idiopathic Intracranial Hypertension and Levonorgestrel Intrauterine Device Use**

Lindsey De Lott<sup>1</sup>, Michelle Moniz<sup>1</sup>, David Musch<sup>1</sup>, Prabha Narayanaswamy<sup>1</sup>, Wayne Cornblath<sup>1</sup>

<sup>1</sup>University of Michigan, Ann Arbor, Michigan, USA,

**Introduction:**

Evidence is limited that levonorgestrel intrauterine device (IUD) contraception may place women at increased risk of idiopathic intracranial hypertension (IIH). Our aim is to assess the feasibility of a longitudinal cohort study of the risk of developing IIH in women using levonorgestrel IUDs.

**Methods:**

Using administrative claims data from beneficiaries continuously enrolled in a large managed care network from January 2001-December 2015, women ages 18 to 45 with at least 2 years of continuous enrollment prior a CPT code for IUD insertion (58300) and device code for Mirena<sup>®</sup> or Liletta<sup>®</sup> (J7302) or Skyla<sup>®</sup> (J7301) will be followed longitudinally for IIH. Subjects with IIH will be identified with at least 2 ICD9 IIH codes (348.2). At least 1 diagnosis of IIH will occur after CPT codes for neuroimaging and lumbar puncture. Subjects will be excluded if they have: dural venous sinus thrombosis (437.6, 325), cerebral edema (348.5), brain tumor (239.6, 191.X, 225.X), prescriptions for vitamin A derivatives or tetracyclines. A Cox proportional hazards model will be used to assess the risk of developing IIH following levonorgestrel IUD use.

**Results:**

There are 22,246,641 beneficiaries in the dataset. Of those, 6,502 women have IIH; 39 had an IUD placed in the 1-6 month period prior to their IIH diagnosis. Twenty-five had Mirena<sup>®</sup> or Liletta<sup>®</sup>, 8 had ParaGard<sup>®</sup> (copper IUD), and 6 did not have a specific device code. Excluding those with ParaGard<sup>®</sup>, the mean ( $\pm$ SD) age at IIH diagnosis was 32.0 ( $\pm$  6.4) years. Most (80.1%) were white and all had at least a high school diploma. Most lived in urban areas (69.2%). The mean ( $\pm$ SD) time from IUD insertion to IIH diagnosis was 103 ( $\pm$ 38.4) days.

**Conclusions:**

Using administrative claims data, a longitudinal cohort study design to assess the risk of developing IIH following levonorgestrel IUD use appears feasible.

**References:** 1. Etmnan M, Lao H, Gustafson, P. Risk of intracranial hypertension with intrauterine levonorgestrel. *Ther Adv Drug Saf.* 2015 June; 6(3): 110-113. 2. Valenzuela RM, Rai R, Kirk B, et al. An estimation of the risk of pseudotumor cerebri among users of the levonorgestrel intrauterine device. *Neuro-Ophthalmology.* 2017; 41(4): 192-197.

**Keywords:** High intracranial pressure/headache, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 191****Venous Sinus Stenting Improves Visual Fields and Cerebrospinal Fluid Opening Pressures in Idiopathic Intracranial Hypertension**

Evan Schloss<sup>1</sup>, Athos Patsalides<sup>2</sup>, Cristiano Oliveira<sup>1</sup>, Jessica Wilcox<sup>3</sup>, Marc Dinkin<sup>1</sup>

<sup>1</sup>Weill Cornell Medicine, Department of Ophthalmology, New York, New York, USA, <sup>2</sup>Weill Cornell Medicine, Department of Neurosurgery, New York, New York, USA, <sup>3</sup>Weill Cornell Medicine, Department of Neurology, New York, New York, USA

**Introduction:**

Idiopathic intracranial hypertension (IIH) causes headache and potentially irreversible visual loss, mostly in obese women of childbearing age. Treatment includes weight loss, acetazolamide, and surgical interventions when medications fail. Venous sinus stenting (VSS) has recently emerged as a promising treatment for IIH patients with dural venous sinus stenosis (DSS) but only a minority of studies have studied post-stent opening pressure (OP) or quantitative visual field scores.

**Methods:**

We reviewed the charts of 52 IIH patients who underwent VSS from 2012-2017. Pre and post-stent 24-2 Humphrey visual field (HVF) mean deviation (MD) scores in each eye and CSF OP were recorded. Student's t-test was used to analyze the continuous variables.

**Results:**

The mean patient age was 30.6 years. 50/52 (96%) patients were female. The two male patients were under 18 years of age. 50/52 (96%) patients had pre-stent HVF within 3 months of stenting. 48/52 (92%) patients had post-stent HVF, ranging from 1-21 months after stenting. All 52 patients had pre-stent lumbar puncture, and 47/52 (90%) had post-stent lumbar puncture (or bolt in 1 case) within 3-7 months. 37/52 (71%) of patients had papilledema. The mean pre and post-stent MD in the papilledema patients were -8.99 and -4.84 dB, respectively. Mean pre and post-stent OP were 36.3 and 20.6 cm H<sub>2</sub>O, respectively. Post-stent MD in papilledema patients improved by 4.40 dB ( $p < 0.001$ ). OP decreased by 16.8 cm H<sub>2</sub>O ( $p < 0.001$ ). 40/52 (77%) patients were on acetazolamide and/or topiramate pre-stent. Among the patients on medications, 18/40 (45%) discontinued treatment completely, and 11/40 (28%) reduced dosing (73% combined.) There were no complications with neurological sequelae.

**Conclusions:**

VSS led to significant improvement in visual field loss and intracranial pressure in patients with IIH and DSS, despite a significant reduction in medical therapy post-stenting. These results add to the growing literature supporting VSS as an effective treatment for IIH.

**References:** None.

**Keywords:** High intracranial pressure/headache, Optic neuropathy, Pseudotumor Cerebri, Vascular disorders, Visual fields

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 192

### Prevalence of Peripapillary and Retinal Folds in Pseudopapilledema and Mild Papilledema

Sara Reggie<sup>1</sup>, Robert Avery<sup>2</sup>, James Bavinger<sup>1</sup>, Imran Jivraj<sup>3</sup>, Cesar Cruz<sup>2</sup>, Maxwell Pistilli<sup>2</sup>, Anita Kohli<sup>4</sup>, Grant Liu<sup>2</sup>, Kenneth Shindler<sup>2</sup>, Ahmara Ross<sup>2</sup>, Randy Kardon<sup>5</sup>, Madhura Tamhankar<sup>1</sup>

<sup>1</sup>University of Pennsylvania Scheie Eye Institute, Philadelphia, Pennsylvania, USA, <sup>2</sup>University of Pennsylvania, Philadelphia, Pennsylvania, USA, <sup>3</sup>University of Toronto, Toronto, Canada, <sup>4</sup>Yale School of Medicine, New Haven, Connecticut, USA, <sup>5</sup>University of Iowa, Iowa City, Iowa, USA

#### Introduction:

Retinal and choroidal folds are often observed on fundus photography as well as on OCT in patients with papilledema secondary to idiopathic intracranial hypertension (1). This study examined whether the presence/absence of retinal and choroidal folds can differentiate between patients with mild papilledema (Frisen grades 1 and 2) and those with presumed pseudopapilledema using both axial and en face OCT images.

#### Methods:

Subjects previously enrolled in a prospective study of optic nerve swelling at the University of Pennsylvania were eligible. Subjects with either presumed pseudopapilledema (defined by lack of change in disc appearance for 6 months) or confirmed papilledema (defined by documented change in disc appearance) were included if their baseline fundus photographs were previously interpreted as either grade 1 or 2 optic nerve swelling. Two masked reviewers were trained on how to observe retinal and choroidal folds on SD-OCT (axial and en face) as previously described (1). Anonymized SD-OCT images were then presented in random order to the masked reviewers who evaluated each eye for the presence/absence of folds.

#### Results:

Thirty-nine subjects were included: 32 eyes had confirmed papilledema and 46 eyes had presumed pseudopapilledema. Using en face images, reviewers were concordant that folds were present in 7.5% of presumed pseudopapilledema eyes and in 27.6% of papilledema eyes. Using axial images, reviewers were concordant that folds were present in 8.8% of presumed pseudopapilledema eyes and in 24.1% of papilledema eyes. Some subjects with presumed pseudopapilledema identified as having retinal folds demonstrated clinical/imaging features suggestive of elevated ICP.

#### Conclusions:

Retinal and choroidal folds are less frequent in grade 1/2 papilledema than previously reported in higher grades (1). Although folds were found more commonly in eyes with papilledema, they may not be useful as a distinguishing feature between pseudopapilledema and true papilledema.

**References:** 1. Sibony PA, Kupersmith MJ, Felton SE, Wang J-K, Garvin M. Retinal and choroidal folds in papilledema. *IOVS*. 2015;56:5676.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Pseudotumor Cerebri, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 193

### A Comparison of UK and USA Idiopathic Intracranial Hypertension (IIH) Patient Populations

Richard Blanch<sup>1</sup>, Caroline Vasseneix<sup>1</sup>, Anthony Liczkowski<sup>2</sup>, Andreas Yiangou<sup>2</sup>, Anuriti Aojula<sup>2</sup>, Jonathan Micieli<sup>1</sup>, Susan Mollan<sup>3</sup>, Nancy Newman<sup>1</sup>, Valerie Biousse<sup>1</sup>, Beau Bruce<sup>1</sup>, Alexandra Sinclair<sup>2</sup>

<sup>1</sup>Emory Eye Center, Emory University, Atlanta, Georgia, USA, <sup>2</sup>University of Birmingham, Birmingham, United Kingdom, <sup>3</sup>University Hospital Birmingham NHS Trust, Birmingham, United Kingdom

#### Introduction:

The management of IIH varies among centers and countries. Demographic factors potentially influencing the presentation/severity of IIH in USA vs UK are obesity, affecting 25.4% of British women and 33.9% of American women<sup>1</sup>, and ethnicity<sup>2</sup>, with 2.81% of the British population identifying as black on the latest census data, compared to 32% in USA and 61% local to our USA referral center. We compared the presenting features of IIH between populations in UK and USA tertiary referral centers, assessing whether population differences cause different presentations.

#### Methods:

209 UK IIH patients and 361 USA IIH patients seen after 2012 in two tertiary centers were included. Data collected included age, race, gender, BMI, recent weight gain, presenting symptoms, visual acuity (VA), visual fields (VF), and CSF-opening pressure (CSF-OP). VFs were graded as severe visual loss when HVF-MD was <-15dB or GVF showed constriction.

#### Results:

USA patients were more commonly of black race (52%vs3.3%) and male (9%vs2.4%; p=0.002) than UK patients, but had a lower mean BMI (37.2±0.50vs39.2±0.69kg/m<sup>2</sup>; p=0.016). Compared to USA patients, the UK cohort had better presenting VA (logMAR 0.04±0.01vs0.13±0.02; p<0.001), Frisén grade (median 1 vs 2; p<0.001) and less severe VF loss (7%vs13%; p=0.025) but there was no difference in mean CSF-OP (36.2±0.82 UK vs 36.6±0.53cmH<sub>2</sub>O US; p=0.699). The prevalence of headache as a presenting symptom was similar in UK and USA patients (49%vs56%; p=0.40). Incidental finding of papilledema on routine examination was more common in UK than USA patients (39%vs23%; p=0.004). About half of patients reported recent weight gain (47%USvs53%UK; p=0.422).

#### Conclusions:

The UK cohort had a higher average presenting BMI. However, visual loss at presentation was more severe in the USA cohort, which may relate to the higher proportion of patients of black race in that population or to different access to care.

**References:** 1. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014;384(9945):766-81. 2. Bruce BB, Preechawat P, Newman NJ, et al. Racial differences in idiopathic intracranial hypertension. *Neurology* 2008;70(11):861-7.

**Keywords:** Pseudotumor Cerebri

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Research to Prevent Blindness, Inc., New York

**Poster 194**

**Optic Disc Drusen (ODD) in the Setting of Idiopathic Intracranial Hypertension (IIH)**

Andrew Sumnicht<sup>1</sup>, Ji Kwan Park<sup>1</sup>, Jan Lloren<sup>1</sup>, Timothy Winter<sup>1</sup>

<sup>1</sup>Loma Linda University, Loma Linda, California, USA

**Introduction:**

Optic disc drusen (ODD) has recently been described to occur following diagnosis of idiopathic intracranial hypertension (IIH). There is great difficulty distinguishing papilledema from anomalous optic nerves or ODD in pediatric patients. This uncertainty leads to extensive testing with associated risks of general anesthesia and/or lumbar puncture (LP). The objective of this study is to describe the association of elevated opening pressure (OP) on LP with presence of ODD among pediatric patients.

**Methods:**

A retrospective review of patients 18 years of age and younger with a diagnosis of IIH, ODD, papilledema, or pseudopapilledema between 2013 and 2017 who received LP was performed. Patients with alternate diagnoses that may cause papilledema were excluded. Recorded data included age, gender, body mass index (BMI), symptoms, acetazolamide use, B-scan ultrasound, fundus auto fluorescence (FAF), Humphrey Visual Field tests, and LPOP. ODD was confirmed with indirect ophthalmoscopy or ancillary testing including ultrasound and FAF. One eye per patient was included in the analysis.

**Results:**

A total of 88 pediatric eyes met inclusion criteria. Seven eyes were confirmed to have ODD. Of those with ODD, mean age was 13.14 years with similar gender distribution. Average BMI was 93.8 percentile. Two patients had headache, nausea, and/or vomiting. Four received intravenous acetazolamide. The mean LPOP for all ODD patients was 26.83 cmH<sub>2</sub>O (SD 15.42 cmH<sub>2</sub>O), and only two were > 28 cmH<sub>2</sub>O. Eyes with ODD had 9.02 cmH<sub>2</sub>O lower mean LPOP than those without ODD. Eyes with LPOP >= 28 cmH<sub>2</sub>O had 65% lower odds of finding an ODD (Odds ratio 0.352 (0.064, 1.663), p = 0.177). Conversely, eyes with LPOP <28 cmH<sub>2</sub>O had 2.84 times greater odds of finding an ODD (p = 0.177).

**Conclusions:**

Patients with elevated LPOP in this pediatric population are less likely to have ODD, though this was not statistically significant.

**References:** None.

**Keywords:** Pediatric neuro-ophthalmology, Pseudotumor Cerebri, High intracranial pressure/headache, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 195

### Direct Retrograde IJ Access for DVSS

Lakshmi Leishangthem<sup>1</sup>, Sudhakar Satti<sup>2</sup>

<sup>1</sup>Albert Einstein Medical Centre, Wyncote, Pennsylvania, USA, <sup>2</sup>Christiana Care Hospital, Newark, Delaware, USA

#### Introduction:

Dural Venous Sinus Stenting (DVSS) is increasingly being performed in select patients with medically refractory IIH. Criteria for stenting includes: significant pressure gradient across the stenosis and an obstructive outflow pattern. Direct retrograde internal jugular access represents a simple, safe, and technically feasible approach with inherent advantages.

#### Description of Case(s):

We present our simplified approach to direct Internal Jugular(IJ) access and discuss some important technical considerations, potential advantages and disadvantages of this approach.. We then present an updated comprehensive meta-analysis on DVSS focusing on success rates and complications. We present 2 patients case examples of direct retrograde IJ DVSS in the setting of medically refractory, progressive symptomatic IIH and a focal dural sinus stenosis with a hemodynamically significant pressure gradient. Ultrasound guided access for retrograde IJ access is key to safe placement of a short vascular sheath. of A triaxial system is then established to minimize the shelf and potential trauma associated with crossing the venous sinus stenosis. Once a Cook 5F shuttle sheath is distal to the target stenosis, a Cordis Precise stent (up to 8 mm diameter) can be safely deployed after the 5F shuttle sheath is withdrawn proximally. If a larger stent is required, a Cook 6F Shuttle or Neuron Max 088 guiding sheath can be substituted to accommodate 10-12 mm stents. We recently performed a meta-analysis of all literature on DVSS stent procedures over the last 14 years and found that DVSS is associated with high technical success, low revision rates (2%) and low complication rates (7.4%). Major complications included subdural hematoma (2.9%) and minor complications included transient hearing loss, retroperitoneal hematoma, urinary tract infections, syncope, femoral aneurysm (4.4%).

#### Conclusions, including unique features of the case(s):

Direct retrograde IJ access for DVSS is safe, associated with high technical success and shorter procedure times with lower cost.

**References:** 1. Satti SR, Leishangthem L, Spiotta A, Chaudry MI. Dural venous sinus stenting for medically and surgically refractory idiopathic intracranial hypertension. *Journal of NeuroInterventional Surgery*. January 2017. Vol. 23(2) 186–193 2. Satti SR, Leishangthem L, Chaudry MI. Meta-analysis of CSF diversion procedures and dural venous sinus stenting in the setting of medically refractory idiopathic intracranial hypertension. *AJNR Neuroradiology*. August 2015. 36: 1899–904. 3. Albuquerque FC, Dashti SR, Hu YC, et al. Intracranial venous sinus stenting for benign intracranial hypertension: clinical indications, technique, and preliminary results. *World Neurosurg* 2011;75:648–52 4. Ahmed RM, Wilkinson M, Parker GD, et al. Transverse sinus stenting for idiopathic intracranial hypertension: A review of 52 patients and of model predictions. *AJNR Am J Neuroradiol* 2011; 32: 1408–1414. 5. Bussiere M, Falero R, Nicolle D, et al. Unilateral transverse sinus stenting of patients with idiopathic intracranial hypertension. *AJNR Am J Neuroradiol* 2010;31:645–50

**Keywords:** Pseudotumor Cerebri, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 196

### Predictive Value of International Classification of Disease Code for IIH in a University Health System

Irma Muminovic<sup>1</sup>, Heather Moss<sup>1</sup>

<sup>1</sup>Stanford University, Palo Alto, California, USA

#### Introduction:

Diagnosis of IIH requires confirming high ICP, excluding secondary causes, and ophthalmic examination. The purpose of this study was to determine the positive predictive value (PPV) of ICD-9/10 codes for IIH(348.2, G93.2) among patients with all necessary testing performed within a university health system.

#### Methods:

24 subjects had incomplete LPs. Of those with full LP results, 77%(n=60) had opening pressure >25cm H<sub>2</sub>O. 54%(n=56) had normal CSF analysis. 51.5%(n=53) had normal neuro-imaging with an additional 17.5%(n=18) having normal neuro-imaging except for ICP associated findings. 39%(n=37) had optic disk edema, and 4.9%(n=5) had other optic disk findings. 56 subjects had definite IIH(with papilledema and without), and an additional 9 had probable IIH. The positive predictive value (PPV) of ICD coding for IIH was 63.10%.

#### Results:

24 subjects had incomplete LPs. Of those with full LP results, 77%(n=60) had opening pressure >25cm H<sub>2</sub>O. 54%(n=56) had normal CSF analysis. 51.5%(n=53) had normal neuro-imaging with an additional 17.5%(n=18) having normal neuro-imaging except for ICP associated findings. 39%(n=37) had optic disk edema, and 4.9%(n=5) had other optic disk findings. 56 subjects had definite IIH(with papilledema and without), and an additional 9 had probable IIH. The positive predictive value (PPV) of ICD coding for IIH was 63.10%.

#### Conclusions:

We estimate a PPV for ICD coding of IIH of 63% in subjects with all necessary testing performed at a single institution. This is similar to a prior estimate of 55% for patients with ER and inpatient visits at a single institution. The results reinforce the potential for misclassification bias when identifying IIH cases by ICD coding alone. Further work is needed to develop algorithms with which increase positive predictive value of coding based case identification.

**References:** Koernor, Deborah, Friedman. Inpatient Emergency Service Utilization in Patients with Idiopathic Intracranial Hypertension, *J Neuroophthal*, 34(3):229-32, 2014. Friedman, Liu, Digre. Revised Diagnostic Criteria for the Pseudotumor Cerebri Syndrome in Adults and Children, *Neurology*, 81(13):1159-1165, 2013.

**Keywords:** High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** NEI K23 024345, Unrestricted Departmental Grant from Research to Prevent Blindness



**Poster 197****Retrospective Analysis of the Effect of Acetazolamide on Anthropometrics in Pediatric Pseudotumor Cerebri Syndrome (PTCS)**

Claire Sheldon<sup>1</sup>, Sara Reggie<sup>2</sup>, Grace Paley<sup>3</sup>, Shana McCormack<sup>2</sup>, Grant Liu<sup>2</sup>

<sup>1</sup>University of British Columbia, Vancouver, Canada, <sup>2</sup>Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA,

<sup>3</sup>Washington University School of Medicine, St Louis, Missouri, USA

**Introduction:**

Oral acetazolamide is a cornerstone of management of pediatric PTCS. Previous studies have suggested that acetazolamide may influence pediatric growth parameters. The purpose of this study was to evaluate this possibility in children with PTCS.

**Methods:**

In a retrospective study, cases of PTCS were identified based on ICD9 code 348.2 and/or physician database (04/1993-04/2013). Clinical data were collected using manual and bioinformatics-based abstraction. Standardized growth charts were used to determine age-/sex-specific height, weight, and BMI Z-scores. Analysis was limited to subjects with > 5 growth parameter measurements over time & clear documentation of acetazolamide use.

**Results:**

Using updated PTCS diagnostic criteria (2013), 34 cases of definite or probable PTCS were identified (60% female, mean age 12.5±4.1yrs). To analyze the effect of acetazolamide on pediatric growth parameters, mean BMI Z-scores were determined prior to, during and following treatment. There was no significant effect of acetazolamide treatment on mean BMI Z-score (1.31±1.08 prior to, 1.20±1.02 during and 1.33±0.45 after acetazolamide treatment; F=0.60). Reviewing records that included anthropometrics before and during acetazolamide treatment (n=22), there was an equal number illustrating an increase or decrease in BMI Z-values (n=11 in each case). This lack of effect was also seen if children of non-overweight status were considered (n=4 showed an increase in BMI Z-score during treatment with acetazolamide vs. n = 3 showed a decrease) or if children <10yrs were considered alone (n=4 showed an increase in BMI Z-score during treatment with acetazolamide vs. n=3 showed a decrease).

**Conclusions:**

Previous studies have suggested that, in the pediatric population, acetazolamide induces growth suppression. This retrospective study included children with PTCS and suggests that, overall, BMI Z-scores remain stable during treatment with acetazolamide. Further studies are required to evaluate if detailed measures of pediatric anthropometrics, including the component elements of BMI, are influenced specifically.

**References:** None.

**Keywords:** Pediatric neuro-ophthalmology, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 198**

**Correlation of Opening Pressure with Unilateral Versus Bilateral Venous Sinus Stenosis in Pseudotumor Cerebri**

Padmaja Sudhakar<sup>1</sup>, Flavius Raslau<sup>1</sup>, Douglas Lukins<sup>31</sup>, Roman Kassa<sup>1</sup>

<sup>1</sup>University of Kentucky, Lexington, Kentucky, USA

**Introduction:**

The pathophysiology behind venous sinus stenosis(VSS) in idiopathic intracranial hypertension (IIH) is unclear. It has been argued that VSS is an independent cause of IIH rather than a consequence and recent data suggest clinical efficacy and safety of venous sinus stenting. In this study we aimed to explore the possible association between unilateral versus bilateral VSS and opening pressure on initial lumbar puncture in IIH.

**Methods:**

Retrospective chart review of IIH patients seen in our neuro-ophthalmology clinic over the past 2 years. VSS on imaging was classified as categorically present or absent.

**Results:**

Our study included 110 IIH patients who had undergone either a CT or MR venogram. They were predominantly women (96.4%) with ages ranging from 18 to 61 years. 62.7% had VSS (n=69); Transverse sinus was predominantly involved (95.7%, n=66) followed by superior sagittal sinus (2.9 %, n=2) and the jugular veins extra-cranially (1.4%, n=1). 80.3% with transverse sinus stenosis had bilateral involvement (n=53) and 19.7% had unilateral involvement (n=13). Interestingly, 76.9% with unilateral transverse sinus stenosis had involvement on the left (n=10). Mean opening pressure was 35.8cm H<sub>2</sub>O (SD +/-8.5) in bilateral transverse sinus stenosis, 33.8cm H<sub>2</sub>O (SD +/-7.6) in unilateral transverse sinus stenosis and 35.5cm H<sub>2</sub>O (SD +/-10) in those with no VSS, suggesting no significant difference between these groups. An intriguing subpopulation of patients with no papilledema but bilateral transverse sinus stenosis had similar mean opening pressure of 32.2cm H<sub>2</sub>O (SD +/-9.1).

**Conclusions:**

Our data show no difference in diagnostic opening pressure in IIH with unilateral or bilateral VSS and in those without VSS. While degree, length of stenosis and venous pressure gradient may play a role in IIH with VSS, we need to look for other contributors among those without VSS. Also, we wonder if the involvement of left transverse sinus has a role in this perplexing entity.

**References:** 1. Dinkin MJ, Patsalides A. Venous Sinus Stenting in Idiopathic Intracranial Hypertension: Results of a Prospective Trial. *J Neuroophthalmol.* 2017 Jun;37(2):113-121. 2. Dinkin MJ, Patsalides A. Venous Sinus Stenting for Idiopathic Intracranial Hypertension: Where Are We Now? *Neurol Clin.* 2017 Feb;35(1):59-81. Review. 3. Kelly LP, Saindane AM, Bruce BB, Ridha MA, Riggeal BD, Newman NJ, Biousse V. Does bilateral transverse cerebral venous sinus stenosis exist in patients without increased intracranial pressure? *Clin Neurol Neurosurg.* 2013 Aug;115(8):1215-9. 4. Aguilar-Pérez M, Martínez-Moreno R, Kurre W, Wendl C, Bänzner H, Ganslandt O, Unsöld R, Henkes H. Endovascular treatment of idiopathic intracranial hypertension: retrospective analysis of immediate and long-term results in 51 patients. *Neuroradiology.* 2017 Mar;59(3):277-287.

**Keywords:** Pseudotumor Cerebri, Optic neuropathy, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 199**

**"Real World" MRI Findings in Idiopathic Intracranial Hypertension**

Philip Garza<sup>1</sup>, Lindsey Delott<sup>1</sup>, Jonathan Trobe<sup>1</sup>, Wayne Cornblath<sup>1</sup>

<sup>1</sup>University of Michigan W. K. Kellogg Eye Center, Ann Arbor, Michigan, USA

**Introduction:**

Neuroimaging is routinely used in the diagnosis of idiopathic intracranial hypertension (IIH), yet many patients with IIH have normal neuroimaging. Previous studies of the neuroimaging correlates of IIH have used expert graders, either fellowship-trained neuroradiologists or neuro-ophthalmologists, to identify imaging abnormalities attributable to IIH. These studies have found imaging abnormalities in as many as 70-80% of patients with IIH. We sought to determine the prevalence of imaging abnormalities on MRI and MR venogram reports generated as part of routine clinical practice at our center.

**Methods:**

We retrospectively reviewed 25 cases of IIH seen at our institution between 2007 and 2017. We included patients aged 18 to 45 years who received an MRI and MR venogram of the brain at our institution and had a documented lumbar puncture opening pressure above 25 cm water, resulting in a new diagnosis of IIH. Patients without bilateral papilledema on fundus examination were excluded. We reviewed clinical imaging reports for documentation of abnormalities commonly seen in IIH.

**Results:**

24/25 (96%) of patients were female, with mean age 26.2 years, mean BMI 34.4 kg/m<sup>2</sup>, and mean opening pressure 42.8 cm water. The most frequently documented MRI abnormality was venous sinus narrowing (11/25, 44%), followed by distention of the optic nerve sheath (6/25, 24%), flattening of the posterior globes (6/25, 24%), empty sella (4/25, 16%), optic nerve head protrusion (2/25, 8%), deformation of the pituitary gland (2/25, 8%), and vertical tortuosity of the optic nerve (2/25, 8%). Widening of the foramen ovale, posterior deviation of the pituitary stalk, and optic nerve head enhancement were not documented.

**Conclusions:**

Neuroimaging abnormalities were documented in clinical imaging reports for fewer than half of patients with definitively-diagnosed IIH, suggesting that the "real world" sensitivity of neuroimaging for IIH is poor. Patients with a clinical picture consistent with IIH require lumbar puncture for accurate diagnosis.

**References:** Butros, Goncalves, Thompson, Agarwal, Lee. Imaging features of idiopathic intracranial hypertension, including a new finding: Widening of the foramen ovale. *Acta Radiologica*, 53, 682-8, 2012. Brodsky, Vaphiades. Magnetic resonance imaging in pseudotumor cerebri. *Ophthalmology*, 105, 1686-93, 1998. Yuh, Zhu, Taoka, Quets, Maley, Muhonen, Schuster, Kardon. MR imaging of pituitary morphology in idiopathic intracranial hypertension. *Journal of Magnetic Resonance Imaging*, 12, 808-13, 2000.

**Keywords:** Pseudotumor Cerebri, Neuroimaging, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Not applicable

## Poster 200

### The Persistence of MRI Findings in Pediatric Pseudotumor Cerebri Syndrome

Anita Kohli<sup>1</sup>, Arastoo Vossough<sup>2</sup>, Robert Mallery<sup>3</sup>, John Woo<sup>4</sup>, Grace Paley<sup>5</sup>, Claire Sheldon<sup>6</sup>, Grant Liu<sup>7</sup>, Christina Szperka<sup>8</sup>

<sup>1</sup>Yale Department of Ophthalmology and Visual Science, New Haven, Connecticut, USA, <sup>2</sup>Children's Hospital of Philadelphia, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA, <sup>3</sup>Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, USA, <sup>4</sup>Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA, <sup>5</sup>Washington University School of Medicine in St. Louis, St. Louis, Missouri, USA, <sup>6</sup>University of British Columbia, Vancouver, Canada, <sup>7</sup>Hospital of the University of Pennsylvania, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA, <sup>8</sup>Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA

#### Introduction:

MRI findings, including optic nerve sheath distention (ONSD), pituitary gland flattening (PGF), flattening of the posterior sclera (FPS) and transverse sinus stenosis (TSS), can be used to diagnose pseudotumor cerebri syndrome (PTCS), when papilledema is absent. At least three imaging findings have a robust specificity for definite PTCS, of which TSS is the most specific. It is not known whether these findings persist on follow-up imaging in the pediatric population.

#### Methods:

In 119 patients with MRI for suspicion of increased intracranial pressure (ICP), 16 had repeat MRI brain (+/-MRV). These follow-up scans were re-reviewed by a masked neuroradiologist to assess for the imaging findings above. Patients were classified based on clinical findings into definite PTCS (n=6), probable PTCS (n=2), intracranial hypertension (IH, n=5), or control groups (n=3). Within the PTCS group (definite and probable, n=8) and not PTCS group (IH and controls, n=8), paired t-tests and McNemar's test were used to describe changes in continuous and categorical variables, respectively.

#### Results:

The average time between original and follow-up MRIs was 17.6 months (with PTCS) and 18.5 months (without PTCS). All patients with PTCS still had papilledema at the time of follow-up MRI. Over time, there was no significant difference in the presence or absence of MRI findings within the PTCS and not PTCS groups ( $p > 0.10$  for all imaging findings). TSS worsened in 3/8 with PTCS. Three of 4 imaging findings were seen initially in 5/6 patients with definite PTCS and persisted in 3 patients.

#### Conclusions:

Imaging findings in patients with PTCS can endure for years, in parallel with the persistence of papilledema, possibly due to incomplete treatment. Obtaining repeat MRI in patients with persistent papilledema and similar clinical symptoms may not be additive to management. On follow-up imaging, TSS and 3/4 imaging findings continue to be seen only in patients with definite PTCS.

**References:** None.

**Keywords:** Neuroimaging, Pediatric neuro-ophthalmology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 202

### Comparison of a Smartphone Application with Ishihara Pseudoisochromatic Plate for Testing Color Vision

Jiawei Zhao<sup>1</sup>, Allen Eghrari<sup>1</sup>

<sup>1</sup>Johns Hopkins Hospital, Baltimore, Maryland, USA

#### Introduction:

Eyehandbook is an accessible smartphone application containing diagnostic tools for eye-care providers with over 25,000 active users globally. It contains a color vision (CV) test similarly designed to the Ishihara pseudoisochromatic color vision test. However, the validity of this CV test has not been assessed in a prospective fashion. The aim of this study is to evaluate and compare the Eyehandbook CV test to Ishihara under simulated CV loss in normal subjects.

#### Methods:

Using ImageJ software, images of Eyehandbook CV test and Ishihara are processed in two different ways: 1) 32 bit-grayscale removes color information from the images to model total color vision loss; 2) Blue channel under Split RGB channel simulates red-green (R-G) deficiency. The unprocessed image simulates that of a person with normal color vision. For each plate, the numeral or pattern seen under each condition was recorded. Preliminary results were obtained by testing the author.

#### Results:

Under 32 bit-grayscale, correct number was identified in 30% of plates in Eyehandbook vs 6% in the Ishihara book. In addition, Eyehandbook lacks special plate designs for differentiation between R-G color deficiency and total color blindness that Ishihara contains. Under the wiggly line design of Ishihara, specific numbers appeared under blue channel whereas no number or line was depicted under 32 bit-grayscale. In contrast, Eyehandbook had an absence of number and pattern under both blue channel and 32 bit-grayscale. Unlike Eyehandbook, Ishihara also contains plates where the unprocessed image shows a different number compared with blue channel images.

#### Conclusions:

The ability to see numbers in 32 bit-grayscale depends on contrast sensitivity. More plates were correctly identified in Eyehandbook, suggesting its results may underestimate the severity of color vision loss in persons with normal contrast sensitivity compared to Ishihara. Furthermore, Eyehandbook lacks the ability to discern R-G color deficiency from total color blindness.

**References:** None.

**Keywords:** Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 203****Development of Nanocarbon Antioxidants for Oxidative Stress Related Injury of the Retina**

William Sikkema<sup>1</sup>, Kimberly Mendoza<sup>2</sup>, James Tour<sup>2</sup>, Veeral Shah<sup>3</sup>

<sup>1</sup>Rice University, Baylor College of Medicine, Houston, Texas, USA, <sup>2</sup>Rice University, Houston, USA, <sup>3</sup>Baylor College of Medicine, Texas Children's Hospital, Houston, Texas, USA

**Introduction:**

Optic neuropathy refers to dysfunction of the optic nerve and to the damage and death of retinal ganglion cells in particular. There are multiple etiologies of optic neuropathy such as genetic, traumatic, inflammatory, and infectious, but oxidative stress is implicated in all of these. Nanocarbon antioxidants (NCA) have been designed to reduce oxidative stress in biological tissue at levels where naturally derived antioxidants are ineffective. These NCAs can specifically target reactive oxygen species (ROS) more efficiently than biological antioxidant cascades, possibly because they specifically target ROS in the mitochondria and don't require cofactors or regeneration. Our central hypothesis is that optimally designed NCA will neutralize and sequester tissue damaging reactive oxygen species. We have demonstrated the safety of the nanoparticle in multiple cells lines, including ocular tissue.

**Methods:**

To compare the efficacy of various nanocarbon antioxidants, 8 carbon nanoparticles were designed from various carbon-rich sources. These NCAs were characterized and screened for their chemical efficacy by electrochemistry and electron paramagnetic resonance. To evaluate the biological antioxidant properties, retina explants are taken from mice and exposed to transient ischemic (TI) conditions in the presence of dihydroethidium (DHE) to monitor oxidative stress. DHE fluorescence is measured by confocal microscopy to quantitate the rescue of TI induced oxidative stress by NCAs.

**Results:**

The nanoparticles derived from single wall carbon nanotubes brought the oxidative stress levels of the retina explants that experienced TI down to that of retinas that experienced no ischemia, while the carbon nanoparticles derived from other sources brought the oxidative stress down 40-70% from the untreated explant that experienced hypoxia. n=4 for each NCA.

**Conclusions:**

We have identified and designed a NCA, whose unique free radical scavenging properties demonstrate a high efficiency, stability, biocompatibility, and resistance to deactivation that would provide a novel and potentially effective antioxidant for mitigating cellular stress injuries.

**References:** None.

**Keywords:** Optic neuropathy, Stroke Trauma, Genetic Disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 205****Inhibitory Deficits in Visual Snow**

Melissa Tien<sup>1</sup>, Janet Chan<sup>2</sup>, Meaghan Clough<sup>3</sup>, Lynette Millist<sup>4</sup>, Allison McKendrick<sup>2</sup>, Heather Mack<sup>5</sup>, Joanne Fielding<sup>3</sup>, Owen White<sup>4</sup>

<sup>1</sup>National Healthcare Group Eye Institute, Tan Tock Seng Hospital, Singapore, Singapore, <sup>2</sup>Optometry and Vision Sciences, University of Melbourne, Melbourne, Australia, <sup>3</sup>Monash Institute of Cognitive and Clinical Neurosciences, Monash University, Melbourne, Australia, <sup>4</sup>Department of Neurology, Royal Melbourne Hospital, Melbourne, Australia, <sup>5</sup>Centre for Eye Research Australia, Melbourne Health, Walter and Eliza Hall, Melbourne, Australia

**Introduction:**

Patients with visual snow (VS) complain of a constant and persistent “static-like” disturbance of the entire visual field, associated with a variety of other phenomena such as palinopsia and tinnitus. The pathophysiology of VS is unknown but cortical hyper-excitability and dysrhythmia have been proposed. We suggest that such dysrhythmia is a consequence of inhibitory dysfunction, leading to the perception of normally convergent, non-visual afferent stimuli. Ocular motor testing has been successfully employed in neurological and psychiatric disorders to demonstrate inhibitory dysfunction. In this study, we used a range of ocular motor tests to investigate inhibitory deficits in patients with VS.

**Methods:**

A prospective pilot study comparing ocular motor tests between 14 patients with VS with 14 healthy controls. Antisaccade, endogenously-cued and visually-guided paradigms were employed. All patients underwent a full neuro-ophthalmic evaluation, including visual electrophysiology.

**Results:**

Patients with VS have significantly higher antisaccade error rates compared to healthy controls ( $p=0.01$ ). Patients with VS also demonstrated shorter saccade latencies across all ocular motor tasks.

**Conclusions:**

The significantly higher antisaccade error rate shown by VS patients suggests underlying inhibitory dysfunction. Likewise, the shorter saccade latencies of VS patients also suggests that VS patients’ neural activity sits much closer to threshold than in healthy controls, likely a consequence of underlying inhibitory deficits. This is the first known ocular motor study demonstrating inhibitory deficits in patients with VS.

**References:** None.

**Keywords:** Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 206**

**Glial Changes In An Animal Model Of Ethambutol-Related Optic Neuropathy**

Hui-Chen Cheng<sup>1</sup>

<sup>1</sup>Taipei Veterans General Hospital, Taipei, Taiwan

**Introduction:**

Ethambutol (EMB)-related optic neuropathy is the most common toxic optic neuropathy, which accounts for 100,000 new cases each year in the world. Glial cells play an essential role in neuronal survival, while dysfunctional glial may result in neuronal cell death.

**Methods:**

A mouse model of EMB-related optic neuropathy was established by intra-peritoneal (IP) injection of phosphate-buffered saline (PBS), EMB 50mg/kg, EMB 200mg/kg to adult C57BL/6J mice for 10 days. Mice are then euthanized and retinal and optic nerve sections were obtained. Immunohistochemistry (IHC) with anti-glial astrocytic fibrillary protein (GFAP), anti-glutamine synthetase (GS) and anti-Brna3a antibody were performed for further analysis.

**Results:**

The results showed a dose-dependent relationship between EMB doses and retinal ganglion cells(RGC) cell numbers, with fewer RGC cell numbers in higher EMB dose. The IHC showed increased GFAP-positive cells in both optic nerve and retinal section in an EMB dose dependent manner, indicating astrocytosis in these areas. In retinal sections, more prominent GS fluorescence was noted in higher EMB doses, implying Muller cell hypertrophy after EMB treatment.

**Conclusions:**

Muller cell hypertrophy and astrocytosis in both optic nerve and retina were observed in an animal model of EMB-related optic neuropathy, which may imply the role of glial changes in the pathogenesis of EMB-related toxicity.

**References:** None.

**Keywords:** Optic neuropathy, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** This study was supported by grants from the Ministry of Science and Technology (MOST-106-2314-B-075-029) and Taipei Veterans General Hospital (VGH 106-B-014).



**Poster 207****Smartphone Tests of Visual Acuity, Hyper-acuity, Contrast Sensitivity and Critical Flicker Fusion**

Jane Bailey<sup>1</sup>, Kasra Zarei<sup>2</sup>, Pieter Poolman<sup>3</sup>, Randy Kardon<sup>2</sup>

<sup>1</sup>University of Iowa Department of Ophthalmology and Visual Sciences, Iowa City, Iowa, USA, <sup>2</sup>University of Iowa, Iowa City, Iowa, USA, <sup>3</sup>University of Iowa and Iowa City Veterans Administration Hospital, Iowa City, Iowa, USA

**Introduction:**

Testing of the afferent visual system within the confines of smartphone hardware limitations would make assessment of visual acuity, contrast sensitivity, and critical flicker fusion available in a wide variety of settings, such as in the emergency department, in outpatient clinics, or in the home. Reliable smartphone-based testing could improve triage, as well as allow patients with known disease to monitor their vision at home frequently, if needed.

**Methods:**

A feasibility study was done to characterize the hardware performance of an iPhone and iPad platform to provide a standardized suite of visual function tests, including Landolt C acuity, Vernier hyper-acuity, Landolt C contrast sensitivity, and critical flicker fusion. An initial version was tested in 27 normal subjects and 16 neuro-ophthalmology patients (age range 18-82 years)

**Results:**

Photometric evaluation of the iPhone and iPad screen intensity showed excellent reproducibility within and across devices. The contrast threshold at which flicker fusion was observed could be determined for both 15Hz and 7.5 Hz. We found that all 4 tests (Landolt C acuity, Vernier hyper-acuity, Landolt C contrast sensitivity, and critical flicker fusion) could be easily completed in minutes, and the intuitive nature of the tests was rapidly accepted by subjects of all ages, including those with eye disease.

**Conclusions:**

These results demonstrate the technical feasibility of visual testing with smartphone and tablet devices for monitoring visual functions such as acuity, contrast sensitivity and critical flicker fusion. A prospective study is currently underway to characterize the sensitivity and specificity of the four test paradigms in a large cohort. Portable and rapid smartphone tests of visual function could aid in the triage and monitoring of patients outside the neuro-ophthalmology office.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy, Miscellaneous, Demyelinating disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 208

### Assessment of Neurocognitive Consequences of Call Duty in Residents Using Saccadic Eye Movements

Michael Ding<sup>1</sup>, Joyce Mbekeani<sup>2</sup>, Yasmina Ahmed<sup>2</sup>, Rosemarie Conigliaro<sup>2</sup>, Ellise Delphin<sup>2</sup>, Anne Durstenfeld<sup>2</sup>, Anand Jagannath<sup>2</sup>, Alina Masters-Israilov<sup>2</sup>, Mark Milstein<sup>2</sup>, Moriah Rabin<sup>2</sup>, Sujatha Ramachandran<sup>2</sup>, Peter Vlismas<sup>2</sup>, David Yang<sup>2</sup>, Moonseong Heo<sup>2</sup>, Jamie Rosenberg<sup>2</sup>

<sup>1</sup>Albert Einstein College of Medicine, Bronx, New York, USA, <sup>2</sup>Montefiore Medical Center | Albert Einstein College of Medicine, Bronx, New York, USA

#### Introduction:

Resident sleep deprivation is an important topic given its negative effect on neurocognitive performance. The King-Devick test (KDT), which tests speed and accuracy of number-reading, requires integrity of saccades, visual processing, and cognition. The purpose of this study is to investigate neurocognitive effects of sleep deprivation in on-call residents using KDT.

#### Methods:

A prospective, cohort study was conducted among 80 residents (PGY2-4) from multiple departments of an urban teaching hospital. KDT was performed at the beginning and end of an overnight call shift for the residents in the experimental group. A control group was tested at the beginning of 2 consecutive day shifts. Estimates of hours of sleep, Karolinska Sleepiness Scale (KSS)(1=extremely alert, 9=extremely sleepy), and time and accuracy of KDT, the primary outcome variable, were recorded. We performed t-test, regression analysis, and correlation analysis. Statistical significance was set at  $p < 0.05$ .

#### Results:

42 residents were tested before and after overnight call shifts and 38 served as controls. Mean age and gender breakdown were similar between groups: age 28.95 years(standard deviation(SD)=2.49) in experimental group and 29.84(SD=3.36) in controls ( $p=0.18$ ); 47.6% female in the experimental group and 47.4% in controls ( $p=0.98$ ). Change in test time was significantly different between the groups, with the experimental group performing 0.54(SD=4.0) seconds slower after their night on call and the control group performing 2.32(SD=3.0) seconds faster on the second day,  $p < 0.001$ . Residents reporting more sleep the night between the two tests had greater improvement in their test times (Pearson  $r = -0.31, p = 0.005$ ). Residents reporting more sleepiness on the KSS had less improvement in their test time ( $r = 0.25, p = 0.027$ ).

#### Conclusions:

Sleep deprivation and self-reported sleepiness were inversely correlated with neurocognitive performance as measured by KDT. More research is required to determine whether this test could help determine resident fatigue or ability to continue working after a long shift.

**References:** 1. Ernst F, Rauchenzauner M, Zoller H, Griesmacher A, Hammerer-Lercher A, Carpenter R, Schuessler G, Joannidis M. Effects of 24 h working on-call on psychoneuroendocrine and oculomotor function: a randomized cross-over trial. *Psychoneuroendocrinology*. 2014 Sep;47:221-31. 2. Rowland LM, Thomas ML, Thorne DR, Sing HC, et al. Oculomotor responses during partial and total sleep deprivation. *Aviat Space Environ Med*. 2005 Jul;76(7 Suppl):C104-13 3. Goel N, Rao H, Durmer JS, Dinges DF. Neurocognitive consequences of sleep deprivation. *Semin Neurol*. 2009 Sep;29(4):320-39. 4. Stocker RP, Khan H, Henry L, Germain A. Effects of Sleep Loss on Subjective Complaints and Objective Neurocognitive Performance as Measured by the Immediate Post-Concussion Assessment and Cognitive Testing. *Arch Clin Neuropsychol*. 2017;32(3):349-368. 5. Davies EC, Henderson S, Balcer LJ, Galetta SL. Residency training: The King-Devick test and sleep deprivation. *Neurology* 2012;78:e103-e106.

**Keywords:** Ocular Motility, Higher visual functions, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 209**

**Clival Mass: An Under Recognized Cause of Sixth Cranial Nerve Palsy**

Talal Derani<sup>1</sup>, Eric Liao<sup>1</sup>, Cherie Farkash<sup>1</sup>, Lindsey De Lott<sup>1</sup>, Johnathan Trobe<sup>1</sup>, Wayne Cornblath<sup>1</sup>

<sup>1</sup>University of Michigan, Ann Arbor, Michigan, USA

**Introduction:**

Imaging is routinely ordered in patients with acute sixth cranial nerve palsies, yet replacement of the clival marrow by malignant tumor is an often under-recognized and potentially life-threatening cause. Neoplastic disease causes loss of the hyperintense clival marrow signal on precontrast T1-weighted MRI sequences, a sign that may be overlooked by radiologists (1-2). While there have been individual cases and small case series reported in the literature (3), we herein report the largest series of patients presenting with a sixth cranial nerve palsy and found to have clivus pathology on imaging.

**Methods:**

This is a retrospective review of patients with sixth cranial nerve palsies found to have neoplastic infiltration of the clivus, diagnosed by fellowship-trained neuro-ophthalmologists from 1994 to 2017. Neuroimaging studies were reviewed by a fellowship-trained neuro-radiologist. Data abstracted from clinical charts included the history, symptoms, imaging findings, and histopathology of the primary tumor. Descriptive statistics were used to summarize clinical variables.

**Results:**

Of 39 patients, 20 were women, and the mean age was 67. A majority had a known history of cancer, though in a significant percentage, sixth nerve palsy was the first sign of metastasis. There was variability regarding whether clival shape was maintained or if there was associated involvement of the calvarium, cervical spine, and whether these findings were mentioned in the original report.

**Conclusions:**

Isolated sixth cranial nerve palsies are often the first presentation of a primary clival mass or a clival metastasis. This can be seen in patients with a known malignancy or as the first sign of malignancy. In patients with a known malignancy the sixth nerve palsy can lead to a search for carcinomatous meningitis when the actual cause is bony metastasis.

**References:** 1. Neelakantan, A., & Rana, A. K., Benign and malignant diseases of the clivus. *Clinical Radiology*, 69(12), 1295–1303, 2014. 2. Loevner, L. A., Tobey, J. D., Yousem, D. M., Sonners, A. I., Hsu, W. C. MR Imaging Characteristics of Cranial Bone Marrow in Adult Patients with Underlying Systemic Disorders Compared with Healthy Control Subjects. *Am. J. Neuroradiol.*, 23(2), 248, 2002. 3. Dekker, S. E., Wasman, J., Yoo, K. K., Alonso, F., Tarr, R. W., Bambakidis, N. C., & Rodriguez, K. Clival Metastasis of a Duodenal Adenocarcinoma: A Case Report and Literature Review. *World Neurosurgery*, 100, 62–68 (2017).

**Keywords:** Neuroimaging, Tumors, Skull Base

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 210****Swept Source OCT Angiography Quantification in Optic Nerve Edema: Preliminary Results**

Marie-Benedicte Rougier<sup>1</sup>, Emilie Tournaire<sup>1</sup>, Jean-François Korobelnik<sup>1</sup>

<sup>1</sup>University Hospital of Bordeaux, Bordeaux, France

**Introduction:**

OCT angiography (OCT-A) is a new imaging tool allowing the visualization of the superficial optic disc vessels and the superficial and deep peripapillary vascular network without any intra-venous dye injection. The morphological features of OCT-A in optic disc edema (papilledema, ischemic and inflammatory) have already been described. With the last development of Swept Source OCT-A software, it is possible to measure the peripapillary vessel density and the vascular flux. The aim of this study is to evaluate the relevance of these metrics in the diagnosis of optic disc edema.

**Methods:**

9 patients with an acute unilateral optic disc edema were evaluated with the routine means and diagnosed with non arteritic ischemic optic neuropathy (NAION, n=4) or papillitis (n=5). Swept source OCT-A (PlexElite 9000, Carl Zeiss Meditec, Dublin, CA) of the peripapillary network was done on both eyes of all 9 patients. Capillary perfusion and capillary flux index were measured in 4 quadrants and on average. Each eye was compared with the contralateral healthy eye. The Wilcoxon test for matched samples was used. A p value less than 0.05 was considered statistically significant.

**Results:**

In NAION eyes, no difference with healthy eye was found for both capillary perfusion and flux index. In papillitis eyes, the average flux index was higher than in the healthy eye with a statistically significant trend (p=0.06).

**Conclusions:**

In NAION eyes we did not find any difference with the healthy eye. This might be due to the presence of artifacts (eye motion, heterogeneous edema) that could alter the measurement. In papillitis eyes, there was a flux index increase trend, which is consistent with the inflammatory mechanisms, but the series is small. Nevertheless, it seems that in optic nerve edema diagnosis, the morphological analysis of Swept Source OCT-A is more reliable than quantified data.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy

**Financial Disclosures:** consultant for Carl Zeiss Meditec

**Grant Support:** None.

**Poster 211****Correlative Image Enhancement: Using Image Processing to Improve Visualization of Optic Neuritis on MRI.**

Leanne Stunkel<sup>1</sup>, Amber Salter<sup>2</sup>, Matthew Parsons<sup>3</sup>, Aseem Sharma<sup>3</sup>, Gregory Van Stavern<sup>4</sup>

<sup>1</sup>Department of Neurology, Washington University in St. Louis School of Medicine, St. Louis, Missouri, USA, <sup>2</sup>Division of Biostatistics, Washington University in St. Louis School of Medicine, St. Louis, Missouri, USA, <sup>3</sup>Mallinckrodt Institute of Radiology, Washington University in St. Louis, St. Louis, Missouri, USA, <sup>4</sup>Department of Ophthalmology and Visual Sciences, Washington University in St. Louis, St. Louis, Missouri, USA

**Introduction:**

Detection of optic neuritis on MRI can be challenging given the nerve's small size and its distance from normal white matter (against which its signal is compared). We aimed to assess the accuracy of Correlative Image Enhancement (CIE), an image post-processing algorithm, for evaluation of optic neuritis (ON) on MRI.

**Methods:**

Retrospective study of 43 patients (32 females; mean age 43 ±14.1) with MRI done for clinical suspicion of ON. Contrast-to-noise ratio (CNR) between optic nerves and ipsilateral white matter on FLAIR and contrast-enhanced images was calculated for baseline and CIE-processed images. Positive result defined as >50% increase in CNR. Sensitivity and specificity values were compared to the original clinical MRI reads. Masked radiologists' review is ongoing.

**Results:**

Out of 86 eyes, 31 had clinically proven ON (ON eyes), 18 eyes had other diagnoses (control, or non-ON eyes), and 37 eyes were asymptomatic (fellow eyes). On FLAIR, mean baseline CNR was 22.2 ±18.4 and baseline MRI read sensitivity was 77% (22/28). Following processing, CNR increased by 75.7 ±43.8 with a positive result in 96.4% (27/28). 1/18 (5.5%) of non-ON control eyes and 1/36 (2.8%) asymptomatic fellow eyes had a positive result, the same false positive rate as the original MRI reads. On contrast-enhanced images, mean baseline CNR was 22.5 ±22.5 and baseline sensitivity was 82% (23/28). Following processing, CNR increased by 79.1 ±53.2 with a positive result in 86% (24/28). A positive result was seen in 5.6% (1/18) non-ON controls and 8.8% (3/34) asymptomatic fellow eyes versus baseline MRI read false positive rate of 5.6% (1/18) and 2.9% (1/34). The proportion with increased CNR on contrast-enhanced images was significantly different for ON vs non-ON control eyes (p=0.0003) and asymptomatic fellow eyes (p<0.001).

**Conclusions:**

CIE increased CNR in most ON-eyes but few control eyes. CIE may improve MRI sensitivity of ON without compromising specificity.

**References:** None.

**Keywords:** Neuroimaging, Demyelinating disease, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 212**

**Optical Coherence Tomography (OCT) Findings in Rat Model of Anterior Ischemic Optic Neuropathy (rAION)**

Tzulun Huang<sup>1</sup>, Yao-Tseng Wen<sup>2</sup>, Rong-Kung Tsai<sup>3</sup>, Kishan kapupara<sup>2</sup>

<sup>1</sup>Department of Ophthalmology, Far Eastern Memorial Hospital, New Taipei City, Taiwan, <sup>2</sup>Institute of Eye Research, Buddhist Tzu Chi General Hospital, Hualien, Taiwan, Hualien, Taiwan, <sup>3</sup>Institute of Medical Sciences, Tzu Chi University, Hualien, Taiwan

**Introduction:**

Optical coherence tomography (OCT) has shown prelaminar tissue thickening which were reversed along with retina nerve fiber layer (RNFL) loss in human NAION. This kind of non-invasive methods gives us an insight of disease mechanism in rAION and provide potential therapeutic outcomes in primate model.

**Methods:**

Outcome measurements included spectral domain OCT image (optic nerve width (ONW) and RNFL), RGCs with retrograde Fluoro-Gold labeling and flash visual-evoked potentials (FVEP). Statistical analysis was performed with IBM SPSS 19. We used Kruskal-Wallis test and Mann-Whitney U test to evaluate differences between the groups.

**Results:**

In OCT, severe swollen disc was observed from the 1st to 3rd day post rAION then recovered completely by the 7th day. Edema change of RNFL last till 3rd day then recovered by the 7th day. There was RNFL loss from the 14th day to 28th day indicated delayed apoptosis in RGCs. At the 28th day, there was significant difference in RNFL thickness between sham and rAION group ( $0.92 \pm 0.15$  mm<sup>2</sup> vs.  $0.51 \pm 0.12$  mm<sup>2</sup>, respectively; \* $p \leq 0.05$ ; n=3-5) FVEPs were measured at 4th week post rAION. The P1-N2 amplitudes in the sham and rAION were  $41.00 \pm 6.15 \mu V$  and  $12.29 \pm 5.5 \mu V$ , respectively. (\*\* $p \leq 0.01$ ; n=3) These data suggests that visual function is decreased in rAION and correlated with RNFL change in our OCT findings. At the 4th week post-infarct, the significant loss of RGC density in the central ( $581 \pm 42$ /mm<sup>2</sup> vs  $1811 \pm 139$ /mm<sup>2</sup>) and mid-peripheral retina ( $389 \pm 71$ /mm<sup>2</sup> vs  $1162 \pm 31$ /mm<sup>2</sup>) compared to sham group was noted. (\*\*\*) $p \leq 0.001$ ; n=3.

**Conclusions:**

OCT may play a role in monitor structural change with correspondent change of RGC survival rate and electrophysiologic visual function in a rAION model.

**References:** None.

**Keywords:** Neuroimaging, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 213****Neuro-ophthalmic Conditions with Discrepancies between OCT findings & Visual Function**

Noel Chan<sup>1</sup>, Jerry Lok<sup>1</sup>, Carmen Chan<sup>1</sup>

<sup>1</sup>Hong Kong Eye Hospital, Hong Kong, Hong Kong

**Introduction:**

Optical coherence tomography (OCT) has been widely employed to evaluate optic nerve pathology in establishing diagnosis, disease monitoring and predicting prognosis. Current literature has demonstrated good correlation between visual function and peripapillary retinal nerve fiber layer thickness (pRNFLT) in glaucoma and other optic neuropathies such as compressive optic neuropathy or multiple sclerosis-related optic neuritis.

**Methods:**

This is a retrospective case series of patients with discrepancies between visual function and OCT findings attending Neuro-ophthalmic clinic in a Tertiary referral Eye Hospital.

**Results:**

We identified 4 young patients with bilateral optic atrophy from our Neuro-ophthalmology clinic who demonstrated marked discrepancies between visual function and OCT findings. Two of them had bilateral optic neuritis, one suffered from tuberculosis meningitis while one had bilateral optic atrophy from unknown cause. All of them enjoyed bilateral good visual acuities (Mean LogMar of 0.012±0.034) with full color vision and completely normal visual fields despite having a mean pRNFLT of 67.25±8.46µm on spectral domain OCT.

**Conclusions:**

Although OCT findings usually correlate well with visual function and it is useful for objective monitoring in most optic neuropathies, exceptions do exist as demonstrated in our study. Clinical correlation with caution is prudent in OCT interpretation especially for young patients.

**References:** None.

**Keywords:** Optic neuropathy, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 214****MRI Features of Demyelinating Diseases Associated with Anti-MOG Antibodies**

Damien Biotti<sup>1</sup>, Deneve Marc<sup>2</sup>, Romain Deschamps<sup>3</sup>, Françoise Heran<sup>4</sup>, Nicolas Menjot de Champfleury<sup>5</sup>, Pierre Labauge<sup>6</sup>, Fabrice Bonneville<sup>7</sup>

<sup>1</sup>CHU Toulouse - Pierre Paul Riquet, Toulouse, cedex 09, France, <sup>2</sup>Radiology - CHU Purpan, toulouse, France, <sup>3</sup>Neurology - Fondation Rothschild +33 5 61 77 55 92, Paris, France, <sup>4</sup>Radiology - Fondation Rothschild, Paris, France, <sup>5</sup>Radiology - CHU Montpellier +33 5 61 77 55 92, Montpellier, France, <sup>6</sup>Neurology - CHU Montpellier +33 5 61 77 55 92, Montpellier, France, <sup>7</sup>Radiology- CHU Purpan, Pierre Paul Riquet, Toulouse, France

**Introduction:**

Almost 25% of patients with neuro-myelitis optica phenotype are seronegative for AQP4-IgG. A quarter to a third of them are found positive to antibodies against oligodendrocyte myelin glycoprotein (MOG-IgG).

**Methods:**

To provide additional data on the radiological characteristics of CNS inflammatory disorders associated with anti-MOG antibodies; to confirm the previously described features of optic nerve involvement, and to deepen our knowledge of the spinal cord involvement, less described. Methods : Multicenter, retrospective and descriptive study. Fifty-three patients with anti-MOG antibodies related clinical events were included between January 2011 and April 2017. MRI were all reviewed by two neuro-radiologists.

**Results:**

The MRI characteristics of the symptomatic optic nerve were reproducible among the patients, with the presence of an extensive T2 hyperintense signal and contrast enhancement, predominant in the anterior segments of the optic nerve. Contrary to anti-AQP4-related optic neuritis, anti-MOG optic nerve lesions respected the chiasm and the optic tracts. A bilateral, edematous and perinervous inflammation was commonly seen. Concerning the spinal cord, we observed patients with T2 extensive transverse hyperintense lesions (>3 vertebral segments) comparable to the lesions seen among AQP4-IgG+ myelitis, but also patients with short lesions (<2 vertebral segments), involving indifferently any part of the spinal cord. Conus medullaris location, frequently associated with a pseudo-dilatation of the central canal of the spinal cord seemed frequent and evocative of MOG positivity.

**Conclusions:**

We confirm some previously described features of optic nerve and spine involvement during MOG-spectrum disorders and we add some new features. A better radiological knowledge of MOG-spectrum disorders can facilitate early diagnosis and management.

**References:** None.

**Keywords:** Demyelinating disease, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Neuroimaging, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 215****Role of Early Neuroimaging in the Management of Acute Isolated Ocular Motor Nerve Palsy**

Daniel Rappoport<sup>1</sup>, Niv Levy<sup>1</sup>, Hana Leiba<sup>1</sup>, Tal Paz<sup>1</sup>

<sup>1</sup>*Kaplan Medical Center, Rehovot, Israel*

**Introduction:**

The indications for early neuroimaging in older individuals who present with acute isolated ocular motor nerve palsies are unclear and controversial. We thus conducted a retrospective study in order to examine the approach differences between neurology and ophthalmology regarding the utility of early neuroimaging in the evaluation of acute isolated ocular motor nerve palsy.

**Methods:**

Retrospective chart review of patients 50 years of age or older with vasculopathic risk factors alone, who presented with acute isolated 3/4/6 cranial nerve palsy. We compared the rate of early neuroimaging referral between neurologists and ophthalmologists at initial presentation, and assessed the proportion of cases in which the final diagnosis has changed after early neuroimaging.

**Results:**

Fifty six patients were enrolled in the study. Analyses was performed on patients without third nerve palsy (for which there is consensus regarding early imaging). Our results indicate that the rate of patients referred to early neuroimaging was significantly greater when presented initially to a neurologist compared with an ophthalmologist ( $p < 0.0001$ ). Out of 39 patients presented with fourth or sixth cranial nerve palsies, 29 patients were referred to early neuroimaging. Only 4/39 (10.2%) were found to have a cause other than presumed microvascular ischemia. Two of them (2/39, 5.1%) were subjects having a causative lesion on early neuroimaging. Overall, 10.7% of patients (6/56) were found to have a cause other than presumed microvascular ischemia, including: pituitary adenoma, myasthenia gravis and meningioma.

**Conclusions:**

The rate of patients referred to early neuroimaging was significantly greater when presented initially to a neurologist compared with an ophthalmologist. In older patients with 4th or 6th nerve palsies and vasculopathic risk factors alone, the yield from early neuroimaging was low (5%). Decision to perform early neuroimaging could be weighed against observation alone, and should be obtained if there is non-resolution of the palsy.

**References:** None.

**Keywords:** Neuroimaging, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 216

### Health-Related Quality of Life in Patients With Giant Cell Arteritis Treated With Tocilizumab

Vibeke Strand<sup>1</sup>, Sophie Dimonaco<sup>2</sup>, Katie Tuckwell<sup>3</sup>, Micki Klearman<sup>3</sup>, Neil Collinson<sup>2</sup>, John Stone<sup>4</sup>

<sup>1</sup>Division of Immunology/Rheumatology, Stanford University, Portola Valley, California, USA, <sup>2</sup>Roche Products Ltd, Welwyn Garden City, United Kingdom, <sup>3</sup>Genentech, South San Francisco, California, USA, <sup>4</sup>Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, Massachusetts, USA

#### Introduction:

Superior rates of sustained glucocorticoid-free remission were shown in patients with giant cell arteritis (GCA) treated with weekly (QW) or every-other-week subcutaneous tocilizumab 162 mg+26-week prednisone taper (TCZ+26) for 52 weeks compared with placebo+26-week or 52-week prednisone taper (PBO+26 or PBO+52) in a phase 3 randomized controlled trial (GIACTA). Improvements in patient-reported SF-36 Physical Component Summary (PCS) score and Patient Global Assessment of Disease Activity were also reported for TCZ versus PBO+52 (1).

#### Methods:

Analysis of patient-reported outcomes at week 52 was performed in patients treated with QW TCZ+26 (n=100) versus PBO+26 (n=50) or PBO+52 (n=51) for 52 weeks based on observed data, including all patients and post-escape data.

#### Results:

Improvements in SF-36 PCS and Mental Component Summary (MCS) scores in the QW TCZ+26 group (4.18 and 8.10, respectively) exceeded PBO+52 (-0.40 and 1.89, respectively [both p<0.001]), exceeded PBO+26 for PCS (-0.98 [p<0.001]), and exceeded the minimal clinically important difference of 2.5 for rheumatoid arthritis. Improvements with QW TCZ+26 exceeded age- and sex-matched norms for the domains physical function, role physical, bodily pain, vitality, and social function and were statistically significant for physical function, role physical, general health, and vitality versus PBO+26 and for role physical, bodily pain, general health, vitality, social function, and mental health versus PBO+52. Improvements in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue were statistically greater with QW TCZ+26 than with PBO+26 and PBO+52 (both p<0.01). The median cumulative prednisone dose over 52 weeks was 1911.0 with QW TCZ+26 (n=57), 3860.5 with PBO+26 (n=37), and 3863.5 with PBO+52 (n=42).

#### Conclusions:

Patients with GCA treated with weekly TCZ 162 mg and a 26-week taper reported improvements in health-related quality of life and fatigue compared with those treated with 26-week or 52-week prednisone taper alone, in part ascribed to lower prednisone doses.

**References:** 1. Stone JH, Tuckwell K, Dimonaco S, et al, Trial of tocilizumab in giant-cell arteritis, N Engl J Med, 377, 317-328, 2017.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Vascular disorders

**Financial Disclosures:** Consulting fees or other remuneration from AbbVie, Amgen, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Celltrion, CORRONA, Crescendo, EMD Serono, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Protagen, Regeneron, Samsung, Sandoz, Sano

**Grant Support:** This study was funded by F. Hoffmann-La Roche Ltd (Roche). Roche was involved in the study design, in the collection, analysis, and interpretation of data, and in the writing of the abstract in collaboration with the authors.

**Poster 217****Retina Nerve Fiber Layer Segmentation with OCT in Patients with Neurodegenerative Diseases**

Marcia Marques<sup>1</sup>, Elena Martin<sup>2</sup>, Luis Julvez<sup>2</sup>

<sup>1</sup>Instituto de Molestias Oculares Brasil Hospital Universitário Miguel Servet Spain, São Paulo, Brazil, <sup>2</sup>Miguel Servet University Hospital- Zaragoza , Spain, Zaragoza, Spain

**Introduction:**

Retinal thickness measurement around optic nerve is a direct measure of axonal damage on neurodegenerative diseases: Multiple Sclerosis ( MS), Alzheimer Disease ( AD), Charlevoix Saguenay Ataxia ( CSA) and Parkinson Disease ( PD)

**Methods:**

We used Spectralis OCT Fourier domain to study retinal nerve fiber layer and optic nerve using macular cube and retinal nerve fiber layer protocol. Images were processed with segmentation software in cross sectional and case study. We've studied 129 PD patients, 204 MS patients , 150 AD patients and 5 CSA patients . All patients were compared to a control group. All individuals underwent complete ophthalmological exam, OCT study with fast macular cube and RNFL-N Axonal Analytics and analysis of retinal layers. Neurologic trial was made to determine stage and severity of each disease: MS the Expanded Disability Status Scale was used, the Hoehn Yahr scale for PD and the MMSE Score for AD.

**Results:**

PD patients had statistically significant reduction on retina layers and showed greater decrease on those with at least 10 years of disease. Ganglionar cell layer thickness correlated inversely with PD duration and Hoehn Yahr Scale. ACS Patients had an increase of the three inner retinal layers OCT showed thickness decrease in all retinal layers except the inner limiting membrane in MS patients. We've noticed significant reduction in retinal layers in AD, specially on those with disease longer than 3 years. The ganglion cell layer and RNFL thickness correlated inversely with duration and MMSE score. Ganglionar cell layer changes can predict axonal damages on MS, PD and AD.

**Conclusions:**

OCT retinal segmentation allows measurement of retinal layer thickness in patients with neurodegenerative diseases. Each layer is differently affected in each disease and the change of thickness of retinal layers can predict the axonal damage of the neurological condition.

**References:** None.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Demyelinating disease, Genetic Disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 218****Non-arteritic Anterior Ischemic Optic Neuropathy and its Association with Obstructive Sleep Apnea**

Ming-Hui Sun<sup>1</sup>, Chia-Yi Lee<sup>2</sup>, Yaping Joyce Liao<sup>3</sup>, Chi-Chin Sun<sup>1</sup>

<sup>1</sup>*Department of Ophthalmology, Chang Gung Memorial Hospital, Taoyuan, Taiwan,* <sup>2</sup>*Department of Medicine, Chang Gung University, College of Medicine, Taoyuan, Taiwan,* <sup>3</sup>*Department of Ophthalmology, Stanford University, School of Medicine, Palo Alto, California, USA*

**Introduction:**

Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in old age. Although there are several known risk factors, the influence of obstructive sleep apnea (OSA) has not been completely revealed. The aim of this study was to evaluate the association between NAION and OSA.

**Methods:**

This retrospective, longitudinal cohort study used the national health insurance database of Taiwan covering the period 1996-2013. Patients without NAION at diagnosis of OSA or with NAION developed one year later than diagnosis of OSA were enrolled in the study. The tracing was continued until the patient's death or the last day of tracing. Cox proportional hazard regression was used to compute the hazard ratio (HR) and 95% confidence interval (CI) to survey the association between OSA and NAION.

**Results:**

There were 10,819 patients in the OSA group and 43,276 in the control group (without OSA), for a ratio of approximately 1:4. The percentages of NAION were 0.36% and 0.17% in the OSA and control groups, respectively, with a statistically significant difference ( $P < 0.01$ ; chi-square test), and this significant difference remained in multivariate analysis ( $P < 0.01$ ) with a significantly higher HR (2.05; 95% CI: 1.39-3.03). There were significant differences in the 0-29 and 30-39 years age groups in multivariate analysis (both  $P < 0.01$ , HR: 9.33 and 6.30, respectively).

**Conclusions:**

There was a strong association between NAION and OSA, and the patients with OSA had a higher risk of NAION. Further large-scale, prospective studies are warranted to evaluate the effect of OSA on developing NAION.

**References:** None.

**Keywords:** Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** This study was supported by Chang Gung Medical Research Project Foundation (CLRPG2C0021, CLRPG2C0022, CLRPG2C0023).

**Poster 219****Cabin Pressures on Commercial Aircraft and Non-Arteritic Ischemic Optic Neuropathy**

Terry Wood<sup>1</sup>, Maleeha Syed<sup>2</sup>, Samir Nazarali<sup>2</sup>, Henry Liu<sup>2</sup>, Anna Ter-Zakarian<sup>3</sup>, Alfredo Sadun<sup>3</sup>, Rustum Karanjia<sup>3</sup>

<sup>1</sup>WVU, Morgantown, West Virginia, USA, <sup>2</sup>University of Ottawa, Ottawa, Canada, <sup>3</sup>Doheny Eye Institute, Los Angeles, California, USA

**Introduction:**

United States Federal Aviation guidelines suggest cabin pressures less than 8,000 ft. Current Commercial aircraft are commonly pressurized between 6,000 to 8,000 ft depending on the type of aircraft and composite materials of the fuselage. However, this variability can significantly impact patients with NAION, who may be predisposed to hypoxia induced complications, thus resulting in transient changes in vision from lower partial pressures of oxygen at higher altitudes. The purpose of this study was to investigate the variations in cabin pressurization of commercial aircraft at cruising altitude.

**Methods:**

Altimeters were used to measure the altitude and cabin pressure at cruising altitude aboard 106 commercial aircraft flights, including 47 narrow-body and 59 wide-body planes. Narrow body aircraft was characterized as single-aisle aircraft with a fuselage width of 10-13 ft, while twin-aisle aircraft with a fuselage width of 16-20 ft were considered wide-body.

**Results:**

The mean cabin pressure among all flights was  $6,355 \pm 863$  ft. Narrow-body aircraft had a significantly greater mean cabin pressure of  $6,864 \pm 750$  ft compared to wide-body aircraft with a mean cabin pressure of  $5,951 \pm 725$  ft. ( $p < 0.001$ ). With respect to service date, newer generation aircraft (service date later than 1990) had a mean cabin pressure of  $6,082 \pm 830$  ft., which was lower than the mean cabin pressure of older aircraft  $6,757 \pm 754$  ft ( $p < 0.001$ ).

**Conclusions:**

The innovation of composite material within aircraft fuselage has offered the ability to fly at greater altitudes, while maintaining lower cabin pressures. All flights studied maintained pressurization below suggested guidelines, however, the newest generation of wide body aircraft studied, B787 and A350, were found to cruise at the lowest mean cabin pressure of all groups. Those at risk of ischemic events such as patients with NAION may want to consider aircraft type when air travel is required.

**References:** None.

**Keywords:** Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 220****Longitudinal Analysis of Contrast Acuity in Friedreich Ataxia**

Ali Hamedani<sup>1</sup>, Lauren Hauser<sup>2</sup>, Susan Perlman<sup>3</sup>, Katherine Mathews<sup>4</sup>, George Wilmot<sup>5</sup>, Theresa Zesiewicz<sup>6</sup>, S.H. Subramony<sup>7</sup>, Tetsuo Ashizawa<sup>8</sup>, Martin Delatycki<sup>9</sup>, Alisha Brocht<sup>10</sup>, David Lynch<sup>2</sup>

<sup>1</sup>University of Pennsylvania, Philadelphia, Pennsylvania, USA, <sup>2</sup>Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA, <sup>3</sup>University of California at Los Angeles, Los Angeles, California, USA, <sup>4</sup>University of Iowa, Iowa City, Iowa, USA, <sup>5</sup>Emory University, Atlanta, Georgia, USA, <sup>6</sup>University of South Florida, Tampa Bay, Florida, USA, <sup>7</sup>University of Florida, Gainesville, Florida, USA, <sup>8</sup>Houston Methodist Hospital, Houston, Texas, USA, <sup>9</sup>Murdoch Children's Research Institute, Melbourne, Australia, <sup>10</sup>University of Rochester, Rochester, New York, USA

**Introduction:**

Optic neuropathy is part of the clinical syndrome of Friedreich ataxia, and low-contrast vision loss correlates with disease severity in cross-sectional studies. However, longitudinal studies are lacking.

**Methods:**

In the Friedreich Ataxia – Clinical Outcomes Measures Study (FA-COMS), an ongoing prospective multicenter cohort study of patients with Friedreich ataxia, participants (n=764) underwent binocular high- and low-contrast visual acuity testing at annual study visits. Information regarding GAA repeat length, disease duration, and other clinical and demographic characteristics was also collected. Mixed effects linear regression was used to model visual acuity as a function of time, with random intercepts and slopes to account for intra-individual correlation of repeated measurements. A time-varying covariate was used to adjust for diabetes, and interaction terms were used to assess for effect modification by GAA repeat length, disease duration, and other variables.

**Results:**

Across a median of 4.4 years of follow-up, visual acuity decreased significantly at 100% contrast (-0.37 letters/year, 95% CI: -0.52 to -0.21), 2.5% contrast (-0.81 letters/year, 95% CI: -0.99 to -0.65), and 1.25% contrast (-1.12 letters/year, 95% CI: -1.29 to -0.96 letters/year) after adjusting for diabetes. There was a significant interaction between time and GAA repeat length such that the rate of decrease in visual acuity was greater for those with higher GAA repeat lengths at 2.5% contrast (p=0.018) and 1.25% contrast (p=0.043) but not 100% contrast. There was no effect modification by age of onset after adjusting for GAA repeat length.

**Conclusions:**

Low-contrast visual acuity decreases linearly over time in Friedreich ataxia, and the rate of decline is greater at higher GAA repeat lengths. Contrast sensitivity has the potential to serve as a biomarker and surrogate outcome in future studies of Friedreich ataxia.

**References:** None.

**Keywords:** Genetic Disease, Optic neuropathy, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 221

### Ocular Bartonellosis (Cat Scratch Disease) : A Case Series

Lakana Kumar Thavaratnam<sup>1</sup>, NESHALENE RATNA KRISHNAN<sup>2</sup>, Nor Azita Ahmad Tarmidi<sup>2</sup>, Hamisah Ishak<sup>2</sup>, wan hazabah wan hitam<sup>3</sup>, wan haslina wan abdul halim<sup>4</sup>

<sup>1</sup>General Hospital Kuala Lumpur Eye Department, Kuala Lumpur, Malaysia, <sup>2</sup>GENERAL HOSPITAL KUALA LUMPUR, KUALA LUMPUR, Malaysia, <sup>3</sup>Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia, <sup>4</sup>hospital universiti kebangsaan malaysia, kuala lumpur, Malaysia

#### Introduction:

Ocular Bartonellosis is a clinical diagnosis supported by serological evidence, which may have various presentations<sup>1</sup>. The common presentation of ocular Bartonellosis is neuroretinitis defined by the presence of exudative optic disc swelling with macula star<sup>2</sup>. The less common presentation of ocular bartonellosis is intermediate uveitis<sup>3,4</sup>.

#### Methods:

Case series

#### Results:

We report a case series of 6 patients with ocular Bartonellosis. Three had history of contact with cats. All patients presented with a decrease vision ranging from 6/9 to perception to light. Four of the patients had unilateral neuroretinitis and two had bilateral involvement. Of the six, one presented with bilateral intermediate uveitis and another had aseptic meningitis evidenced by high CSF opening pressure, raised total white cell count and papilledema. All patients had serological evidence of Bartonella Hensalae with OCT findings of sub-retinal fluid in the affected eye which resolved after treatment. All patients were treated with antibiotics. Two received intravenous corticosteroid followed by oral steroids, while three received oral steroids and one had topical steroids for bilateral intermediate uveitis. All patients regained visual acuity of at least 6/12 or better except for one which had 6/18.

#### Conclusions:

Optic neuropathy is a serious complication of ocular Bartonellosis associated with macular edema presenting as macula star. Although it is a self-limiting disease, high dose corticosteroids and antibiotic therapy helps in improving the visual outcome as seen in all our cases especially the patient with aseptic meningitis.

**References:** 1. Metzker-Cotter E, Kletter Y, Avidor B, et al. Long-term serological analysis and clinical follow-up of patients with cat scratch disease. Clin Infect Dis. 2003;37(9):1149–1154 2. Harper SL, Chorich LJ, III, Foster CS. Bartonella. In: Foster CS, Vitale AT, editors. Diagnosis and treatment of uveitis. Philadelphia: WB Saunders; 2002. pp. 260–263. 3. Rothova A, Kerkhoff F, Hooft HJ, et al. Bartonella serology for patients with intraocular inflammatory disease. Retina 1998;18:348-55. 4. Martinez-Osorio H, Calonge M, Torres J, et al. Cat-scratch disease (ocular bartonellosis) presenting as bilateral recurrent iridocyclitis. Clin Infect Dis 2005;40:E43–E45.

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion), Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 222****Nasopharyngeal Carcinoma, A Masquerade: Case Series**

Lakana Kumar Thavaratnam<sup>1</sup>, Shelva Meena Gurusamy<sup>2</sup>, Wan Hazabbah Wan Hitam<sup>3</sup>, Azhany Yaakub<sup>3</sup>

<sup>1</sup>Neuro-ophthalmologist Eye Department, Hospital Kuala Lumpur, Malaysia, Kuala Lumpur, Malaysia, <sup>2</sup>University Science Malaysia Ophthalmology Department Hospital Kuala Lumpur, Kuala Lumpur, Malaysia, <sup>3</sup>Universiti Sains Malaysia, Kubang Krian, Kelantan, Kelantan, Malaysia

**Introduction:**

To exemplify rare and common presentations of nasopharyngeal carcinoma (NPC).

**Methods:**

Retrospective case series of 5 patients

**Results:**

Case 1: 60 years old, Malay gentleman presented with sinusitis diagnosed on CT scan. Patient had LE swollen optic disc with optic neuropathy. Vision LE 1/60 and RE 6/6. Patient was treated with intravenous antibiotics with impression of LE optic neuritis secondary to sinusitis, vision improved to 6/18, 1 week later deteriorated to 6/60. Antibiotics continued. 2 weeks later, vision deteriorated to Counting Fingers. Patient was admitted and treated as atypical optic neuritis with high dose corticosteroid and discharged with 6/9 vision on tapering dose of oral steroids. 2nd relapse 2 weeks later to perception of light (PL). Nasal endoscopy showed an inverted papilloma. Differentials were steroid dependent optic neuritis or compressive optic neuropathy. Intravenous corticosteroids recommenced and referred to neuro-ophthalmologist with BE 6/120 vision and optic neuropathy. Review of CT scan and MRI showed left nasal mass extending into left pterygopalatine fossa, left orbital apex, cavernous sinus and sphenoid sinus atypical of an inverted papilloma. Endoscopic tumour resection and HPE revealed NPC. He underwent chemo and radio therapy. Post radiotherapy developed RE neurotropic corneal ulcer and BE radiation induced optic neuropathy. Vision RE 3/60, LE no PL. RE penetrating keratoplasty was done. Currently his vision RE 6/120 LE NPL. Case 2: 69 year old Chinese gentleman presented with right eye 3rd nerve palsy and pupil involvement suspicious of Posterior Communicating Artery Aneurysm (PCOM). CTA showed no aneurysm but CT imaging revealed a sella mass extending to right nasopharynx with bony erosion. Nasal endoscopy and biopsy revealed NPC. The 3rd, 4th and 5th cases had common 6th nerve palsy presentations.

**Conclusions:**

NPC commonly presents as 6th nerve palsy, but it can masquerade from an atypical optic neuritis to a PCOM aneurysm.

**References:** None.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Orbit/ocular pathology, Optic neuropathy, Tumors, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 224****Ocular Motor Abnormalities in Autoimmune Ataxias**

Xiaojun Zhang<sup>1</sup>, Ali Saber Tehrani<sup>2</sup>, Diana Londono<sup>1</sup>, Jorge Kattah<sup>1</sup>

<sup>1</sup>University of Illinois College of Medicine at Peoria, Peoria, Illinois, USA, <sup>2</sup>Neuro-ophthalmology, Mass. Eye and Ear Infirmary, Harvard Medical School, Boston, Massachusetts, USA

**Introduction:**

Immune-mediated ataxias are usually of rapid onset with a relentless progressive course and early diagnosis is critical to halt the progression by establishing prompt immunotherapy. We hypothesize that oculomotor findings might guide earlier diagnosis. We sought to characterize the spectrum of oculomotor abnormalities among patients with immune mediated cerebellar ataxias and to correlate them with specific autoantibodies.

**Methods:**

A retrospective chart review of patients diagnosed with autoimmune ataxia at neuro-vestibular clinic at Illinois Neurological Institute from 2001-2016. We included adult patients with acute or subacute onset of diplopia, dizziness, disorders of gait and balance and/or limb ataxia in our study, and were positive for at least one antibody known to cause immune-mediated cerebellar ataxia. Patients with stroke, positive family history of hereditary/degenerative, toxic/metabolic, demyelinating, nutritional ataxias were excluded. We report head impulse test and abnormal oculomotor findings, neuro-imaging, CSF analysis results, and abnormal CSF antibodies.

**Results:**

Twelve patients were included in the study. The median age of symptoms onset was 68 (46-89) years; 6 patients (50%) were female. 75% of the patients had physical findings consistent with cerebellar dysfunction, alone or in combination, including truncal ataxia 4 (30%), positive Romberg's 3 (25%), abnormal Fukuda step test 5 (42%), or abnormal tandem gait 5 (42%). Importantly, no acute intracranial abnormalities were found on the first MRI. All patients had normal CSF protein and glucose levels, with lymphocytic pleocytosis in 50% of the patients. All patients had at least one autoantibody detected in either serum or CSF samples.

**Conclusions:**

Abnormal oculomotor findings can be a useful clinical tool to guide early diagnosis of patients with autoimmune cerebellar ataxia with noncontributory MRI and CSF studies. Clinicians should be familiar with the appropriate examination of eye movements and interpretation of findings. Further studies are needed to correlate autoantibodies with specific oculomotor and vestibular neuron targets.

**References:** None.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Nystagmus, Ocular Motility, Ocular manifestations of vestibular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 225****Evaluation And Correlation Between Neurophysiological And Visual Functional Tests In Multiple Sclerosis.**

Elena Garcia-Martin<sup>1</sup>, Elisa Vilades<sup>1</sup>, Marcia Marques<sup>2</sup>, Elvira Orduna<sup>1</sup>, Maria Rodrigo<sup>1</sup>, Vicente Polo<sup>1</sup>, Jose Larrosa<sup>1</sup>, Maria Satue<sup>1</sup>, Luis Pablo<sup>1</sup>

<sup>1</sup>Miguel Servet University Hospital, Zaragoza, Spain, <sup>2</sup>Ocular Discomfort Institute, Sao Paolo, Brazil

**Introduction:**

The purpose was to evaluate best corrected visual acuity (BCVA), contrast sensitivity (SC), pattern electroretinogram (pERG), multifocal electroretinogram (mfERG), and multifocal visual evoked potentials (mfVEP) in multiple sclerosis (MS) and compare with healthy controls.

**Methods:**

Fifty-eight eyes were included in this cross-sectional study: 14 of healthy controls and 44 of subjects with MS (of whom 17 presented a previous episode of optic neuritis). The BCVA was recorded at 100% contrast, 2.5% and 1.25%, contrast sensitivity vision (CSV) was measured with CSV1000 test (at 3, 6, 9 and 12 cycles per degree) and Pelli Robson test. The pERG, mfERG and mfVEP electrophysiology tests were performed with the Roland Consult's Reti-port / scan device.

**Results:**

Patients with MS showed a significant reduction of BCVA at 100% contrast ( $p = 0.013$ ), 2.5% ( $p < 0.001$ ) and 1.25% ( $p = 0.008$ ), CSV-1000 was also affected at 3 ( $p = 0.017$ ), 9 ( $p = 0.017$ ), and 12 cycles per degree ( $p = 0.048$ ), and also Pelli Robson ( $p < 0.001$ ). The mfERG showed in MS patients a significant affectation for amplitude and latency at the inferonasal and superonasal quadrants ( $p = 0.045$  and  $0.042$  respectively), and the overall values of the mfPEV shown abnormalities at N1 and P1 amplitudes ( $p = 0.019$  and  $p = 0.039$ , respectively).

**Conclusions:**

Patients with MS have a clear impairment of visual function in both psychophysical and electrophysiological tests.

**References:** - Retinal and Optic Nerve Degeneration in Patients with Multiple Sclerosis Followed up for 5 Years. Garcia-Martin E, Ara JR, Martin J, et al. *Ophthalmology*. 2017;124(5):688-696. -Electropysiologic evaluation of the visual pathway in patients with multiple sclerosis. Rodriguez-Mena D, Almarcegui C, Dolz I, et al. *J Clin Neurophysiol*. 2013;30(4):376-81. -Neuro-ophthalmologic evaluation, quality of life, and functional disability in patients with MS. Garcia-Martin E, Rodriguez-Mena D, Herrero R, et al. *Neurology*. 2013 2;81(1):76-83.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 226****Eyetracking in Pediatric Multiple Sclerosis**

Andrew Yousef<sup>1</sup>, Michael Deveruex<sup>1</sup>, Pierre-Antoine Gourraud<sup>1</sup>, Soren Jonzson<sup>1</sup>, Leena Suleiman<sup>1</sup>, Janet Chong<sup>1</sup>, Emmanuelle Waubant<sup>1</sup>, Ari Green<sup>1</sup>, Jennifer Graves<sup>1</sup>

<sup>1</sup>University of California, San Francisco, San Francisco, California, USA

**Introduction:**

Efferent visual dysfunction in children with multiple sclerosis (MS) may lead to significant impairment to quality of life, including school and athletic performance. Modern eye tracking technology can be used to detect subtle efferent dysfunction that may be missed on a bedside exam. We aimed to determine the feasibility of applying eye-tracking technology to the pediatric MS population.

**Methods:**

Participants meeting published criteria for pediatric MS and healthy controls were recruited. Each MS patient received a full clinical assessment that included an expanded disability status scale (EDSS) and a symbols digit modalities test (SDMT). All participants completed an eye-tracking exam with the Eye Brain Tracker 2. Paradigms for testing included measurements of saccadic latency and anti-saccadic latency. Intra-class correlation coefficients (ICC) were generated to determine inter-test reliability. Generalized estimating equations (GEE) were used to compare latencies with case status, EDSS and SDMT scores, adjusting for age and inter-eye correlations.

**Results:**

We eye-tracked 15 children with MS (N=30 eyes, mean age 15.6 ± 2.1) with mean disease duration of 3.9 years and median EDSS of 1.5 and compared them to 6 healthy controls (N=12 eyes, age 14.3 ± .95). The ICC for repeated trials was 0.86. In the GEE model adjusted for age, saccadic latency was 60ms longer for cases than controls (95%CI=26.4,93.8; p=0.0005). In a similar model for antisaccadic latency there was no difference seen in cases and controls (p=0.85). There were no associations observed between EDSS or SDMT and saccadic latency.

**Conclusions:**

There was high inter-test reliability supporting use of eye-tracking technology in children with MS. Even in this pilot study, differences in saccadic latency were seen between children with MS and healthy controls despite short disease duration and low EDSS scores in pediatric MS.

**References:** None.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Demeylinating disease, ,

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 227**

**Abnormal Chewing Gum Test Results in Patients with Giant Cell Arteritis: A Case Series**

Clare Fraser<sup>1</sup>, Chih-Hung Kuo<sup>1</sup>, Anthony Sammel<sup>2</sup>, Jessica Tong<sup>3</sup>, Hamish Dunn<sup>2</sup>, Peter McCluskey<sup>1</sup>, Clare Fraser<sup>1</sup>

<sup>1</sup>Save Sight Institute, Sydney, Australia, <sup>2</sup>Royal North Shore Hospital, Sydney, Australia, <sup>3</sup>Concord Repatriation Hospital, Sydney, Australia

**Introduction:**

Jaw claudication is a specific symptom and positive predictor for patients with suspected giant cell arteritis (GCA). The chewing gum test (CGT) is a method of reproducing and characterising jaw claudication, by asking patients to chew a piece of gum at one chew per second for up to 5 minutes. Abnormal results have been described in two cases of patients with GCA in the literature.

**Methods:**

Participants with biopsy proven GCA were identified from the prospective studies of the Chewing Gum Test Study and Giant Cell Arteritis and PET Scan (GAPS) Study. Characteristics of the abnormal test results and the clinical details were recorded and analyzed.

**Results:**

5 individuals with biopsy-proven GCA and abnormal CGT results were identified. All the biopsies showed transmural inflammation. One patient with temporal mandibular joint dysfunction was included for comparison. 5/5 patients reported symptoms along the distribution of the masseter muscle. 2/5 patients reported no or resolution of jaw claudication symptoms prior to the test. There seemed to be a correlation between shorter duration of onset of symptoms and higher inflammatory markers at the time of testing.

**Conclusions:**

This small case series of abnormal chewing gum test results suggests that true jaw claudication has certain characteristics, in terms of location, timing, reproducibility. Some patients may have abnormal test results despite reporting no or resolved jaw symptoms.

**References:** Kuo, C.H., McCluskey, P., Fraser, C.L. Chewing gum test for jaw claudication in giant-cell arteritis. *N Engl J Med.* 2016;374:1794–1795.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 228****Characteristics and Prognosis of Patients with Ocular Myasthenia Gravis (OMG) and Thymoma.**

Su Ann Lim<sup>1</sup>, Melissa Chih Hui Tien<sup>1</sup>, Chee Fang Chin<sup>1</sup>

<sup>1</sup>*Tan Tock Seng Hospital, Singapore, Singapore*

**Introduction:**

Fifteen percent of patients with myasthenia have a thymoma.(1) Little data is available regarding OMG and thymoma. This study aims to determine the characteristics and prognosis of patients with OMG and thymoma.

**Methods:**

Retrospective case series of patients with OMG and thymoma. Records of 10 patients with OMG and thymoma were reviewed. Epidemiological data, size of thymoma, cell type and stage of disease, management and control of MG pre and post surgery as well as and conversion to generalised MG was studied.

**Results:**

Thymoma was detected on a screening CT scan of the thorax in 9 patients, the remaining patient had a history of invasive thymoma 10 years before. One patient refused surgery. Fifty percent of the patients were female and the mean age was 60.2 years. All nine patients in whom antibodies against acetylcholine receptors were tested were positive and 3/5 patients tested positive for anti-skeletal muscle antibodies. There was no association with size of thymoma and stage or cell type of tumour. Majority of patients had stage IIA disease (4/8). Two patients developed generalised myasthenia before thymectomy was performed. Of the 8 patients with thymectomy performed, OMG control improved in 3, was unchanged in 2 and deteriorated in 3 patients. Mean follow-up period was 23.2 months.

**Conclusions:**

There is no association of the size of the mass with the stage or cell type of thymoma. All patients with OMG should be monitored closely for development of generalised disease while awaiting thymectomy. Repetitive nerve stimulation and lung function test may be useful pre-operatively to ensure safe surgery. Although no patient in our series who had OMG developed generalised disease post operatively, patients should still be followed up closely to ensure no deterioration of symptoms.

**References:** (1) Fredrik Romi. Thymoma in myasthenia gravis, from diagnosis to treatment. *Autoimmune Diseases*. Volume 2011, Article ID 474512, 5 pages, doi 10.1061\2011\474512.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Tumors, Paraneoplastic syndromes,

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 229****Remote Ischemia Conditioning Protects Retinal Ganglion Cells in Streptozotocin Induced Diabetic Rats**

Xuxiang Zhang<sup>1</sup>, Yunneng Jizhang<sup>2</sup>, Changhong Ren<sup>3</sup>, Dachuan Liu<sup>1</sup>

<sup>1</sup>Xuanwu Hospital, Capital Medical University, Beijing, China, <sup>2</sup>University of Pittsburgh School of Medicine, Pittsburgh, USA, <sup>3</sup>Beijing Key Laboratory of Hypoxia Conditioning Translational Medicine, Beijing, China

**Introduction:**

Limb remote ischemic conditioning (LRIC) provides a physiologic strategy for harnessing the body's endogenous protective capabilities against reactive oxygen species induced injury. This research aims to investigate the protective effects of RIPC in retinal ganglion cell in streptozotocin (STZ) induced Type 1 diabetes rats.

**Methods:**

35 healthy male Sprague-Dawley rats were randomly assigned to control group, control+ RIPC group, diabetes rats and diabetic+ RIPC group. Diabetic rat model was induced by a single intraperitoneal injection of streptozotocin (STZ, 60 mg/kg in 0.1mol/L) dissolving in sodium citrate solution. RIPC was conducted by tightening a tourniquet around the upper thigh and releasing for three cycles daily. After 12 weeks of RIPC, eyes were enucleated. Expression of Brn3a positive RGC, GFAP and Nrf2 in different groups was examined by immunohistochemical study.

**Results:**

Over the course of experiment, control rats showed a gradual gain in weight. Body weight were lower in diabetic rats than in the corresponding control groups. Blood glucose levels were increased in diabetic rats compared with non-diabetic controls. There was a significant decrease of Brn3a+ cells between diabetic group and control group. The number of RGC was significantly increased in diabetic+ RIPC group than that in diabetic group. In control group and control+ RIPC group, glial fibrillary acidic protein (GFAP) expression was distributed throughout all layers of the retina in diabetic rats and was upregulated compare to that in control rats (p=0.001). The average of density of expressions of GFAP was significant decreased in diabetic+ RIPC group in comparison to diabetic group. LRIC treatment remarkably increased the activities of superoxide dismutase and glutathione peroxidase in plasma, and decreased serum level of nitric oxide.

**Conclusions:**

These results suggest that the antioxidative activities of LRIC may be important mechanisms involved in the protective effect of LRIC in STZ-induced diabetic rats.

**References:** None.

**Keywords:** Vascular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Beijing Municipal Administration of Hospitals Clinical Medicine Development of Special Funding Support (ZY L X 2 0 1 7 0 6)

**Poster 230****Visual Sequelae in Children with Primary CNS Tumors**

Yin Allison Liu<sup>1</sup>, Timothy Winter<sup>2</sup>

<sup>1</sup>Loma Linda University Children's Hospital, Loma Linda, California, USA, <sup>2</sup>Loma Linda University Medical Center, Loma Linda, California, USA

**Introduction:**

The prevalence of visual sequelae in children with brain tumors has received limited attention in the literature. They are oftentimes unrecognized due to limited patient/caregiver report. As survival improves with emerging treatments, systematic neuro-ophthalmologic evaluations may help improve long-term visual outcomes and quality-of-life.

**Methods:**

We reviewed outcomes of 142 children with primary brain tumors.

**Results:**

A total of 68 patients (Male=32, Female=36) and 222 ophthalmology evaluations were reviewed. The median age at diagnosis was 7 (0-18) years. Nine children (13%) presented with visual symptoms. Hydrocephalus was present in 65% of all patients. Tumor types mainly included glioma (35%), medulloblastoma (13%), and ependymoma (10%). Tumor locations were on the optic pathway (45%) and in the posterior fossa and brainstem (55%). Surgery was performed on 93% of patients. Gross total resection was achieved in 51% from initial surgery. A total of 54% received chemotherapy and/or radiation. Overall survival was 84% over a median follow-up of 28 months (1-180 months). Median time from tumor diagnosis to initial ophthalmological evaluation was 9 months (0-94 months). Initial complaints included abnormalities in vision (35%), gaze (34%), none (22%), visual field (4.4%), and other (7.4%). Exam found 62% with visual acuity impairment, 51% with strabismus, 37% with amblyopia, 35% with papilledema, 19% with visual field defects, 17.6% with optic nerve atrophy with or without papilledema, 15% with exposure keratopathy (30% required tarsorrhaphy or corneal transplant). Discrepancy between the prevalence of patient/caregiver reported eye symptoms and abnormal ophthalmologic exam findings was significant (P=0.011). Noticeably, there were 74 patients with mainly low grade brain tumors were never evaluated by an ophthalmologist (overall survival = 86.5%).

**Conclusions:**

Both afferent and efferent visual sequelae are prominent in children with brain tumors, even when asymptomatic. A single ophthalmologic evaluation is suggested to evaluate for complications from tumor and/or treatment to prevent vision threatening disease.

**References:** None.

**Keywords:** Pediatric neuro-ophthalmology, Tumors, Visual fields, Optic neuropathy, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 231****The Relationship of Retinal Nerve Fiber Layer Thickness to Alzheimer's Disease Biomarkers**

Victoria Pelak<sup>1</sup>, Prem Subramanian<sup>1</sup>, Jonathan Woodcock<sup>1</sup>, Huntington Potter<sup>1</sup>, Brianne Bettcher<sup>1</sup>

<sup>1</sup>University of Colorado School of Medicine, Aurora, Colorado, USA

**Introduction:**

For patients with Alzheimer's disease (AD), retinal nerve fiber layer (RNFL) thickness is decreased compared to age-matched controls and this is consistent with histopathological data revealing degeneration of retinal ganglion cell axons, retinal ganglion cells, and the optic nerve.(1,2) The mechanism, visual impact, and the stage of onset of this degeneration is unknown. We seek to investigate the relationship between RNFL thickness and threshold visual field perimetry, cortical volumes, cerebral amyloid, and cognition for people within the aging and AD spectrums.

**Methods:**

Subjects representing the aging spectrum (healthy control to mild cognitive impairment) and amyloid spectrum (negative to positive) will be comprehensively characterized and further screened for eligibility to participate. The relationship between RNFL optical coherence tomography (OCT) thickness to visual field threshold perimetry, MRI cortical volumes, PET amyloid, and cognition will be analyzed.

**Results:**

Participants have been comprehensively characterized with brain MRI, cognitive assessments, informant report, and neurological/physical exam. Sixty-five healthy controls and MCI subjects are eligible for further screening and testing, and approximately 18 have undergone PET-amyloid imaging from the parent study.

**Conclusions:**

Interim analysis regarding the associations between RNFL OCT, visual field threshold perimetry, MRI cortical volumes, PET amyloid, and cognition will be presented. How the results inform our understanding of the mechanism and visual impact of RNFL degeneration will be discussed, along with insights into the stage of aging and AD that RNFL loss can be detected.

**References:** 1. Coppola, G. et al. Optical Coherence Tomography in Alzheimer's Disease: A Meta-Analysis. PloS one 10, 2015. 2. Hinton D, Sadun AA, Blanks JC, Miller CA. Optic-nerve degeneration in Alzheimer's disease. N Engl J Med 315, 485-487, 1986.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Visual fields

**Financial Disclosures:** 1. Royalties from Up-To-Date, Inc; unrelated to this study 2. Quark pharmaceutical study support; unrelated to this study

**Grant Support:** North American Neuro-ophthalmology Society and the Rocky Mountain Alzheimer's Disease Center



**Poster 232****Asynchronous Onset in Leber's Hereditary Optic Neuropathy.**

Rustum Karanjia<sup>1</sup>, Henry Liu<sup>2</sup>, Chiara LaMorgia<sup>3</sup>, Samir Nazarali<sup>2</sup>, Lidia Di Vito<sup>3</sup>, Michele Carbonelli<sup>4</sup>, Alexander Pearson<sup>2</sup>, Neringa Jurkute<sup>5</sup>, Piero Barboni<sup>4</sup>, Anna Maria De Negri<sup>6</sup>, Patrick Yu-Wai Man<sup>7</sup>, Valerio Carelli<sup>3</sup>, Alfredo Sadun<sup>8</sup>

<sup>1</sup>University of Ottawa and Doheny Eye Institute and Department of Ophthalmology UCLA, Ottawa, Canada, <sup>2</sup>University of Ottawa, Ottawa, Canada, <sup>3</sup>IRCCS Institute of Neurological Sciences of Bologna, Bellaria Hospital, Bologna, Italy, <sup>4</sup>Studio Oculistico d'Azeglio, Bologna, Italy, <sup>5</sup>UCL and Moorfields Eye Hospital, London, United Kingdom, <sup>6</sup>Azienda Ospedaliera San Camillo-Forlanini, Roma, Italy, <sup>7</sup>University of Cambridge, Cambridge, United Kingdom, <sup>8</sup>Doheny Eye Institute and Department of Ophthalmology UCLA, Los Angeles, California, USA

**Introduction:**

Leber's hereditary optic neuropathy (LHON) is an inherited mitochondrial disease characterized by asynchronous subacute vision loss. The purpose of this study was to determine if there was a correlation between age of onset and synchronicity of vision loss and the different mutation types.

**Methods:**

Age of onset, unilateral versus bilateral presentation, interval between first and second eye involvement, and the mtDNA mutations were retrieved from clinical registries at the investigators' institutions.

**Results:**

Clinical data from 300 LHON patients with classical LHON mutations were evaluated (m.11778G>A, n = 216; m.3460G>A, n = 40; m.14484T>C, n = 44; non-dominant mutations, n = 39). Bilateral eye involvement was clinically documented in 99.4% of cases with 50.3% of all patients demonstrating sequential onset. In these latter cases the median inter-eye delay was 12.8 weeks. The m.14484T>C mutation resulted in the lowest age at onset ( $19.2 \pm 10.6$  years) compared to m.11778G>A ( $25.8 \pm 15.3$  years), m.3460G>A ( $20.9 \pm 14.5$  years) and non-dominant mutations ( $22.9 \pm 12.1$  years) (p A, m.3460G>A, m.14484T>C and non-dominant mutations were 3.5:1, 1.7:1, 4.5:1 and 3.8:1 respectively). Interestingly, the m.14484T>C mutation exhibited more simultaneous onset than sequential onsets compared with the other mutation subtypes (p C showed a shorter and more reproducible interval between eyes (inter-eye onset range = 1–44 weeks) versus m.11778G>A (range = 1–2016 weeks), m.3460G>A (range = 2–816 weeks), non-dominant mutations (range = 1–108 weeks) for sequential presentations.

**Conclusions:**

The m.14484T>C mutation, though least penetrant, manifested at an earlier age and resulted in a smaller inter-eye delay interval range and higher incidence of simultaneous involvement compared to the other classical and non-dominant mutations in LHON.

**References:** None.

**Keywords:** Optic neuropathy, Genetic Disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 233****Physiologic Dysfunction Precedes Retinal Ganglion Cell Loss in Mice with Neurofibromatosis and Optic Pathway Gliomas**

Steven Stasheff<sup>1</sup>, Francisco Nadal-Nicolas<sup>2</sup>, Emmanuelle Jecrois<sup>3</sup>, Wei Li<sup>4</sup>, Miriam Bornhorst<sup>3</sup>, Yuan Zhu<sup>3</sup>

<sup>1</sup>*Gilbert Neurofibromatosis Institute National Eye Institute, Washington, District of Columbia, USA*, <sup>2</sup>*Retinal Neurophysiology Section, The National Eye Institute, Bethesda, Maryland, USA*, <sup>3</sup>*Gilbert Neurofibromatosis Institute, Children's National Health System, Washington, District of Columbia, USA*, <sup>4</sup>*National Eye Institute, Bethesda, Maryland, USA*

**Introduction:**

We report previously unrecognized developmental abnormalities of retinal ganglion cell (RGC) anatomy and physiology that may help explain a striking disparity in young children with neurofibromatosis type 1 (NF1) who develop optic pathway gliomas (OPGs): the degree of visual loss is inadequately predicted by tumor characteristics or treatment response. In an animal model, we find RGC loss in discrete sectors months after tumor formation, but also greatly disrupted physiology among surviving retinal ganglion cells (RGCs).

**Methods:**

Using in vitro multielectrode recording, we measured spontaneous and light-evoked responses of RGCs in retinas from transgenic mice with the neurofibromin (Nf1) gene knocked out in glial precursor cells. These NF1-OPG mice proliferate atypical glial cells and develop OPGs by P15-21, with progressive loss of RGCs beginning at 2-4 months of age. We recorded RGCs, histologically analyzed the recorded retinas and optic nerves, and measured behavioral light responsiveness using a modified open field test, across these developmental stages.

**Results:**

Between 2 and 7 months of age, discrete sectors of NF1-OPG retinas progressively lose RGCs until they are virtually absent. Even in neighboring regions with normal RGC density, many have no recordable activity. Those that do have higher spontaneous discharge rates but less vigorous responses to light - correlating with decreased behavioral light responses.

**Conclusions:**

Our results highlight substantial abnormalities in RGC function accompanying NF1-OPGs, despite normal histopathologic appearance of these cells; i.e., functional deficits precede anatomic loss of RGCs/optic nerve axons. This early developmental disruption in the retina's "message" to the brain may explain the disparity between visual loss and tumor characteristics or treatment response. Ongoing experiments aim to more precisely identify developmental stages at which promising treatments (e.g., MEK inhibitors) can be more effective. Ideally, these principles will translate to earlier clinical detection of visual dysfunction.

**References:** None.

**Keywords:** Genetic Disease, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Pediatric neuro-ophthalmology, Genetic Disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Gilbert Family Neurofibromatosis Institute

**Poster 235****Epidemic Bhutanese Optic Atrophy**

Philip Skidd<sup>1</sup>, Eman Hawy<sup>2</sup>, Kinjal Thakor<sup>1</sup>

<sup>1</sup>Larner College of Medicine, University of Vermont, Division of Ophthalmology, Burlington, Vermont, USA, <sup>2</sup>Emory University School of Medicine, Department of Ophthalmology, Atlanta, Georgia, USA

**Introduction:**

Beginning in the early 1990's, tens of thousands of ethnic Nepali Bhutanese were forced out of Bhutan as a result of the Bhutanese government's policy of "one nation and one people." A majority of these persons resided, for up to twenty years, in camps along the Eastern Nepal border with Bhutan before resettlement in third-party countries. Vitamin B12, among other micronutrient deficiencies, was common in these camps. More than 100,000 individuals have been resettled, with over 80% coming to the United States, with less than 3,000 Bhutanese refugee arriving in Vermont. A number of patients from the local Bhutanese refugee population were evaluated in the neuro-ophthalmology clinic at our academic medical center and found to have optic atrophy (OA) without identifiable cause. To better understand the scale and potential etiology of this problem, all cases of OA, from this group, referred to the neuro-ophthalmology clinic, were reviewed.

**Methods:**

A retrospective chart review was conducted of all patients with optic atrophy of Nepali/Bhutanese referred to the neuro-ophthalmology clinic.

**Results:**

Thirteen cases of optic atrophy were identified in a population of less than 3,000 individuals. No clear cause was identified, however toxic/metabolic etiology is suspected, with evidence supporting micronutrient deficiencies including vitamin B12.

**Conclusions:**

Good estimates for the incidence of unexplained OA in the general population are not available. One study, identified only 73 patients over eight years seen at two major referral centers. To date, the best studied epidemic of OA, identified no clear etiology, but strongly implicated limited food availability and access to micronutrients. While much larger in scale, the incidence and proposed etiology of OA during that epidemic was similar to that described here. To our knowledge this is the first report of epidemic OA in the Bhutanese refugee population.

**References:**

1. The United States Refugee Admissions Program (USRAP) Report to Congress FY 2017; <https://static1.squarespace.com/static/580e4274e58c624696efadc6/t/583c72eb37c5810ef265fd3e/1480356588974/Report+to+Congress+for+FY+2017+USRAP.pdf> 2. Cuffe K, Stauffer W, Painter J, Shetty S, Montour J, Zhou W. Update: vitamin B12 deficiency among Bhutanese refugees resettling in the United States, 2012. *MMWR Morb Mortal Wkly Rep.* 2014 Jul 18;63(28):607-3. Department of State (DOS) Bureau of Population, Refugees, and Migration (PRM), The Refugee Processing Center (RPC) <http://www.wrapsnet.org/admissions-and-arrivals/> 4. Lee AG, Chau FY, Golnik KC, Kardon RH, Wall M. The diagnostic yield of the evaluation for isolated unexplained optic atrophy. *Ophthalmology* 2005; 112(5):757-759. 5. The Cuba Neuropathy Field Investigation Team. Epidemic Optic Neuropathy in Cuba - clinical characterization and risk factors. *N Engl J Med.* 1995 Nov 2; 333(18):1176-8

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 236

### The Utility of Nomograms for Suspected Giant Cell Arteritis

Nurhan Torun<sup>1</sup>, Edsel Ing<sup>2</sup>, Gabriela Lahaie Luna<sup>3</sup>, John Chen<sup>4</sup>, Andrew Toren<sup>5</sup>, Royce Ing<sup>6</sup>, Nitika Arora<sup>4</sup>, Otana Jakpor<sup>7</sup>, J. Alexander Fraser<sup>8</sup>, Felix Tyndel<sup>2</sup>, Arun Sundaram<sup>2</sup>, Vivek Patel<sup>9</sup>, Christian Pagnoux<sup>10</sup>, Cindy Lam<sup>2</sup>, Martin ten Hove<sup>3</sup>

<sup>1</sup>Beth Israel Deaconess Hospital, Boston, Massachusetts, USA, <sup>2</sup>University of Toronto, Toronto, Ohio, Canada, <sup>3</sup>Queens University, Kingston, Canada, <sup>4</sup>Mayo Clinic, Rochester, Minnesota, USA, <sup>5</sup>Laval University, Laval, Kansas, Canada, <sup>6</sup>Toronto Eyelid Strabismus & Orbit Surgery Clinic, Toronto, Ohio, Canada, <sup>7</sup>Harvard Medical School, Boston, Massachusetts, USA, <sup>8</sup>Western University, London, Ohio, Canada, <sup>9</sup>University of Southern California (Roski Eye), Los Angeles, USA, <sup>10</sup>Mt. Sinai Hospital, Toronto, Canada

#### Introduction:

Giant cell arteritis (GCA) can be difficult to diagnose. Logistic regression prediction models (LRPM) exist, but the average clinician is not facile synthesizing multiple odds ratios and p values into an output probability. A nomogram is a chart or graph of scaled variables that facilitates the approximate computation of a mathematical function via intersecting lines. A GCA nomogram can help gauge the need for temporal artery biopsy and the decision for glucocorticoid initiation.

#### Methods:

A ten factor nomogram was developed from our recently validated LRPM for biopsy-proven GCA using the "nomolog" plug-in for Stata 15 and the covariates of age, gender, new onset headache, clinical temporal artery abnormality, jaw claudication, vision loss, diplopia, log ESR, log CRP, and platelets. Age and serology values were maintained as continuous variables. The nomogram from the non-histologic ACR classification criteria was compared with our model.

#### Results:

Our nomogram had a maximum output probability of 0.99. Statistically significant predictors with non-null odds ratios had a longer nomogram scale than weak covariates. Age and platelets had the greatest potential to augment the risk score, followed by CRP >4.5, jaw claudication and vision loss. The 1.005 odds ratio for platelets seemed insignificant but the nomogram revealed its strong effect. ESR > 50 had a moderate risk. Gender, diplopia headache and temporal artery abnormality were weak predictors. The ACR nomogram had a maximum output probability 0.45, and there was no scale for age because our subjects were all over 50 years old.

#### Conclusions:

Calculators for LRPM are available, [https://docs.google.com/spreadsheets/d/1wLRFGLeW2Vf-LlyImY76KSTzIAf1TrX5U\\_1770HhD1Y/edit#gid=0](https://docs.google.com/spreadsheets/d/1wLRFGLeW2Vf-LlyImY76KSTzIAf1TrX5U_1770HhD1Y/edit#gid=0) but nomograms allow visualization of the relative importance of covariates. "Actuarial" methods for medical decision-making usually outperform clinical intuition. Nomograms can objectify and optimize the individualized risk assessment of GCA patients.

**References:** Ing EB, Lahaie Luna G, Torun N, Chen JJ, ten Hove M et al, "Multivariate Prediction Model for Suspected Giant Cell Arteritis: Development and Validation", *Clinical Ophthalmology*, accepted October 2017.

**Keywords:** Vascular disorders, Optic neuropathy, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 238****Reduction of Photopic Negative Response(PhNR) in Optic Neuropathies Obtained Using a Handheld Electroretinogram Device**

Fareshtha Khushzad<sup>1</sup>, Megh Patel<sup>2</sup>, Heather Moss<sup>2</sup>

<sup>1</sup>Stanford University, Palo Alto, California, USA, <sup>2</sup>Stanford School of Medicine, Palo Alto, California, USA

**Introduction:**

The PhNR, the negative wave following the B wave in the full field flash photopic electroretinogram(ERG) is reduced in optic neuropathies. Our purpose was to determine if the PhNR is altered between eyes within patients with unilateral or asymmetric optic neuropathies.

**Methods:**

18 subjects were recruited (ages 26-88, 61% female); 9 with either unilateral or highly asymmetric optic neuropathies (optic neuritis(3), NAION(2), infectious(1), drusen(2), and atrophy(1)) and 9 with no ocular or neurological disease(controls). A portable handheld ERG device with skin electrodes(RETeval/LKC) was used to provide full field stimulation(red flashes at 3.4Hz on a blue background) and record ERG waveforms. Customized MATLAB software was used to evaluate PhNRamplitude, P-ratio( $PR = \text{PhNRamplitude} / \text{Bamplitude}$ ), and W-ratio( $WR = (\text{Bamplitude} - \text{PhNRamplitude}) / (\text{Bamplitude} - \text{Aamplitude})$ ). Humphrey Visual Field mean deviation(HVF-MD) and ganglion cell complex average thickness(GCC, Cirrus/Zeiss) were obtained in optic neuropathy patients. Paired t-tests were done to compare HVF-MD, GCC, PhNR, P-ratio and W-ratio between the good and bad eyes within subjects with optic neuropathies. T-tests for independent samples were used to compare intereye PhNR, PR and WR difference between optic neuropathy and control subjects.

**Results:**

GCC and HVF-MD were reduced in affected vs. less/unaffected eyes. PR and WR but not PhNR were decreased in eyes with an optic neuropathy compared with less or unaffected eyes in the same subjects(PR:mean diff 0.053+/-0.063,p=0.03; WR:mean diff: 0.087+/-0.060,p=0.002; PhNR:mean diff: 0.059mV+/-1.73,p=0.34). Control subjects had less intereye difference in PR, but not in WR or PhNR compared with optic neuropathy subjects(PR:mean diff 0.009+/-0.044,p=0.03; WR:mean diff: 0.03+/-0.8,p=0.10; PhNR:mean diff -0.16+/-1.66,p=0.6).

**Conclusions:**

P and W-ratios were decreased in optic neuropathy eyes compared with fellow eyes. However, the magnitude of the inter-eye difference was less than controls only for the P-ratio. P-ratio is a candidate marker for detecting asymmetric optic neuropathies.

**References:** None.

**Keywords:** Optic neuropathy, Optic nerve trauma and treatment, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 239****Spinocerebellar Ataxia Type 7: A Case Series and Review**

DonRaphael Wynn<sup>1</sup>, Judith Warner<sup>1</sup>, Bradley Katz<sup>1</sup>, Alison Crum<sup>1</sup>, Kathleen Digre<sup>1</sup>

<sup>1</sup>John A Moran Eye Center, University of Utah, Salt Lake City, Utah, USA

**Introduction:**

This report describes a series of 10 cases of spinocerebellar ataxia type 7 from the same family.

**Methods:**

We performed a retrospective chart review was performed on 2 male and 8 female patients aged between 5 and 80 from 3 different generations of the same family. The first and last visit charts were reviewed for ocular abnormalities, including decreased visual acuity, visual field defects, Flynn phenomenon, loss of color perception (including tritan-type color blindness), abnormalities in extraocular movements (including restriction in movements and slow saccades) and changes on funduscopic exam such as mottling pigmentary changes in the macula. Neurological exam abnormalities were reviewed as well, which included gait and limb ataxia, dysarthria, dysphagia, and upper motor neuron findings such as hyper-reflexia, spasticity, ankle clonus, and up-going toes. We collected age of symptoms onset, first symptom reported, sex, and other demographic information.

**Results:**

The mean age of symptom onset ranged from 15.5 years (the 3rd generation) to 45 years (the 1st generation). Patients in the younger generation almost all presented with visual symptoms and signs (including changes in color vision), while those of the older generation presented with neurological symptoms. Early ocular signs included tritan-type color blindness and a beaten bronze-appearance to the macula, often prior to any significant reduction in visual acuity. The most common neurologic signs in the first generation were ataxia and dysarthria.

**Conclusions:**

In our series, younger generations showed anticipation and tend to present at younger ages. This is consistent with the known genetic characteristics of SCA-7, which is an autosomal dominant disease that has been found to exhibit marked anticipation of age of onset [1]. Patients from the youngest generation also tend to initially present with visual complaints which is characteristic of SCA-7 as reported in other series [2].

**References:** Johansson J, Forsgren L, Sandgren O, et. al.. Expanded CAG repeats in Swedish spinocerebellar ataxia type 7 (SCA7) patients: effect of CAG repeat length on the clinical manifestation. *Hum Mol Genet* 1998; 7:171-176. Van de Warrenburg BP, Frenken CW, Ausems MG, et. al. Striking anticipation in spinocerebellar ataxia type 7: the infantile phenotype. *J Neurol* 2001; 248:911-914.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Optic neuropathy, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Supported in part by an Unrestricted Grant from Research to Prevent Blindness, Inc., New York, NY, to the Department of Ophthalmology & Visual Sciences, University of Utah.

**Poster 240****The Great Imitator on the Rise: Optic Disc Involvement in Syphilis Patients**

Dvir Koenigstein<sup>1</sup>, Michaela Goldstein<sup>2</sup>, Naomi Fischer<sup>2</sup>, Shiri Shulman<sup>2</sup>, Zohar Habet-Wilner<sup>2</sup>, Ainat Klein<sup>2</sup>

<sup>1</sup>Tel Aviv medical center, Tel Aviv-Yafo, Israel, <sup>2</sup>Ophthalmology Division, Tel Aviv medical center, Tel Aviv, Israel

**Introduction:**

Syphilis is an infectious venereal disease caused by the spirochete *Treponema pallidum*. Ocular manifestations, are reported in the literature in 2-10% of the cases can occur at any stage of the disease and may involve any ocular structure. During the last decade the number of syphilis cases has been on the rise in developed countries. As a result, ocular syphilis has become more common too. The purpose of this study was to report the current incidence and characteristics of optic nerve involvement in patients with newly diagnosed syphilis

**Methods:**

A retrospective, single center study. We reviewed medical records of hospitalized patients between January 2009 and January 2017 with a new documented diagnosis of Syphilis

**Results:**

We have located 123 newly diagnosed patients. Only ten of them reported ocular symptoms that triggered their workup. The rest, 83 patients, were evaluated by an ophthalmologist as part of a routine workup. Twenty three (22%) had clinical findings on examinations. Seven patients had isolated optic disc edema (usually bilateral), 4 patients had neuroretinitis and 4 had disc edema combined with pan or posterior uveitis. One patient was found to have optic atrophy. There were 4 cases of anterior uveitis and 3 cases of intermediate or posterior uveitis with no optic nerve involvement. All patients were treated with intravenous penicillin G. Six patients required topical administration of steroids and one patient was treated with oral prednisolone due to severe optic neuropathy. While initial best corrected visual acuity (VA) ranged from 20/25 to hand movement. Final VA ranged from 20/20 to 20/160.

**Conclusions:**

Ocular Syphilis is more common than previously reported and optic nerve involvement can affect up to 17% of the patients. High index of suspicion for *Trponema* infection is required in order to preserve vision as well as prevent life threatening complications.

**References:** None.

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion), Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 241****Pediatric Research Collaboration ExPLoring Tests In Ocular Neuroimmunology (PERCEPTION)**

Jennifer Graves<sup>1</sup>, Amy Waldman<sup>2</sup>, Ben Greenberg<sup>3</sup>, Gena Heidary<sup>4</sup>, Amy Lavery<sup>2</sup>, Darrel Conger<sup>5</sup>, Leslie Benson<sup>4</sup>

<sup>1</sup>UCSF, San Francisco, California, USA, <sup>2</sup>Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA, <sup>3</sup>University of Texas Southwestern, Dallas, Texas, USA, <sup>4</sup>Boston Children's Hospital, Boston, Massachusetts, USA, <sup>5</sup>UTSW, Dallas, Texas, USA

**Introduction:**

Multiple potential therapies are in various stages of development for both neuroprotection and remyelination trials in adults with multiple sclerosis (MS), but there are no such trials that target pediatric MS. Our preliminary data demonstrate that knowledge gained from adult studies cannot be directly translated into pediatric populations. The rarity of pediatric MS and the paucity of validated paradigms and outcomes threaten the ability to study such therapies in children.

**Methods:**

We developed the PEdiatric Research Collaboration ExPLoring Tests in Ocular Neuroimmunology (PERCEPTION) to address the gaps in knowledge regarding visual outcome metrics and their interpretation in pediatric neuroinflammatory diseases. Children with central nervous system neuroinflammatory diseases are being enrolled at 4 academic centers. These centers were chosen based on their respective visual sciences research interests with expertise in both pediatric neurology and neuro-ophthalmology. Longitudinal data (at least yearly evaluations), including clinical features, high- and low-contrast visual acuity, optical coherence tomography, and additional metrics are being collected using a shared research protocol.

**Results:**

The PERCEPTION team participates in regular conference calls and in-person meetings. Initial discussions were focused on protocol development to ensure uniform and consistent data collection across the Centers. Recruitment for longitudinal data collection using the implemented protocol commenced on April 1, 2016[WAT1]. Data is entered into a Research Electronic Data Capture (REDCap) database with all sites having full access to the data. [WAT1]Anyone remember the date?

**Conclusions:**

The PERCEPTION database will contain cross sectional and longitudinal data on visual metrics to enable the design of clinical trials with appropriate sample sizes relative to outcome measures in pediatric neuroinflammatory diseases. PERCEPTION was designed to determine the impact of potential therapies on visual function, optic nerve myelination and optic nerve axon density.

**References:** None.

**Keywords:** Demyelinating disease, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 242**

**Neuro-ophthalmic Consequences of Firearms-Related Trauma in the United States**

Jimmy Hu<sup>1</sup>, Afshin Parsikia<sup>2</sup>, Joyce Mbekeani<sup>3</sup>

<sup>1</sup>Montefiore Medical Center, Bronx, New York, USA, <sup>2</sup>Surgery, Jacobi Medical Center, Bronx, New York, United States, Bronx, New York, USA, <sup>3</sup>Surgery (Ophthalmology), Jacobi Medical Center, Bronx, New York, United States, Bronx, New York, USA

**Introduction:**

The United States has the highest rate of firearms-related injuries amongst all affluent nations. Neuro-ophthalmic injuries, often associated with traumatic brain injury (TBI), may result in long-term disabilities. Our study seeks to characterize neuro-ophthalmic consequences of firearms-related trauma.

**Methods:**

Retrospective analysis of patients admitted with firearms-related trauma and neuro-ophthalmic manifestations were identified from the National Trauma Data Bank (2008-2014) using ICD-9CM codes. Data analysis was performed, using student t-test, Chi-squared test and odds ratio (OR) calculations, with SPSS software. Statistical significance was set at  $p < 0.05$ .

**Results:**

1188(13.6%) out of 8715 patients with firearms-related ocular trauma, had neuro-ophthalmic manifestations. The mean(SD) age was 33(16)years. Most were males (83.8%). Whites accounted for 46.5%, Blacks, 37.2% and Hispanics, 12.5%. Frequently associated non-neuro-ophthalmic injuries were orbital (28.3%) open globe (19.9%) and contusions (12%). Mean(SD) injury severity score (ISS) was 20.1(11.1) (severe); 32.4% were classified  $>24$  (very severe). Mean(SD) Glasgow Coma Score (GCS) was 11.2(4.8), with 65 years suffered most from self-inflicted trauma (OR=5.85, 95%CI=3.35-10.22;  $p < 0.001$ ) as did males (OR=1.43, 95%CI=1.01-2.01;  $p = 0.04$ ) and Whites (OR=12.55, 95%CI=9.25-17.02;  $p < 0.001$ ). Blacks were most likely victims of assault (OR=10.21, 95%CI=7.46-13.98) as were Hispanics (OR=2.91, 95%CI=1.94-4.36);  $p < 0.001$ . Mean(SD) hospital stay was 13.8(15.9)days and mortality was 8.9%.

**Conclusions:**

Neuro-ophthalmic consequences of firearms-related trauma were associated with TBI and severe ISS. Optic, facial and oculomotor neuropathies were the commonest forms of nerve damage. Assault and self-inflicted trauma were the most frequent intentions and were variably associated with age, gender, race and ethnicity.

**References:** None.

**Keywords:** Stroke Trauma

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 243

### IVIG Treatment in the Management of Corticosteroid Unresponsive Optic Neuritis: Case Series of 15 Cases

Yu Zhao<sup>1</sup>, Angela Herro<sup>2</sup>, William Feuer<sup>3</sup>, Norman Schatz<sup>3</sup>, John Guy<sup>3</sup>

<sup>1</sup>Minneapolis Clinic of Neurology, Minneapolis, Minnesota, USA, <sup>2</sup>Barrow Neurological Institute, Phoenix, Arizona, USA, <sup>3</sup>Bascom Palmer Eye Institute, Miami, Florida, USA

#### Introduction:

Corticosteroid (CS) unresponsive optic neuritis is a clinical challenge. Intravenous immunoglobulin (IVIG) has been used in multiple autoimmune diseases since 1980 due to its anti-inflammatory and immune-modulating effects. In this retrospective study, we demonstrated our experience with IVIG in the management of 15 cases of CS unresponsive optic neuritis.

#### Methods:

This is an Institutional Review Board (IRB) approved retrospective chart review study of patients from 2010 to 2017 in our academic tertiary center with diagnosis of optic neuritis. All the patient did not respond to or could not tolerate intravenous (IV) CS. Totally 15 cases meet the criteria, including 11 cases of auto-immune optic neuritis /neuropathy (AON), 2 cases of Neuromyelitis Optica (NMO), 1 case of autoimmune-related retinopathy and optic neuropathy (ARRON) and 1 case of multiple sclerosis (MS). All the patients' vision are monitored by visual acuity (VA) (Snellen acuity chart) and/or Humphrey visual field (HVF) or Goldman visual field (GVF).

#### Results:

13 patients (86.7%) responded to IVIG treatment with both subjective and objective improvement. 1 patient (case 3) has improvement with mean deviation (MD) of HVF but has worsened VA without any subjectively improvement. 1 patient (case 11) has improvement of VA in left eye (OS) by record but had no subjective improvement. 9 patients (60%) have at least 2 lines of improvement in one eye on snellen's VA. 7 patients (46.7%) have at least 2 dB MD improvement on HVF in one eye. There are total of 11 patients (73.3%) have either 2 lines of VA improvement or 2 MD improvement on HVF in at least one eye. 1 patient has significant improvement on HVF although no VA change.

#### Conclusions:

IVIG is an important medical treatment of CS unresponsive optic neuritis and in some cases the only tolerable and effective treatment to preserve the patients' vision.

**References:** 1. Petzold, A., Wong, S. & Plant, G. T. Chapter 20 – Autoimmunity in visual loss. in Handbook of Clinical Neurology 133, 353–376 (2016). 2. Lam, B. Retinal Ganglion Cell Thickness to assess the optic nerve. J. Neuroophthalmol. 35, 107–108 (2015). 3. Miller, N., Subramanian, P. & Patel, V. Walsh and Hoyt's Clinical Neuro-ophthalmology. The essentials. (Wolters Kluwer). 4. Gaier, E. D., Boudreault, K., Rizzo, J. F., Falardeau, J. & Cestari, D. M. Atypical Optic Neuritis. Curr. Neurol. Neurosci. Rep. 15, (2015). 5. Golnik, K., Malik, A. & Ahmed, M. Treatment options for atypical optic neuritis. Indian J. Ophthalmol. 62, 982–982 (2014). 6. Galetta, S. & Cornblath, W. Should most patients with optic neuritis be tested for neuromyelitis optica antibodies and should this affect their treatment? J. Neuroophthalmol. 30, 376–8 (2010). 7. Nakamura, M. et al. Early high-dose intravenous methylprednisolone is effective in preserving retinal nerve fiber layer thickness in patients with neuromyelitis optica. Graefes Arch Clin Exp Ophthalmol 248, 1777–85 (2010).

**Keywords:** Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 244**

**The Heidenhain Variant of Creutzfeldt-Jakob Disease: The New Zealand Experience 1997-2016**

Benson Chen<sup>1</sup>, Eoin Mulroy<sup>1</sup>, Nicholas Cutfield<sup>2</sup>, Neil Anderson<sup>1</sup>

<sup>1</sup>Department of Neurology, Auckland City Hospital, Auckland, New Zealand, <sup>2</sup>University of Otago and Southern District Health Board, Dunedin, New Zealand

**Introduction:**

Creutzfeldt-Jakob Disease (CJD) is a transmissible spongiform encephalopathy resulting in a progressive dementia with associated neurological features. The Heidenhain variant produces a rapid disease course with prominent early visual symptoms which may precede dementia or other neurologic signs. We identified Heidenhain cases retrospectively from the New Zealand CJD Registry (1997 to 2016). Clinical features including neuro-ophthalmic and neurologic findings, electroencephalograms (EEG), magnetic resonance images (MRI), cerebrospinal fluid (CSF) samples, and neuropathological studies were evaluated if available.

**Description of Case(s):**

Eleven cases (six female) with a median age of 72 years (range, 58-86 years) were identified. The median disease duration from onset of symptoms until death was 3.0 months (range 1.2-48.8 months). Three cases were initially referred to ophthalmology and symptoms attributed to other diagnoses (cataracts in two and temporal arteritis in one). Visual symptoms at disease onset included reduced visual acuity and higher visual processing deficits, such as visual hallucination, dysmorphopsia, dyschromatopsia and visuospatial inattention. All cases later developed additional neurologic symptoms allowing a clinical diagnosis of CJD. All cases had occipital lobe cortical signal disturbance on initial DWI or FLAIR MRI sequences. CSF 14-3-3 was positive in seven (78%) of nine tested samples. Eight cases had EEG, with typical CJD changes observed in four (50%). Post-mortem neuropathology was available in four cases, all showing neuronal loss, spongiform change, and gliosis in the grey matter of the cerebral cortex. Staining for human prion protein was positive.

**Conclusions, including unique features of the case(s):**

The Heidenhain variant of CJD should be considered in patients with visual symptoms of unclear origin, particularly when ocular causes are excluded. Screening for disorders of higher visual processing can be helpful when the diagnosis is being considered. A diagnosis of CJD can be made on the basis of clinical features, with the support of MRI, EEG and CSF findings.

**References:** None.

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion), Higher Visual Cortical functions, Higher visual functions, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 245****Failure to Find Evidence for a Strong Association Between Herpes Zoster and Giant Cell Arteritis**

Charles Grose<sup>1</sup>, Erin Buckingham<sup>1</sup>, Nasreen Syed<sup>1</sup>, Morton Smith<sup>2</sup>, Todd Margolis<sup>2</sup>, Matthew Thurtell<sup>1</sup>, Randy Kardon<sup>1</sup>

<sup>1</sup>University of Iowa, Iowa City, Iowa, USA, <sup>2</sup>Washington University in St. Louis, St. Louis, Missouri, USA

**Introduction:**

The etiology of the inflammatory process in giant cell arteritis (GCA) is unknown. Prior studies of herpes zoster antigen and GCA have conflicting results ranging from 74% with zoster antigen in one study to none with zoster antigen in a second study. Therefore, we re-examined whether zoster viral antigen was detectable in temporal artery (TA) biopsies taken from individuals with GCA.

**Methods:**

This was a retrospective comparative microscopic case study of TA biopsies of from patients with GCA-positive and GCA-negative histopathology. Sections of formalin-fixed paraffin-embedded arteries were examined first by H&E and elastin staining to establish the diagnosis of GCA. Adjacent sections of the same biopsy were then examined by immunohistochemistry, using 2 different monoclonal antibodies against a major viral antigen known as gE. Pathological specimens were obtained from patients who underwent TA biopsies at two university medical centers.

**Results:**

The study included TA biopsies from 25 patients with both symptoms of GCA and granulomatous arteritis seen on biopsy and 25 patients with symptoms compatible with GCA but negative H&E pathology. Among the GCA-positive group, biopsies from three patients had positive staining for zoster viral antigen. Among the GCA-negative group, zoster antigen was not detected in any biopsy. In both groups of patients, false positive staining for zoster antigen was detected in areas of calcification within the arteries. Further, false-positive staining was also detected on some extra-arterial skeletal muscle and erythrocytes.

**Conclusions:**

Herpes zoster antigen was detected in only 3/25 temporal arteries from patients with biopsy-proven GCA. One of the three positive cases was noteworthy, because the patient was subsequently found to have had herpes zoster ophthalmicus three weeks before the onset of GCA symptoms. Of equal importance, false-positive staining for zoster antigen was a recurrent problem when testing these TA biopsies.

**References:** None.

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion), Vascular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 246****Retinal And Optic Nerve Degeneration In Patients With Multiple Sclerosis Followed Up For 10 Years**

Elena Garcia-Martin<sup>1</sup>, Marcia Marques<sup>2</sup>, Maria Rodrigo<sup>1</sup>, Elvira Orduna<sup>1</sup>, Elisa Vilades<sup>1</sup>, Marta Cipres<sup>1</sup>, Javier Obis<sup>1</sup>, Maria Satue<sup>1</sup>

<sup>1</sup>Miguel Servet University Hospital, Zaragoza, Spain, <sup>2</sup>Ocular Discomfort Institute, Sao Paulo, Brazil

**Introduction:**

The purpose was to analyze functional and structural changes in the neuro-retina of patients with multiple sclerosis (MS) compared to healthy controls and after 10 years of follow-up.

**Methods:**

Fifty eyes of patients with mild-moderate MS were evaluated and compared to 50 eyes of controls at a baseline visit and at 10 years of follow-up. The following functional parameters were evaluated: best-corrected visual acuity, color vision examined with the Ishihara test, and mean deviation of visual field analyzed using the Humphrey perimetry. The structural parameters of the retinal nerve fiber layer (RNFL) were also studied using the NSITE axonal application of the optical coherence tomograph (OCT) Heidelberg Spectralis.

**Results:**

No differences were found in the functional parameters in MS patients compared to controls, neither at 10 years of follow-up ( $p > 0.05$ ). However a statistically significant decrease was observed in the RNFL thicknesses of MS patients at 10 years of follow-up (mean, nasal, nasal-inferior, temporal-inferior, temporal, temporal-superior, and papillomacular bundle) ( $p < 0.015$ ). The thinning during the follow-up was significant higher in MS patients compared with controls in most of RNFL sector ( $p < 0.001$ ): mean, nasal-inferior, temporal-inferior, temporal, temporal-superior, and papillomacular bundle. A significant increase of the nasal/temporal ratio was found in MS group during the follow-up ( $p < 0.001$ ). A higher functional disability using the Expanded Disability Status Scale was also recorded.

**Conclusions:**

Axonal damage in MS patients can be analyzed and quantified in neuro-retinal structures using the OCT. Patients with MS showed significant RNFL thinning at 10 years of follow-up compared to controls and a progressive axonal death (without outbreaks) that could be detected and quantified using the OCT, but not with the functional tests (best-corrected visual acuity, color vision and visual field).

**References:** -Martinez-Lapiscina EH, Arnow S, Wilson JA, et al. Retinal thickness measured with optical coherence tomography and risk of disability worsening in multiple sclerosis: a cohort study. *Lancet Neurol* 2016;15:574-84. -Pedersen JA, Swartz MA. Mechanobiology in the third dimension. *Ann Biomed Eng* 2005;33(11):1469-90. -Adhi M, Liu JJ, Qavi AH, et al. Choroidal analysis in healthy eyes using swept-source optical coherence tomography compared to spectral domain optical coherence tomography. *Am J Ophthalmol* 2014;157(6):1272-81. -Gordon-Lipkin E, Chodkowski B, Reich DS, et al. Retinal nerve fiber layer is associated with brain atrophy in multiple sclerosis. *Neurology* 2007;69:1603-9.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 247****The Spectrum of Anti-GAD Antibody Associated Neuro-Ophthalmological and Neurological Conditions**

Thirugnanam Umaphathi<sup>1</sup>, Hui Jin Chiew<sup>1</sup>, Shermyn Xiu Min Neo<sup>1</sup>, Pei Xuan Koh<sup>1</sup>, Daniel Chia Theng Oh<sup>1</sup>, Zhiyong Chen<sup>1</sup>, Peng Soon Ng<sup>1</sup>, Nigel Choon Kiat Tan<sup>1</sup>

<sup>1</sup>*National Neuroscience Institute, Singapore 308433, Singapore*

**Introduction:**

Neuro-ophthalmologists are aware of the association between anti-GAD antibodies and nystagmus, in particular downbeat nystagmus. It occurs in the context of diffuse cerebellar degeneration but may be an isolated phenomenon. In addition, anti-GAD antibodies are associated with a number of neurological syndromes and systemic autoimmunity, some of which co-exist and have important diagnostic and therapeutic implications. Neuro-ophthalmologists should therefore be familiar with this spectrum.

**Methods:**

We selected and studied consecutive cases of anti-GAD associated neuro-ophthalmological and neurological conditions seen at our institution from the beginning of 2015.

**Results:**

We discuss, using a series of video-illustrations, the clinical presentation of our ten patients with the following anti-GAD antibody associated syndromes: episodic vertigo, isolated downbeat nystagmus, cerebellar degeneration, stiff person syndrome, focal epilepsy, limbic and extra-limbic encephalitis. The role of underlying malignancy, in particular thymoma, would be examined using an illustrative patient with thymomatous acetylcholine receptor antibody positive-myasthenia gravis co-existing with anti-GAD antibody-related epilepsy. We summarize the treatments that the patients received, both symptomatic eg aminopyridine, benzodiazepines and anticonvulsants as well as immunomodulatory, such as intravenous immunoglobulin and corticosteroids.

**Conclusions:**

Anti-GAD antibody is associated with a wide variety of systemic and neurologic disorders and management, including cancer surveillance, should be tailored to the individual patient's manifestation.

**References:** None.

**Keywords:** Nystagmus, Neuro-opth & systemic disease ( eg. MS, MG, thyroid), Ocular manifestations of vestibular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 248****Temporal Artery Ultrasound in Suspected Giant Cell Arteritis**

Suellen Li<sup>1</sup>, John Pula<sup>2</sup>

<sup>1</sup>University of Chicago Pritzker School of Medicine, Chicago, USA, <sup>2</sup>Northshore University Healthsystem, Chicago, USA

**Introduction:**

Patients frequently present to a neuro-ophthalmologist for suspected giant cell arteritis. The gold-standard for diagnosis is considered to be a temporal artery biopsy, although this procedure is invasive and it has variable sensitivity. We report here our experience with temporal artery ultrasound, particularly those cases where both an ultrasound and biopsy were performed concomitantly.

**Methods:**

This is a retrospective chart review. We analyzed all cases where temporal artery ultrasound was ordered for evaluation of suspected giant cell arteritis. All patients were examined by one neuro-ophthalmologist and all ultrasounds were interpreted by one radiologist. In cases where biopsy was performed, it was completed after the ultrasound.

**Results:**

Twelve patients had temporal artery ultrasound. Four of these also had temporal artery biopsy, three of whom were tissue-positive for giant cell arteritis. In all three biopsy-positive and one biopsy-negative patients, the ultrasound findings correctly predicted the biopsy result. Of the seven patients with temporal artery ultrasound who did not have biopsy, six were negative and one was positive. The six patients negative for arteritis on ultrasound have not gone on to develop arteritis over time at this point. The patient who was positive on ultrasound but did not have a biopsy was treated for arteritis based on high pre-test probability and comorbidities which precluded the procedure.

**Conclusions:**

Temporal artery ultrasound may have a role in the diagnostic evaluation of giant cell arteritis.

**References:** Alberts M. Temporal Arteritis: Improving Patient Evaluation with a New Protocol. Perm J,17(1):56-62, 2013

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Vascular disorders

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 249****Mobile Universal Lexicon Evaluation System in MS: A New Visual Test of Rapid Picture Naming**

Meagan Seay<sup>1</sup>, Omar Akhand<sup>1</sup>, Lucy Cobbs<sup>1</sup>, Lisena Hasanaj<sup>1</sup>, Prin Amorapanth<sup>1</sup>, John-Ross Rizzo<sup>1</sup>, Rachel Nolan<sup>1</sup>, Liliana Serrano<sup>1</sup>, Barry Jordan<sup>2</sup>, Janet Rucker<sup>1</sup>, Steven Galetta<sup>1</sup>, Laura Balcer<sup>1</sup>

<sup>1</sup>New York University School of Medicine, New York, USA, <sup>2</sup>Burke Rehab Hospital, White Plains, USA

**Introduction:**

Vision-based measures of rapid number naming (King-Devick [K-D]) have improved the sensitivity of sports-related concussion screening and also demonstrate slower testing times in patients with multiple sclerosis (MS). K-D requires saccades and vergence, measuring aspects of frontal, parietal and brainstem centers. We developed the Mobile Universal Lexicon Evaluation System (MULES) to capture a more extensive vision network, integrating saccades, color perception, and object identification. This study introduces MULES, a new vision-based test of rapid picture naming, to the visual assessment of patients with MS.

**Methods:**

We administered the MULES and K-D tests in addition to binocular measures of low-contrast letter acuity (LCLA) and high-contrast visual acuity (VA) in an MS cohort and in a group of disease-free controls.

**Results:**

Among 22 patients with MS (median age 37 years, range 20-72) and 22 disease-free controls (median age 34 years, range 19-59), MULES test times were greater (worse) among the patients (59.6 vs. 40.0 seconds). Accounting for age, MS vs. control status was a predictor of MULES test times ( $P=0.03$ , logistic regression). Faster testing times were noted among patients with MS with greater (better) scores for binocular LCLA at 2.5% contrast ( $P<0.001$ , linear regression, accounting for age), binocular high-contrast VA ( $P<0.001$ ), and K-D test times ( $P<0.001$ ). Both groups demonstrated 8-10-second improvements in MULES test times between trials 1 and 2 ( $P<0.0002$ , paired t-tests).

**Conclusions:**

A complex task, the MULES test of rapid picture naming involves a more extensive visual network than the K-D test, capturing color perception and object characterization, in addition to saccades. Color recognition occurs early in object processing and requires area V4 and the inferior temporal projections. MULES scores reflect performance of LCLA, a widely-used measure of visual function in MS clinical trials. These results provide evidence that the MULES test can add visual information to the assessment of patients with MS.

**References:** None.

**Keywords:** Demyelinating disease, Higher visual functions, Miscellaneous, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 250**

**Differential Visual Acuity Data When Utilizing 2 versus 4 Meter ETDRS Charts in Pediatric Patients**

Darrel Conger<sup>1</sup>, Leslie Benson<sup>2</sup>, Jennifer Graves<sup>3</sup>, Amy Waldman<sup>4</sup>, Samuel Hughes<sup>1</sup>, Benjamin Greenberg<sup>1</sup>

<sup>1</sup>University of Texas Southwestern, Dallas, Texas, USA, <sup>2</sup>Boston Childrens, Boston, Massachusetts, USA, <sup>3</sup>University of California San Francisco, San Francisco, California, USA, <sup>4</sup>Childrens Hospital of Philadelphia, Philadelphia, Pennsylvania, USA

**Introduction:**

We developed the PEdiatric Research Collaboration ExPLoring Tests in Ocular Neuroimmunology (PERCEPTION) to address the gaps in knowledge regarding outcome metrics and their interpretation in pediatric neuroinflammatory diseases. Children with central nervous system neuroinflammatory diseases are being enrolled at 4 academic centers. As part of the process of creating a uniform data collection protocol, various assessments were analyzed to determine data reliability.

**Methods:**

Children underwent routine visual acuity testing with the ETDRS backlit charts. Children were tested with 2 meter and 4 meter charts per standardized protocols and their relative visual acuities were assessed.

**Results:**

102 measurements were taken utilizing both the 2 meter and 4 meter ETDRS charts in the same subjects on the same day. The average number of letters read using the 2 meter chart was 54.33 while the average number of letter read using the 4 meter chart was 51.94. Using a two sided t test, the two means were considered different to a statistically significant degree ( $p < 0.0001$ )

**Conclusions:**

Studies collecting visual acuity data in children will need to specify either a 2 meter or 4 meter ETDRS chart as this study suggests the data is not interchangeable.

**References:** None.

**Keywords:** Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid), Pediatric neuro-ophthalmology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 252****Are Video-oculography Findings Linked to Specific Clinical Features in Parkinson's Disease?**

Woong-Woo Lee<sup>1</sup>, Byung-Kun KIM<sup>1</sup>

<sup>1</sup>*Nowon Eulji Medical Center, Eulji University, Seoul, Korea, Republic of*

**Introduction:**

Ocular findings are useful in differentiating some neurodegenerative disorders. In contrast, there were no disease-specific ocular findings which favor Parkinson's disease (PD), although saccadic hypometria, frequent square wave jerks (SWJs), and impaired anti-saccade and/or impaired smooth pursuit have been relatively often reported in PD compared to normal controls. Additionally, there was no well-performed study for the correlation between abnormal ocular signs for brainstem-cerebellar involvement (AOS-BCs) [perverted head-shaking nystagmus, positional downbeat-nystagmus, gaze-evoked nystagmus, and hypermetria], which could be found in part of PD patients. We studied which specific clinical features are correlated with SWJs and AOS-BCs to evaluate their clinical significances in PD.

**Methods:**

We reviewed retrospectively 29 PD patients (14 of male) with video-oculography (VOG) and Unified Parkinson's disease rating scale (UPDRS). VOG should be performed within 1 year prior to UPDRS examination. The age of onset and UPDRS examination were respectively  $48.0 \pm 8.4$  and  $59.2 \pm 6.6$  years.

**Results:**

The patients with the higher frequency of SWJs (defined as over 20/min) were likely to have greater severity of on- ( $p=0.007$ ) and off-period falling ( $p=0.002$ ) in UPDRS part-II. The AOS-BCs were linked to lower off-period tremor scores in UPDRS part-III. ( $p=0.011$ )

**Conclusions:**

The presence of frequent SWJs was correlated to the severity of falling in PD. Progressive supranuclear palsy patients have frequent SWJs and early falling. It is another supportive evidence for the positive correlation between SWJs and falling. The presence of AOS-BCs was inversely correlated to off-period tremor scores. A tremor-dominant PD patient is expected to have a good prognosis. Therefore, the absence of AOS-BCs in PD may correspond with less brainstem pathologic involvements. SWJs and AOS-BCs in PD could be considered as markers for falling and tremor respectively. This abstract was accepted as a poster presentation at the 2017 WCN in Japan and was presented on September 18th 2017.

**References:** None.

**Keywords:** Ocular Motility, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 253****Neurophthalmic Manifestations of ZIKA patients in Venezuela**

Emely Karam<sup>1</sup>, Rafael Muci Mendoza<sup>2</sup>, Jose Murcia<sup>1</sup>

<sup>1</sup>Centro Medico Docente La Trinidad, Caracas, Venezuela, <sup>2</sup>Clinica Avila, Caracas, Venezuela

**Introduction:**

Zika is a re-emergent epidemic disease transmitted by bite of infected Aedes species of mosquitoes. Many descriptions of congenital neurological and Guillan Barre diseases had been described. We report the neurophthalmological manifestations in a series of Venezuela adult patients and children.

**Methods:**

Evaluated the neuro-ophthalmic manifestations of Zika patients

**Results:**

We evaluated 12 adult patients and 4 children with Zika disease. In the adult series the patients developed: One with Guillan Barre who developed also ocular flutter. One patient VI and IV nerve palsy. One patient third nerve palsy. One patient facial and IV nerve palsy. Two patients with VI nerve palsy. Two cases with optic neuropathy one of them bilateral. One patient with neuroretinopathy. One patient with uveitis. One case developed myasthenia and other thyroid ophthalmopathy. . In the children group: Two children with microcephalia and funduscopy findings and children with nystagmos. All children had Zika encephalopathy The arbovirus test was performed in 6 adult patients and the 4 mothers of the children with Zika during the period of pregnancy and the disease. The magnetic resonance imaging study showed meningeal contrast enhancement in one adult patient and brain anomalies in the 4 children.

**Conclusions:**

Zika causes a variety of neurophthalmological manifestations, however in some cases it seems that it can exacerbate immunological diseases as was observed in two cases. Compromise of the afferent visual system is more prone to leave sequel than the affection of the visual efferent system. In congenital Zika, fundoscopic changes and microcephaly were observed when the infection occurred in the first months of pregnancy while in late periods of pregnancy the cardinal symptom was nystagmus. In both groups of children there is cerebral involvement.

**References:** Platt DJ, Miner JJ: Consequences of congenital Zika virus infection. *Curr Opin Virol*, 25;(27):1-7, 2017. Wahid B, Ali A, Rafique S, Idrees M.: Zika: As an emergent epidemic. *Asian Pac J Trop Med*.;9(8):723-9, 2016

**Keywords:** Neuro-ophth & infectious disease (eg, AIDS, prion), Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Ocular Motility, Optic neuropathy, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 254**  
**Optic Meningitis**

Jean-Phillippe Woillez<sup>1</sup>

<sup>1</sup>Centre Hospitalier Universitaire de Lille (France), Lille, France

**Introduction:**

Optic nerve inflammations have common symptoms: Vision decrease, Retro bulbar pain, Rapid, Visual Field (VF) impairments and Visual Evoked Potential (VEP) alterations. These manifestations are identical in both Optic Perineuritis (OP) and Optic Neuritis (ON). Real ON is always associated with a perineuritic reaction. As a neuro-ophthalmologist it is impossible to distinguish between the two entities: ON and OP. Therefore the words Optic Meningitis (OM) should be used. These words express the painful aspect (only the optic nerve's meningeal sheath is sensitive) and the functional impairment (by inflammatory compression or by direct inflammatory axonal or microglial injuries).

**Methods:**

Typical clinical cases analysis using complementary explorations (VF, VEP, Contrast Vision (CV), Color Vision, OCT, MRI c).

**Results:**

After a bibliographic summary, we try to establish a typical analysis of ON and OP. The nosological term « Optic Meningitis » is argued.

**Conclusions:**

Initial neuro-ophthalmological examination of a patient with painful unilateral vision loss, which suggests an optic nerve inflammatory episode, does not allow confirming ON diagnosis. Electrophysiological or neuroradiological investigations only lead results. It is therefore attractive to propose and use the words "Optic Meningitis" as a first-sight in this very frequent clinical fact.

**References:** Bergman O(1), Andersson T(1), Zetterberg M(1)(2). Optic perineuritis: a retrospective case series. *Int Med Case Rep J.* 2017 Jun 8;10:181-188. doi: 10.2147/IMCRJ.S125972. eCollection 2017. Purvin V, Kawasaki A, Jacobson DM. Optic perineuritis: clinical and radiographic features. *Arch Ophthalmol.* 2001;119:1299–306. Byon IS, Jung JH, Choi J-H, et al. Evaluation of retinal nerve fiber layer in patients with idiopathic optic perineuritis using optical coherence tomography. *Neuroophthalmology.* 2015;39:34–8. Pakdaman MN. Orbital inflammatory disease: pictorial review and differential diagnosis. *WJR.* 2014;6:106–15. Coppens S, Petzold A, de Vries-Knoppert WA. Pain in Optic Perineuritis: Author Response. *Neuroophthalmology.* 2015 May 4;39(2):101-102. eCollection 2015 Apr. PubMed PMID: 27928342; PubMed Central PMCID: PMC5123112.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Demyelinating disease, Optic neuropathy, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 255****Saccadic Intrusions Are Rare in Multiple Sclerosis**

Lisa DePledge<sup>1</sup>, Pavle Repovic<sup>2</sup>, James Bowen<sup>2</sup>, Peiqing Qian<sup>2</sup>, Bobbie Severson<sup>2</sup>, Steven Hamilton<sup>3</sup>, Bonnie Keung<sup>3</sup>, Eugene May<sup>3</sup>

<sup>1</sup>Gonzaga University, Spokane, Washington, USA, <sup>2</sup>Multiple Sclerosis Center, Swedish Neuroscience Institute, Seattle, Washington, USA, <sup>3</sup>Neuro-ophthalmology Clinic, Swedish Neuroscience Institute, Seattle, Washington, USA

**Introduction:**

Saccadic intrusions (SI) are spontaneous abnormal eye movements that occur due to a number of neurologic conditions, and are indicative of pathology in a wide variety of neuroanatomical sites. Square wave jerks, macro-saccadic oscillations, and ocular flutter have been described in case reports and short series of patients with multiple sclerosis (MS). The prevalence of SI in the general MS population has not been systematically studied.

**Methods:**

All patients with MS seen at an MS center between June 12, 2017 and August 17, 2017 were evaluated for the presence of SI. If the examining provider suspected SI, the patient was evaluated by a neuro-ophthalmologist. Demographic, clinical, and MRI information about affected patients was tabulated. Visual quality of life questionnaires were completed.

**Results:**

Three patients were found to have SI out of 614 screened, indicating a prevalence of 0.49%. Two patients had macro-square wave jerks (MSWJ) and one had ocular flutter. Both MSWJ patients had SPMS with significant disability, with MS plaques on MRI scattered throughout the brainstem, the cerebellum, and both cerebral hemispheres. There was a relation to visual quality of life scores. The patient with flutter had relapsing remitting MS, a single MS plaque in the cerebellar peduncle, no other brainstem lesions, and several hemispheric lesions.

**Conclusions:**

We estimate the prevalence of SI in the general MS population to be approximately 0.5%, making them rare in this group of patients. The examining providers may not have detected all patients with SI, so this is likely to be an underestimate of true prevalence. Based on the patients we identified, MSWJ may be more likely present in individuals with significant disability, secondary progressive MS, and widespread multi-level plaques. Ocular flutter may occur in individuals with less extensive brainstem and cerebellar burden of disease.

**References:** None.

**Keywords:** Ocular Motility, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 256****The Role of Neuro-Ophthalmology in Atypical Parkinsonism: Clinical Findings on a Standardized Ocular Motor Exam**

Meagan Seay<sup>1</sup>, Andrea Lee<sup>1</sup>, Steven Frucht<sup>1</sup>, Janet Rucker<sup>1</sup>

<sup>1</sup>New York University School of Medicine, New York, USA

**Introduction:**

Parkinsonian disorders can be divided into idiopathic Parkinson's disease and atypical parkinsonism, including progressive supranuclear palsy (PSP), multisystem atrophy (MSA), dementia with Lewy bodies (DLB), and corticobasal syndrome (CBS). Diagnostic challenges include phenotypic overlap and delayed development of classic features, making early diagnosis difficult. Eye movement exam may assist with diagnosis, particularly early when findings are subtle. For example, supranuclear gaze palsy (SGP) of PSP demonstrates absent optokinetic fast phases as the earliest manifestation; downbeat nystagmus may indicate MSA; and ocular motor apraxia (OMA)/Balint syndrome may indicate CBS or DLB. The aim of this study was to categorize findings of a standardized clinical ocular motor examination in atypical parkinsonism.

**Methods:**

Retrospective chart review in patients with atypical parkinsonism referred to neuro-ophthalmology from 2014-2017.

**Results:**

Fifty patients, mean age  $70.0 \pm 8.5$  years, were included. Patients were grouped according to eye movement deficits: SGP suggesting PSP (n=26), SGP plus cerebellar suggesting PSP or PSP-mimic (n=8), OMA/Balint suggesting DLB or CBS (n=6), cerebellar only suggesting MSA (n=4), and no abnormality (n=6). SGP was vertical greater than horizontal in 71% and vertical only in 29%. Of those with decreased vertical OKN (n=27), 93% involved upward and downward and 7% upward only. SGP was mild in 21%, moderate in 26%, and severe in 53%. Of those with cerebellar involvement, downbeat nystagmus was present in 42% (positional only in 1 patient), gaze-evoked nystagmus in 69%, and saccadic dysmetria in 69%. Convergence insufficiency was present in 98% of all patients: symptomatic in 56%. Saccadic intrusions were present in 78%, of which 62% were pathologic square wave jerks.

**Conclusions:**

Eye movement abnormalities provide clues to distinguish between various forms of atypical parkinsonism. Referral patterns and diagnostic contribution are assessed in a corresponding study. Systematic ocular motor examination, especially for subtle signs, may assist in diagnosis.

**References:** None.

**Keywords:** Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Ocular Motility, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 258****Internuclear Ophthalmoplegia in Pediatric Patients**

Emely Karam<sup>1</sup>

<sup>1</sup>*Centro Medico Docente La Trinidad, Caracas, Venezuela*

**Introduction:**

Internuclear ophthalmoplegia is a localization sign of the lesion of the medial longitudinal fasciculus (LMF). Damage of the LMF causes deficit of ipsilateral adduction with contralateral abduction nystagmus. The internuclear ophthalmoplegia can be unilateral, frequently associated with skew deviation or bilateral in greater relation with vertical nystagmus. The most frequent cause in elderly patients is ischemia of the brainstem and in young adults or teenager multiple sclerosis. Internuclear ophthalmoplegia in pediatric patients is rare. We report 9 patients under 10 years of age with internuclear ophthalmoplegia

**Methods:**

Report the internuclear ophthalmoplegia in pediatric patients

**Results:**

Unilateral ophthalmoplegia (adduction deficit with contralateral abduction nystagmus and skew deviation) was observed in a patient with brain stem tumor. Bilateral internuclear ophthalmoplegia or WEBINO (wall-eyed bilateral internuclear ophthalmoplegia) syndrome was found in 8 patients: 2 of them after cranioencephalic trauma, one with inborn error of metabolism and 5 in premature patients with perinatal hypoxia. In all cases there was deficit of adduction with abduction nystagmus and skew deviation; except in the group of premature patients due to perinatal hypoxia; they did not develop abduction nystagmus. The studies of brain magnetic resonance showed a compromise of the median longitudinal fasciculus.

**Conclusions:**

Internuclear ophthalmoplegia in children is uncommon. An important observation found was in preterm infants with perinatal hypoxia. These patients did not trigger nystagmus in abduction. Probably the delay in the maturation of the middle longitudinal fasciculus causes its absence, since it is known that this system reaches maturity in the first year of life. This would also explain the great angle of deviation that these patients present.

**References:** Rizzo JL, Lloyd M, Ohara M: Pediatric internuclear ophthalmoplegia, *Journal of Neuro-Ophthalmology* ;33:134–136, 2013. Shaikh AG, Ghasia FS: Fixational saccades are more disconjugate in adults than in children. *Plus One*. 13;12(4), 2017

**Keywords:** Pediatric neuro-ophthalmology, Ocular Motility, Ocular manifestations of vestibular disorders, Miscellaneous,

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 259****Focal Thickness Alterations in the Intraretinal Layers in Patients Multiple Sclerosis**

Hong Jiang<sup>1</sup>, Ce Shi<sup>2</sup>, Silvia Delgado<sup>3</sup>, Yuqing Deng<sup>2</sup>, Jianhua Wang<sup>2</sup>

<sup>1</sup>Bascom Palmer Eye Institute, Department of Neurology, University of Miami, Miami, Florida, USA, <sup>2</sup>Bascom Palmer Eye Institute, University of Miami, Miami, Florida, USA, <sup>3</sup>Department of Neurology, University of Miami, Miami, Florida, USA

**Introduction:**

Detecting the locations with most profound changes in the intraretinal layers may provide more sensitive information on neurodegeneration in patients with multiple sclerosis. The goal of this study was to map the thicknesses of intraretinal layers and identify the locations of the most profound thickness alterations by ultra-high-resolution optical coherence tomography (UHR-OCT).

**Methods:**

Fifty-three relapsing and remitting multiple sclerosis (RRMS) patients, and 53 (age  $\pm$  5 yrs) and gender-match healthy subjects were recruited. Custom made UHR-OCT (axial resolution  $\sim$ 3  $\mu$ m) was used to acquire three dimensional volumes of the macula of the right eye of each subject. Automated segmentation software (Orion, Voxeleron LLC) was used to segment the thickness of GCIPL in a diameter of 6 mm centered on the fovea. The thickness differentiation maps were calculated by subtracting the thickness of the control group from the MS groups in each pixel and partition was done using the Early Treatment Diabetic Retinopathy Study (ETDRS).

**Results:**

Focal thinning of the total retina, retinal nerve fiber layer and ganglion cell-inner plexiform layer (GCIPL) was located in the nasal side of the map. The most profound thinning of GCIPL was located in an area with diameter of 1 mm which was about 1.8 mm nasal from the fovea (We named it as "Miami GCIPL MS thinning zone). The averaged thinning in the Miami zone was 9.4  $\mu$ m, which was thinner than any other sectors and provided the discrimination power (area under the curve) was 0.77. In contrast, thickening was evident in the outer plexiform layer with focal alteration at the inferior sector.

**Conclusions:**

Focal thickness alteration of the intraretinal layers was evident in patients with RRMS, and their detection may help develop more sensitive image biomarkers of retinal neurodegeneration in MS.

**References:** None.

**Keywords:** Demyelinating disease, Neuro-ophth & systyemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 260****Comparing the Smooth Pursuit and Saccadic Eye Movements in Rugby Players to a Normative Database**

Clare Fraser<sup>1</sup>, Premkumar Gunasekaran<sup>2</sup>, Adrian Cohen<sup>1</sup>, Christopher Hodge<sup>2</sup>

<sup>1</sup>University of Sydney, Sydney, Australia, <sup>2</sup>University of Technology Sydney, Sydney, Australia

**Introduction:**

There is increasing evidence to suggest ocular-based tools may improve the sensitivity of sideline concussion detection protocols. Currently, normative saccadic and smooth pursuit eye movements in the general population have been documented for digital eye-tracking tests such as the RightEye Neuro Vision™ test (RightEye). However, this normative database may not accurately represent athletes. This study examined the saccadic and smooth pursuit systems in premiership-grade young rugby athletes as compared to published population means. It also investigated impacts of age and previous concussion within the last 12 months on oculomotor function.

**Methods:**

During the 2017 competition pre-season, forty-two premiership-grade male players (mean age=20.61±3.0 years) from a semi-professional rugby club were recruited. Prior history of concussion was documented including quantity and dates of medically-diagnosed concussions. Players with present symptoms of concussion were excluded. All players performed 3 smooth pursuit tests (horizontal, vertical and circular) and 2 saccade tests (horizontal and vertical) on the RightEye apparatus. Ocular variables were calculated and recorded by the eye-tracking system.

**Results:**

No statistical difference ( $p>0.05$ ) was determined when comparing between players with a history of concussion ( $n=6$ ) and those without ( $n=36$ ). No statistical difference ( $p>0.05$ ) was found between players below ( $n=20$ ) and over 20 years ( $n=22$ ). Faster horizontal smooth pursuits were demonstrated in 85.7% of the players than the population mean. In the vertical pursuit test, 83.3% of the rugby cohort had faster vertical smooth pursuits, while 78.6% exhibited faster circular smooth pursuits than the population. Additionally, 73.8% had greater saccade numbers in the horizontal and vertical axis than the normative mean.

**Conclusions:**

We found that young premiership-grade rugby players possess faster smooth pursuit and saccadic ocular systems than the general population. Additionally, previous history of concussion and age have no significant impact on smooth pursuit and saccades. Future studies should include a comparative control athlete population.

**References:** None.

**Keywords:** Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 261****Peripapillary Vessel Density Changes in Alzheimer's Type Dementia ; A Pilot Study.**

Paareena Chaitanuwong<sup>1</sup>, Supharat Jariyakosol<sup>1</sup>, Supanut Apinyawasisuk<sup>1</sup>, Hathairat Lawanlattanagul<sup>1</sup>, Parima Hirunwiwatkul<sup>1</sup>

<sup>1</sup>Chulalongkorn University, Bangkok, Thailand

**Introduction:**

Alzheimer's type dementia (ATD) is a common disorder affecting elderly adult. From previous study, there's an evidence of retinal pathology in ATD. This study aims to identify ophthalmic findings including retinal thickness and retinal vascular density in ATD compared to normal subjects.

**Methods:**

This is a comparative descriptive study. We collected participants from institution's Alzheimer center [SA1]. Participants' medical history was taken and the participants with glaucoma and other retinal disorders were excluded. Complete ophthalmic examinations were performed. Spectral domain optical coherence tomography angiography (SD-OCTA) was used to analyze retinal thickness and retinal vascular density. Ocular surface disease index (OSDI) score was used to evaluate ocular surface symptoms. Blink rate was counted by a well-trained observer. Cognitive function was evaluated using Thai Mental State Examination (TMSE) score. [SA1] Check the right name of the center

**Results:**

We included 24 ATD patients, and 39 normal participants as a control group. Demographic data was not statistically different between 2 groups. In ATD group, the TMSE score was significantly lower than the control group ( $p < 0.001$ ). The differences of OSDI score, tear breakup time (TBUT), and blink rate between 2 groups were not statistically significant. The parafoveal and perifoveal macular thickness of the ATD group were significantly lower than the control group ( $p < 0.05$ ). Retinal nerve fiber layer (RNFL) thickness of the optic disc was significantly thinner in ATD group ( $p = 0.001$ ). Some vessel density parameters of the ATD group were significantly lower than in the control group, including whole macular vessel density ( $p < 0.001$ ), optic disc's vessel density at the nerve head level (both the whole volume and peripapillary density) ( $p < 0.05$ ), and optic disc's vessel density at the radial peripapillary capillary (RPC) level (both the whole volume and peripapillary density) ( $p < 0.05$ ).

**Conclusions:**

Patients with ATD are more likely to have lower retinal vessel density of the optic disc and macular region.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Miscellaneous,

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 262

### Kayser-Fleischer Ring Detection and Quantification in Wilson's disease using Optical Coherence Tomography

Ruchika Batra<sup>1</sup>, Pearse Keane<sup>2</sup>, David Nicholl<sup>3</sup>, Gideon Hirschfield<sup>4</sup>, Alastair Denniston<sup>5</sup>, Susan Mollan<sup>5</sup>

<sup>1</sup>Birmingham Neuro-ophthalmology Unit, Birmingham, Great Britain, <sup>2</sup>NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital, London, Great Britain, <sup>3</sup>Department of Neurology, City Hospital, Birmingham, Great Britain, <sup>4</sup>Centre for Liver Research, NIHR Biomedical Research Unit, University of Birmingham, Birmingham, Great Britain, <sup>5</sup>University Hospitals Birmingham NHS Trust, Queen Elizabeth Hospital, Birmingham, Great Britain

#### Introduction:

Delays in the diagnosis of Wilson's Disease (WD) arising from the challenging heterogeneity of presentation, lead to avoidable morbidity and mortality. Clinically a Kayser-Fleischer (KF) ring is useful in diagnosis, reported as being present in nearly all neurological WD, half of hepatic WD and less than half of presymptomatic WD. Most KF rings regress with medical therapy or liver transplantation, however, may return when treatment ceases. Lifelong monitoring of serum and urine is cumbersome for the patient and a reliable non-invasive disease activity score is sought. The aim of the study was to establish the feasibility of quantitative analysis of KF rings in established WD using non-invasive anterior segment optical coherence tomography (AS-OCT).

#### Methods:

Six patients with neurological WD and six healthy controls were included in this pilot study. Clinical and laboratory parameters were noted. Using AS-OCT, cross-sectional corneal images were taken and remotely assessed for evidence of a KF ring. Using validated software, images were analysed to produce an OCT reflectance value at the level of Descemet's membrane for the total band and for the peripheral portion in both WD and controls.

#### Results:

Total band AS-OCT signal intensity at the level of Descemet's membrane, was significantly higher in the WD group with a mean ( $\pm$  SD) of 0.607 ( $\pm$  0.098) vs 0.473 ( $\pm$ 0.111) in the control group (student T-test:  $p=0.011$ ). When directed at the peripheral portion of the band only, the difference between WD and controls was even greater, with a mean ( $\pm$  SD) of 0.549 ( $\pm$  0.156) in WD and 0.261 ( $\pm$  0.096) in controls (student T-test:  $p=0.008$ ).

#### Conclusions:

This study reports unique AS-OCT findings of statistically significant increase in the AS-OCT reflectance value at the level of Descemet's membrane in WD compared to normals. Further characterisation within the range of the disease phenotype is required.

**References:** 1 Walshe JM. The eye in Wilson disease. QJM 2011;104:451-453. 2 Demirkiran M, Jankovic J, Lewis RA, Cox DW. Neurologic presentation of Wilson disease without Kayser-Fleischer rings. Neurology 1996;46:1040-1043. 3 Esmaeli B, Burnstine MA, Martonyi CL, Sugar A, Johnson V, Brewer GJ. Regression of Kayser-Fleischer rings during oral zinc therapy: correlation with systemic manifestations of Wilson's disease. Cornea 1996;15:582-588. 4 Fenu M, Liggi M, Demelia E, Sorbello O, Civolani A, Demelia L. Kayser-Fleischer ring in Wilson's disease: a cohort study. Eur J Intern Med 2012;23:e150-156. 5 Sturniolo GC, Lazzarini D, Bartolo O, Berton M, Leonardi A, Fregona IA, Parrozzani R, Midena E. Small fiber peripheral neuropathy in Wilson disease: an in vivo documentation by corneal confocal microscopy. Invest Ophthalmol Vis Sci 2015;56:1390-1395.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 263

### Surgical Anatomy of the Superficial Temporal Artery to Prevent Facial Nerve Injury During Arterial Biopsy

Hyun Jin Shin<sup>1</sup>, Kang-Jae Shin<sup>2</sup>, Shin Hyo Lee<sup>3</sup>, Ki-Seok Koh<sup>4</sup>, Wu-Chul Song<sup>4</sup>

<sup>1</sup>Department of Ophthalmology, Konkuk University School of Medicine, Seoul, Korea, Republic of, <sup>2</sup>Department of Anatomy, Yonsei University College of Medicine, Seoul, Republic of Korea, Seoul, Korea, Republic of, <sup>3</sup>Department of Anatomy, Konkuk University School of Medicine, Seoul, Korea, Republic of, <sup>4</sup>Konkuk University School of Medicine, Department of Anatomy, Seoul, Korea, Republic of

#### Introduction:

To investigate the topographic relationship between the frontal branch of the superficial temporal artery (FSTA) and the temporal branch of the facial nerve (TFN) with the aim of preventing nerve injury during FSTA biopsy.

#### Methods:

Fifty-seven hemifaces of 33 Korean cadavers were dissected. Vertical lines drawn to the lateral orbital margin (LOM) and superior root of the helix were used as the anterior and posterior reference positions, respectively. Horizontal lines drawn through the supraorbital margin and between the LOM and the superior root of the helix were used as the superior and inferior reference points, respectively. The depth and course relationships of the FSTA and TFN were examined.

#### Results:

The TFN crossed the inferior and superior reference lines at means of 49.0 and 33.0 mm posterior to the anterior reference line, respectively. The FSTA generally runs within the superficial temporal fascia (STF), while the TFN runs within the fibrofatty layer deep to the STF at a distance of 1–2 cm anteriorly and inferiorly to the FSTA. However, in two cases (3.6%) the TFN ran just underneath the FSTA with only a very small safe distance, which makes it highly vulnerable to iatrogenic injury.

#### Conclusions:

When performing an FSTA biopsy, the surgeon should not perform dissection below the STF. Also, surgical incisions should be made outside of the area delineated by an oblique line passing through the points 6 and 4.5 cm posterior to the anterior reference line at the level of the LOM and the supraorbital margin, respectively.

**References:** Yoon MK, Horton JC, McCulley TJ. Facial nerve injury: a complication of superficial temporal artery biopsy. *Am J Ophthalmol.* 2011;152:251-255. Gunawardene AR, Chant H. Facial nerve injury during temporal artery biopsy. *Ann R Coll Surg Engl.* 2014;96:257-260. Albertini JG, Ramsey ML, Marks VJ. Temporal artery biopsy in a dermatologic surgery practice. *Dermatol Surg.* 1999;25:501-508.

**Keywords:** Optic neuropathy, Orbit/ocular pathology, Optic nerve trauma and treatment

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 264****Relation of Quantitative Eye Movements with Cognitive Dysfunction in Patients with Concussion**

Doria Gold<sup>1</sup>, John Martone<sup>1</sup>, Yuen Shan Christine Lee<sup>1</sup>, Amanda Childs<sup>1</sup>, Yuka Matsuzawa<sup>1</sup>, Felicia Fraser<sup>1</sup>, Joseph Ricker<sup>1</sup>, WeiWei Dai<sup>2</sup>, John-Ross Rizzo<sup>1</sup>, Todd Hudson<sup>1</sup>, Ivan Selesnick<sup>2</sup>, Steven Galetta<sup>1</sup>, Laura Balcer<sup>1</sup>, Janet Rucker<sup>1</sup>

<sup>1</sup>New York University Langone Medical Center, New York, New York, USA, <sup>2</sup>New York University, New York, New York, USA

**Introduction:**

Inter-saccadic interval (ISI) prolongation during rapid number naming on King-Devick (K-D) testing has been shown to underlie longer test times in patients with a history of concussion. The ISI is a measure of time between saccades, representing saccadic latency and fixation duration. Prolongation may result from increased saccade latency either as a result of, or in concert with, impaired attention and/or cognition. We sought to determine the relation of ISI prolongation and neuropsychological testing in a range of cognitive domains in concussion.

**Methods:**

Analysis of sixteen patients with a concussion history (mean age 41.7 +/-13.6 years, range 24-65) who performed K-D with eye movement recordings (EyeLink 1000+) and underwent neuropsychological testing. Primary neuropsychological measures included tests assessing effort, pre-morbid intellectual functioning, processing speed, attention and working memory, executive function, and mood as part of a concussion battery. Spearman rank-correlations were performed to examine the relation of ISI and neuropsychological measures.

**Results:**

Among 16 participants, aged 41.7 +/- 13.6 years, mean K-D test time was 72.6s +/-20.7; this is longer than the expected control value of 41.5s (prior studies). Mean ISI was 379.1msec +/-199.1. Greater ISI prolongation was associated with lower scores on measures of processing speed and attention/working memory: Trails Making Test Part A (rs=-0.64, P=0.009); Stroop Color Word (rs=-0.69, P=0.003); Digit Span Backward (rs =-0.59 P =0.02) and Digit Span Total (rs =-0.65 P =0.006).

**Conclusions:**

Results demonstrate associations between ISI prolongation and worse neuropsychological scores among patients with a history of concussion. Such deficits may reflect involvement of the dorsolateral prefrontal cortex (DLPFC) and subcortical structures in concussion, as these facilitate saccades, processing speed, and working memory. Ongoing studies will further refine cognitive function domains most associated with eye movement physiology in concussion.

**References:** None.

**Keywords:** Ocular Motility, Stroke Trauma

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 265****The Effect of Horizontal Rectus Muscle Surgery on Distance-Near Incomitance**

Paul Phillips<sup>1</sup>, Katherine Fray<sup>1</sup>, Adriana Grigorian<sup>2</sup>, Hanya Qureshi<sup>3</sup>, Brita Rook<sup>1</sup>, Lamonda Corder<sup>3</sup>, Robert Lowery<sup>1</sup>

<sup>1</sup>University of Arkansas for Medical Sciences Arkansas Children's Hospital, Little Rock, Arkansas, USA, <sup>2</sup>UH Cleveland Medical Center, Cleveland, Ohio, USA, <sup>3</sup>Arkansas Children's Hospital, Little Rock, Arkansas, USA, <sup>5</sup>University of Arkansas for Medical Sciences Arkansas Children's Hospital, Little Rock, Arkansas, USA

**Introduction:**

Patients with neurologic disorders often have horizontal deviation with distance-near incomitance such as divergence insufficiency esotropia. The purpose of this study is to determine the effect of horizontal rectus muscle surgery on distance-near incomitance.

**Methods:**

Prospective evaluation of patients > 7 years old who had medial rectus or lateral rectus muscle surgery between 12/09 and 7/12. Prism and alternate cover testing was performed at distance (6 meters) and near (0.3 meters) after > 1 hour of monocular occlusion at the pre-operative and post-operative examinations. The change in distance-near incomitance was calculated. The choice of strabismus surgery was at the surgeon's discretion. Post-operative examinations within 1 week and closest to 1 year after surgery were analyzed. Patients with vertical muscle surgery, muscle fibrosis, or paralysis were excluded.

**Results:**

Forty-five patients met inclusion criteria. Twenty-three patients had esotropia treated with medial rectus muscle recessions (21 patients) or lateral rectus muscle resections (2 patients). Twenty-two patients had exotropia treated with lateral rectus muscle recessions (18 patients) or medial rectus muscle resections (4 patients). Post-operative examinations within one week after surgery were obtained in 44 patients. The change in distance-near incomitance was  $\leq 5$  prism diopters in 37 patients,  $\leq 10$  prism diopters in 42 patients. Follow-up examinations 6 – 24 months after surgery were obtained in 28 patients. The change in distance-near incomitance was  $\leq 5$  pd in 20 patients,  $\leq 10$  pd in all 28 patients. Change in distance-near incomitance did not correlate with the specific surgical procedure.

**Conclusions:**

Horizontal rectus muscle surgery does not have a clinically significant effect on distance-near incomitance. It is not necessary to consider distance-near incomitance when choosing between medial rectus and lateral rectus muscle surgery.

**References:** None.

**Keywords:** Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 266

### Molecular Findings Among Patients with Nystagmus Referred for Targeted Next-Generation Sequencing

Jinu Han<sup>1</sup>, John Hoon Rim<sup>2</sup>, Seung-Tae Lee<sup>3</sup>, Hye Young Kim<sup>4</sup>, Hye Won Park<sup>1</sup>, Sueng-Han Han<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, Yonsei University College of Medicine, Seoul, Korea, Republic of, <sup>2</sup>Department of Medicine, Yonsei University Graduate School of Medicine, Seoul, Korea, Republic of, <sup>3</sup>Department of Laboratory Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of, <sup>4</sup>Department of Ophthalmology, National Health Insurance Service Ilsan Hospital, Goyang, Korea, Republic of

#### Introduction:

Infantile nystagmus syndrome (INS) is a group of disorders presenting with genetic and clinical heterogeneities, and patients often undergo numerous investigations including brain MRI. This study aimed to assess the utility of next-generation sequencing (NGS) to enhance the diagnosis of INS.

#### Methods:

A single-center retrospective case series involving 74 unrelated, consecutive patients with INS, who underwent genetic testing between June 2015 and September 2017. NGS analysis was performed using a target panel that included 113 genes associated with INS (n=48) or 429 genes associated with known ocular phenotypes (n=25) or a TruSight One sequencing panel that included 4813 genes associated with known human phenotypes (n=1). Patients underwent a detailed ophthalmic examination, including electroretinogram (ERG) and optical coherence tomography (OCT), if feasible.

#### Results:

Among the 74 patients, 13 (18%) had a family history of nystagmus. Forty (53%) were men and all patients were of single ethnicity (Korean). The mean age at genetic testing was  $10.2 \pm 10.6$  years. ERG was done in 41 patients (55%) and OCT scan was available in 49 patients (66%). Variants that were highly likely to be causative were identified in 46 of the 74 patients, corresponding to a molecular diagnostic yield of 62.2% (95% CI: 50.8~73.5%). NMNAT1, FRMD7, and PAX6 mutations appeared to be the major genetic causes of INS in our cohort. Notably, 14 (19%) were reclassified to a different diagnosis based on NGS testing, enabling accurate clinical management and genetic counselling.

#### Conclusions:

These findings suggest that NGS can be used as an initial diagnostic tool to enable accurate molecular diagnosis of INS because ERG and OCT tests are not easily applicable in young infants. Accurate NGS application in early childhood not only facilitated early molecular diagnosis, but also led to improved personalized management in patients with INS.

**References:** None.

**Keywords:** Nystagmus, Genetic Disease, Pediatric neuro-ophthalmology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** This study was funded by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2016R1D1A1B03934725).

**Poster 267**

**Clinical Significance of Perverted Head-Shaking Nystagmus**

Sun-Young Oh<sup>1</sup>, Tae-Ho Yang<sup>1</sup>

<sup>1</sup>*Chonbuk National University, Jeonju-City, Korea, Republic of*

**Introduction:**

Perverted head-shaking nystagmus (pHSN) refers to the nystagmus that develops in the plane other than that being stimulated by head shaking, i.e., downbeat or upbeat head shaking nystagmus (HSN) after horizontal head shaking.

**Methods:**

We reviewed the medical records of 822 consecutive subjects who were referred to a dizziness clinic of Chonbuk National University hospital from January 2010 to December 2010.

**Results:**

In unspecified dizziness group, SN was observed in 1.9% (4/208), HSN was observed in 13.0% (27/208), perverted HSN was observed in 1.9% (4/208). Perverted HSN was frequently observed in central vestibular disorders such as stroke, vestibular migraine, cerebellar ataxia, and vertebro-basilar insufficiency (VBI). However, pHSN was also observed at higher rate than expected in peripheral vestibular disorders including BPPV especially involving the vertical canals, Meniere disease and even in the unilateral vestibulopathy (39/397, 9.8%).

**Conclusions:**

Our results show that the perverted HSN in dizzy populations was frequently observed not only in cases of central vestibular disorders but also in peripheral disorders. Perverted after head-shaking nystagmus can develop by any conditions that cause the difference in the vestibular velocity storage in vertical component of vestibular-ocular reflex.

**References:** None.

**Keywords:** Ocular manifestations of vestibular disorders, Nystagmus

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 268****Clinical and Molecular Genetic Features of Congenital Nystagmus with FRMD7 mutations**

Jae-Hwan Choi<sup>1</sup>, Eun Hye Oh<sup>1</sup>, Jae-Ho Jung<sup>2</sup>, Seo Young Choi<sup>1</sup>, Kwang-Dong Choi<sup>1</sup>, Sang-Ho Kim<sup>3</sup>, Hak-Seung Lee<sup>4</sup>

<sup>1</sup>Department of Neurology, Pusan National University Yangsan Hospital, Yangsan, Korea, Republic of, <sup>2</sup>Department of Ophthalmology, Pusan National University Yangsan Hospital, Yangsan, Korea, Republic of, <sup>3</sup>Department of Neurology, Dong-A University Hospital, Busan, Korea, Republic of, <sup>4</sup>Department of Neurology, Wonkwang University Hospital, Iksan, Korea, Republic of

**Introduction:**

Congenital nystagmus (CN) is the involuntary oscillation of the eyes with onset in the first few months of life. CN can be an idiopathic disease (idiopathic infantile nystagmus, IIN) or can be a feature of other ocular diseases. The most common form of inheritance is X-linked, and mutations in FRMD7 gene are a major cause. The aim of this study is to determine the clinical and molecular genetic features of CN with FRMD7 mutations.

**Methods:**

We recruited 37 unrelated Korean patients (13 familial cases and 24 sporadic cases) with CN. All patients underwent detailed ophthalmic examinations and eye movement recording. To identify the mutation of FRMD7, we performed PCR-based direct sequencing using genomic DNA from the patient's peripheral blood. We compared clinical features and eye movement recordings between FRMD7 group and non-FRMD7 group.

**Results:**

In 13 (35%) of 37 patients, five different mutations of FRMD7 were detected: start codon mutation c.1A>G, splice site mutation c.162+6T>C, and three missense mutations c.575A>C, c.722A>G, and c.875T>C. Four of them were novel mutations. In particular, the known mutation (c.875T>C) was identified in one family and six sporadic cases. A cup-to-disc ratio (C/D ratio) was significantly decreased in FRMD7 groups ( $p<0.001$ ), while a disc-macula distance to disc diameter ratio (DM/DD ratio) was significantly increased in FRMD7 group when compared with non-FRMD7 group ( $p=0.015$ ). A macular hypoplasia and anomaly of anterior segments were not observed in any patients with FRMD7 mutations. There were no significant differences in waveform and frequency of nystagmus between two groups.

**Conclusions:**

Our study shows that FRMD7 mutations are the underlying molecular pathogenesis of CN and the missense mutation, c.875T>C may be common mutation among Korean CN patients. The optic nerve head hypoplasia is associated with FRMD7 mutations and could be an important etiological factor in the development of nystagmus.

**References:** None.

**Keywords:** Genetic Disease, Nystagmus

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 269**

**Modulation of Vertical Nystagmus by Convergence: Correlation with Positional Nystagmus**

Sun-Uk Lee<sup>1</sup>, Jeong-Yoon Choi<sup>1</sup>, Hyo-Jung Kim<sup>1</sup>, Seong-Ho Park<sup>1</sup>, Ji-Soo Kim<sup>1</sup>

<sup>1</sup>Seoul National University Bundang Hospital, Seongnam-si, Korea, Republic of

**Introduction:**

This study aimed to delineate the mechanisms of nystagmus modulation during convergence by comparing the modulation patterns observed during convergence and lateral gazes, and while supine and straight head hanging.

**Methods:**

We analyzed the modulation of nystagmus during convergence and lateral gazes, and in supine and straight head hanging positions in 63 patients with vertical nystagmus (30 men, mean age±SD=45±18, range: 13~86), 34 with downbeat and 29 with upbeat nystagmus. We correlated the findings between the patients with and without convergence-induced nystagmus (CIN).

**Results:**

During convergence, downbeat nystagmus remained unchanged in 15 (15/34, 44%), but increased in nine (9/34, 26%), decreased in six (6/34, 18%), or changed into upbeat in four patients (4/34, 12%). Patients with modulation of downbeat nystagmus during convergence showed a modulation during lateral gazes ( $p=0.034$ ) and in the supine or straight head hanging positions ( $p=0.005$ ) more frequently than those without CIN. Significant modulation of upbeat nystagmus was also found during convergence in 23 (23/29, 79%) patients, augmented in 16 (16/29, 55%), reversed to downbeat in five (5/29, 17%), and suppressed in the remaining two (2/29, 7%). Patients with modulation of upbeat nystagmus during convergence showed positional modulation of the nystagmus ( $p=0.008$ ) more frequently than those without. The direction of CIN mostly coincided with the direction of vertical nystagmus induced by lying down ( $p=0.001$ ) or SHH ( $p=0.02$ ). While supine, convergence decreased downbeat nystagmus ( $p=0.011$ ), but did not affect upbeat nystagmus ( $p=0.657$ ).

**Conclusions:**

Vertical nystagmus may increase, decrease or alter its direction during convergence. Patients with a modulation of vertical nystagmus during convergence showed positional modulation of the nystagmus more frequently than those without. These findings indicate that the otolith-ocular reflex may be involved in modulation of vertical nystagmus during convergence.

**References:** None.

**Keywords:** Nystagmus

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

## Poster 270

### The New MULES: A Sideline-Friendly Test of Rapid Picture Naming for Concussion

Omar Akhand<sup>1</sup>, Matthew Galetta<sup>1</sup>, Lucy Cobbs<sup>1</sup>, Lisena Hasanaj<sup>1</sup>, Nikki Webb<sup>2</sup>, Julia Brandt<sup>1</sup>, Prin Amorapanth<sup>1</sup>, John-Ross Rizzo<sup>1</sup>, Rachel Nolan<sup>1</sup>, Liliana Serrano<sup>1</sup>, Janet Rucker<sup>1</sup>, Barry Jordan<sup>3</sup>, Arlene Silverio<sup>1</sup>, Steven Galetta<sup>1</sup>, Laura Balcer<sup>1</sup>

<sup>1</sup>New York University School of Medicine, New York, New York, USA, <sup>2</sup>New York University, New York, New York, USA, <sup>3</sup>Burke Rehabilitation Hospital, White Plains, New York, USA

#### Introduction:

Measures of rapid automatic naming (RAN) have been used for over 50 years to capture vision-based aspects of cognition. The Mobile Universal Lexicon Evaluation System (MULES) is a test of rapid picture naming under investigation. MULES was designed as a series of 54 grouped color photographs (fruits, random objects, animals) that integrates saccades, color perception and contextual object identification. Recent changes to the MULES test have been made to improve ease of use on the sidelines. Originally an 11x17-inch single-sided paper, the test has been reduced to a laminated 8.5x11-inch double-sided version. We identified performance changes associated with transition to the new, more sideline-friendly MULES. We also examined MULES on the sideline for sports-related concussion.

#### Methods:

We administered the new laminated MULES to youth and collegiate athletes during pre-season baseline testing. Healthy volunteers (office staff) also participated. Athletes with concussion underwent sideline testing after injury. Time scores for the new laminated MULES were compared to those for the larger version (big MULES).

#### Results:

Among 503 athletes and office volunteers (age 16±7 years, range 6-59, 30% female), average test times at baseline were 45.6±15.5 seconds for the new laminated MULES (n=197) and 48.2±17.1 seconds for big MULES (n=249). Both versions were completed by 57 participants, with excellent agreement (P<0.001, linear accounting for age). Age was a predictor of test times for both MULES, with longer times noted for younger participants (P<0.001). Among 4 athletes with concussion thus far during the fall sports season (age 14±5 years) all showed worsening of MULES scores from pre-season baseline (median 3.0 seconds, range 2.1-14.4).

#### Conclusions:

The MULES test has been converted to a more sideline-friendly laminated version, with excellent agreement between versions across age groups. Feasibly administered at pre-season and in the office setting, the MULES shows preliminary evidence of capacity to identify athletes with sports-related concussion.

**References:** 1. Cobbs L, Hasanaj L, Amorapanth P, Rizzo JR, Nolan R, Serrano L, Raynowska J, Rucker JC, Jordan BD, Galetta SL, Balcer LJ. Mobile Universal Lexicon Evaluation System (MULES) test: a new measure of rapid picture naming for concussion. *J Neurol Sci* 2017;372:393-398.

**Keywords:** Higher visual functions, Higher Visual Cortical functions, Miscellaneous, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Supported by New York University.

## Poster 271

### Long-term Memory Of Object Locations And Strabismus Angle Requires Oculomotor Proprioception

Linus Sun<sup>1</sup>, Wangzikang Zhang<sup>1</sup>, Amrita Singh<sup>2</sup>, Stephen Lomber<sup>3</sup>, Vincent Sanchez<sup>1</sup>, Michael Goldberg<sup>1</sup>

<sup>1</sup>Columbia University College of Physicians and Surgeons, New York, New York, USA, <sup>2</sup>Columbia University, New York, USA, <sup>3</sup>University of Western Ontario, London, Canada

#### Introduction:

In humans, the accuracy of saccades to remembered spatial locations deteriorates linearly with the first few intervening saccades between the initial target presentation and the final saccade to the remembered target location. As the number of intervening saccades increases, the degree of deterioration decreases until it asymptotes. One explanation for the asymptote of saccadic error is that when the number of intervening saccades is low, the brain relies on a corollary discharge of the saccade to remap the retinotopic receptive field, with the error being additive with each remapping, consistent with Helmholtz's postulate[1]. The asymptote of saccadic error may be due to a switch from a retinotopic remapping process to a stable craniotopic representation which can be accessed repeatedly without concurrent increases in saccadic inaccuracy and is consistent with Sherrington's postulate[2, 3]. We hypothesized that the late, stable representation is dependent upon a proprioceptive mechanism[4].

#### Methods:

To test this we trained a monkey to make a saccade to the spatial location of a briefly presented target after a random set of up to nine intervening visually guided saccades. The monkey's accuracy asymptotes as the number of saccades increases. We used an implanted cryoloop to inactivate the oculomotor proprioceptive region of sensorimotor cortex (Area 3a)[5].

#### Results:

The monkey made accurate memory-guided saccades to the spatial location of vanished targets contralateral to the cortical inactivation after one or two intervening saccades, but made significantly inaccurate, frequently ipsilateral, saccades after five to nine intervening saccades. Inactivation did not affect saccades to ipsilateral memory target locations. In addition, inactivation caused a small latent deviation divergence movement and increased variability of visual ocular fixations.

#### Conclusions:

These data indicate that remembering the location of a target after five or more intervening visually guided saccades requires oculomotor proprioception. Furthermore, cortical proprioception appears to control strabismus angle and ocular fixation accuracy.

**References:** 1. von Helmholtz, H., Handbook of Physiological Optics, 3rd Edition, translated by J.P.C. Southall. 1928, Optical Society of America: New York. p. 242-281. 2. Karn, K.S., P. Møller, and M.M. Hayhoe, Reference frames in saccadic targeting. Experimental brain research, 1997. 115(2): p. 267-282. 3. Poletti, M., D.C. Burr, and M. Rucci, Optimal multimodal integration in spatial localization. The Journal of neuroscience : the official journal of the Society for Neuroscience, 2013. 33(35): p. 14259-14268. 4. Sun, L.D. and M.E. Goldberg, Corollary Discharge and Oculomotor Proprioception: Cortical Mechanisms for Spatially Accurate Vision. Annu Rev Vis Sci, 2016. 2: p. 61-84. 5. Lomber, S.G., B.R. Payne, and J.A. Horel, The cryoloop: an adaptable reversible cooling deactivation method for behavioral or electrophysiological assessment of neural function. J Neurosci Methods, 1999. 86(2): p. 179-94.

**Keywords:** Higher Visual Cortical functions, Ocular Motility, Adult strabismus with a focus on diplopia, Pediatric neuro-ophthalmology, Higher visual functions

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** This work was partially supported by the National Eye Institute (K08EY023265 to L.D. Sun, PI; and P30EY019007, R01EY014978, and R01EY017039 to M.E. Goldberg, PI) and partially supported by grants from the Zegar, Keck, Kavli, and Dana Foundations.

**Poster 272****Association between Convergence Insufficiency and EVestG Extracted Features in Post-Concussion Syndrome**

Behzad Mansouri<sup>1</sup>, Abdelbaset Suleiman<sup>1</sup>, Zahra Moussavi<sup>1</sup>, Brian Lithgow<sup>1</sup>

<sup>1</sup>*University of Manitoba, Winnipeg, Canada*

**Introduction:**

Electrovestibulography (EVestGTM) is a novel technology that objectively measures the vestibular response. Our data suggests EVestG recordings may distinguish short-and long-term post-concussion syndrome (S-PCS3 months) from each other and from the healthy controls. EVestG signals are recorded non-invasively from the external ear whilst stationary or in response to vestibular stimuli; the signals consist of the brainstem and peripheral sensory vestibulo-acoustic signals modulated by the cortical responses. It has been shown that the prevalence of Convergence Insufficiency (CI) increases in PCS significantly. In this study, we investigated the correlation of CI and extracted averaged field potentials (FPs) of EVestG signals and the Rivermead post-concussion questionnaire (RPQ) score in individuals with PCS.

**Methods:**

48 PCS individuals were tested using EVestG, out of which 23 completed the RPQ. FPs were obtained from stationary (i.e. background recording) part of the EVestG signals. CI was measured at near vision using a prism-bar and a cross-cover test by a neuro-ophthalmologist (author BM).

**Results:**

CI was negatively correlated with FP ( $R=-0.68$ ,  $P<<0.05$ ). This finding is consistent with our previous finding where we showed FP correlated with PCS. A positive correlation ( $R=0.7$ ,  $P<<0.05$ ) was found between CI and RPQ3-the score of the first three symptoms of RPQ (i.e. Headache, Dizziness and Nausea).

**Conclusions:**

To the best of our knowledge, this is the first study that objectively demonstrates a correlation between PCS and its severity and CI: (A) the EVestG and CI results significantly correlated in patients with PCS, and (B) the RPQ results showed an association between the CI and severity of the PCS. This study suggests that CI quantification may help in assessment of PCS and its recovery.

**References:** None.

**Keywords:** Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 273****Evaluation of a Novel Smartphone App For the Automated Evaluation of Strabismus Measurements**

Dean Cestari<sup>1</sup>, Gabby Madriz<sup>1</sup>, Peggy Bouzika<sup>1</sup>, Eric Gaier<sup>1</sup>, Malgorzata Rajtar<sup>2</sup>, Ara Keshishian<sup>2</sup>, Elizabeth Fortin<sup>1</sup>

<sup>1</sup>MEEI, Harvard Medical School, Boston, Massachusetts, USA, <sup>2</sup>None, Pasadena, California, USA

**Introduction:**

The sensorimotor examination can detect, assess, and monitor strabismic conditions including esotropia, exotropia, and hypertropia. The exam requires an experienced examiner to reliably record and interpret the findings. There can be great variability in the recorded deviations in the same patient among different examiners. We have developed an app that can automatically calculate these deviations using standard photos taken from any smartphone device.

**Methods:**

Patients were evaluated prospectively in the Neuro-ophthalmology/Adult Strabismus Clinic at the Massachusetts Eye & Ear Infirmary. Measurements were taken by an experienced neuro-ophthalmologist and compared to the measurement taken by either a second year ophthalmology resident or a neuro-ophthalmology fellow. These measurements were then compared with automated measurements that were generated by the app from standard photos taken with a smartphone.

**Results:**

32 consecutive patients were evaluated prospectively. Data was analyzed on 26 patients and 6 were excluded for technical reasons. 6 patients had exotropia, 5 patients had esotropia, 3 patients had hypertropia, and 5 patients had a combination of horizontal and vertical deviation. 7 patients were ortho. The average horizontal deviation measured by the attending, trainee and automated app was 8.4, 10.5, and 9.2 PD respectively. The average vertical deviation was 6.8, 10.1, 7.2 PD respectively.

**Conclusions:**

The sensorimotor examination is time consuming and requires the skill of an experienced clinician. We have developed a smartphone app that can give automated strabismic measurements based on standard smartphone photos. We believe this app can be used by health care professions to accurately assess ocular misalignments and it can be further developed to help clinicians differentiate neurogenic from non-neurogenic etiologies.

**References:** None.

**Keywords:** Adult strabismus with a focus on diplopia, Ocular Motility

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 274****Magnetic Resonance Imaging (MRI) Reveals Compartmental Violations of Sherrington's Law in Horizontal Fusional Vergence**

Joseph Demer<sup>1</sup>, Robert Clark<sup>2</sup>

<sup>1</sup>Stein Eye Institute and Dept. of Neurology, UCLA, Los Angeles, California, USA, <sup>2</sup>Department of Ophthalmology, UCLA, Los Angeles, California, USA

**Introduction:**

Fusional vergence prevents latent misalignment from manifesting strabismus. We employed functional MRI to clarify compartmental mechanisms of horizontal vergence.

**Methods:**

Orbital MRI was performed during fusion and alternate monocular fixation. For medial (MR) and lateral rectus (LR) muscles, changes in posterior partial volume (PPV) of superior (MRs and LR<sub>s</sub>) and inferior (MR<sub>i</sub>) and LR<sub>i</sub>) compartments reflected contractility considered significant at  $P < 0.05$ . Fusion of prism induced phoria in normal subjects was compared with fusion of intermittent exotropia [X(T)] and esotropia [E(T)].

**Results:**

In 11 normals, fusion of a monocularly-aligned, 15cm distant target was implemented in the converging eye by similar relaxation of LR<sub>i</sub> and LR<sub>s</sub> but relaxation of MR<sub>s</sub> > MR<sub>i</sub>. In the aligned eye, both inferior and superior compartments of LR and MR similarly relaxed. Fusion of 50PD X(T) at distance was associated with similar relaxation in LR<sub>i</sub> and LR<sub>s</sub>, but contraction of MR<sub>i</sub> > MR<sub>s</sub>. Fusion of 35PD X(T') at near was associated with similar relaxation of LR<sub>i</sub> and LR<sub>s</sub>, but contraction of MR<sub>s</sub> > MR<sub>i</sub>. In 10 normals, fusional divergence induced by viewing of a 20cm near target through 8PD base in prism was implemented by equal contraction of LR<sub>i</sub> and LR<sub>s</sub>, but relaxation only of MR<sub>s</sub> while MR<sub>i</sub> maintained activity. In 8 normals, fusional divergence to 4PD base-in prism during 500cm distant target viewing was associated with similar contraction of LR<sub>i</sub> and LR<sub>s</sub> but no MR relaxation. In 4 patients, fusion of 30PD E(T) was implemented by similar contraction in LR<sub>i</sub> and LR<sub>s</sub>, but relaxation only in MR<sub>s</sub> while MR<sub>i</sub> maintained activity.

**Conclusions:**

Selective compartmental activity of MRs is intrinsic to physiological near horizontal vergence and compensation of intermittent strabismus. However, MRs does not play this role in X(T) at distance. There is unexpectedly little MR relaxation during normal fusional divergence. Horizontal fusional vergence therefore violates Sherrington's Law of reciprocal antagonist activity.

**References:** 1. Demer, J. L., Kono, R., Wright, W. Magnetic resonance imaging of human extraocular muscles in convergence. *J. Neurophysiol.* 9: 2072-2085, 2003. 2. Demer, J. L. and Clark R. A. Differential compartmental function of medial rectus muscle during conjugate and converged ocular adduction. *J. Neurophysiol.* 112:845-55, 2014. 3. Demer, J. L. and Clark, R. A. Magnetic resonance imaging demonstrates compartmental muscle mechanisms of human vertical fusional vergence. *J. Neurophysiol.* 113:2150-63, 2015.

**Keywords:** Adult strabismus with a focus on diplopia, Ocular Motility, Pediatric neuro-ophthalmology, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** USPHS NIH NEI grant EY008313 and Research to Prevent Blindness

**Poster 275****Quantitative Relationship Between Ocular Motility and Superior Oblique Muscle Hypoplasia in Unilateral Superior Oblique Palsy**

Ji Eun Lee<sup>1</sup>, Hee Kyung Yang<sup>2</sup>, Jae Hyoung Kim<sup>3</sup>, Jeong-Min Hwang<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, Maryknoll Medical Center, Busan, Korea, Republic of, <sup>2</sup>Department of Ophthalmology, Seoul National University College of Medicine, Seongnam, Korea, Republic of, <sup>3</sup>Department of Radiology, Seoul National University College of Medicine, Seongnam, Korea, Republic of

**Introduction:**

To investigate the relationship between ocular motility and the degree of superior oblique muscle hypoplasia in subjects with unilateral superior oblique palsy (SOP).

**Methods:**

A total of 166 patients with unilateral SOP were divided into three groups according to their etiology. Seventy nine patients with congenital SOP and trochlear nerve agenesis (absent group), 40 patients with congenital SOP and a normal trochlear nerve (present group), and 47 patients with acquired SOP (acquired group) who all had a normal trochlear nerve were included. Cross sectional areas of bilateral SO muscles at the optic nerve-globe junction were analyzed on high resolution thin-section MR images. The degree of SO hypoplasia was defined as the ratio of SO area between paretic and normal sides. Multivariate analysis was performed to determine the correlation of SO hypoplasia and ocular motility parameters in each group.

**Results:**

The degree of SO hypoplasia showed an inverse correlation with the difference in hypertropia between both tilt positions (ipsilateral-contralateral tilt) in all groups ( $P < 0.001$  in the absent group,  $P = 0.034$  in the present group,  $P = 0.002$  in the acquired group). Regarding the difference in hypertropia between both side gazes (contralateral-ipsilateral gaze), SO hypoplasia showed a positive correlation in the absent group ( $\beta = 0.405$ ,  $P < 0.001$ ) and the acquired group ( $\beta = 0.420$ ,  $P = 0.001$ ), but not in the present group. None of the other ocular motility parameters including ipsilateral underdepression or overelevation in adduction were related to the degree of SO hypoplasia in all groups.

**Conclusions:**

In unilateral SOP, the degree of SO hypoplasia significantly correlated with the difference in hypertropia during both head tilt positions regardless of etiology, suggesting that the cyclovertical function of the paretic SO during head tilt corresponds mainly to its relative size compared to its fellow eye.

**References:** None.

**Keywords:** Ocular Motility, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 276****Clinical Characteristics of Neuro-Ophthalmology Patients Seen by One Orthoptist at a Large Urban Academic Institution**

Alex Christoff<sup>1</sup>

<sup>1</sup>*The Wilmer Eye Institute at Johns Hopkins Hospital, Baltimore, Maryland, USA*

**Introduction:**

Certified orthoptists are routinely asked to examine neuro-ophthalmology patients with symptomatic strabismus. The importance of creating a differential diagnosis and providing cost-effective, non-surgical treatment options is an important part of delivering effective and affordable healthcare.

**Methods:**

This work was a descriptive study and retrospective review of the most common clinical characteristics of adult neuro-ophthalmology and oculo-plastics patients seen over a 9-year period by one orthoptist in a large urban academic institution in the United States.

**Results:**

575 subjects were identified based on inclusion criteria. Ninety-one percent of the cohort was referred by neuro-ophthalmologists at the institution. Racial demographics matched that of the state. Hypertension was a statistically significant medical risk factor for acquired strabismus and diplopia in this adult cohort. Pupil-sparing oculomotor palsy (CN3) occurred as frequently as pupil-involving CN3, with tumor associated more frequently than aneurysm in both groups. Trochlear nerve palsy (CN4) was more often associated with hydrocephalus than abducens nerve palsy (CN6), and trauma remained a common association with acquired CN4 palsy. In patients with thyroid eye disease (TED), esotropia occurred with similar frequency as exotropia. Myasthenia gravis (MG) remained rare in these patients, as has been previously reported in the literature 1-2, occurring with similar frequency in patients with both types of horizontal strabismus. In patients with ptosis, asymmetry was not more predictive of MG than symmetry. Prism was used most frequently, followed by surgery, to address symptoms. Lastly, there was a statistically significant association of acquired symptomatic strabismus in female subjects with breast cancer and no past ocular history of childhood strabismus or amblyopia.

**Conclusions:**

Orthoptic examination is an important adjunct in determining differential diagnosis and in the treatment adult neuro-ophthalmology patients with symptomatic strabismus. Press-On™ or ground-in spectacle prism was a commonly used treatment for diplopia.

**References:** 1. Ohno M, Hamada N, Yamakawa J, Noh J, Morii H, Ito K: Myasthenia gravis associated with Graves' disease in Japan. *Jpn J Med*1987; 26:2- 6. 2. Yaman A, Yaman H: Ocular myasthenia gravis coincident with thyroid. *Ophthalmopathy Neurol India*2003; 51:100- 101.

**Keywords:** Adult strabismus with a focus on diplopia, Ocular Motility, Myasthenia

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 277**

**Improvement of Interictal Ocular Motor Abnormalities in Vestibular Migraine following Migraine Preventive Therapy.**

Stacy Smith<sup>1</sup>, Shin Beh<sup>2</sup>

<sup>1</sup>Houston Methodist Neurological Institute, The Woodlands, Texas, USA, <sup>2</sup>UT Southwestern Medical Center, Dallas, Texas, USA

**Introduction:**

Vestibular migraine (VM) is a debilitating disorder associated with dizziness and migrainous features, and often associated with interictal central vestibular dysfunction.(1-2) Expert opinion and small studies support the use of migraine preventive therapies for symptomatic relief, but there is limited data on their effect on objective examination findings.(3-5)

**Methods:**

Through an IRB approved retrospective chart review protocol, we identified 13 vestibular migraine patients with an abnormal baseline neuro-otologic examination and the evolution of these findings over time after initiation of a migraine preventive agent. Neuro-otologic examination included assessment in the upright position with and without fixation and with provocative maneuvers (mastoid vibration, head-shaking, and hyperventilation), as well as positional testing (Dix-Hallpike, head-hanging, supine, and supine head right/left positions).

**Results:**

The patients included 11 females and 2 males, with an average age 55 years. Nine had a documented history of migraine or headache. Follow up ranged from 2-22 months (median 11 months). In the upright position, nystagmus was only observed in three patients (two with downbeat nystagmus in eccentric horizontal gaze, and one with right beating nystagmus in right gaze). With removal of fixation, 2 patients had upbeat nystagmus. Head-shaking and mastoid vibration each provoked nystagmus in 4 patients. Hyperventilation produced nystagmus (typically downbeat) in 8 patients. Central positional nystagmus was seen in 8 patients. Treatments included topiramate, amitriptyline, lamotrigine, and non-pharmacologic supplements (magnesium and riboflavin). The majority of patients demonstrated an improvement in exam findings in conjunction with symptomatic improvement on the migraine preventive therapy.

**Conclusions:**

VM is associated with eye movement abnormalities both during the ictal and interictal periods. In our small cohort of patients, we observed an improvement in these abnormalities that correlated with symptomatic improvement on migraine preventive therapy, providing evidence that the underlying central vestibular dysfunction responsible for VM responds to migraine preventive therapy.

**References:** 1. Celebisoy N, Gokcay F, Sirin H, Bicak N. Migrainous vertigo: clinical, oculographic and posturographic findings. *Cephalalgia*, 28(1):72-77, Jan 2008. 2. Rogalinski S, Rambold HA. Probing early motion processing with eye movements: differences of vestibular migraine, migraine with and without aura in the attack free interval. *Headache*, Sep 25, 2017 (epub). 3. Baier B, Winkenwerder E, Dieterich M. "Vestibular migraine": effects of prophylactic therapy with various drugs. A retrospective study. *J Neurol*, 256(3):436-442, Mar 2009. 4. Liu F, Ma T, Che X, Wang Q, Yu S. The efficacy of venlafaxine, flunarizine, and valproic acid in the prophylaxis of vestibular migraine. *Front Neurol*, 8:524, Oct 2017. 5. Salmito MC, Duarte JA, Morganti LOG, Brandao PVC, Nakao BH, et al. Prophylactic treatment of vestibular migraine. *Braz J Otorhinolaryngol*, pii: S1808-8694(16)30103-3, Jun 2016.

**Keywords:** Nystagmus, Vestibular, Ocular manifestations of vestibular disorders, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** This project was supported by the Fight For Sight/NANOS Research Award 2016/2017. This included \$3000 for the project expenses, as well as additional funds toward travel for the NANOS 2018 meeting to present the work.

**Grant Support:** Fight for Sight/NANOS Research Award 2016/2017 with Travel Grant for NANOS 2018 Annual Meeting.

**Poster 278****'Sandbagging' a Vision Test for Concussion-based Sideline Assessment: An Eye Movement Investigation reveals the Strategies**

John-Ross Rizzo<sup>1</sup>, Todd Hudson<sup>1</sup>, Weiwei Dai<sup>1</sup>, John Martone<sup>1</sup>, Yash Chaudhury<sup>1</sup>, Oluchi Ihionu<sup>1</sup>, Lisena Hasanaj<sup>1</sup>, Ivan Selesnick<sup>2</sup>, Laura Balcer<sup>1</sup>, Steven Galetta<sup>1</sup>, Janet Rucker<sup>1</sup>

<sup>1</sup>NYU School of Medicine, New York, New York, USA, <sup>2</sup>NYU Tandon, Brooklyn, New York, USA

**Introduction:**

Athletes may under-report concussion symptoms, leading to inappropriate return-to-play and increased risk of re-injury. Thus, attention has been directed toward tests to identify concussion, such as the K-D, for which longer test times compared to baseline are associated with concussion. There is concern that, in order to facilitate staying in the game in the event of concussion, athletes may attempt to prolong pre-season baseline testing times.

**Methods:**

Twenty-six healthy participants (mean age 29.1+/-7.6 years, range 20-59) with no concussion history performed K-D after reading a randomly selected cue card instructing them to intentionally prolong their reading time. Cards indicated that the examiner was blinded to this strategy. Twenty participants also performed K-D with standard instructions: to read as quickly as possible. Eye movements were recorded with video-oculography (EyeLink 1000+).

**Results:**

K-D testing times were substantially longer among participants whose scripts instructed them to 'sandbag' (91.6s vs 46.2s,  $p < 0.001$ ), as were inter-saccadic intervals (ISI) (413.9.9ms vs 273.2ms,  $p < 0.01$ ). Greater numbers of saccades (overall) (176.8 vs 140.5,  $p < 0.01$ ), as well as saccades in the wrong direction (reversed reading progression) (21.2% vs 10.8%,  $p < 0.001$ ), were generated during 'sandbagging'. Saccade peak velocities and durations showed no differences between participants instructed to read the K-D as usual vs. sandbagging.

**Conclusions:**

K-D test 'sandbagging' results in eye movement behavior differences that are easily detectable by eye movement recordings and differentiable from prior reported findings in concussion. Specifically, ISI prolongation and greater numbers of saccades and reverse saccades occur with 'sandbagging'. Such values detected on baseline assessment may suggest an invalid test score. Objective eye movement recording during K-D performance shows promise for distinguishing between best effort and injury, as well as for identifying red flags on intentionally prolonged baseline performance.

**References:** Carney N, Ghajar J, Jagoda A, et al. Concussion guidelines step 1: systematic review of prevalent indicators. *Neurosurgery*. 2014 Sep;75 Suppl 1:S3-15. Giza CC, Hovda DA. The new neurometabolic cascade of concussion. *Neurosurgery*. 2014 Oct;75 Suppl 4:S24-33. Cantu RC. Recurrent athletic head injury: risks and when to retire. *Clin Sports Med*. 2003 Jul;22(3):593-603, x. Heitger MH, Jones RD, Macleod AD, Snell DL, Frampton CM, Anderson TJ. Impaired eye movements in post-concussion syndrome indicate suboptimal brain function beyond the influence of depression, malingering or intellectual ability. *Brain*. 2009 Oct;132(Pt 10):2850-70. Galetta KM, Brandes LE, Maki K, et al. The King-Devick test and sports-related concussion: study of a rapid visual screening tool in a collegiate cohort. *J Neurol Sci*. 2011 Oct 15;309(1-2):34-9. Galetta MS, Galetta KM, McCrossin J, et al. Saccades and memory: baseline associations of the King-Devick and SCAT2 SAC tests in professional ice hockey players. *J Neurol Sci*. 2013 May 15;328(1-2):28-31. Carpenter RH. The neural control of looking. *Curr Biol*. 2000 Apr 20;10(8):R291-3.

**Keywords:** Ocular Motility, Higher visual functions, Higher Visual Cortical functions

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Sources of funding: 5K12HDOO1097 NICHD and NCMRR, National Institutes of Health Rehabilitation Medicine Scientist Training Program (JRR). Empire Clinical Research Investigator Program (ECRIP) (JRR, TEH, LJB, JCR).

**Poster 279****Misdiagnosis of Third Nerve Palsy**

Richard Schroeder<sup>1</sup>, Leanne Stunkel<sup>1</sup>, Eric Eggenberger<sup>2</sup>, James Ebot<sup>2</sup>, Gregory Van Stavern<sup>1</sup>

<sup>1</sup>Washington University in St. Louis, St. Louis, Missouri, USA, <sup>2</sup>Mayo Clinic, Jacksonville, Florida, USA

**Introduction:**

Third (3rd) nerve palsy is characterized by some combination of ptosis, limited adduction, supraduction, infraduction, and pupillary function. Causes include microvascular ischemia, compression, and aneurysms. Accurate diagnosis is essential to avoid potentially life-threatening consequences and unnecessary testing. We assessed the frequency of 3rd nerve palsy misdiagnosis based upon referrals to two high volume tertiary care neuro-ophthalmology services, and characterized the specific diagnostic errors.

**Methods:**

A retrospective review of patients with 3rd nerve palsy among patients identified by searching for variations of “3rd nerve palsy” in scheduling comments for referrals and final diagnosis of “3rd nerve palsy”. Patients were excluded from the review if they lacked adequate referral documentation or had a known history of compressive brain mass or aneurysm. Incorrect referral diagnoses were analyzed using the DEER criteria. We also collected and analyzed patient characteristics including past medical history, age, gender, referring provider specialty, and results of diagnostic imaging.

**Results:**

69 patients were reviewed with 44 meeting inclusion criteria. Among the cohort referred for 3rd nerve palsy, 24% were found to have alternate diagnoses including myasthenia gravis, thyroid ophthalmopathy, congenital strabismus, and internuclear ophthalmoplegia. Among subjects with final diagnosis of 3rd nerve palsy, 25% were referred for diagnoses including myasthenia gravis, vision loss, and unspecified diplopia. The most common reason identified for misdiagnosis was misinterpretation of exam findings. Failure in hypothesis generation, inadequate physical exam, and failure to weigh clinical history were also common reasons for misdiagnosis.

**Conclusions:**

Misdiagnosis of 3rd nerve palsy was common in referrals to two tertiary neuro-ophthalmology centers. Careful attention to physical exam and a focused differential diagnosis are key factors in correct diagnosis of 3rd nerve palsy.

**References:** Graber, Franklin, Gordon., Diagnostic Error in Internal Medicine. Arch Intern Med,165:1493-9, 2005 Norman, Young, Brooks. Non-analytical models of clinical reasoning: the role of experience. Medical Education 2007; 41: 1140–1145, 2006 Eva, Cunnington, The difficulty with experience: does practice increase susceptibility to premature closure?, J Contin Educ Health Prof, 26:192–8, 2006 Voytovich, Rippey, Suffredini, Premature conclusions in diagnostic reasoning, J Med Educ, Apr;60(4):302-7, 1985 Crosskerry, The Importance of Cognitive Errors in Diagnosis and Strategies to Minimize Them, Acad. Med, 78:775–780, 2003 Trobe, Searching for brain aneurysm in third cranial nerve palsy. J Neuroophthalmol, 29:171-173, 2009

**Keywords:** Ocular Motility, Neuroimaging

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 280**

**New Onset Binocular Diplopia in Patients Over 65 Years**

Daniel Rappoport<sup>1</sup>, Tal Paz<sup>1</sup>, Hana Leiba<sup>1</sup>, Niv Levy<sup>1</sup>

<sup>1</sup>*Kaplan Medical Center, Rehovot, Israel*

**Introduction:**

Diplopia may be caused by various etiologies, and its incidence rises with age. We conducted a retrospective study in order to describe its epidemiology, etiology and the effects of different treatments in patients 65 years of age and older.

**Methods:**

Retrospective chart review of patients 65 years of age and older with a new onset binocular diplopia presenting between January 2012 and December 2016. Data collected included demographics, etiology of misalignment, alignment in cardinal positions, clinical course and treatment methods.

**Results:**

One hundred and eleven patients were included. The most common type of new-onset strabismus was paralytic (78.3 %,  $p < 0.01$ ), followed by restrictive (12.6%), decompensated phoria/tropia (6.3%) and divergence insufficiency (3.6%). Among the paralytic group, isolated cranial nerve palsy was the most common cause (57%), and most cases spontaneously resolved within 1-3 months. All decompensations were documented during 6 months after cataract excision. Of all patients, 13 (11.7%) were candidates for strabismus surgery, but only 53% underwent surgery, with complete success rate of 71.4%. Nine patients were treated with prisms, and five of them (55%) improved.

**Conclusions:**

Paralytic strabismus was the most common cause of diplopia in patients 65 years of age and older. Identifying and understanding the different causes of diplopia in this age group may improve prevention and diagnosis.

**References:** None.

**Keywords:** Adult strabismus with a focus on diplopia, Ocular Motility, Myasthenia, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid), Orbit/ocular pathology

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 281****Ocular Myasthenia Gravis Thymectomy Cohort Study**

Ali Hamedani<sup>1</sup>, Maxwell Pistilli<sup>1</sup>, Kenneth Shindler<sup>1</sup>, Robert Avery<sup>1</sup>, Madhura Tamhankar<sup>1</sup>, Grant Liu<sup>1</sup>

<sup>1</sup>*University of Pennsylvania, Philadelphia, Pennsylvania, USA*

**Introduction:**

The benefit of thymectomy in reducing prednisone requirement, symptom severity, need for immunosuppression, and hospitalization in patients with seropositive generalized myasthenia has recently been established. It is unclear whether this benefit applies to patients with purely ocular myasthenia.

**Methods:**

We conducted a retrospective single-center cohort study of patients with ocular myasthenia. Diagnoses was confirmed by acetylcholine receptor antibodies, abnormal electrophysiology, or a positive edrophonium test and they had at least one year of clinical follow-up. At each visit, ocular and generalized symptom severity was ascertained using a 4-point scale, and prednisone dose, steroid-sparing agent use, and need for IVIG or plasmapheresis were recorded. The effect of thymectomy on time-weighted prednisone dose and symptom severity score was assessed using linear regression models. To adjust for non-randomization of thymectomy, we employed inverse probability weighting using a propensity score model derived from the pre-thymectomy observation period for thymectomy patients and a 6-month lead-in period for non-thymectomy patients that incorporated age, sex, acetylcholine receptor seropositivity, disease severity (as defined by both symptom severity and treatment requirement), and treating physician preferences.

**Results:**

Seventy eight patients (29 thymectomy, 49 non-thymectomy) were included. In unadjusted analyses, time-weighted daily prednisone dose was 2.9mg higher in thymectomy compared to non-thymectomy (95% CI: 0.2-5.7), but after inverse probability weighting, this was no longer statistically significant (difference = 2.0 mg, 95% CI: -0.6 to 4.6). There was no statistically significant difference in symptom severity score (adjusted difference = 0.35, 95% CI: -0.02 to 0.72).

**Conclusions:**

There was no significant difference in prednisone dose or symptom severity after thymectomy in ocular myasthenia. A trend towards higher prednisone dose and symptom severity in patients with thymectomy likely reflects incomplete adjustment for confounding by indication. Future analysis of other outcomes (need for steroid-sparing agent, risk of generalization) is needed and will be performed.

**References:** None.

**Keywords:** Myasthenia

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 282****Tonic vs. Phasic Fiber Dysfunction in Isolated, Unilateral Sixth Cranial Nerve Palsy**

Elizabeth Fortin<sup>1</sup>, Dean Cestari<sup>1</sup>, Stephanie Tin<sup>2</sup>, Joseph Rizzo<sup>1</sup>

<sup>1</sup>Massachusetts Eye and Ear, Boston, Massachusetts, USA, <sup>2</sup>Washington University in St Lewis, St Lewis, Missouri, USA

**Introduction:**

Sixth nerve palsy is a relatively common cause of diplopia. We have observed an apparent non-linearity between the degree of deficit in abduction vs. static ocular misalignment among patients. We hypothesized that this disparity might be due to relative differences in impairment of phasic vs. tonic muscles fiber function. We selected isolated sixth nerve palsies because of the singular innervation of this cranial nerve to the lateral rectus muscle to examine the relationship between the degree of esotropia and limitation of abduction.

**Methods:**

Twenty consecutive patients examined by JR with isolated sixth nerve palsy underwent quantification of the esotropia using prisms and the alternate cover test. An assessment of misalignment was made having the patient fixate on a optotype placed at 16 feet in primary position, then with the head turned 30 and 45 degrees away from the side of the palsy. The amount of head turn amplitude was measured with a protractor centered over the orbit of the affected eye. The abduction deficit was measured by attempted ipsilateral abduction and recorded on a categorical five-point scale (0 to -4).

**Results:**

The relationship between the limitation of abduction and static misalignment of the eyes was: 1) for primary position ( $R^2=0.4645$ ); 2) at 30° ( $R^2=0.3825$ ); and 3) at 45° ( $R^2=0.5722$ ).

**Conclusions:**

Our measurements revealed a poor linear correlation between the degree of limitation of abduction and the degree of static ocular misalignment. This result is consistent with our hypothesis and would suggest that tonic and phasic fibers of the lateral rectus muscle, which each receive a different type of innervation, can be differentially affected by dysfunction of the sixth cranial nerve. We are in the process of obtaining additional patients to compare the outcomes for idiopathic versus non-idiopathic etiologies to assess if measurements obtained in the acute phase might predict the potential for recovery.

**References:** None.

**Keywords:** Ocular Motility, Adult strabismus with a focus on diplopia

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 283****Role of OCT in Monitoring for Ethambutol Induced Optic Neuropathy**

Sona Chaudhry<sup>1</sup>, Crandall Peeler<sup>1</sup>

<sup>1</sup>*Boston Medical Center, Boston, Massachusetts, USA*

**Introduction:**

Toxic optic neuropathy is a rare but serious complication of ethambutol use. The incidence of optic neuropathy increases with sustained periods of the drug's standard loading dose (25 mg/kg/day). To date, there are no known strategies for detecting subclinical ethambutol-induced toxicity, which if detected early may be reversed upon stopping the drug. We assess the utility of ocular coherence tomography (OCT) in detecting subclinical ethambutol-induced optic neuropathy.

**Methods:**

We present a prospective case series of seven patients started on ethambutol and referred to the ophthalmology clinic for monthly screening while on the medication. Visual acuity, color vision, automated perimetry, and OCT of the optic nerve head with retinal nerve fiber layer (RNFL) analysis were obtained and analyzed. Progression analysis from the Heidelberg OCT was utilized to track the RNFL thickness over time. Statistical significance was defined as a p-value <0.05.

**Results:**

All seven patients had a baseline BCVA of 20/20, full color vision, and normal RNFL thickness on OCT. All but one patient had full baseline visual field testing. Ethambutol doses ranged from 12.5mg/kg/day to 26.0mg/kg/day. Mean follow up was 4.6 months from initial screening (Range 1-9 months). No patients in the cohort developed afferent visual dysfunction but three of seven cases showed an upward trend in RNFL thickness, although not statistically significant (p-value 0.48 to 1.0).

**Conclusions:**

We demonstrate an upward trend in RNFL thickness in patients following initiation of ethambutol therapy. We hypothesize that this thickening results from subclinical optic nerve toxicity, manifest as subtle axonal swelling that may precede the development of frank optic atrophy. Larger studies are required to determine whether a "threshold" value of thickening exists that is associated with clinical changes in afferent visual function.

**References:** Barron GJ, Tepper L, Iovine G. Ocular toxicity from ethambutol. *Am J Ophthalmol*, 77(2):256–260, 1974. Chai SJ, Foroozan R. Decreased retinal nerve fibre layer thickness detected by optical coherence tomography in patients with ethambutol-induced optic neuropathy. *Br J Ophthalmol*, 91: 895–897, 2007. Jones AL, Sheen NJ, North RV, Morgan JE. The Humphrey optical coherence tomography scanner: quantitative analysis and reproducibility study of the normal human retinal nerve fibre layer. *Br J Ophthalmol*, 85(6):673–677, 2001. Kim KL, Park SP. Visual function test for early detection of ethambutol induced ocular toxicity at the subclinical level. *Cutan Ocul Toxicol*, 35(3): 228–232, 2016. Zoumalan CI, Agarwal M, Sadun AA. Optical coherence tomography can measure axonal loss in patients with ethambutol-induced optic neuropathy. *Graefe's Arch Clin Exp Ophthalmol*, 243:410–416, 2005.

**Keywords:** Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 284****Nonmydriatic Fundus Photography in the Emergency Department for Patients Presenting with Acute Vision Loss.**

Caroline Vasseneix<sup>1</sup>, Beau Bruce<sup>1</sup>, Samuel Bidot<sup>2</sup>, Nancy Newman<sup>1</sup>, Valerie Biousse<sup>1</sup>

<sup>1</sup>Emory Eye Center, Atlanta, Georgia, USA, <sup>2</sup>Rotschild Hospital, Paris, France

**Introduction:**

Acute visual loss (AVL) is a common chief complaint in Emergency Department (ED) patients, but its evaluation is made difficult by the lack of ophthalmologists readily available in most EDs. We evaluated whether non-mydriatic fundus photography (NMFP) obtained in the ED helps triage patients presenting to the ED with AVL, whether interpreted by ED providers (EPs) or remotely by neuro-ophthalmologists.

**Methods:**

213 patients with AVL evaluated in the ED with NMFP as part of FOTO-ED (phases 1-3) [1-4] were included. Demographics, referral patterns, results of fundus photographs, and final diagnoses were recorded.

**Results:**

A final ophthalmologic diagnosis was made in 109/213 patients (51%) who presented to the ED with a chief complaint of AVL. NMFP allowed a definite diagnosis in 52/109 (38%) patients: 10 acute retinal ischemia (arterial or venous retinal occlusions, or related to diabetic or hypertensive retinopathy); 14 optic neuropathies, 10 papilledema, 4 retinal detachments, 1 retinal hemorrhage, 2 choroidal metastases, 1 vitreous hemorrhage, 4 maculopathies, 6 glaucoma. However, in 57/109 (52%) patients, NMFP was not diagnostic even when interpreted remotely by neuro-ophthalmologists because they had disorders that could not be diagnosed with NMFP (e.g., transient visual loss, diplopia misinterpreted as “visual loss”, anterior segment disorders or peripheral retinal tear in 2 patients, posterior vitreous detachment in 8 patients).

**Conclusions:**

Although NMFP allowed a rapid diagnosis in 52/213 (25%) patients with AVL, NMFP did not help the EPs' triage and referral decisions, emphasizing the limitations of tele-ophthalmology in remotely detecting ocular diseases in the ED, particularly when fundus photography only involves the posterior pole (non-mydriatic imaging) and information about patients' histories and symptoms is missing [5]. NMFP complements ophthalmology consultations in the ED but will not replace them.

**References:** [1] Bruce BB, Lamirel C, Wright DW, Ward A, Heilpern KL, et al. Nonmydriatic ocular fundus photography in the emergency department. *N Engl J Med*, 364: 387–389, 2011. [2] Bruce BB, Lamirel C, Biousse V, Ward A, Heilpern KL, et al. Feasibility of nonmydriatic ocular fundus photography in the emergency department: phase I of the FOTO-ED study. *Acad Emerg Med*, 18: 928–933, 2011. [3] Bruce BB, Thulasi P, Fraser CL, Keadey MT, Ward A, et al. Diagnostic accuracy and use of nonmydriatic ocular fundus photography by emergency physicians: phase II of the FOTO-ED study. *Ann Emerg Med*, 62: 28–33.e1, 2013. [4] Bruce BB, Bidot S, Hage R, Clough L, Fajoles-Vasseneix C, et al. What happens when you try to teach emergency providers to read fundus photographs? Presented at the 42nd Annual NANOS Meeting, February 27 - March 3, 2016, Tuscon, Arizona. [5] Woodward MA, Bavinger JC, Amin S, Blachley TS, Musch DC, et al. Telemedicine for ophthalmic consultation services: use of a portable device and layering information for graders. *J Telemed Telecare*, 23(2):365-370, 2017.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Supported by Research to Prevent Blindness and by the Philippe Foundation.

**Poster 285****Episcleral Delivery System for Neuroprotection in Optic Neuropathy**

Kimberly Cockerham<sup>1</sup>, Katie Topping<sup>1</sup>, Andrea Kossler<sup>1</sup>, Jeffrey Goldberg<sup>1</sup>

<sup>1</sup>Stanford, Department of Ophthalmology, Stockton, California, USA

**Introduction:**

For many optic nerve disorders, there are limited therapeutic options to preserve vision. Under successive DOD Awards, a sustained choroid/retinal Episcleral Delivery System (EDS) has been developed to deliver drugs for weeks to years. The IND enabling work to date includes Episcleral Brimonidine for acute neuroprotection, EC-4565 (stabilizes mitochondria/catalytic anti-oxidant/oxygen free radical scavenger) for sustained neuroprotection and dexamethasone to mitigate inflammation. The EDS can deliver any small molecule that is currently used as an eye drop and most intravitreal injections and intravenous infusions.

**Methods:**

In a bilateral macula-off retinal detachment rabbit model, the EDS was placed unilaterally. A small incision was made in the conjunctiva and the EDS was secured to the superotemporal sclera with tissue glue. Local and systemic toxicity were monitored. Complete eye examinations, fundus photography and ERG were performed. The globes were studied histopathologically including meticulous cell counts per high powered field.

**Results:**

In contrast to the control eyes, there was complete structural and functional cellular preservation in both the EDS of Brimonidine and EC4565 treated eyes with macula-off retinal detachment model. The unidirectional drug delivery through the sclera precluded drug loss through the conjunctival lymphatics; no drugs were detected in serum testing. The EDS were well tolerated without ocular toxicity. Once through the sclera, the therapeutic agents were distributed throughout the choriocapillaris resulting in therapeutic pharmacokinetics even distal to the location of the EDS.

**Conclusions:**

Episcleral delivery of neuroprotective agents effectively prevents apoptosis in the rabbit model. A phase 1 dose escalation clinical study in patients with optic neuropathies without clinical options is planned to begin in early 2018. Primary outcome measures will include dose limiting toxicity and determination of recommended dose for phase 2 studies. Secondary outcome measures will include ETDRS visual acuity, HVF, OCT and Flavoprotein Fluorescence (FPF), a unique device that quantifies mitochondrial health.

**References:** References: 1. Saylor et.al. Arch Ophthalmol. Experimental and clinical evidence for Brimonidine as an optic nerve and retinal neuroprotective agent: an evidence-based review. 127:402-6, 2009. 2. Green et al., Neuroscience. Nuclear estrogen receptor-independent neuroprotection by estratrienes: a novel interaction with glutathione. 84: 7-10, 1998. 3. Knels et al., J Neurochem. Effects of advanced glycation end products-inductor glyoxal and hydrogen peroxide as oxidative stress factors on rat retinal organ cultures and neuroprotection by UK-14, 304. 106(4): 1876-87, 2008. 4. Kumar et al., Free Radical Biol Med, Role of nonfeminizing estrogen analogues in neuroprotection of rat retinal ganglion cells against glutamate-induced cytotoxicity. 38: 1153-1163, 2005. 5. Liu et al., Stroke, Neuroprotective effects of a novel non-receptor-binding estrogen analogue: in vitro and in vivo analysis. 33: 2481-2491, 2002. 6. Field MG, et al. Retinal flavoprotein fluorescence correlates with mitochondrial stress, apoptosis, and chemokine expression. Exp Eye Res. Vol. 93, p. 548-555, 2011.

**Keywords:** Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic nerve trauma and treatment, Neuro-ophth & systemic disease ( eg. MS, MG, thyroid)

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Department of Defense

**Poster 286****Microvascular Changes in Macula and Optic Nerve Head in Non-Arteritic Anterior Ischemic Optic Neuropathy**

Satya Karna<sup>1</sup>, Abdul Rawoof<sup>1</sup>, Sruthi Surendran<sup>1</sup>, Rohit Shetty<sup>1</sup>, Abhijit SinhaRoy<sup>1</sup>, Nivedhita G<sup>1</sup>

<sup>1</sup>Narayana Nethralaya, Bangalore, Karnataka, India

**Introduction:**

To determine the microvascular changes in macula and optic nerve head in Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION).

**Methods:**

A total of 26 eyes of normal Indian subjects and 6 eyes of (NAION) patients with mean age ( $59 \pm 4.1$ ) underwent OCTA imaging centered on the fovea and optic nerve head. Local fractal analysis was applied to the superficial and deep retinal OCTA images and optic disc centered images obtained from Optovue. For optic disc centered images, Garway Heath Map was used to analyze the images by dividing the image around optic disc into sectors (Temporal, Nasal, Superior-Temporal, Superior-Nasal, Inferior-Temporal, and Inferior-Nasal).

**Results:**

In the superficial layer, normal eyes had significantly higher vessel density ( $p < 0.001$ ) lower spacing between large and small vessels ( $p < 0.001$ ) compared with NAION patients. Foveal Avascular Zone (FAZ) area had no prominent changes compared to the normal subjects in superficial ( $P = 0.51$ ) and deep layer ( $P = 0.45$ ). Vessel Density ( $P = 0.012$ ), spacing between large vessels ( $P = 0.004$ ) and spacing between small vessels ( $P = 0.008$ ) were significant from normal. Vessel Density enface and all the sectors of NAION were statistically significant ( $P < 0.001$ ) from the normal subjects. In ROC analysis, superficial layer had higher area under curve compared to deep layer. Among the vascular parameters spacing between large vessels ( $0.97 \pm 0.02$ ) and vessel density ( $0.95 \pm 0.04$ ). In optic disc centered images, the sectors (N,T,ST) had the highest area under curve ( $0.97 \pm 0.03$ ) and a sensitivity of 100%.

**Conclusions:**

OCTA analysis of macula and optic disc prove to be a good factor in differentiating NAION from normal subjects. However in macula centered superficial layer showed significant changes compared to deep layer. In case of disc centered images all the vascular parameters prove to be statistically significant.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 288**

**Optical Coherence Tomographic Angiography in Non-arteritic Anterior Ischemic Optic Neuropathy Reveals Biphasic Microvascular Changes**

Eric Gaier<sup>1</sup>, Mengyu Wang<sup>2</sup>, Aubrey Gilbert<sup>1</sup>, Joseph Rizzo<sup>1</sup>, Dean Cestari<sup>1</sup>, John Miller<sup>1</sup>

<sup>1</sup>Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, USA, <sup>2</sup>Schepens Eye Research Institute, Boston, Massachusetts, USA

**Introduction:**

Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common cause of non-glaucomatous optic neuropathy in older adults. Optical coherence tomographic angiography (OCT-A) is an emerging, non-invasive method to study the microvasculature of the posterior pole, including the optic nerve head. The goal of this study was to assess the vascular changes in the optic nerve head and peripapillary area associated with NAION using OCT-A.

**Methods:**

In this retrospective comparative case series, we performed OCT-A in 25 eyes (7 acute and 18 non-acute) in 19 patients with NAION. Fellow, unaffected eyes were analyzed for comparison. Macro- and microvascular densities were quantified in the papillary and peripapillary regions of unaffected, acutely affected, and non-acutely affected eyes and compared across these groups according to laminar segment and capillary sampling region, and with respect to performance on automated visual field testing.

**Results:**

In acutely affected eyes, OCT-A revealed a reduction in the signal from the major retinal vessels and dilation of the superficial capillaries in the peripapillary area. By contrast, non-acutely affected eyes showed attenuation of the capillaries in the peripapillary area. The peripapillary choriocapillaris was obscured by edema in acute cases, but was similar between non-acute and unaffected eyes. The degree of dilation of the superficial microvasculature in the acute phase and attenuation in the non-acute phase each correlated inversely with visual field performance. The region of reduced capillary density correlated with the location of visual field defects in 80% of acute cases and 80% of non-acute cases.

**Conclusions:**

OCT-A reveals a dynamic shift in the superficial capillary network of the optic nerve head with strong functional correlates in both the acute and non-acute phases of NAION. Further study may validate OCT-A as a useful adjunctive diagnostic tool in the evaluation of ischemic optic neuropathy.

**References:** None.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy, Vascular disorders, Visual fields

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 289****Comparison of Peripapillary Retinal Vessel Density of Optic Atrophy after Optic Neuritis and NAION**

Parima Hirunwiwatkul<sup>1</sup>, Hathairat Lawanlattanagul<sup>2</sup>, Supharat Jariyakosol<sup>1</sup>, Supanut Apinyawasisuk<sup>2</sup>

<sup>1</sup>Department of Ophthalmology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, <sup>2</sup>King Chulalongkorn Memorial Hospital, Bangkok, Thailand

**Introduction:**

Identifying cause of unknown optic atrophy (OA) can be challenging and problematic since the optic disc pallor is the end result of various types of optic neuropathy. Optic neuritis (ON) and non-arteritic anterior ischemic optic neuropathy (NAION) are among the leading causes. The purpose of this study is to quantitatively compare the retinal vessel density between post-ON and post-NAION optic atrophy. Both conditions need different management to prevent complications in the future.

**Methods:**

Retrospective chart review of patients definitely diagnosed with ON and NAION was performed. We included the patients who had either condition more than 3 months. Exclusion criteria are patients with retinal diseases and glaucoma. All patients were invited to undergo the Spectral domain optical coherence tomography angiography (SD-OCTA) of the optic disc. The angio-vessel density and grid-based vessel density around the disc in nerve head and radial peripapillary capillary (RPC) protocol of both groups were compared and analyzed.

**Results:**

We included 33 OA patients, comprising 18 post-ON patients (26 eyes) and 15 post-NAION patients (21 eyes) The vessel density was analyzed by t-test. The optic nerve head vessel density in post-NAION group was lower than post-ON in superotemporal (P=0.002, 95%CI 3.48-15.13) and superonasal segment (P=0.009, 95%CI 2.10-14.40). The same as in RPC, the vessel density was lower in superotemporal (P=0.01, 95%CI 2.10-14.85) and superonasal segment (P=0.022, 95%CI 1.17-14.17). In post-NAION group, there are a significant difference between the peripapillary retinal vessel density in superior part and inferior part (P=0.002), which was not found in the post-ON (P=0.86).

**Conclusions:**

Peripapillary retinal vessel density evaluated by OCTA can be used to differentiate NAION from ON in atrophic stage. The retinal vessel density could be another potential biomarker for assessing the cause of optic neuropathy.

**References:** Lui CH, Kao LY, Sun MH, Wu WC, Chen HS. Retinal vessel density in optical coherence tomography angiography in optic atrophy after Nonarteritic anterior ischemic optic neuropathy. *Journal of Ophthalmology*, vol. 2017, Article ID 9632647, 7 page  
Chen JJ, AbouChehade JE, Iezzi RJr, LeavittJA, Kardon RH. Optical coherence angiography demonstration of retinal changes from chronic optic neuropathy. *Neuroophthalmology*, vol.41(2),76-83, 2017 Ghasemi FG, Tian JJ, Akil H, Garcia GA, Sadda SR, Sadun AA. Swept-source optical coherence tomography angiography of the optic disk in optic neuropathy. *Retina*, vol.36, 168-177, 2016.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** Ratchadapisaksomphot Funding by Faculty of Medicine, Chulalongkorn University

**Poster 290****Retinal Amyloid Imaging in Patients with Alzheimer's Disease**

Oana Dumitrascu<sup>1</sup>, Yosef Koronyo<sup>1</sup>, Steven Verdooner<sup>2</sup>, Keith Black<sup>1</sup>, Maya Koronyo-Hamaoui<sup>1</sup>

<sup>1</sup>*Cedars-Sinai Medical Center, Los Angeles, California, USA*, <sup>2</sup>*NeuroVision, Sacramento, California, USA*

**Introduction:**

Alzheimer's disease (AD) conveys major burden to the society and healthcare system. Retinal pathology in AD is complex, one hallmark characteristic being amyloid  $\beta$ -protein (A $\beta$ ) deposition, which is shown to correlate with brain A $\beta$  plaque burden. We assessed a novel retinal curcumin-labeled amyloid imaging technique in patients with probable AD.

**Methods:**

We performed retinal imaging in two subjects with probable AD and two healthy controls before and after two days of solid-lipid curcumin formula ingestion. Curcumin fluorescence imaging (SLO with laser excitation at 488 nm and 532 nm) and optical coherence tomography (Spectralis OCT) were conducted. Post-image processing and analysis were performed to detect and quantify increased curcumin fluorescence signal. Subsequently, the retinal amyloid indexes (RAI) were calculated.

**Results:**

Both subjects with probable AD (ages 70 and 72; MMSE scores 14 and 19) had bilateral A $\beta$ retinal deposits in the supero-temporal greater than the infero-temporal quadrant, in the mid and far-periphery. No A $\beta$ deposits were noted in the posterior pole. The two control subjects had MMSEs of 30 and were 53 and 69 years-old. AD patients' retinas exhibited higher A $\beta$  deposition (RAI 78.6 and 85.3) in the supero-temporal quadrants compared with controls (RAI 23.4 and 21.0). More intense curcumin fluorescence was noted at day 2 compared to the baseline. On high-definition OCT, curcumin fluorescent spots were detected in AD patients above the retinal pigment epithelium, in the inner retina layers, without affecting the RPE integrity. No OCT retinal deposits were seen in the controls.

**Conclusions:**

Retinal A $\beta$  burden detected by curcumin fluorescence imaging and high-definition OCT was greater in the two subjects with mild probable AD compared to controls. Further studies evaluating retinal fluorescence imaging and OCT in larger patient-populations with AD are mandated in order to define a standard protocol for use in clinical practice and clinical research studies.

**References:** None.

**Keywords:** Pupils Retina, Higher visual functions, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** NIH/NIA AG044897 and AG056478 Awards The Saban and The Marciano Private Foundations

**Poster 291**

**Is Pink the New Black? Comparison of OCT –GCL mapping to Humphrey Perimetry in hemianopia**

Oded Hauptman<sup>1</sup>

<sup>1</sup>*Royal Victorian Eye and Ear Hospital Melbourne, East Melbourne, Australia*

**Introduction:**

OCT is commonly used as an efficient neurological screen. Its utility in diagnosing occipital stroke is questioned.

**Methods:**

A retrospective study from patient records over 10 years found 29 examples of patients with quadrantanopia and hemianopia that had both perimetry and OCT-GCL exams. These were correlated.

**Results:**

Two patients were excluded for pathology from bitemporal hemianopia. 12 of the remaining 27 – (the correlated group) had good correlation between the OCT-CGC and the perimetry. Of the other 15 (the negative group) with poor correlation, 5 were excluded for artefact clouding the results from planoid macula, epi-retinal membrane and severe glaucomatous neuropathy. Three had hemianopia from neglect without a discrete occipital lesion. Seven had normal OCT-GCL maps. Of these 5 had central sparing and/or very partial quadrantanopia. Of the remaining two, the time delay between estimated time of stroke and OCT examination was 86 days and 177 days. This compares with the correlated group of earliest time was 124 days with median 888 days. This compares with the negative group of earliest scan at 31 days with median of 177 days.

**Conclusions:**

Trans-geniculate degeneration occurs after occipital stroke and paints the OCT-GCL map in a similar manner to perimetry in the absence of significant artefact from other of retinal pathology and where there is no central sparing and there has been a delay of at least 6 months which is much earlier than previous reports.

**References:** Tsutomu Yamashita et al: Retinal Ganglion Cell Atrophy in Homonymous Hemianopia due to Acquired Occipital Lesions Observed Using Cirrus High-Definition-OCT J Ophthalmol. 2016

**Keywords:** Optic neuropathy, Stroke Trauma, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 292****Pseudo-Papilledema Detection and Prevalence**

Richard Blanch<sup>1</sup>, John Horsburgh<sup>2</sup>, Alexandra Creavin<sup>3</sup>, Michael Burdon<sup>2</sup>, Cathy Williams<sup>3</sup>

<sup>1</sup>Neuroscience and Ophthalmology, University of Birmingham, Birmingham, United Kingdom, <sup>2</sup>University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom, <sup>3</sup>Bristol Medical School, University of Bristol, Bristol, United Kingdom

**Introduction:**

Papilledema, caused by raised intracranial pressure, must be distinguished from pseudo-swelling when the optic disc appears swollen but is not. Anecdotally, pseudo-papilledema referrals are often based on abnormal disc appearances on fundus imaging and may precipitate unnecessary invasive investigations. The prevalence of pseudo-papilledema is not reported. We aimed to: (1), determine the population-prevalence of pseudo-papilledema (2), determine the sensitivity and specificity for papilledema detection on fundus imaging.

**Methods:**

We conducted a prospective assessment in groups of 4 Neuro-ophthalmologists (NO), Ophthalmologists (O), Neurologists (N) and Emergency Medicine physicians (EM), presenting a forced choice task where we required raters to assign fundus photos to not swollen or swollen groups. We used a bank of 200 randomly-selected images derived as follows: 150 normal images of 12-13 year olds from a longitudinal study of parents and children community database; 10 papilledema images from the hospital database; 28 images without papilledema from the hospital database; 10 duplicate images.

**Results:**

The prevalence of pseudo-papilledema in the community population, defined as images mistaken as papilledema by  $\chi\%$  of raters (P $\chi$ ) varied from P100=0% to P50=21.3±3.9%. In the hospital population, P50=7.1±10.8%. Sensitivity for papilledema detection approached 100%, though 3 raters incorrectly labelled the same patient with unilateral disc swelling as normal, all other cases were detected by all raters. Individual specificities for papilledema detection ranged from 42.7-100%, being lowest amongst EM physicians (NO, 85±2.0%; O, 90±1.70%; N, 87±2.1%; ED, 53±3.6% p<0.001) and lower for community than hospital images (75±2.2%; vs 87±3.1%; p=0.007). Cronbach's alpha was 0.920 and intra-class correlation coefficient 0.360, indicating consistent responses across all raters but low individual agreement.

**Conclusions:**

There is a high rate of pseudo-papilledema in our teenage community sample (P50=21.3%), though raters often disagree on what constitutes pseudo-papilledema. The missed papilledema case suggests an educational requirement to highlight that papilledema may be unilateral.

**References:** None.

**Keywords:** Miscellaneous, Pediatric neuro-ophthalmology, Pseudotumor Cerebri

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.



**Poster 293**

**Optical Coherence Tomography Findings in Papilledema Versus Optic Disc Drusen**

Laura Dell'Arti<sup>1</sup>, Alba Xhepa<sup>1</sup>, Gordon Plant<sup>1</sup>

<sup>1</sup>*Moorfields Eye Hospital, London, United Kingdom*

**Introduction:**

The role of optical coherence tomography (OCT) to differentiate between papilledema (PE) and optic disc drusen (ODD) has been largely studied, however, it is still not clear whether this type of imaging is able to distinguish between the 2 entities. Indeed, whether peripapillary retinal nerve fiber layer (RNFL) as measured by OCT is thicker in eyes with PE than in eyes with ODD is still an open question. Furthermore, in recent reports, eyes with PE displayed peripapillary hyperreflective mass lesions, simulating buried ODD.

**Methods:**

en patients (10 eyes) with clinical diagnosis of PE (confirmed by lumbar puncture) and 10 patients (10 eyes) with diagnosed buried ODD (based on autofluorescence imaging) were retrospectively evaluated. In addition to autofluorescence, all subjects underwent imaging with OCT of the RNFL and volumetric scans through the optic nerve head using the Enhanced Depth Imaging (EDI) mode. The two groups were compared with regard to RNFL qualitative and quantitative changes and to the presence on volumetric scans of peripapillary hyperreflective mass lesions.

**Results:**

In eyes with PE, RNFL had an average thickness significantly increased than buried ODD ( $p=0.001$ ) and was significantly increased in all the inferior and superior sectors (superotemporal  $p=0.004$ , superonasal  $p=0.006$ , inferotemporal  $p=0.002$ , inferonasal  $p=0.004$ ). Nine out of 10 eyes with PE showed 4 or more sectors with increased RNFL thickness, while 80% of the eyes with buried ODD showed thickening of 3 or less sectors. Nine eyes out of ten with buried ODD demonstrated peripapillary hyperreflective mass lesions. However, all the eyes with PE also displayed the same finding.

**Conclusions:**

Qualitative and quantitative RNFL thickness evaluation can help in accurately classifying eyes as PE or ODD. The presence of peripapillary hyperreflective mass lesions on volumetric scans is not specific for ODD and this finding, if used in isolation, can lead to misdiagnosis of PE as ODD.

**References:** Chang, Velez, Demer, Bonelli, Quiros, Accuracy of Diagnostic Imaging Modalities for Classifying Pediatric Eyes as Papilledema Versus Pseudopapilledema, *Ophthalmology*, 885, 1-10, 2017. Traber, Weber, Sabah, Keane, Plant, Enhanced Depth Imaging Optical Coherence Tomography of Optic Nerve Head Drusen: A Comparison of Cases with and without Visual Field Loss, *Ophthalmology*, 124, 66-73, 2017. Lee, Woo, Hwang, Differentiation of optic nerve head drusen and optic disc edema with spectral-domain optical coherence tomography, *Ophthalmology*, 118, 971-7, 2011.

**Keywords:** Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy, Pseudotumor Cerebri, High intracranial pressure/headache

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** None.

**Poster 295**

**Study of Age Correlation of the Intrinsically-photosensitive Retinal Ganglion Cell (ipRGC)-Medicated Pupil Light Reflex (PLR)**

Yanjun Chen<sup>1</sup>, Karen Cruickshanks<sup>1</sup>, Adam Paulsen<sup>1</sup>

<sup>1</sup>University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA

**Introduction:**

The eye serves two fundamental physiologic functions: image-forming and non-image-forming function. The non-image-forming function is a collection of non-visual, vital physiologic activities including pineal melatonin suppression, sleep, body temperature, hormonal secretion, and pupil light reflex. Here, we present a preliminary analysis of age correlation of the ipRGC-mediated PLR in an epidemiologic cohort.

**Methods:**

We are conducting a cross-sectional study to collect pupil reactivity in the ongoing examination of 10-year follow up examination of the Beaver Dam Offspring Study (BOSS), an established, large longitudinal epidemiologic, multi-sensory study of aging. The pupil reactivity was recorded using a binocular infrared pupillometer (DP2000 Human Laboratory Pupillometer, Neur-Optics, Inc., Irvine, CA). The stimulus consisted of a pair of 1-sec red (640±10 nm) and blue (467±17 nm) light stimulus at the stimulus intensity of 2.0 log cd/m<sup>2</sup>. The stimulus pair was repeated once within a trial of recording and two trials of recordings were collected during the study visit. The ipRGC-mediated PLR was calculated as post-illumination pupil response (PIPR) at 6-sec after termination of the 1-sec light stimulus.

**Results:**

76 BOSS participants (34 men and 42 women) were included in this preliminary analysis, with age ranging from 37 to 80 years (mean±SD: 58.8±10.2). The baseline pupil diameter decreases with increasing age (linear regression,  $y=-0.044x+7.89$ ,  $R^2=0.23$ ). The percent PIPR demonstrates a modest decline with age and a stronger association with baseline pupil diameter (linear regression,  $y=0.048x-0.092$ ,  $R^2=0.24$ ).

**Conclusions:**

(1) The preliminary analysis of this selected BOSS cohort demonstrated a modest trend of age-related decline in percent PIPR, (2) the percent PIPR appears to increase with baseline pupil diameter, and (3) the relation between percent PIPR, age and baseline pupil diameter needs to be further defined by mathematical model that incorporates age, baseline pupil diameter, and other age-related sensory markers.

**References:** 1. Berson DM, Dunn FA, Takao M. Phototransduction by retinal ganglion cells that set the circadian clock. *Science* 2002;295:1070-1073. 2. Dacey DM, Liao HW, Peterson BB, et al. Melanopsin-expressing ganglion cells in primate retina signal colour and irradiance and project to the LGN. *Nature* 2005;433:749-754. 3. Loewenfeld IE. "Simple central" anisocoria: a common condition, seldom recognized. *Transactions Section on Ophthalmology American Academy of Ophthalmology and Otolaryngology* 1977;83:832-839. 4. Lucas RJ, Douglas RH, Foster RG. Characterization of an ocular photopigment capable of driving pupillary constriction in mice. *Nat Neurosci* 2001;4:621-626. 5. Park JC, Moura AL, Raza AS, Rhee DW, Kardon RH, Hood DC. Toward a clinical protocol for assessing rod, cone, and melanopsin contributions to the human pupil response. *Invest Ophthalmol Vis Sci* 2011;52:6624-6635.

**Keywords:** Pupils Retina, Miscellaneous

**Financial Disclosures:** The authors had no disclosures.

**Grant Support:** The study is supported by NIA, R01AG021917, unrestricted grant from Research to Prevent Blindness, University of Wisconsin Department of Ophthalmology and Visual Sciences research funding, and F.A. David fund for vision research

## WEDNESDAY, MARCH 7

6:30 am - 7:30 am	Breakfast.....	Grand Promenade
6:30 am - 7:30 am	CME Committee Meeting .....	Kona 1
6:30 am - 5:30 pm	Registration/Help Desk .....	Grand Promenade

7:30 am - 9:30 am	<b>VZV in Neuro-Ophthalmology .....</b>	<b>Grand Ballroom</b>
	<i>Moderators: Judith Warner, MD, John Chen, MD, PhD</i>	

This session will review the ocular and central nervous system manifestations of Varicella Zoster Virus. We will provide an update on treatments for the various neuro-ophthalmic manifestations of Varicella Zoster. We will also review the evidence for and against the connection between Varicella Zoster and Giant Cell Arteritis.

At the conclusion of this course, the attendees should be able to: 1) describe the neuro-ophthalmic manifestations of Varicella Zoster; 2) discuss the treatment of Varicella Zoster when it affects the eyes or CNS and; 3) debate the connection between Varicella Zoster and giant cell arteritis.

7:30 am - 8:00 am	<b>VZV and the CNS, Joseph Berger, MD</b>
8:00 am - 8:25 am	<b>What to Do When VZV Affects the Reina, Optic Nerve, and Makes the Patient See Double?, Sachin Kedar, MD, MBBS</b>
8:25 am - 8:45 am	<b>Q&amp;A</b>
	<b>Debate</b>
8:45 am - 9:00 am	<b>VZV IS the Cause of GCA, Joseph Berger, MD</b>
9:00 am - 9:15 am	<b>VZV IS NOT the Cause of GCA, Alfredo Sadun, MD, PhD</b>
9:15 am - 9:30 am	<b>Q &amp; A</b>

9:30 am - 10:00 am	Coffee Break .....	Grand Promenade
--------------------	--------------------	-----------------

10:00 am - 11:15 am	<b>Is IIH Idiopathic? .....</b>	<b>Grand Ballroom</b>
	<i>Moderators: Matthew Thurtell, MBBS, MSc, FRACP, Michael Wall, MD</i>	

Idiopathic intracranial hypertension (IIH) is one of the most common disorders seen in neuro-ophthalmic practice, yet its etiology remains elusive. In this session, factors contributing to the pathophysiology of IIH will be reviewed with special attention to the potential roles of metabolic factors, endocrine factors and cerebral venous dynamics. Upon completion of this session, participants should be able to: 1) describe metabolic factors that may play a role in the etiology of IIH; 2) describe endocrine factors that may play a role in the etiology of IIH; 3) discuss the role of cerebral venous dynamics in the pathophysiology of IIH and 4) discuss whether the findings of the IIHTT contribute to our understanding of the pathophysiology of IIH.

10:00 am - 10:20 am	<b>Metabolic Underpinnings, Alex Sinclair, MD</b>
10:20 am - 10:40 am	<b>Contributions of Venous Dynamics and Implications for Therapy, Marc Dinkin, MD</b>
10:40 am - 11:00 am	<b>Pathophysiology of IIH and the IIHTT, Michael Wall, MD</b>
11:00 am - 11:15 am	<b>Q &amp; A</b>

11:20 am - 12:00 pm	<b>Jacobson Lecture: Vascular Supply of the Occipital Lobe Explains Why Certain Patterns of Visual Field Loss from Embolic Stroke Are Common and Others Are Prohibited.....</b>	<b>Grand Ballroom</b>
	<i>Moderator: Jonathan Trobe, MD</i>	
	<i>Presenter: Jonathan Horton, MD, PhD</i>	

The cerebral cortex is supplied by microvascular lobules, comprised of half a dozen penetrating arterioles surrounding a single, central draining venule. Surface arterioles that supply penetrating arterioles form an anastomotic plexus. Consequently, embolic occlusion of a small surface vessel does not cause a local infarct, because collateral flow is available. Nor does an infarct occur after occlusion of a single penetrating arteriole. Infarction of striate cortex requires occlusion of a major arterial trunk vessels – e.g., the inferior or superior calcarine artery. The fixed relationship between the vascular supply of the occipital lobe and the retinotopic map causes stereotypical patterns of visual field defects after stroke. In this lecture, allowed and forbidden scotomas will be reviewed and explained.

12:00 pm - 1:30 pm	Lunch Break (on your own)	
12:15 pm - 1:30 pm	Research Committee Meeting Luncheon .....	Kona 1

**1:30 pm - 2:30 pm                      We are WIN .....Kona 4-5**

Aloha! Women in Neuro-Ophthalmology would like to welcome you to an informal networking event, "We Are WIN." Come catch up with old friends and meet new ones over light refreshments after lunch. We will be interacting with each other through an informal ice-breaker and table discussions on topics ranging from life outside work to empowering ourselves and our colleagues, with a special focus on developing mentoring relationships. No registration is required.

**2:30 pm - 4:00 pm                      International Infections: What Lies Beyond the Eye .....Grand Ballroom**

*Moderators: Susan Mollan, MBCHB, FRCOPHTH, Claire Fraser, MBBS, FRANZCO  
Neuroradiologist: Swarupsinh Chavda, MD*

In this global community, where travel to and from countries outside America is becoming more frequent, it is increasingly likely that doctors will be seeing patients with diseases that would otherwise not be common in their country. This symposium is designed to introduce five systemic infections that can have devastating consequences for the patient and their vision.

Each presenter will highlight a challenging case from their practice, they will update us on the current thoughts of how to diagnose, investigate and manage that infection. Neuroradiology interpretation will be provided by Dr. Chavda. In the closing minutes of their presentation there will be comments to the future and anticipation of any changes that we can expect in the coming years for the infectious disease described. There will be ample time for questions and reflections from the floor after each presentation.

At the conclusion of this course, the attendees should be able to: 1) recognize and distinguish five common infectious diseases that affect the central nervous system and eye; 2) plan an appropriate series of investigations and evaluate the results regarding such diseases and; 3) recommend treatment plans for these diseases.

**Surely Not Syphilis**, *Claire Fraser, MBBS, FRANZCO*  
**Damning Dengue**, *Dan Milea, MD, PhD*  
**Terrible TB**, *Tim Matthews, MBBS, FRCS, FRCOphth*  
**Lurid Lyme**, *Francois Xavier Borruat, MD, PhD, MER*  
**Cunning CJD**, *Susan Mollan, MBCHB, FRCOPHTH*  
**Neuroradiology**, *Swarupsinh Chavda, MD*

*Brief Break Between Sessions (15 minutes)*

**4:15 pm - 5:45 pm                      Generation Next: Genetic Testing for Inherited Neuro-Ophthalmic Diseases.....Grand Ballroom**

*Moderator: Veeral Shah, MD, PhD*

This CPNO event is to promote the role of practicing neuro-ophthalmologists to translate genetic testing and genomic medicine tools into management and intervention. With increasing accessibility of genetic testing, the burden of ordering, interpreting, and translating genetic testing information into clinical management, many times falls on the practicing neuro-ophthalmologist. With limited availability of a geneticist or genetic counselor, neuro-ophthalmologists may feel overwhelmed when evaluating genomic medicine data and translating this information into clinical management and genetic counseling. The purpose of this new skill transfer workshop is to introduce the use of online genomic tools and databases and to empower neuro-ophthalmologist to interpret genetic testing and translate this information into clinical management. This course will begin with a brief didactic session on genetic testing followed by a representative neuro-ophthalmology case-based presentation that applies and utilizes online-based genomic tools.

At the conclusion of this course, the attendees will be able to: 1) identify candidates for genomic testing, and select the appropriate test for a patient; 2) learn the different type of genetic testing: single-, multi-gene assays, and whole exome/genome sequencing; 3) utilize web-based databases (i.e. OMIM, ClinVar) that describe genotype, phenotype, and pathogenicity to make accurate diagnosis of genetic diseases; 4) interpret genomic medicine data and translate this information into clinical management and genetic counseling. The program's goal is to introduce a framework to evaluate genetic testing that would have broad appeal among both practicing adult and pediatric neuro-ophthalmologists.

Attendees are strongly encouraged to bring their laptops to this session or will need to share with other attendees.

**6:30 pm - 12:00 am                      Annual NANOS Reception and Banquet.....Lanai/Grand Promenade/Kohala Ballroom**

*Join colleagues for a fun, casual evening of socializing, dining and a little hula at the NANOS Annual Banquet! Dinner will take place in the Grand Promenade/Lanai, and the dance will proceed in the Kohala Ballroom. This event is complimentary for registered attendees; guests must purchase tickets for \$100 per person.*

## VARICELLA ZOSTER VIRUS INFECTION AND THE NERVOUS SYSTEM

**Joseph R. Berger, M.D.**  
**Professor of Neurology**  
**Perelman School of Medicine**  
**University of Pennsylvania**

### **Background**

Primary infection with Varicella zoster virus (VZV) causes varicella (chickenpox). Following primary infection, this ubiquitous human neurotropic virus establishes latency in cranial nerve ganglia, dorsal root ganglia and autonomic ganglia, sites from which it can reactivate, most often occurring as cell-mediated immunity wanes with advancing age and immunosuppression. Reactivation results in zoster (shingles), a painful dermatomal rash occasionally followed by postherpetic neuralgia. Centripetal spread at the time of reactivation may result in other neurological complications including meningoencephalitis, myelopathy and VZV vasculopathy. Diagnosis of these neurological conditions is aided by polymerase chain reaction (PCR) to detect VZV DNA in CSF and serological studies of antibody in the CSF to VZV in CSF.

### **Virology**

VZV is a member of the alpha subfamily in the herpes virus group (human herpesvirus type 3). On electron microscopy, it is 180–200 nm in diameter. It was the first herpesvirus to be entirely sequenced genetically. Unlike other viruses, such as, smallpox, it is exceedingly labile and unable to survive for long periods in scabs or on fomites. Under laboratory conditions, VZV DNA replication spreads in cell culture within 8 hours of infection and reaches its maximum titer in infected cells within 40 hours.

### **Epidemiology**

Varicella is a highly contagious, typically mild disease of childhood. Its spread is by direct contact or by respiratory transmission and the incubation period is 9-21 days. Prior to widespread vaccination in 1995 in the U.S., the annual incidence was 4 million cases. Less than 2% of varicella cases occur in adults and virtually all adults are VZV seropositive. Chickenpox is characterized by an exanthem of macules and papules on the trunk the spreads centrifugally and evolves into vesicles with an erythematous halo. Patients are considered infectious from 2 days before rash until all vesicles have crusted, typically 6 days after the onset of rash. Subclinical reinfection with VZV is common.

### **Shingles – Zoster Radiculopathy**

Zoster is typically characterized by a painful rash confined to one or two dermatomes affecting one million persons, generally the elderly, in the U.S. annually. Zoster is twice as common over age 50 years than under 50 and there is an 8 to 10-fold increase after age 60 as a consequence of immunosenescence. Pain may precede rash by weeks to months. Although zoster can develop anywhere on the body, thoracic zoster is most common, followed by lesions on the face, most often in the ophthalmic division of the trigeminal nerve. Ophthalmic zoster accounts for 10-15% of zoster accompanied in about one-third of cases by involvement of the nasociliary branch with a rash on the side or tip of the nose (Hutchinson's sign) as well as supraorbital and trochlear branches. Conjunctivitis, keratitis, scleritis, iridocyclitis, and extraocular muscle palsies may occur with ophthalmic zoster. Any cranial nerve may be affected by zoster. Optic neuritis, sometimes bilateral, may develop after zoster. Third nerve palsies are more common than those in the sixth; least affected is the fourth and combinations of cranial nerve involvement are not uncommon. The Ramsay-Hunt syndrome is characterized by reactivation affecting the seventh and often eighth cranial nerve. It is characterized by ipsilateral facial muscle weakness associated with vesicles in the external auditory canal, the tympanic

membrane (zoster oticus), or the ipsilateral anterior two-thirds of the tongue or hard palate. Tinnitus, hearing loss, nausea, vomiting, vertigo and nystagmus are frequent concomitants. Detection of VZV DNA or anti-VZV IgG antibody in CSF is helpful in instances of otherwise unexplained cranial mononeuritis or polyneuritis which may occur in the absence of a rash. Zoster paresis is also observed following radicular involvement of a limb or the trunk.

### **Postherpetic Neuralgia**

By definition, pain persisting more than 3 months after resolution of a zoster rash is postherpetic neuralgia (PHN). While rare in individuals under age 50, more than 40% of patients over 50 develop PHN with increased frequency in women and after trigeminal involvement. The mechanism of PHN remains uncertain. At times, the pain can occur in the absence of a rash; a disorder that is referred to as zoster sine herpete. Treatment of zoster with antivirals, e.g., valacyclovir and famciclovir, appears to decrease the risk of PHN. A wide variety of medications have been employed with varying success in the treatment of PHN.

### **VZV Meningoencephalitis**

Reactivation of VZV may present as meningitis, meningoencephalitis, meningoradiculitis, or cerebellitis (gait ataxia and tremor). These neurological manifestations may occur in the absence of rash and diagnosis is predicated on detecting VZV DNA in the CSF by PCR or antibody in the CSF.

### **VZV Myelopathy and Myelitis**

VZV myelopathy may occur as either an acute infection of the spinal cord or as a postinfectious manifestation following varicella or zoster. The former is typically observed in immunocompetent individuals days to weeks after varicella or zoster. It is self-limited and improves with corticosteroid administration. A mild CSF mononuclear pleocytosis, with a normal or slightly elevated protein is often seen. On the other hand, VZV myelitis is a progressive disorder seen most often in immunocompromised individuals. A rash on the trunk is often but not invariably present. VZV myelitis is a cause of longitudinally extensive transverse myelitis. CSF PCR or antibody studies can confirm the diagnosis. Aggressive treatment with antivirals is necessary. Spinal cord infarction from VZV vasculitis has also been described.

### **VZV CNS Vasculitis**

In any patient with TIAs, ischemic or hemorrhagic stroke, chronic headache or altered mental status following zoster, VZV vasculopathy should be suspected. This condition occurs as a consequence of transaxonal spread of the virus to the adventitia of cranial arteries following reactivation with subsequent transmural spread. In about 30% of patients with virologically-verified VZV vasculopathy, the rash is absent. CSF VZV PCR is positive in only a minority of individuals; therefore, the diagnosis is dependent on the demonstration of anti-VZV IgG antibody in CSF with a reduced serum/CSF ratio of anti-VZV IgG confirming intrathecal synthesis of anti-VZV IgG. VZV vasculopathy is treated with intravenous acyclovir, 10-15 mg/kg given 3 times daily for 14 days. Immunocompromised patients may require longer durations of treatment. The addition of corticosteroids is recommended.

### **VZV and Giant Cell Arteritis and Other Vasculitides**

This topic is the subject of the debate

## WHAT TO DO WHEN VZV AFFECTS THE RETINA, OPTIC NERVE, AND MAKES THE PATIENT SEE DOUBLE?

Sachin Kedar MBBS, MD  
Department of Neurological Sciences and Stanley M Truhlsen Eye Institute  
University of Nebraska Medical Center  
Omaha NE

### LEARNING OBJECTIVES

1. List neuro-ophthalmic presentations secondary to varicella zoster infection
2. Discuss pertinent diagnostic studies for confirming ocular zoster infections.
3. Describe anti-viral agents commonly used in ophthalmic varicella zoster.
4. Manage the neuro-ophthalmological manifestations of varicella-zoster infection
5. Describe the evidence for and against the connection between varicella-zoster and giant cell arteritis

### CME QUESTIONS

1. Following primary infection, varicella zoster virus (VZV) exists in a life-long state of latency within neurons comprising the cranial, dorsal root, autonomic and enteric ganglia
  - a. True
  - b. False
2. Which of these neuro-ophthalmic presentations have been reported to occur following VZV reactivation:
  - a. Necrotizing retinopathy
  - b. Acute optic neuropathy
  - c. Acute orbitopathy
  - d. Isolated cranial neuropathy
  - e. All of the above
3. You evaluate an otherwise healthy 60-year-old with acute unilateral blurred vision following herpes zoster ophthalmicus. Examination reveals panuveitis and you suspect acute retinal necrosis on dilated fundus examination. How will you manage this patient:
  - a. Observation with daily ophthalmic examination
  - b. Perform aqueous tap and start intravenous acyclovir if polymerase chain reaction (PCR) testing confirms varicella zoster
  - c. Perform aqueous tap and start intravenous acyclovir without waiting for results of polymerase chain reaction (PCR)
  - d. Perform aqueous tap and start systemic corticosteroids to decrease intraocular inflammation while waiting for results of polymerase chain reaction (PCR)

### KEYWORDS (5 Max)

1. Varicella Zoster
2. Acute retinal necrosis
3. Ophthalmoplegia
4. Optic neuropathy
5. Anti-viral medication

## HIGHLIGHTS

### INTRODUCTION

VZV is an exclusive human neurotropic alpha herpes virus, which produces chicken pox. Greater than 95% human population demonstrates serological evidence of VZV infection before adolescence. Primary infection results in a lifelong period of latency in the neurons of the cranial, dorsal root, autonomic and enteric ganglia (1). VZV reactivation due to waning cell (T-cell) mediated immunity with advancing age or immunocompromised condition, results in replication of the virus in the ganglia followed by trans-axonal spread to the mucocutaneous surfaces where it produces zoster (shingles) in the corresponding dermatome (2). Mucocutaneous zoster is characterized by a painful vesicular dermatomal rash, which in most patients resolves within 4-6 weeks. Approximately 1 million new episodes of zoster are estimated to occur annually in the US with a lifetime risk of 30%. The incidence of zoster across different populations is approximately 4-4.5 per 1000 person-years and appears to be increasing (3).

Neurological and ophthalmological complications can result from both primary infection as well as reactivation. Due to the widespread distribution of latent VZV in the ganglia, reactivation can affect the neuraxis at all levels. The thoracic and trigeminal distributions are most common since the face and thorax carry the highest cutaneous lesion load and viral particles during the primary infection.

Post herpetic neuralgia is the most common sequela of zoster characterized by pain persisting 3 months after the initial episode of zoster. VZV can produce a myriad of neurological complications including meningitis/meningoencephalitis, cerebellitis, myelitis, acute inflammatory demyelinating polyneuropathy (AIDP) and AIDP variants including multiple cranial neuropathy and radiculoneuropathy. Rarely, primary and reactivation results in VZV vasculopathy from direct infection of the arteries resulting in ischemic or hemorrhagic stroke, transient ischemic attacks, intracranial aneurysms and venous sinus thrombosis (4).

#### HERPES ZOSTER OPHTHALMICUS (HZO)

HZO results from reactivation of VZV along the V1 division of the trigeminal nerve and accounts for 10-20% of all herpes zoster; about half of these will have ocular involvement (5). The frontal branch of V1 is most commonly affected (6). Involvement of the nasociliary branch characterized by skin lesions along the side of the nose, increases the risk for corneal denervation and ocular inflammatory disease (Hutchinson's sign) by 4.02 and 3.35 times respectively (7). HZO is a chronic and recurrent disease with a 5- year recurrence rate of 25% (8). Dermatologic involvement with painful vesicular rash, periorbital edema and ptosis is common although ocular involvement without rash (zoster sine herpete) occurs in a few patients. Common anterior segment manifestations of HZO include various forms of conjunctivitis, keratitis, uveitis, keratouveitis, episcleritis, scleritis, acute and long term ocular surface abnormalities from neurotrophic and exposure keratopathy (9, 10).

#### RETINAL DISEASE

VZV can produce retinal perivasculitis and various forms of necrotizing retinopathy such as acute retinal necrosis (ARN) and progressive outer retinal necrosis (PORN). While the former occurs in immunocompetent individuals, the latter occurs in those with severe immunosuppression. ARN is diagnosed clinically using criteria established by the Executive Committee of the American Uveitis Society. These include- presence of one or more clearly defined foci of retinal necrosis located in the retinal periphery, rapid disease progression in the absence of antiviral treatment, circumferential spread, occlusive vasculitis with arteritis and significant anterior and posterior segment inflammation (11). Varicella retinitis is a devastating disease with poor visual outcomes; visual acuity is worse than 20/200 in about half of the affected eyes due to secondary complications such as retinal detachment, chronic vitritis, epiretinal membrane and maculopathy (12). Systemic antiviral treatment should be initiated immediately in a patient suspected of having varicella retinitis without waiting for diagnostic



confirmation. A 7-10 day course of intravenous acyclovir (10mg/kg 3 times daily) followed by oral antiviral therapy for several months results in improvement in visual outcomes by promoting regression of retinitis, reducing rates of retinal detachment and fellow eye involvement (13, 14). Without antiviral treatment, about 60-70% will develop bilateral disease (13). Recently, it has been shown that appropriately dosed oral valacyclovir, an orally administered prodrug of acyclovir, achieves equivalent plasma acyclovir levels as well as equivalent therapeutic efficacy compared to traditional doses of intravenous acyclovir therapy (15-17). Hence, patients with ARN *without neurological involvement* may be treated with a 7-10 day induction course of oral valacyclovir (6000-8000 mg daily) followed by longer term maintenance therapy with valacyclovir 1000 daily for 6 months or more (18). Addition of intravitreal foscarnet to systemic antiviral therapy results in better visual outcomes and reduced incidence of retinal detachment (19, 20).

#### OPTIC NERVE

Optic neuropathy (ON) is an uncommon sequela of herpes zoster which occurs in less than 0.5% patients with HZO (21). ON may develop in the acute or late stages of HZO. It may accompany anterior and/or posterior forms of HZO. Presentation is variable and includes disc swelling, posterior optic neuropathy or optic atrophy (22). A close temporal association of ON with HZO and exclusion of other etiology, forms the basis for diagnosis. Modest improvement of visual function has been reported to occur with systemic antiviral medications. Use of systemic corticosteroids as adjunctive treatment is controversial with case reports suggesting an increased risk of disease extension from the optic nerve to the retina, without improvement in visual outcomes (23). The pathophysiology of ON in HZO is unclear and multiple mechanisms including continuous and hematogenous viral spread to the optic nerve as well as ocular ischemia from vascular inflammation have been proposed (24-26). Recently, an association between giant cell arteritis (GCA) and VZV was proposed by investigators who detected VZV virion, antigen, and DNA within vessel walls of temporal arteries of patients with GCA (27).

#### DIPLOPIA

Reports of diplopia following VZV reactivation are relatively uncommon in the literature. Diplopia can result from internuclear ophthalmoplegia, skew deviation, isolated or combined ocular motor cranial nerve III,IV, VI) palsy and orbital myositis (28-31). Ocular motor cranial neuropathy has been reported to occur in 7-31% HZO. Prognosis for recovery of ophthalmoplegia was reported to be excellent in 2 large series (31, 32). HZO can rarely present with acute orbital signs such as proptosis, ptosis, chemosis, ophthalmoplegia and visual loss accompanied by radiological evidence of orbital inflammation. The current consensus recommends radiological studies such as MRI brain ( $\pm$  orbit) to exclude alternate cause and treatment with systemic antiviral medications.

#### SUMMARY

VZV reactivation can produce abnormalities of both afferent and efferent visual pathways. Involvement of the retina, optic nerve, orbit and cranial nerves are relatively uncommon compared to dermatologic and ocular anterior segment manifestations. Diagnosis can be straightforward in the presence of a characteristic rash; however, additional investigations may be necessary when the presentation is atypical such as absence of rash or unusual clinical findings. Imaging studies (such as MRI brain  $\pm$  orbit) may be necessary to exclude other more common etiologies of optic nerve or ocular motor disease. VZV DNA detection using PCR is the most sensitive method reaching 95–100% sensitivity and specificity. Real time PCR in combination with serology on paired serum and CSF or intra-ocular fluid in patients sampled more than 2-3 weeks after disease onset is the method of choice for diagnosis of zoster with neurological or ophthalmological complications (33). These patients should be treated with systemic antiviral medications such as intravenous acyclovir or equivalent doses of oral valacyclovir in

uncomplicated cases without neurological involvement. There does not appear to be a role for systemic steroids in improving visual outcomes in complicated HZO.

#### CME ANSWERS

1. A
2. E
3. C

#### REFERENCES

1. Gilden DH, Vafai A, Shtram Y, Becker Y, Devlin M, Wellish M. Varicella-zoster virus DNA in human sensory ganglia. *Nature*. 1983; 306(5942):478-480
2. Steiner I, Kennedy PG, Pachner AR. The neurotropic herpes viruses: herpes simplex and varicella-zoster. *Lancet Neurol*. 2007; 6(11):1015-1028
3. Yawn BP, Gilden D. The global epidemiology of herpes zoster. *Neurology*. 2013; 81(10):928-930
4. Nagel MA, Jones D, Wyborny A. Varicella zoster virus vasculopathy: The expanding clinical spectrum and pathogenesis. *J Neuroimmunol*. 2017; 308:112-117
5. Liesegang TJ. Herpes zoster ophthalmicus natural history, risk factors, clinical presentation, and morbidity. *Ophthalmology*. 2008; 115(2 Suppl):S3-12
6. Edgerton AE. Herpes Zoster Ophthalmicus: Report of Cases and a Review of the Literature. *Trans Am Ophthalmol Soc*. 1942; 40:390-439
7. Zaal MJ, Volker-Dieben HJ, D'Amario J. Prognostic value of Hutchinson's sign in acute herpes zoster ophthalmicus. *Graefes Arch Clin Exp Ophthalmol*. 2003; 241(3):187-191
8. Tran KD, Falcone MM, Choi DS, Goldhardt R, Karp CL, Davis JL, Galor A. Epidemiology of Herpes Zoster Ophthalmicus: Recurrence and Chronicity. *Ophthalmology*. 2016; 123(7):1469-1475
9. Liesegang TJ. Corneal complications from herpes zoster ophthalmicus. *Ophthalmology*. 1985; 92(3):316-324
10. Kaufman SC. Anterior segment complications of herpes zoster ophthalmicus. *Ophthalmology*. 2008; 115(2 Suppl):S24-32
11. Holland GN. Standard diagnostic criteria for the acute retinal necrosis syndrome. Executive Committee of the American Uveitis Society. *Am J Ophthalmol*. 1994; 117(5):663-667
12. Butler NJ, Moradi A, Salek SS, Burkholder BM, Leung TG, Dunn JP, Thorne JE. Acute Retinal Necrosis: Presenting Characteristics and Clinical Outcomes in a Cohort of Polymerase Chain Reaction-Positive Patients. *Am J Ophthalmol*. 2017; 179:179-189
13. Palay DA, Sternberg P, Jr, Davis J, Lewis H, Holland GN, Mieler WF, Jabs DA, Drews C. Decrease in the risk of bilateral acute retinal necrosis by acyclovir therapy. *Am J Ophthalmol*. 1991; 112(3):250-255
14. Blumenkranz MS, Culbertson WW, Clarkson JG, Dix R. Treatment of the acute retinal necrosis syndrome with intravenous acyclovir. *Ophthalmology*. 1986; 93(3):296-300
15. Aizman A, Johnson MW, Elnor SG. Treatment of acute retinal necrosis syndrome with oral antiviral medications. *Ophthalmology*. 2007; 114(2):307-312
16. Tibbetts MD, Shah CP, Young LH, Duker JS, Maguire JI, Morley MG. Treatment of acute retinal necrosis. *Ophthalmology*. 2010; 117(4):818-824
17. Taylor SR, Hamilton R, Hooper CY, Joshi L, Morarji J, Gupta N, Lightman SL. Valacyclovir in the treatment of acute retinal necrosis. *BMC Ophthalmol*. 2012; 12:48-2415-12-48
18. Schoenberger SD, Kim SJ, Thorne JE, Mruthyunjaya P, Yeh S, Bakri SJ, Ehlers JP. Diagnosis and Treatment of Acute Retinal Necrosis: A Report by the American Academy of Ophthalmology. *Ophthalmology*. 2017; 124(3):382-392

19. Wong R, Pavesio CE, Laidlaw DA, Williamson TH, Graham EM, Stanford MR. Acute retinal necrosis: the effects of intravitreal foscarnet and virus type on outcome. *Ophthalmology*. 2010; 117(3):556-560
20. Yeh S, Suhler EB, Smith JR, Bruce B, Fahle G, Bailey ST, Hwang TS, Stout JT, Lauer AK, Wilson DJ, Rosenbaum JT, Flaxel CJ. Combination systemic and intravitreal antiviral therapy in the management of acute retinal necrosis syndrome. *Ophthalmic Surg Lasers Imaging Retina*. 2014; 45(5):399-407
21. Marsh RJ, Cooper M. Ophthalmic herpes zoster. *Eye (Lond)*. 1993; 7 ( Pt 3)(Pt 3):350-370
22. de Mello Vitor B, Foureaux EC, Porto FB. Herpes zoster optic neuritis. *Int Ophthalmol*. 2011; 31(3):233-236
23. Nakamoto BK, Dorotheo EU, Biousse V, Tang RA, Schiffman JS, Newman NJ. Progressive outer retinal necrosis presenting with isolated optic neuropathy. *Neurology*. 2004; 63(12):2423-2425
24. Gunduz K, Ozdemir O. Bilateral retrobulbar neuritis following unilateral herpes zoster ophthalmicus. *Ophthalmologica*. 1994; 208(2):61-64
25. Mathias M, Nagel MA, Khmeleva N, Boyer PJ, Choe A, Durairaj VD, Bennett JL, Mandava N, Gilden D. VZV multifocal vasculopathy with ischemic optic neuropathy, acute retinal necrosis and temporal artery infection in the absence of zoster rash. *J Neurol Sci*. 2013; 325(1-2):180-182
26. Salazar R, Russman AN, Nagel MA, Cohrs RJ, Mahalingam R, Schmid DS, Kleinschmidt-DeMasters BK, VanEgmond EM, Gilden D. Varicella zoster virus ischemic optic neuropathy and subclinical temporal artery involvement. *Arch Neurol*. 2011; 68(4):517-520
27. Gilden D, White T, Khmeleva N, Boyer PJ, Nagel MA. VZV in biopsy-positive and -negative giant cell arteritis: Analysis of 100+ temporal arteries. *Neuro Neuroimmunol Neuroinflamm*. 2016; 3(2):e216
28. Al-Abdulla NA, Rismondo V, Minkowski JS, Miller NR. Herpes zoster vasculitis presenting as giant cell arteritis with bilateral internuclear ophthalmoplegia. *Am J Ophthalmol*. 2002; 134(6):912-914
29. Verhulst E, Van Lammeren M, Dralands L. Diplopia from skew deviation in Ramsey-Hunt syndrome. A case report. *Bull Soc Belge Ophtalmol*. 2000; (278)(278):27-32
30. Kawasaki A, Borruat FX. An unusual presentation of herpes zoster ophthalmicus: orbital myositis preceding vesicular eruption. *Am J Ophthalmol*. 2003; 136(3):574-575
31. Marsh RJ, Dulley B, Kelly V. External ocular motor palsies in ophthalmic zoster: a review. *Br J Ophthalmol*. 1977; 61(11):677-682
32. Chhabra MS, Golnik KC. Recovery of ocular motor cranial nerve palsy after herpes zoster ophthalmicus. *J Neuroophthalmol*. 2014; 34(1):20-22
33. Werner RN, Nikkels AF, Marinovic B, Schafer M, Czarnecka-Operacz M, Agius AM, Bata-Csorgo Z, Breuer J, Girolomoni G, Gross GE, Langan S, Lapid-Gortzak R, Lesser TH, Pleyer U, Sellner J, Verjans GM, Wutzler P, Dressler C, Erdmann R, Rosumeck S, Nast A. European consensus-based (S2k) Guideline on the Management of Herpes Zoster - guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV), Part 1: Diagnosis. *J Eur Acad Dermatol Venereol*. 2017; 31(1):9-19

## Should Anti-Viral/Anti-VZV Treatment Be Used in Patients with GCA?

### Introduction:

Recent reports show that varicella zoster virus (VZV) antigen is found in temporal artery (TA) biopsies in patients with giant cell arteritis (GCA). Two experts debate whether anti-viral therapy should be used routinely in patients with GCA.

### Pro: Anti-VZV therapy should be considered in the treatment of patients with GCA

Y. Joyce Liao, MD, PhD

GCA is the most prevalent vasculitis with predisposition to cranial arteries in the elderly and has an incidence of 19.8 per 100,000 annually (1). It is associated with large and medium vessel granulomatous inflammation, which leads to thrombosis and ischemia (2, 3). The most feared and most common neurologic consequence of GCA is irreversible vision loss due to arteritic anterior ischemic optic neuropathy (A-AION) (2, 3). Diagnosis of GCA is based on clinical suspicion, elevated systemic inflammatory markers, and, most importantly, temporal artery biopsy (TAB) to look for the presence of transmural inflammation, medial smooth muscle cell damage, and multinucleated giant cells in noncontiguous skip lesions. The mainstay of GCA treatment is chronic, high dose corticosteroid treatment (4, 5), which is limited because it has many short- and long-term side effects, and some patients continue to exhibit symptoms despite treatment. On the cellular level, corticosteroid therapy is limited because it only reduces CD4<sup>+</sup> T help T<sub>H</sub>17- but not T<sub>H</sub>1-mediated tissue-destructive immune responses (3).

The cause of GCA remains unknown, and many infectious organisms have been postulated but none proven. In 2002-2005, varicella zoster virus (VZV) was found in the extracranial superficial temporal arteries of patients with clinical manifestations of anterior ischemic optic neuropathy (AION) associated with temporal headache, jaw claudication, and herpes zoster ophthalmicus, leading to the suspicion that VZV infection may contribute to GCA-like clinical manifestations (6). VZV is an alpha herpesvirus that causes chicken pox (varicella) and shingles (herpes zoster). Historically, the association between VZV and GCA (and other vasculitides) has been difficult to show due to the challenge of finding evidence of VZV in formalin-fixed tissues. VZV exhibits a tropism for intracranial blood vessels, and VZV infection leading to VZV vasculitis is well known to be an important cause of vasculitis, ischemic stroke, and development of intracerebral aneurysms. The identification of VZV in TABs in patients with suspect GCA leads to the speculation that VZV is involved in the pathogenesis of GCA (6, 7). VZV reactivation due to reduced cell-mediated immunity or viral-induced effects on the blood vessel local milieu may contribute to GCA pathogenesis. VZV vasculitis is an especially important consideration in severe cases of GCA that are refractory to treatment or has intracranial involvement.

There are several compelling reasons that the diagnosis of overlapping VZV infection or VZV-triggered immune-mediated effects should be considered when approaching patients with possible GCA and acute vision loss: 1) overlapping neuro-ophthalmic and systemic manifestations, 2) nearly identical histological changes and co-localization of disease in tunica adventitia of the blood vessels in the early phase of disease, and 3) prominent cell-mediated inflammation and cytokine release in both conditions.

**Overlapping neuro-ophthalmic and systemic manifestations.** Patients presenting with vision loss and symptoms of GCA can be indistinguishable from that of VZV infection because they both present with neurological symptoms plus systemic manifestations, symptoms are highly variable and can wax and wane, and disease has a protracted course that last for months to more than one year (8). These overlapping clinical manifestations can be diagnostic dilemmas and lead to a delay in initiation of the appropriate treatment. Although VZV does not typically present as A-AION, this has been reported (9) and can present with or without acute retinal necrosis or herpes zoster ophthalmicus and may not be

associated with rash (zoster sine herpete) (8). In one study of 9 surgically removed eyes using both DNA in situ hybridization for VZV DNA (and immunohistochemistry using anti-VZV antibody in some cases for the presence of VZV antigen), 44% (4/9) eyes exhibit optic neuritis; 89% (8/9), perineuritis; and 89% (8/9), perivasculitis of the *posterior ciliary arteries* (10), the same blood vessels that are predominantly involved in AION (10). Although the authors do not comment on which layer of the vessel was involved, they do comment on the frequent association of viral DNA with vascular rather than with neuronal structures (10). Not surprisingly, this vascular association underlies typical manifestations of VZV, including transient ischemic attack, stroke, aneurysm, and venous sinus thrombosis (11, 12). Although strokes are more commonly associated with VZV infection, intracranial involvement such as stroke has also been reported in GCA (13-15). Below the cranium, like GCA, VZV vasculopathy can also present as granulomatous aortitis or nonspecific vasculitis (11, 12). In 2017, England et al. used two independent health care provider datasets (Medicare, MarketScan) and determined that prior zoster infection is associated with a significantly increased hazard ratio of developing GCA (16). Although prior VZV vaccination has not been shown to decrease the incidence of GCA (17), this could be due to different reasons such as waning immunity with aging, limited size of study, and heterogenous population.

**Prevalence of VZV in the superficial temporal artery biopsies.** The localization of VZV antigens and DNA in TABs, especially in patients with suspect GCA, has been more extensively studied since its initial observation in a small number of patients. Recent studies identifying VZV DNA by polymerase chain reaction (PCR) or presence of VZV antigen by immunostaining with multiple anti-VZV antibodies have shown that VZV is found in a significantly higher percentage of TABs in both GCA-positive as well as negative patients (18, 19). In one large study, VZV antigen was found in 68/93 (73%) GCA-positive TABs and in 45/70 (64%) of GCA-negative TABs, which is significantly higher than the 11/49 (22%) in control TABs (19). A masked study of 10 TAB in 9 patients using both PCR of formalin-fixed and fresh frozen TABs and immunostaining using anti-VZV antibody found that VZV antigen was detected in 78% of GCA-positive and GCA-negative TABs (18). These findings are consistent with the well-known tissue tropism of VZV for the trigeminal ganglia and transaxonal spread of infection along the superficial temporal branches to the extracranial vessels like the superficial temporal artery and that VZV alone is not sufficient to produce GCA (20). Although the presence of VZV in aorta (not cranial or extracranial vessels) has not been well studied in GCA patients, one study using 3 different anti-VZV antibodies identified significantly greater prevalence of VZV antigen in 100% (11/11) of aortas with pathologically confirmed granulomatous aortitis compared to 28% (5/18) of control aortas at autopsy (21). Again, this co-localization does not prove a causal relationship but provides further evidence of the tissue tropism of VZV and presence of VZV in the vessels most commonly affected in GCA.

**Histologic overlap in tunica adventitia.** Histologically, VZV vasculopathy and GCA have virtually identical pathological findings in the blood vessels. In both conditions, the pathology is characterized by granulomatous arteritis, in which inflammation, often transmural, is seen, along with necrosis in the arterial media; multinucleated giant cells, epithelioid macrophages or both are also present (11). Strikingly, the greatest amount of VZV antigen in TABs from patients with GCA is localized in the *tunica adventitia* (12), the outermost layer of the vessel wall. In one study, one TAB specimen that was obtained 3 days after onset of vision loss from A-AION revealed an early, prominent co-localization of the VZV antigen and inflammatory cells, including T cells, activated macrophages, and rare B cells in the adventitia and intima (22). In VZV vasculopathy, VZV antigen is also found in the adventitia early in disease (from transaxonal spread) and then later on in the media and intima through transmural spread of the virus within the vessel wall (8). This co-localization of the VZV antigen and avid vasculitis in one patient with acute A-AION and GCA does not prove a causal relationship, but it does highlight the important role of the adventitia in the development of vasculitis in both VZV-associated vasculitis and in GCA vasculitis.

**Prominent immune activation in the tunica adventitia.** The adventitia is particularly important in the early phase of the development of GCA, and much more is known about the cell-mediated vasculitis in GCA than in VZV vasculopathy. In the adventitia, both VZV infection and GCA lead to local, prominent inflammation. In VZV vasculitis, the CSF has significantly elevated proinflammatory cytokines, IL-8 and IL-6, along with elevated MMP-2 (23). A proinflammatory environment bathing the anterior optic nerve in the posterior ciliary artery territory can certainly cause breakdown of blood-optic nerve-barrier and vasculitis leading to A-AION.

VZV-infected adventitial cells down-regulate the expression of programmed death ligand 1 (PD-L1) in a post-translational fashion, which contributes to persistent vascular inflammation (24). In GCA, T cells interact with endothelial cells in the adventitia in a tightly controlled and antigen-specific manner that shape the evolution of vasculitis through activation of T<sub>H</sub>1 and T<sub>H</sub>17 T helper cells and chemokine and cytokine production, including interferon  $\gamma$  (IFN $\gamma$ ), tumor necrosis factor  $\alpha$  (TNF $\alpha$ ), and interleukins (IL6, IL17) (3, 25).

In patients with GCA, adventitial inflammation was seen adjacent to VZV immunoreactivity in 26 (52%) of 58 GCA-negative subjects whose temporal arteries contained VZV antigen, and no inflammation was seen in normal temporal arteries containing VZV antigen, thought to reflect subclinical reactivation in some people over age 50 (18). The presence of VZV in the adventitia may contribute to a milieu of vasculitis, which is a critical part of vasculitis development. In GCA patients (unknown in VZV vasculopathy), this process involves up-regulation of Jagged1 in adventitial endothelial cells, which synergizes with activation of the Notch receptor and biasing the CD4 T cell repertoire toward T<sub>H</sub>1 and T<sub>H</sub>17 fate, excessive inflammatory activity and production of cytokines, and destructive granulomas and vessel thrombosis (26). It will be interesting to see if these molecular and cellular changes can be dampened by anti-viral therapy.

**Con: Anti-VZV therapy should not be considered in the treatment of patients with GCA**

**Sachin Kedar, M.D.**

An association between VZV and GCA was demonstrated by a group of investigators studying formalin fixed paraffin embedded (FFPE) sections of TABs (27). Based on these results, the investigators proposed empirically treating GCA, with a combination of steroids and oral antiviral medications for 4-12 weeks depending on the initial response. They also propose treating GCA recurrence during steroid taper by adding antiviral medications to the steroids rather than increase the steroid dosage. The authors acknowledge that in the absence of randomized or non-randomized clinical trials, their recommendations are based on “Level 5 class of evidence: expert opinion without critical appraisal, or based on physiology, bench research” (28). I will argue that it is premature to consider the empiric use of anti-viral medications in GCA.

GCA is a chronic, systemic vasculitis of the elderly, affecting medium and large arteries, especially branches of the internal and external carotid artery. Disease manifestation depends on the vascular territory involved and results in end organ complications such as ischemic optic neuropathy, myocardial infarction, stroke, mesenteric ischemia, and aortitis and aortic aneurysms (29). Long-term corticosteroid therapy remains the mainstay of treatment for GCA, but results in considerable treatment-related morbidity and mortality (30-32). Numerous steroid sparing agents have proven ineffective in GCA (32). Recently, tocilizumab, an interleukin-6 receptor alpha inhibitor has shown promise but the rates of infection are high and comparable to chronic steroid usage (33). There clearly is need for safer treatment options for GCA.

Risk factors for GCA include advanced age, Caucasian race, female gender and geographic distribution. Genetic susceptibility is suggested by an association with genetic polymorphisms of the human leukocyte antigen loci HLA-DRB1\*04 as well as non-HLA loci such as PTPN 22 (34). Activation of

dendritic cells result in an immunological cascade leading to recruitment of T-cells and macrophages within the arterial wall. This leads to granulomatous inflammation within the arterial wall, disruption of internal elastic lamina, necrosis of arterial media, intimal hyperplasia and luminal obstruction (35). The inciting event for dendritic cell activation has remained elusive, although, an infectious cause has long been suspected based on the cyclical and seasonal fluctuation seen in GCA (36). After sifting through a number of potential agents such as Epstein - Barr virus, Parvovirus B19 and Chlamydia pneumonia, VZV has recently emerged as the primary suspect (37).

VZV is an exclusively human neurotropic alpha herpes virus, which produces chicken pox. Greater than 95% human population demonstrates serological evidence of VZV infection before adolescence. Primary infection results in a lifelong period of latency in the cranial, dorsal root, autonomic and enteric ganglia. VZV reactivation due to a waning of cell (T-cell) mediated immunity with advancing age or immunocompromised condition, results in replication of the virus in the ganglia and trans-axonal spread to the mucocutaneous surfaces where it produces zoster (shingles) in the corresponding dermatome (38). On rare occasions, reactivation produces VZV vasculopathy through direct infection of the arteries and may cause a number of cerebrovascular diseases (28).

A group of investigators have proposed that VZV may play a substantial role in causing GCA based on studies performed on FFPE sections of temporal arteries in biopsy positive GCA, biopsy negative GCA and postmortem specimens from normal controls (12,19,27). VZV antigen was detected in the arterial vessel wall using immunohistochemistry in 70% biopsy positive GCA, 58% biopsy negative GCA and 18% normal controls. The VZV antigen was 3.89 times more likely to be present in the vessel wall of biopsy-positive GCA and 3.22 times more likely in biopsy negative GCA compared to controls. The VZV antigen was found in the perineural cells expressing claudin-1 around nerve bundles adjacent to areas of adventitial inflammation in a majority of GCA positive biopsy specimens. Based on these observations, the investigators hypothesized that GCA results from trans-axonal transport of the reactivated VZV from ganglia to the wall of temporal artery, resulting in activation of dendritic cells followed by an inflammatory cascade.

These results are impressive but do not provide evidence for a causal role of VZV in GCA for the following reasons:

**Lack of reproducibility.** Multiple groups of investigators have explored the role of VZV in GCA and only 2 other groups have found evidence of VZV in TAB specimens. VZV DNA was not detected in 13 biopsy positive and 17 biopsy negative TAB specimens by Helweg-Larsen et.al. (37), 15 biopsy positive and 7 control TAB specimens by Kennedy et.al (39) and 50 GCA positive and 97 biopsy negative TAB specimens by Rodriguez-Pla et.al. (40). Procop et. al. failed to detect VZV DNA using two different validated PCR methods in 31 thoracic aorta specimens including 8 with GCA and 11 TAB specimens including 5 with GCA obtained and processed in a surgically sterile manner (41).

Mitchell et.al. demonstrated VZV DNA in 9/35 (26%) biopsy positive GCA compared to 0/29 control specimens and proposed an association (42). Alvarez-Lafuente et.al. however, found VZV DNA in 18/57 GCA and 18/56 control TAB specimens and proposed a lack of association between VZV and GCA (43). Using both immunohistochemistry and PCR methods, Nordborg et. al failed to show evidence for VZV DNA or antigen in 10 biopsy positive TAB specimens (23), while Muratore et. al found VZV antigen in one and VZV DNA in none of the 79 TAB specimens which included 34 biopsy positive TAB (4). Some investigators have questioned the specificity of the antibodies used in the immunohistochemistry studies after finding significant cross-reactivity of VZV antibodies with various muscle tissue due to shared epitopes between VZV protein and muscular elements in the vessel wall (45).

**Lack of temporal relationship.** There is no convincing evidence that GCA is preceded by antecedent infections such as herpes zoster (HZ) (46). In a retrospective study of approximately 17

million subjects from two large administrative datasets from the United States, only 4% (236/5942) GCA was preceded by zoster. Although antecedent zoster increased the risk of GCA, there was variable and significant time lag (months to years) between the 2 events (47). I was unable to find literature which showed an increase in serological markers for VZV in patients with GCA. Not only does this weaken the hypothesis that VZV causes GCA, it raises serious questions about the rationale and timing for empiric treatment of GCA with antiviral medications.

**Lack of consistency with epidemiological studies.** Approximately 1 million new episodes of zoster are estimated to occur annually in the US with a lifetime risk of 30%. The incidence of zoster across different populations is approximately 4–4.5 per 1000 person-years and appears to be increasing (48). A causal relationship between VZV and GCA should be reflected by an increasing incidence of GCA. However, the annual incidence of GCA is considerably less (~18 per 100,000 in Olmsted County, Minnesota), varies significantly across different population groups and does not appear to be increasing (49). Conversely, interventions to decrease VZV reactivation have not led to a decrease in the incidence of GCA. Vaccination using attenuated VZV has been demonstrated to be effective in decreasing the incidence of zoster by at least 50% (50). Studies using large administrative data sets of subjects >50 years age, have not shown a corresponding decrease in the incidence of GCA in the vaccinated compared to the non-vaccinated population (47,51).

In summary, there appears to be an association between VZV and GCA. The evidence, however, is weak and does not support a causal role for VZV. Using antiviral medications in the management of GCA makes sense only if there is concurrent VZV infection. At present, there is no evidence for a consistent temporal relationship between VZV reactivation and GCA, which makes recommendations for empiric use of antiviral agents for treatment of GCA premature and without sound rationale.

### **Rebuttal: Dr. Liao**

According to the Koch's postulate (52), there is no evidence linking VZV as the causative agent for GCA. The Koch's postulate dictates that: 1) the microorganism or other pathogen must be present in all cases of the disease, 2) the pathogen can be isolated from the diseased host and grown in pure culture, 3) the pathogen from the pure culture must cause the disease when inoculated into a healthy, susceptible laboratory animal, and 4) the pathogen must be re-isolated from the new host and shown to be the same as the originally inoculated pathogen. In this case, there is no evidence that any of the 4 postulates are fulfilled.

This lack of evidence does not mean that we should deny our patients the benefit of effective, potentially life-saving anti-viral therapies. Diagnostic testing for VZV infection or other causes of vasculitis in the *atypical* GCA cases should be performed. High clinical suspicion of VZV involvement should immediately prompt consideration of anti-viral/anti-VZV treatment, potentially before diagnostic testing results are available. When prescribed in the right setting, there is relatively low risk of anti-viral treatment in patients, who are refractory to traditional treatment.

Another reason for consideration of anti-viral therapy in atypical GCA cases is the limited efficacy of current treatment choices for GCA. Although corticosteroid is the mainstay of treatment for GCA, it effectively dampens  $T_H17$ -mediated responses but not  $T_H1$ -mediated immune responses ((53), and some patients with repeat TAB after long-term corticosteroid treatment still show active disease. As Dr. Kedar pointed out, newer therapies such as tocilizumab are associated with significantly increased risk of infections, and there is no evidence that it actually helps save vision.

With advancing age and decline in VZV-specific cell mediated immunity, there is a rise in the incidence of herpes zoster (48). The estimated incidence of herpes zoster is 3.4–4.82 per 1,000 person



years in the general population, which increases to more than 11 per 1,000 person-years in those above 80 years old. In a prospective study of 11 patients with treated GCA compared with 26 age- and sex-matched healthy controls, the treated GCA patients exhibited significantly reduced *VZV-specific* T-cell-mediated immunity, but no difference in the total number of CD3<sup>+</sup> T cells, the frequencies of IFN $\gamma$ -, TNF $\alpha$ , and IL-2-producing CD4<sup>+</sup> T cells, the frequency of cytokine-producing CD4<sup>+</sup> or CD8<sup>+</sup> T cells following stimulation with VZV, or humoral immunity as measured using serum VZV-IgG levels (54). These results mean that separate from GCA, these patients are at greater risk of VZV infection than age-matched healthy controls, so VZV vaccination is particularly important in this population.

Until we know for sure the role of VZV in the pathogenesis of GCA, the most prudent approach is to be aware of the clinical overlap and to consider the possibility of VZV reactivation and anti-viral therapy in those with compelling clinical presentation or in those who are refractive to traditional immunomodulatory therapies. Anti-viral treatment with acyclovir or valacyclovir is easy to administer and typically well tolerated. If VZV is contributory to GCA pathogenesis or persistence of granulomatous vasculitis in even a fraction of patients, anti-viral therapy has the potential to reduce cell-mediated immunity at the vessels, which may be more effective than corticosteroid treatment, especially since corticosteroid therapy does not appropriately address all of the immune derangements in patients with suspected GCA (3).

VZV vaccination contains live-attenuated virus, which is not typically recommended in those on immunosuppressive therapy because of concerns of infection and possible reduced efficacy. The non-live-attenuated vaccine is becoming available and can reduce the risk of infection and has been shown to be more effective than live-attenuated vaccine. Because of the importance of vaccination in this group of patients and concerns of the impact of immunosuppressive medication, some have proposed vaccination at the time of diagnosis, before high dose corticosteroid becomes effective (54). In the United States and many other countries, herpes zoster vaccination is recommended for adults aged 60 years or older because there is known age-related waning of VZV immunity and because of the increased prevalence of VZV reactivation such as shingles even in immunocompetent individuals. The typical herpes zoster vaccination is a live, attenuated virus that is the same strain as the varicella vaccine that is recommended for children but is 14 times more potent. Since vaccination with live-attenuated virus is not recommended in those on immunomodulatory therapy, vaccination is not recommended in the acute phase of GCA. However, once patients are out of the acute phase of disease and no longer on high dose corticosteroids, vaccination, especially recombinant herpes zoster virus, can be considered. Alternatively, the new adjuvanted recombinant subunit HZ vaccine is associated with a lower risk of infection than the live-attenuated virus and is thought to be more effective (50,55). Because patients with GCA have reduced cell-mediated immunity to VZV, as measured by interferon  $\gamma$  (IFN $\gamma$ ) enzyme-linked immunospot and intracellular cytokine flow cytometry measurements, VZV vaccination in the non-acute setting may help reduce relapse in GCA patients (54).

#### **Rebuttal: Dr. Kedar**

Dr. Liao and I agree that recent literature supports a clinical and histological overlap between VZV and GCA. Let us consider these three possibilities regarding the association between VZV and GCA:

1. **Innocent bystander:** Nearly all humans harbor the VZV virus lifelong, in a latent state within ganglia, along the entire neuraxis following primary infection. A significant number will have VZV reactivation during their lifetime, but a much smaller number develop GCA. Since both VZV reactivation and GCA are diseases of the elderly, it is possible that VZV was “in the wrong place at the wrong time”. In this scenario, treatment of GCA with antivirals would not be justified.

2. **Indirect causation:** The clinical, immunological and histopathological overlap between VZV and GCA suggests that the role of VZV may be more than an “innocent bystander”. Whether VZV triggers the immunopathology of GCA or vice versa is not clear. A recent study found that GCA might cause decreased immunity to VZV (56). If VZV does trigger immunopathology of GCA, the time to clinical presentation is not known. Patients with GCA do not have elevated serological markers for a recent VZV infection. In this scenario, concurrent use of antiviral treatment in all GCA cannot be justified.
3. **Direct causation:** Besides a few case reports, which show VZV vasculopathy causing cerebrovascular events including ischemic optic neuropathy, there is no evidence that VZV is immediately responsible for GCA. Unless there is serological or biopsy evidence for recent and/or concurrent VZV reactivation, there is no rationale for treating either primary, recurrent or intractable GCA with antiviral medications.

Lastly, let us not forget that we have been down this road before. A number of microorganisms such as Chlamydia pneumonia, parvovirus B19, human papillomavirus and Burkholderia-like bacterium have all been assigned blame for triggering GCA pathogenesis (57). None of these agents currently have a proven role in the pathogenesis (or management) of GCA. The current antiviral medications such as acyclovir and valacyclovir are safe to administer, but this should not be a justification for empiric treatment in GCA. As discussed, none of the three scenarios described above would support the use of anti-viral treatment at present. Rather, all of these scenarios support VZV vaccination in the elderly.

### **Conclusions: Drs. Lee and Van Stavern**

The overlap in histopathology and clinical manifestations between VZV vasculopathy and GCA are suggestive of an association but not necessarily a causal association. However, the data are conflicting and until there is clear evidence of a true, causal relationship, standard use of anti-viral therapy for all patients with GCA is an intriguing but unproven treatment option. The current work has been useful for hypothesis generating but is not sufficient for hypothesis testing. For now, perhaps it is reasonable to consider the possibility that treatment of VZV might be beneficial for select patients with GCA, perhaps those with a recent history of zoster infection, or those who fail to respond to treatment. Further studies are needed to better elucidate this relationship and a randomized, clinical trial of anti-viral therapy could be considered.

### **References**

1. Chandran AK, Udayakumar PD, Crowson CS, Warrington KJ, Matteson EL. The incidence of giant cell arteritis in Olmsted County, Minnesota, over a 60-year period 1950-2009. *Scand J Rheumatol* 2015;44:215-218.
2. Gonzalez-Gay MA, Garcia-Porrúa C, Llorca J, et al. Visual manifestations of giant cell arteritis. Trends and clinical spectrum in 161 patients. *Medicine (Baltimore)* 2000;79:283-292.
3. Weyand CM, Liao YJ, Goronzy JJ. The immunopathology of giant cell arteritis: diagnostic and therapeutic implications. *J Neuroophthalmol* 2012;32:259-265.
4. Buttgereit F, Dejaco C, Matteson EL, Dasgupta B. Polymyalgia Rheumatica and Giant Cell Arteritis: A Systematic Review. *JAMA* 2016;315:2442-2458.
5. Jivraj I, Tamhankar M. The Treatment of Giant Cell Arteritis. *Curr Treat Options Neurol* 2017;19:2.
6. Nagel MA, Gilden D. Developments in Varicella Zoster Virus Vasculopathy. *Curr Neurol Neurosci Rep* 2016;16:12.

7. Gildeen DH, Kleinschmidt-DeMasters BK, Wellish M, Hedley-Whyte ET, Rentier B, Mahalingam R. Varicella zoster virus, a cause of waxing and waning vasculitis: the New England Journal of Medicine case 5-1995 revisited. *Neurology* 1996;47:1441-1446.
8. Nagel MA. Varicella zoster virus vasculopathy: clinical features and pathogenesis. *J Neurovirol* 2014;20:157-163.
9. Salazar R, Russman AN, Nagel MA, et al. Varicella zoster virus ischemic optic neuropathy and subclinical temporal artery involvement. *Arch Neurol* 2011;68:517-520.
10. Wenkel H, Rummelt V, Fleckenstein B, Naumann GO. Detection of varicella zoster virus DNA and viral antigen in human eyes after herpes zoster ophthalmicus. *Ophthalmology* 1998;105:1323-1330.
11. Nagel MA, Jones D, Wyborny A. Varicella zoster virus vasculopathy: The expanding clinical spectrum and pathogenesis. *J Neuroimmunol* 2017;308:112-117.
12. Gildeen D, White T, Khmeleva N, et al. Prevalence and distribution of VZV in temporal arteries of patients with giant cell arteritis. *Neurology* 2015;84:1948-1955.
13. Buttner T, Heye N, Przuntek H. Temporal arteritis with cerebral complications: report of four cases. *Eur Neurol* 1994;34:162-167.
14. Lariviere D, Sacre K, Klein I, et al. Extra- and intracranial cerebral vasculitis in giant cell arteritis: an observational study. *Medicine (Baltimore)* 2014;93:e265.
15. Alsolaimani RS, Bhavsar SV, Khalidi NA, et al. Severe Intracranial Involvement in Giant Cell Arteritis: 5 Cases and Literature Review. *J Rheumatol* 2016;43:648-656.
16. England BR, Mikuls TR, Xie F, Yang S, Chen L, Curtis JR. Herpes Zoster as a Risk Factor for Incident Giant Cell Arteritis. *Arthritis Rheumatol* 2017.
17. Lotan I, Steiner I. Giant cell arteritis following varicella zoster vaccination. *J Neurol Sci* 2017;375:158-159.
18. Gildeen D, White T, Khmeleva N, Katz BJ, Nagel MA. Blinded search for varicella zoster virus in giant cell arteritis (GCA)-positive and GCA-negative temporal arteries. *J Neurol Sci* 2016;364:141-143.
19. Nagel MA, White T, Khmeleva N, et al. Analysis of Varicella-Zoster Virus in Temporal Arteries Biopsy Positive and Negative for Giant Cell Arteritis. *JAMA Neurol* 2015;72:1281-1287.
20. Gildeen D, Nagel MA. Varicella zoster virus triggers the immunopathology of giant cell arteritis. *Curr Opin Rheumatol* 2016;28:376-382.
21. Gildeen D, White T, Boyer PJ, et al. Varicella Zoster Virus Infection in Granulomatous Arteritis of the Aorta. *J Infect Dis* 2016;213:1866-1871.
22. Nagel MA, Traktinskiy I, Stenmark KR, Frid MG, Choe A, Gildeen D. Varicella-zoster virus vasculopathy: immune characteristics of virus-infected arteries. *Neurology* 2013;80:62-68.
23. Jones D, Alvarez E, Selva S, Gildeen D, Nagel MA. Proinflammatory cytokines and matrix metalloproteinases in CSF of patients with VZV vasculopathy. *Neurol Neuroimmunol Neuroinflamm* 2016;3:e246.
24. Jones D, Blackmon A, Neff CP, et al. Varicella-Zoster Virus Downregulates Programmed Death Ligand 1 and Major Histocompatibility Complex Class I in Human Brain Vascular Adventitial Fibroblasts, Perineurial Cells, and Lung Fibroblasts. *J Virol* 2016;90:10527-10534.
25. Ma-Krupa W, Jeon MS, Spoerl S, Tedder TF, Goronzy JJ, Weyand CM. Activation of arterial wall dendritic cells and breakdown of self-tolerance in giant cell arteritis. *J Exp Med* 2004;199:173-183.
26. Loureiro M, Rothwell R, Fonseca S. Nodular Scleritis Associated with Herpes Zoster Virus: An Infectious and Immune-Mediated Process. *Case Rep Ophthalmol Med* 2016;2016:8519394.

27. Gilden D, White T, Khmeleva N, Boyer PJ, Nagel MA. VZV in biopsy-positive and -negative giant cell arteritis: Analysis of 100+ temporal arteries. *Neurol Neuroimmunol Neuroinflamm.* 2016; 3(2):e216
28. Nagel MA, Jones D, Wyborny A. Varicella zoster virus vasculopathy: The expanding clinical spectrum and pathogenesis. *J Neuroimmunol.* 2017; 308:112-117
29. Salvarani C, Pipitone N, Versari A, Hunder GG. Clinical features of polymyalgia rheumatica and giant cell arteritis. *Nat Rev Rheumatol.* 2012; 8(9):509-521
30. Mukhtyar C, Guillevin L, Cid MC, Dasgupta B, de Groot K, Gross W, Hauser T, Hellmich B, Jayne D, Kallenberg CG, Merkel PA, Raspe H, Salvarani C, Scott DG, Stegeman C, Watts R, Westman K, Witter J, Yazici H, Luqmani R, European Vasculitis Study Group. EULAR recommendations for the management of large vessel vasculitis. *Ann Rheum Dis.* 2009;68(3):318-323
31. Proven A, Gabriel SE, Orces C, O'Fallon WM, Hunder GG. Glucocorticoid therapy in giant cell arteritis: duration and adverse outcomes. *Arthritis Rheum.* 2003; 49(5):703-708
32. Almarzouqi SJ, Morgan ML, Lee AG. Treatment of giant cell arteritis. *Curr Opin Ophthalmol.* 2015; 26(6):469-475
33. Stone JH, Tuckwell K, Dimonaco S, Klearman M, Aringer M, Blockmans D, Brouwer E, Cid Collinson N. Trial of Tocilizumab in Giant-Cell Arteritis. *N Engl J Med.* 2017; 377(4):317-328
34. Weyand CM, Hicok KC, Hunder GG, Goronzy JJ. The HLA-DRB1 locus as a genetic component in giant cell arteritis. Mapping of a disease-linked sequence motif to the antigen binding site of the HLA-DR molecule. *J Clin Invest.* 1992; 90(6):2355-2361
35. Génèreau T, Lortholary O, Pottier M, Michon-Pasturel U, Ponge T, De Wazières B, Liozon E, Pinède L, Hachulla E, Roblot P, Barrier J, Herson S, Guillevin L. Temporal artery biopsy: A diagnostic tool for systemic necrotizing vasculitis. *Arthritis & Rheumatism.* 1999; 42(12):2674-2681
36. Weyand CM, Goronzy JJ. Giant cell arteritis as an antigen-driven disease. *Rheum Dis Clin North Am.* 1995; 21(4):1027-1039
37. Helweg-Larsen J, Tarp B, Obel N, Baslund B. No evidence of parvovirus B19, Chlamydia pneumoniae or human herpes virus infection in temporal artery biopsies in patients with giant cell arteritis. *Rheumatology (Oxford).* 2002; 41(4):445-449
38. Steiner I, Kennedy PG, Pachner AR. The neurotropic herpes viruses: herpes simplex and varicella-zoster. *Lancet Neurol.* 2007; 6(11):1015-1028
39. Kennedy PG, Grinfeld E, Esiri MM. Absence of detection of varicella-zoster virus DNA in temporal artery biopsies obtained from patients with giant cell arteritis. *J Neurol Sci.* 2003; 215(1-2):27-29
40. Rodriguez-Pla A, Bosch-Gil JA, Echevarria-Mayo JE, Rossello-Urgell J, Solans-Laque R, Huguet-Redecilla P, Stone JH, Vilardell-Tarres M. No detection of parvovirus B19 or herpesvirus DNA in giant cell arteritis. *J Clin Virol.* 2004; 31(1):11-15
41. Procop GW, Eng C, Clifford A, Villa-Forte A, Calabrese LH, Roselli E, Svensson L. Varicella Zoster Virus and Large Vessel Vasculitis, the Absence of an Association. *Pathog Immun.* 2017; 2(2):228-238
42. Mitchell BM, Font RL. Detection of varicella zoster virus DNA in some patients with giant cell arteritis. *Invest Ophthalmol Vis Sci.* 2001; 42(11):2572-2577
43. Alvarez-Lafuente R, Fernandez-Gutierrez B, Jover JA, Judez E, Loza E, Clemente D, GarciaAsenjo JA, Lamas JR. Human parvovirus B19, varicella zoster virus, and human herpes virus 6 in temporal artery biopsy specimens of patients with giant cell arteritis: analysis with quantitative real time polymerase chain reaction. *Ann Rheum Dis.* 2005; 64(5):780-782
- Nordborg C, Nordborg E, Petursdottir V, LaGuardia J, Mahalingam R, Wellish M, Gilden DH. Search for varicella zoster virus in giant cell arteritis. *Ann Neurol.* 1998; 44(3):413-414

44. Muratore F, Croci S, Tamagnini I, Zerbini A, Bellafiore S, Belloni L, Boiardi L, Bisagni A, Pipitone N, Parmeggiani M, Cavazza A, Salvarani C. No detection of varicella-zoster virus in temporal arteries of patients with giant cell arteritis. *Semin Arthritis Rheum.* 2017; 47(2):235-240
45. Pisapia DJ, Lavi E. VZV, temporal arteritis, and clinical practice: False positive immunohistochemical detection due to antibody cross-reactivity. *Exp Mol Pathol.* 2016;100(1):114-115
46. Rhee RL, Grayson PC, Merkel PA, Tomasson G. Infections and the risk of incident giant cell arteritis: a population-based, case-control study. *Ann Rheum Dis.* 2017; 76(6):1031-1035
47. England BR, Mikuls TR, Xie F, Yang S, Chen L, Curtis JR. Herpes Zoster as a Risk Factor for Incident Giant Cell Arteritis. *Arthritis Rheumatol.* 2017
48. Yawn BP, Gilden D. The global epidemiology of herpes zoster. *Neurology.* 2013; 81(10):928-930
49. Crowson CS, Matteson EL. Contemporary prevalence estimates for giant cell arteritis and polymyalgia rheumatica, 2015. *Semin Arthritis Rheum.* 2017; 47(2):253-256
50. Gagliardi AM, Andriolo BN, Torloni MR, Soares BG. Vaccines for preventing herpes zoster in older adults. *Cochrane Database Syst Rev.* 2016; 3:CD008858
51. Lotan I, Steiner I. Giant cell arteritis following varicella zoster vaccination. *J Neurol Sci.* 2017; 375:158-159
52. Evans AS. Causation and disease: a chronological journey. The Thomas Parran Lecture. *Am J Epidemiol* 1978;108:249-258.
53. Deng J, Younge BR, Olshen RA, Goronzy JJ, Weyand CM. Th17 and Th1 T-cell responses in giant cell arteritis. *Circulation* 2010;121:906-915.
54. Rondaan C, van der Geest KSM, Eelsing E, et al. Decreased Immunity to Varicella Zoster Virus in Giant Cell Arteritis. *Front Immunol* 2017;8:1377.
55. Esposito S, Principi N. Herpes zoster prevention: A difficult problem to solve. *Vaccine* 2017.
56. Rondaan C, van der Geest KSM, Eelsing E, Boots AMH et al. Decreased immunity to VZV in Giant Cell Arteritis. *Front Immunol* 2017;8:1377
57. van Timmeren MM, Heeringa P, Kallenberg CG. Infectious triggers for vasculitis. *Curr Opin Rheumatol.* 2014; 26(4):416-423

# VENOUS DYNAMICS IN IDIOPATHIC INTRACRANIAL HYPERTENSION AND THERAPEUTIC STENTING OF VENOUS SINUS STENOSIS

Marc Dinkin, MD  
Associate Professor of Neurology and Ophthalmology  
Weill Cornell Medical College  
New York, NY

## LEARNING OBJECTIVES

1. The attendee will be able to describe the evidence for an association between stenosis at the transverse-sigmoid sinus junction and idiopathic intracranial hypertension (IIH).
2. The attendee will be able to explain the difference between intrinsic and extrinsic stenosis and describe the positive feedback loop theory for extrinsic stenosis and IIH.
3. The attendee will be able to summarize the outcomes of venous stenting for IIH among the published studies, including its effect on symptoms, visual acuity, visual fields, papilledema, and intracranial pressure.
4. The attendee will be able to evaluate the complications reported after venous stenting, including restenosis.

## CME QUESTIONS

1. MRI evidence suggests that the majority of patients with idiopathic intracranial hypertension (IIH) have stenosis at:
  - a. The upper internal jugular veins, either unilaterally or bilaterally.
  - b. The proximal superior sagittal sinus
  - c. The junction of the transverse and sigmoid sinuses, either unilaterally or bilaterally.
  - d. The vein of Galen.
2. Which of the following is true about the venous sinus stenosis found in IIH?
  - a. The stenosis is fixed and does not reverse with a reduction in CSF pressure
  - b. The stenosis is dynamic and reverses with reduction in CSF pressure.
  - c. The stenosis is dynamic and reverse with calcium channel blockers.
  - d. Both A and B may be true depending on the patient.
  - e. Both A and C may be true depending on the patient.
3. The evidence that venous sinus stenting can result in improvement in CSF pressure, papilledema, symptoms of IIH and visual field defects comes from:
  - a. Anecdotal case reports only.
  - b. Retrospective case series and several uncontrolled prospective series.
  - c. A placebo-controlled, physician-blinded prospective trial.
  - d. There is no evidence. The concept of venous sinus stenting as a therapy for IIH is theoretical only.
4. All of the following are complications reported after venous stent placement for IIH except:
  - a. Guidewire perforation and intracranial hemorrhage
  - b. Transient hearing loss
  - c. Stent migration

- d. Cavernous sinus thrombosis
- e. In-stent thrombosis
- f. Acute worsening of intracranial hypertension

## KEY WORDS

1. Idiopathic intracranial hypertension
2. Papilledema
3. Venous sinus stenosis
4. Venous stenting
5. Magnetic resonance venography

## SUMMARY

### Introduction

Idiopathic intracranial hypertension (IIH) is a disease predominantly of women of childbearing age with elevated body mass index in which there is elevated intracranial pressure (ICP) without tumor or meningitic inflammation as its cause. Typical symptoms include position-dependent headache, a pulsatile whooshing, horizontal diplopia (from abducens palsies) and transient visual obscurations, blurry vision or visual field defects due to papilledema. Up to 10% of IIH patients do not respond or do not tolerate medical therapy, and therefore require surgical treatments for fast and dependable control of ICP to prevent progressive vision loss and manage symptoms. Furthermore, up to 2.9% of patients present with fulminant vision loss, such that they cannot wait for a gradual reduction in ICP with medical treatment and must be treated from the start with surgery. Over the last few decades, it has been increasingly recognized that the majority of IIH patients have stenosis along the junction of the transverse sinus (TS) and sigmoid sinus (SS). This observation of venous sinus stenosis (VSS) has led to numerable studies evaluating treatment with venous sinus stenting.

### Evidence for association of venous stenosis and IIH and radiological assessment techniques

In 1995, King and colleagues demonstrated elevated venous pressures in the superior sagittal sinus and transverse sinus in patients with IIH. As Farb and colleagues later showed in 2003, stenosis at the junction of the TS and SS is found in the majority of patients with IIH, with a suggesting that the stenosis causes the elevated venous pressure. Using the auto-triggered elliptic-centric-ordered three-dimensional gadolinium-enhanced MR venography (ATECO MRV) technique, Farb found that a combined venous conduit score (CSS, which accounted for the degree of stenosis bilaterally) of <5.0 predicted IIH with high sensitivity and specificity (both 93%). More recently, Lublinsky and colleagues have developed a computer assisted detection (CAD) method for vessel cross section analysis to enable accurate evaluation of the shape and size of the dural sinuses in a quantitative manner.

### Theoretical Underpinnings

#### *Evidence for reversible (Extrinsic) stenosis*

Several case reports and series have demonstrated reversal of venous hypertension and venous sinus stenosis with reduction in ICP, and a recent report demonstrated reversal of the trans-stenotic gradient and resolution of the stenosis using intravascular ultrasound. Critics of venous sinus stenting have therefore argued that the procedure simply and needlessly reverses a downstream effect of IIH.

#### *Evidence for irreversible (Intrinsic) stenosis*

On the other hand, others have demonstrated stenoses that persist even as ICP is lowered, providing evidence that at least in some cases the stenoses are primary anatomical features that are not purely a result of high ICP. Indeed, such intrinsic stenoses may be caused by arachnoid granulations, septal bands or occult prior thrombosis. Thus two forms of VSS were recognized, an intrinsic form, which is typically appears as a sharp cut off and is unresponsive to changes in ICP, and an extrinsic form resulting from intracranial hypertension, which appears more tapered and reverses with CSF removal.

#### *Positive feedback loop theory of stenosis-ICP elevation-stenosis and Starling resistor model*

The “self-limiting venous collapse feedback loop model” strives to explain why stenting of the stenosis might treat IIH even if the stenosis was secondary to elevated ICP. In certain individuals with compressible regions of the sinus, an inciting event causing a mild elevation in CSF pressure (weight gain or obstructive sleep apnea for example) might therefore result in stenosis of the susceptible region, in turn leading to localized venous hypertension. CSF drainage into the venous system is therefore compromised, resulting in elevation of ICP, which in turn compresses the susceptible sinus even more. The resulting positive feedback loop can ultimately result in the clinical entity of IIH. This system of a partially compressible sinus surrounded by a compartment whose pressure is related to the flow through that sinus has been mathematically modelled as a Starling-like resistor.

#### *The role of dural incompetence and venous sinus pulsatility*

Lazzaro and colleagues described three patients with IIH and VSS in which direct manometry revealed an increase in the pulsatility amplitude, in addition to an increase in the mean venous pressure. They postulated that this increase in pulsatility reflected a greater transmission of the CSF waveform through the CSF-venous interface (i.e. the dural wall) and that this resulted from ICP-induced dural wall incompetence.

#### *Venous sinus stenosis and obesity*

A recent study demonstrated a correlation between BMI and mean intracranial venous pressure, as well as with the trans-stenotic gradient. This finding offers more evidence in support of the theory that weight gain serves as an inciting event that raises the venous pressure to the point where the collapsible sinus feedback model takes over.

### **Outcomes of stenting (combining available studies and case series to date, 464 patients)**

Over 22 studies evaluating VSS have been published to date since Higgins’ first study in 2002, including Donnet’s series of 10, Ahmed’s series of 54 patients and two small prospective series. ,

#### *Change in trans-stenotic gradient*

Of 346 patients in the literature in which pre and post-stent mean trans-stenotic gradients were reported, the mean reduced from 20.4 to 2.4 mm Hg.

#### *Change in intracranial pressure*

Of 90 patients with both pre and post-stent ICP measurements, the mean ICP reduced from 32.8 cm H<sub>2</sub>O to 17.6 cm H<sub>2</sub>O (46.3% reduction)

#### *Symptoms*

Of 424 presenting with headaches, 72.6% experienced either resolution or improvement. Of 102 patients presenting with transient visual obscurations (TVOs), 68 (66.7%) experienced complete resolution. Of 36 patients presenting with diplopia, 33 (91.7%) experienced resolution following stenting, and of 126 presenting with pulsatile tinnitus, 112 (88.9%) reported resolution.



## Visual Exam

Mean visual acuity prior to stenting in patients with quantitative acuity assessment was LogMAR 0.25 (Snellen 20/36) and improved to 0.136. (Snellen 20/27). Quantitative pre and post assessment of visual fields was available in 71 eyes and showed an improvement of average mean deviation from -10.35 to -7.05 dB. Papilledema was typically reported by the patient. Of 308 patients with definite papilledema, 174 (60%) experienced complete resolution and an additional 83 (26.9%) experienced improvement in grade. Optic atrophy was noted in 27 patients (8.8%) post-stent. Optical coherence tomography (OCT) was performed in 73 eyes and demonstrated a reduction from a mean pre-stent RNFL thickness of 225.4  $\mu\text{m}$  to 87.6  $\mu\text{m}$  post-stent.

## Side effects, complications and recurrence rates

The most frequent adverse symptom was headache ipsilateral to the stent, likely due to dural stretch and lasting several days, in 104/464 (22.4%). Thrombosis in either the stent (n=3) or adjacent transverse sinus (n=1) was relatively rare (together 0.65%), as was intracranial hemorrhage (n=4, 0.86%). There were two deaths, one due to malignant intracranial hypertension, with possible contribution from anesthesia, and a severe cerebellar hemorrhage, presumably from guidewire perforation. Other complications include retroperitoneal hemorrhage (n=2), femoral Pseudoaneurysm (n=5) and transient hearing loss (n=4). Recurrent stenosis, sometimes accompanied by a clinical relapse, was reported in a total of 35 patients (5.52%), 8 of whom developed recurrent in-stent stenosis and 27 of whom developed stent adjacent stenosis (SAS). Most received a new stent. Proposed risk factors predictive of recurrent adjacent stenosis include a higher opening pressure pre-stent, extrinsic stenosis and a failure of the venous pressure distal to the stenosis to decrease following stenting.

## Conclusion

The apparent efficacy and safety of venous stenting as a treatment for IIH is, to date, based on retrospective studies and two uncontrolled and un-blinded prospective studies, as well as its theoretical underpinnings. Available results must be looked at in that context, taking into account the placebo effect, lack of direct comparison with alternative surgical therapies, and possible under-reporting of complications when performed outside of a research protocol. Several planned prospective trials comparing stenting to shunting may offer more scientific evidence of its utility in medically-refractory IIH.

## REFERENCES

1. Wall M, George D. Idiopathic intracranial hypertension. A prospective study of 50 patients. *Brain J Neurol*;114 (Pt 1A):155-180, 1991
2. Thambisetty M, Lavin PJ, Newman NJ, Biousse V. Fulminant idiopathic intracranial hypertension. *Neurology*, 68(3):229-232, 2007
3. King JO, Mitchell PJ, Thomson KR, Tress BM. Cerebral venography and manometry in idiopathic intracranial hypertension. *Neurology*, 45(12):2224-2228, 1995
4. Farb RI, Vanek I, Scott JN, Mikulis DJ, Willinsky RA, Tomlinson G, terBrugge KG. Idiopathic intracranial hypertension: the prevalence and morphology of sinovenous stenosis. *Neurology*, 13;60(9):1418-24, 2003
5. Lublinsky S, Friedman A, Kesler A, Zur D, Anconina R, Shelef I. Automated Cross-Sectional Measurement Method of Intracranial Dural Venous Sinuses. *AJNR Am J Neuroradiol*, 37(3):468-74, 2016.
6. King JO, Mitchell PJ, Thomson KR, Tress BM. Manometry combined with cervical puncture in idiopathic intracranial hypertension. *Neurology*, 8;58(1):26-30, 2002.

7. Rohr A, Dörner L, Stingle R, Buhl R, Alfke K, Jansen O. Reversibility of venous sinus obstruction in idiopathic intracranial hypertension. *AJNR Am J Neuroradiol*, 28(4):656-9, 2007
8. Buell TJ, Raper DMS, Pomeranec IJ, Ding D, Chen CJ, Taylor DG, Liu KC. Transient resolution of venous sinus stenosis after high-volume lumbar puncture in a patient with idiopathic intracranial hypertension. *J Neurosurg*, 25:1-4, 2017
9. Bono F, Giliberto C, Mastrandrea C, Cristiano D, Lavano A, Fera F, Quattrone A. Transverse sinus stenoses persist after normalization of the CSF pressure in IIH. *Neurology*, 11;65(7):1090-3, 2005
10. De Simone R, Ranieri A, Montella S, Bilo L, Cautiero F. The role of dural sinus stenosis in idiopathic intracranial hypertension pathogenesis: the self-limiting venous collapse feedback-loop model. *Panminerva Med*, 56(3):201-9, 2014
11. Lazzaro MA, Darkhabani Z, Remler BF, Hong SH, Wolfe TJ, Zaidat OO, Fitzsimmons BF. Venous sinus pulsatility and the potential role of dural incompetence in idiopathic intracranial hypertension. *Neurosurgery*, 71(4):877-83, 2012
12. Raper DMS, Ding D, Buell TJ, Crowley RW, Starke RM, Liu KC. Effect of Body Mass Index on Venous Sinus Pressures in Idiopathic Intracranial Hypertension Patients Before and After Endovascular Stenting. *Neurosurgery*, Epub ahead of print, 2017
13. Higgins JN, Cousins C, Owler BK, Sarkies N, Pickard JD. Idiopathic intracranial hypertension: 12 cases treated by venous sinus stenting. *J Neurol Neurosurg Psychiatry*, 74(12):1662-6, 2003
14. Ahmed RM, Wilkinson M, Parker GD, Thurtell MJ, Macdonald J, McCluskey PJ, Allan R, Dunne V, Hanlon M, Owler BK, Halmagyi GM. Transverse sinus stenting for idiopathic intracranial hypertension: a review of 52 patients and of model predictions. *AJNR Am J Neuroradiol*, 32(8):1408-14, 2011
15. Dinkin MJ, Patsalides A. Venous Sinus Stenting in Idiopathic Intracranial Hypertension: Results of a Prospective Trial. *J Neuroophthalmol*, 37(2):113-121, 2017
16. Liu KC, Starke RM, Durst CR, Wang TR, Ding D, Crowley RW, Newman SA. Venous sinus stenting for reduction of intracranial pressure in IIH: a prospective pilot study. *J Neurosurg*, 23:1-8, 2016
17. Ahmed R, Friedman DI, Halmagyi GM. Stenting of the transverse sinuses in idiopathic intracranial hypertension. *J Neuroophthalmol*. 2011
18. *J Neuroophthalmol*. 2011
19. Lavoie P, Audet MÈ, Gariépy JL, Savard M, Verreault S, Gourdeau A, Milot G, Carrondo Cottin S. Severe cerebellar hemorrhage following transverse sinus stenting for idiopathic intracranial hypertension. *Interv Neuroradiol*. 2017
20. Goodwin CR, Elder BD, Ward A, Orkoulas-Razis D, Kosztowski TA, Hoffberger J, Moghekar A, Radvany M, Rigamonti D. Risk factors for failed transverse sinus stenting in pseudotumor cerebri patients. *Clin Neurol Neurosurg*, 127:75-8, 2014.
21. Kumpe DA, Seinfeld J, Huang X, Mei Q, Case DE, Roark CD, Subramanian PS, Lind KE, Pelak VS, Bennett JL. Dural sinus stenting for idiopathic intracranial hypertension: factors associated with hemodynamic failure and management with extended stenting. *J Neurointerv Surg*, 9(9):867-874, 2017
22. Raper D, Buell TJ, Ding D, Chen CJ, Starke RM, Liu KC. Pattern of pressure gradient alterations after venous sinus stenting for idiopathic intracranial hypertension predicts stent-adjacent stenosis: a proposed classification system. *J Neurointerv Surg*. Epub ahead of print, 2017
23. *J Neurointerv Surg*. Epub ahead of print, 2017
24. Chandran A, Pulhorn H, McMahan C. Idiopathic intracranial hypertension VISION (venous intervention versus shunting in IIH for optic nerve disc swelling) trial: patient perspective questionnaire. *Br J Neurosurg*. 2017 Sep 21:1-5.

## PATHOPHYSIOLOGY OF IIH AND THE IIHTT

Michael Wall, MD  
University of Iowa  
Iowa City, IA

### LEARNING OBJECTIVES

1. To understand what is known about the genetics of IIH
2. To know what has and what has not been investigated regarding sex hormones and IIH
3. To understand interactions of weight regulation hormones and their possible influence on IIH.

### CME QUESTIONS

1. There appears to be a genetic component to IIH (True or False)
2. The evidence from the IIHTT suggest there is no substantial link between vitamin A and the cause of IIH(True or False).
3. Steroid withdrawal is associated with intracranial hypertension (True or False).

### KEYWORDS (5 Max)

1. Idiopathic Intracranial Hypertension
2. Pseudotumor cerebri
3. Genetics

### HIGHLIGHTS

The cause of IIH has been elusive. In the IIHTT, 5% of subjects had a family member with IIH and an underpowered GWAS was inconclusive. A comprehensive vitamin A study was done in the IIHTT with negative results. Endocrine and sex hormone abnormalities have been sought in some small and poorly designed studies with no consistent abnormality found; the same conclusion holds for obesity hormones. While many causes of IIH have been suggested, none have been able to explain the predominance of the disease in obese females.

### SUMMARY

Genetics of IIH: 5% of subjects in the IIHTT had family members with IIH and there are many reports of families with multiple cases of IIH. A GWAS from the IIHTT<sup>1</sup> was limited by its modest size but suggested several variants and loci were that might be candidates for follow up studies. Three chromosomal regions were identified that each contain multiple SNPs, all at p-values between  $3 \times 10^{-7}$  and  $9 \times 10^{-6}$ . Loci on chromosomes 5, 13, and 14 were identified that were highly suggestive of association with IIH. Each of these loci contained multiple SNPs which strengthens support for true association of these regions despite the fact that genome wide statistical significance was not reached. The locus on chromosome 5 is not located in the vicinity of known genes, but those on chromosome 13 and 14 are located within the genes for LINC00359 and FOXN3, respectively. LINC00359 is a species of long non-coding RNA. While its precise function is not known, long non-coding RNAs are often involved in pre- and post-translational regulation of gene expression and may affect the activity of multiple genes.

FOXP3 is a forkhead family transcription factor with a role in craniofacial development and it is expressed in a variety of tissues including the brain. Variants in this gene have also been associated with altered fasting blood glucose and the regulation of glucose utilization by hepatocytes. Further studies with a larger sample size are needed.

Vitamin A IIHTT study: Vitamin A and its metabolites (retinoids) have been thought to play a role in the development of IIH. In the IIHTT we obtained measures of serum vitamin A and its metabolites from 96 IIHTT subjects, and 25 controls with similar gender, age and body mass index (BMI). These included retinol, retinol binding protein, all-trans retinoic acid (ATRA), alpha- and beta-carotenes, and beta-cryptoxanthin. The IIHTT subjects also had CSF and serum vitamin A and metabolite measurements obtained at study entry and at six months. At study entry, of the vitamin A metabolites, only serum ATRA was significantly different in IIHTT subjects (median 4.33 nM) and controls (median 5.04 nM,  $p=0.02$ ). The BMI of IIHTT subjects showed mild significant negative correlations with serum ATRA, alpha- and beta-carotene, and beta-cryptoxanthin. In contrast, the control subject BMI correlated only with serum ATRA. At six months, the serum retinol, alpha-carotene, betacarotene, and CSF retinol were increased from baseline in the acetazolamide treated group, but only increases in alpha carotene ( $p=0.02$ ) and CSF ATRA ( $p=0.04$ ) were significantly greater in the acetazolamide group compared with the placebo group. No other vitamin A measures were significantly altered. Weight loss correlated with only with the change in serum beta-carotene ( $r = -0.44$ ,  $p = 0.006$ ) and the change in CSF retinol ( $r = -0.61$ ,  $p = 0.02$ ). The study concluded vitamin A toxicity is unlikely a contributory factor in the causation of IIH.

IIHTT Metabolomics and hormone studies: Blood from IIHTT subjects is currently under analysis.

Endocrine associations: IIH has been reported in patients with chronic adrenal insufficiency and steroid withdrawal (not steroid use) but no consistent abnormalities in cortisol metabolism have been found. Papilledema has been associated with primary, secondary and pseudohypoparathyroidism. It is thought that hypocalcemia in patients with hypoparathyroidism may lead to an increase in intracellular sodium and water that in turn interferes with transport of CSF through the arachnoid granulations.

Sex Hormones: Studies of female and male hormones including estrogen, progesterone, FSH, LH, prolactin, androstenedione, estrone and estradiol have been conducted at various times during the subjects' course and during various stages of treatment. Blood and CSF have been examined. IIH patients showed increased CSF estrone levels and decreased CSF androstenedione levels – the significance of these findings is unclear as there were normal values of these parameters observed in plasma/ In summary, hormone surveys of IIH patients have not yielded a consistent abnormality. These hormones have not yet been studied in a careful and controlled way.

Obesity Hormones: Leptin, secreted by adipocytes, acts as a signaling factor regulating body weight homeostasis and energy balance. With forced weight gain, leptin levels increase while insulin, glucose and corticosteroid levels decrease; in an attempt to return weight to baseline with weight loss, leptin levels decrease. Therefore, defective production of the leptin protein may be one of the causes for development of obesity. The mean concentration of leptin in plasma of lean subjects is much lower than that of obese ones. In addition, leptin levels are three times greater in women than men! And leptin concentrations in CSF are strongly correlated to the plasma level. Lastly, leptin binding sites are found in leptomeninges and choroid plexus, the primary site of cerebrospinal fluid production. mRNA for the leptin receptor is expressed not only in the hypothalamus, but also in the choroid plexus. Since CSF pressure is a function of both secretion rate and absorption, leptin has been postulated to play a role. Weight loss might lower leptin levels resulting in decreased secretion of CSF and resultant reduction of CSF pressure. The kidney has been shown to express mRNA for the full length Ob-Rb leptin receptor. In

addition, leptin increases renal sodium and water excretion, apparently through a direct tubular action, suggesting leptin may exert functional effects to raise intracranial pressure. Leptin and related ghrelin levels in serum and CSF have not been conclusively shown to be different in IIH compared to controls.

Other purported causes of IIH that do not pass the filter: “There do not appear to be any differences between women and men.” are spinal meningeal compliance, glymphatic circulation through cranial nerve and spinal nerve root sheaths, and aquaporin.

#### **CME ANSWERS**

1. True
2. True
3. True

**REFERENCES** Wall M, McDermott MP, Kieburtz KD, et al. Effect of Acetazolamide on Visual Function in Patients with Idiopathic Intracranial Hypertension and Mild

## THURSDAY, MARCH 8

6:30 am - 7:30 am	Breakfast.....	Grand Promenade
6:30 am - 12:00 pm	Registration/Help Desk .....	Grand Promenade
7:30 am - 9:30 am	<b>Unexplained Visual Loss: You have some nerve sending me that patient!</b> .....	Grand Ballroom
	<i>Moderators: Joseph Rizzo, MD, Hong Jiang, MD, PhD</i>	

This session will provide a selection of cases that pertain to unexplained visual loss. The cases will demonstrate how varied and sometimes subtle these clinical presentations can be. The risk of misdiagnosis non-organic features will be addressed.

At the conclusion of this course, the attendees should be able to: 1) better identify subtle causes of blindness; 2) improve known inventory of disorders that can produce non-obvious causes of blindness and; 3) describe risks misdiagnosis non-organic visual loss.

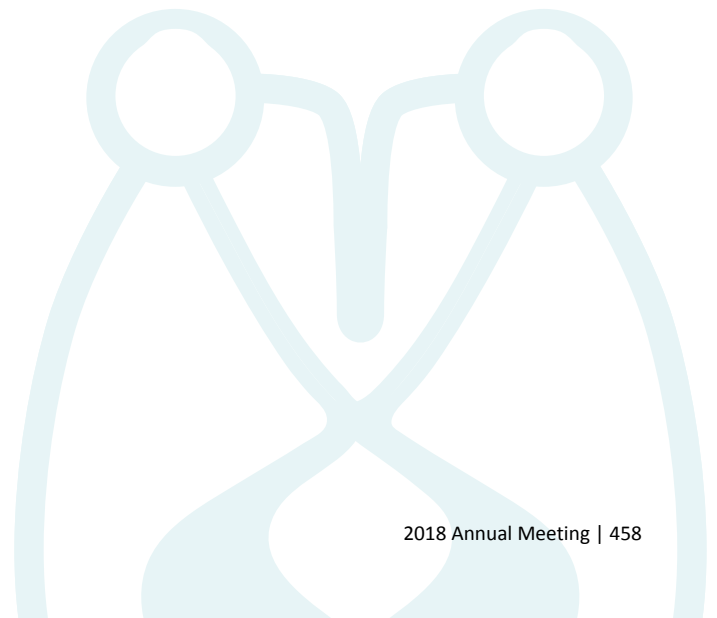
7:30 am - 7:50 am	<b>Anterior Segment Afflictions</b> , <i>Greg Kosmorsky, DO</i>
7:50 am - 8:10 am	<b>Posterior Segment Possibilities</b> , <i>Tariq Bhatti, MD</i>
8:10 am - 8:30 am	<b>Neurologic Visual Nuances</b> , <i>Jonathan Trobe, MD</i>
8:30 am - 9:20 am	<b>Case Presentation</b>
9:20 am - 9:30 am	<b>Q &amp; A</b>

9:30 am - 10:00 am	Coffee Break .....	Grand Promenade
10:00 am - 12:00 pm	<b>Eye Movement: Diagnostic &amp; Treatment Pearls for the Daily Clinic</b> .....	Grand Ballroom
	<i>Moderators: John Pula, MD, Matthew Thurtell, MBBS, MSc, FRACP</i>	

This session will involve the subject of eye movements and include a review of diagnostic and treatment pearls for the daily clinic. Orbital disorders, cerebellar disorders, and brainstem disorders will be discussed, with case studies to follow.

At the conclusion of this course, the attendees should be able to: 1) identify localized eye movement disorders; 2) create a different diagnosis in patients with eye movement problems and; 3) improve accuracy of treatments for patients with eye movement disorders.

10:00 am - 10:35 am	<b>Orbital Disorders</b> , <i>Joseph Demer, MD, PhD</i>
10:35 am - 11:10 am	<b>Brainstem Disorders</b> , <i>Dan Gold, MD</i>
11:10 am - 11:45 am	<b>Cerebellar Disorders</b> , <i>David Zee, MD</i>
11:45 am - 12:00 pm	<b>Q &amp; A</b>



## UNEXPLAINED VISUAL LOSS: YOU HAVE SOME NERVE SENDING ME THAT PATIENT!

### ANTERIOR SEGMENT AFFLICTIONS

Greg Kosmorsky, DO  
Cleveland Clinic Main Campus  
Cleveland, OH

#### LEARNING OBJECTIVES

1. The attendee will be able to understand the reason for diminished visual acuity when surface abnormalities of the cornea are present.
2. The attendee will be able to discern whether a lenticular abnormality or IOL complication could be the cause of the patient's visual problem.
3. The attendee will be able to discern if an abnormality in the shape of the cornea could be responsible for an abnormal visual perception.

#### CME QUESTIONS:

1. A patient presents with a history of slowly progressive, painless visual loss in the right eye over a one year period with no other neurologic symptoms. Which of the following is not a likely cause?
  - a. Nuclear sclerotic cataract
  - b. Keratoconus
  - c. Epithelial corneal edema
  - d. Posterior capsular opacification
  - e. None of the above
2. A 72 year old woman undergoes an uncomplicated phacoemulsification procedure in her left eye. She complains bitterly about a shadow in her temporal visual field since the procedure. A chiasmatic lesion has been excluded by a normal MRI of the brain. Which of the following is the most likely cause?
  - a. Decentered IOI
  - b. Posterior capsular opacification
  - c. Negative dysphotopsia
  - d. Insertion of a diffractive IOL
  - e. All of the above
3. A 35 year old woman notes progressive painless visual loss in her left eye greater than her right eye over the past year and has no neurologic symptoms other than menstrual migraines. What test(s) would be used to uncover corneal ectasia as the cause?
  - a. Retinoscopy
  - b. Topography
  - c. Orbscan
  - d. Slit lamp examination
  - e. All of the above

## KEY WORDS

1. Cataract
2. Keratoconus
3. Negative dysphotopsia
4. Posterior capsular opacification
5. Diffractive IOL

## HIGHLIGHTS

1. Surface abnormalities- in this section disorders such as ABMD (anterior basement membrane dystrophy), dry eyes, corneal scars, epithelial edema, etc. will be discussed with reference to their impact on light refraction and diffraction with subsequent light scatter resulting in subnormal visual acuity.
2. Corneal ectasia – Keratoconus and pellucid marginal degeneration cause irregular astigmatism that result in blur. These disorders are easily missed during a general eye exam and can result in referral to the neurophthalmologist. The use of the retinoscope and topography will be reviewed to uncover these disorders.
3. LASIK and other refractive procedures – When the geometry of the cornea is altered by these procedures, the optical effects are induced that can mimic neurologic disease.
4. Lenticular abnormalities- cataracts and other lens opacities can scatter light and lead to a poor focus in the eye resulting in diminished visual potential. These abnormalities can be missed or under-appreciated and thought to have a neurologic origin.
5. Pupillary abnormalities – Any deviation from a round pupil will cause undesirable optical effects that can be misinterpreted as neurologic disease due to the perceived blur.
6. Artificial intraocular lens (IOL's) – Although the vast majority of IOL's result in a substantial improvement in visual acuity certain complications may result in a degradation of acuity. Problems such as decentered IOL's, diffractive IOL's, IOL dysphotopsias and PCO (posterior capsular opacification) will be reviewed.

## SUMMARY:

Corneal surface abnormalities occur commonly and are a source of light scatter. The scattering of light results in abnormal focusing of light on the retina with poor image formation in the macula resulting in diminished visual acuity.(1) Further, since the cornea is responsible for 2/3 of the refractive power of the eye, even small abnormalities of the corneal surface can result in visual symptoms. Conditions like ABMD (anterior basement membrane dystrophy), corneal scars, epithelial edema and dry eye disrupt the light ray at the front surface of the cornea. In reality, the first place that light encounters the eye is not the corneal epithelium but rather the air/tear-film interface. This is why dry eye can have such a profound effect on vision, as dryness results in a change in shape of the epithelial cells (clinically seen as punctate epithelial erosions or PEE) and this change results in light scatter.(2) (3) ABMD is seen clinically in approximately 2% of the Caucasian population by electron microscopic studies reveal a true incidence of about 15%. ABMD (AKA map/dot/fingerprint dystrophy) is a reduplication of the epithelial cells that



create hills and valleys on the corneal surface and cause light scatter. (4) Additionally, ABMD can result in recurrent corneal erosions that produce pain and these lesions can be detected by anterior segment OCT.(5) Likewise, corneal scars cause light to scatter and can reduce visual acuity.

Treatment for these conditions is aimed at smoothing the corneal surface. In the case of dry eye artificial tears are a mainstay of therapy in an attempt to heal the epithelium and re-establish the normal shape of the epithelial surface. Given that dry eye has been shown to be secondary to a chronic low-grade inflammatory response in the tear producing cells, therapy with anti-inflammatory medications often proves to be helpful. Drugs like Restasis (cyclosporine) and Alrex (0.1% loteprednol) quell this inflammatory response and can have an ameliorating response on people with dry eyes.(6)

Treatment of ABMD and surface scars can be accomplished by using PTK (phototherapeutic keratectomy).(7, 8) PTK uses a laser to smooth the surface and requires the use of a masking agent (usually celluvisc) to fill in the valleys so the laser smooths the peaks to meet the valleys of the irregular corneal surface thereby smoothing the corneal surface. This technique can be used for any surface abnormality including superficial corneal scars and some corneal dystrophies.

An irregular geometry of the cornea results in rays of light not being focused properly on the macula. Disorders such as keratoconus (KCN) and pellucid marginal degeneration result from an abnormality of the tensile strength of the corneal collagenous matrix. This matrix is akin to a cable suspension bridge and is constituted of a series of overlapping cables that cross the cornea from one end of the corneal-scleral junction to the other. Deficiency of the tensile strength of these fibers causes the cornea to “sag” resulting in an abnormal corneal shape. Rather than having a regular geometry (the geometry of a sphere) the geometry is more like a breast where there is superior flattening and the majority of the tissue is inferiorly displaced. This abnormal geometry causes rays from a point source of light to be bent to variable regions on the retina resulting in a reduction in visual acuity and visual quality.(9) These disorders can be easily mistaken for neurologic disease when the cornea is not recognized as the problem, particularly when the process is early and subtle. Retinoscopy generally reveals a scissoring of the corneal reflex and is the first tool used when this condition is suspected. Corneal topography is vital in uncovering this group of disorders and usually shows inferior steepening. Corneal OCT can also reveal focal thinning of the cornea and aid in the diagnosis of KCN or other ectasias. Other tools such as a Pentacam can also assist with the diagnosis.(10) Lasik surgeons are always on the lookout for these disorders as performing LASIK further thins the cornea (to change its shape thereby changing the refraction) and performing LASIK in a keratoconic patient can induce post LASIK corneal ectasia, potentially requiring a corneal transplant.(11) Since the majority of the tensile strength of the cornea is anterior, LASIK can unmask the presence of ectasia. Newer methods of stabilizing the cornea include corneal cross-linking.(12) This methodology uses a photo-excited dimer that is activated by UV (ultraviolet) light to cross-link the abnormal collagen fibers that can “slide by” each other leading to the corneal ectasia. This newly approved therapy offers new hope for patients with corneal ectatic disorders to have more normal vision without resorting to a penetrating keratoplasty (corneal transplant).

Cataracts and other lens opacities can scatter light and lead to poor focus in the eye resulting in diminished visual potential.(13, 14) These abnormalities can be missed or under-appreciated and thought to have a neurologic origin. Cataracts are the most common cause of treatable blindness in the world. Aging is the most common pathology to induce a change in both the shape and the clarity of the crystalline lens. Many different sorts of cataracts have been documented, yet the optical result is always the same, that is, light is improperly refracted and scattered leading to a reduction in visual acuity and visual quality. Although the vast majority of cataracts can be easily identified and treated, more subtle

forms of cataract can be missed and the patient thought to have a neurologic problem. An “oil-drop” cataract is a form of nuclear sclerosis where the index of refraction of one portion of the lens is different than another and can result in rapid progression of myopia.(15) This difference in refractive power between adjacent regions of the natural lens results in light being bent differentially and therefore not coming to a clean focus on the macula. Because these differences can be subtle, they can easily be missed. The use of the retinoscope will reveal scissoring of the light reflex indicating abnormal refraction of light. Utilizing the slit lamp with a direct beam and looking for posterior scatter can reveal the central defect of the oil-drop cataract. Phacoemulsification is curative in these cases.

Posterior subcapsular cataracts (PSC) are much more common than an oil-drop cataract, but early on can certainly be overlooked and are often caused by steroid use.(16) The clue to a PSC is that this form of cataract tends to reduce near acuity out of proportion to distance acuity. This is because the focal point moves posteriorly to the back surface of the lens during accommodation causing the light rays to be more scattered while doing near tasks. In this situation, obtaining both the distance acuity and near acuity and noticing the discrepancy between distance vision and worse near vision is necessary to suggest the presence of the PSC.

Pupillary abnormalities can induce optical aberrations as any deviation from a round pupil will cause undesirable optical effects that can be misinterpreted as neurologic disease due to the perceived blur. In order for light to be regularly distributed on the retina it must pass through a regularly sized pupil.(17) Any deviation from a spherical shape of the iris will result in light rays being abnormally distributed on the retina resulting in decreased acuity and glare. The aperture of the iris is only somewhat relevant in that a very small iris aperture can reduce the overall amount of light reaching the retina and tends to reduce nighttime visual acuity. A very widely dilated pupil at night (as would be seen in an acute Adie’s tonic pupil or with dilating drops) will cause the light rays to not only pass through the central portion of the crystalline lens but also through the most peripheral parts of the lens that has a higher index of refraction. This optical effect increases the size of the conoid of Sturm and results in a myopic shift and glare. The size of the pupil is neurally adapted to the ambient lighting conditions in order to ameliorate these optical effects. Patients can perceive these changes as pathologic and be referred for neurophthalmic consultation. When a patient perceives an otherwise normal phenomenon as pathologic we refer to these perceptions as an entoptic phenomenon.

At times, the ophthalmologist will purposely induce an iris abnormality resulting in a second pupil effect. This procedure is termed an LPI (laser peripheral iridotomy) and is performed in patients with narrow angles in order to create an equalization of pressure between the anterior and posterior chambers of the eye and helping to allow the iris to “fall back” and away from the trabecular meshwork thereby reducing the risk of angle closure glaucoma. Recent studies have suggested that removal of the natural lens might be a more effective method to prevent angle closure glaucoma, but this procedure would be hard to justify in a younger patient with a clear lens. Performing an LPI causes light to not only enter through the normal pupillary aperture, but also through the LPI and this can result in significant night blur and glare as there are now two pupillary apertures (particularly in those with lids that are anatomically high and don’t block the opening).(18) Other disorders can also result in breaks or holes in the iris and these include the ICE (irido-corneal syndromes), trauma and cataract surgery (Phaco tip damage to the iris or severe iris prolapse during surgery) and others.

Although the vast majority of IOL’s (intraocular lenses) result in a substantial improvement in visual acuity certain complications may result in a degradation of acuity. Problems such as decentered IOL’s, side effects of diffractive IOL’s, IOL dysphotopsias and PCO (posterior capsular opacification) are known

to occur. Cataract surgery is the most performed surgery in the world, and on the whole results in miraculous restoration of vision. Quality indicators of surgical procedures have demonstrated that cataract surgery is the most appreciated surgical procedure in terms of patient satisfaction. However, complications of cataract surgery can result in reduced best-corrected visual acuity. The modern IOL (intraocular lens) is an aspheric implant that can exert the same power across its surface even when somewhat decentered. However, if there is zonular dehiscence or significant capsular contraction, the IOL can become so decentered that the original power of the IOL is no longer available and the light rays are no longer brought to focus on the macula resulting in decreased visual acuity.(19)

Diffractional IOL's are a technology that utilizes different curvatures at varying distances from the center of the IOL. These various curvatures are meant to create differing refractions from the central portion of the IOL and have the effect of allowing more myopic viewing. This technology does not produce a lot of near power (averaging only 1.5 diopters, and this isn't much different than the pseudoaccommodation produced by monofocal IOL's). Further, the "steps" cut into these IOL's result in diffractional effects that induce significant night glare in some people. Considering that one of the major complaints of patients with cataracts is night glare, some patients are very disturbed that it can be even worse, particularly if this potential side effect is not revealed preoperatively. This annoying symptom may go away on its own, but in a substantial minority of patients an explant of the diffractional IOL with an IOL exchange is needed. Also, because the central portion of the IOL is relatively small, decentration of a multifocal IOL can result in a substantial change in the visual results.(20)

In rare patients a refractive scotoma, referred to as a negative dysphotopsia is recognized after cataract surgery. The exact mechanism of this scotoma is unknown but it is believed to be the result of light rays being differentially bent between the edge of the IOL and the aphakic region at the termination of the IOL. This can result in a peripheral visual field defect and be referred for neurologic evaluation. Another potential cause can be anterior capsular fibrosis and some patients appear to have had their abnormal perception cured by doing a YAG laser of the anterior capsule.(21, 22)

PCO (posterior capsular opacification) is very common postoperative sequelae of cataract surgery. Although usually easily recognized by the ophthalmologist it is occasionally very difficult to fully appreciate how badly the scarring of the posterior capsule can affect the best-corrected visual acuity. YAG laser of the offending posterior capsule can result in a rapid improvement of blurred vision induced by the scarring of the posterior capsule.(23)

## **CME ANSWERS**

1. C
2. C
3. E

## **REFERENCES:**

1. van der Mooren M, Rosen R, Franssen L, Lundstrom L, Piers P. Degradation of Visual Performance With Increasing Levels of Retinal Stray Light. *Investigative ophthalmology & visual science*. 2016 Oct 01;57(13):5443-8. PubMed PMID: 27760270.
2. Baudouin C. The pathology of dry eye. *Survey of ophthalmology*. 2001 Mar;45 Suppl 2:S211-20. PubMed PMID: 11587145.

3. Koh S. Mechanisms of Visual Disturbance in Dry Eye. *Cornea*. 2016 Nov;35 Suppl 1:S83-S8. PubMed PMID: 27583799.
4. Klintworth GK. Corneal dystrophies. *Orphanet journal of rare diseases*. 2009 Feb 23;4:7. PubMed PMID: 19236704. Pubmed Central PMCID: 2695576.
5. Diez-Feijoo E, Duran JA. Optical coherence tomography findings in recurrent corneal erosion syndrome. *Cornea*. 2015 Mar;34(3):290-5. PubMed PMID: 25532997.
6. Al-Saedi Z, Zimmerman A, Bachu RD, Dey S, Shah Z, Baugh R, et al. Dry Eye Disease: Present Challenges in the Management and Future Trends. *Current pharmaceutical design*. 2016;22(28):4470-90. PubMed PMID: 27296759.
7. Fagerholm P. Phototherapeutic keratectomy: 12 years of experience. *Acta ophthalmologica Scandinavica*. 2003 Feb;81(1):19-32. PubMed PMID: 12631015.
8. Dedes W, Faes L, Schipper I, Bachmann LM, Thiel MA. Phototherapeutic keratectomy (PTK) for treatment of recurrent corneal erosion: Correlation between etiology and prognosis - prospective longitudinal study. *Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie*. 2015 Oct;253(10):1745-9. PubMed PMID: 25900814.
9. Mas Tur V, MacGregor C, Jayaswal R, O'Brart D, Maycock N. A review of keratoconus: Diagnosis, pathophysiology, and genetics. *Survey of ophthalmology*. 2017 Jul 06. PubMed PMID: 28688894.
10. Martinez-Abad A, Pinero DP. New perspectives on the detection and progression of keratoconus. *Journal of cataract and refractive surgery*. 2017 Sep;43(9):1213-27. PubMed PMID: 28991620.
11. Santhiago MR, Giacomini NT, Smadja D, Bechara SJ. Ectasia risk factors in refractive surgery. *Clinical ophthalmology*. 2016;10:713-20. PubMed PMID: 27143849. Pubmed Central PMCID: 4844427.
12. Kobashi H, Rong SS. Corneal Collagen Cross-Linking for Keratoconus: Systematic Review. *BioMed research international*. 2017;2017:8145651. PubMed PMID: 28691035. Pubmed Central PMCID: 5485290.
13. Sharma KK, Santhoshkumar P. Lens aging: effects of crystallins. *Biochimica et biophysica acta*. 2009 Oct;1790(10):1095-108. PubMed PMID: 19463898. Pubmed Central PMCID: 2743770.
14. Gholami S, Reus NJ, van den Berg T. Changes in Intraocular Straylight and Visual Acuity with Age in Cataracts of Different Morphologies. *Journal of ophthalmology*. 2017;2017:5649532. PubMed PMID: 28831307. Pubmed Central PMCID: 5554999.
15. Hodges JS, Marcus S, Page E. It's not a tumor, it's a cataract! rapid myopic progression and diplopia secondary to the formation of an oil-drop cataract. *Military medicine*. 2013 Mar;178(3):e372-5. PubMed PMID: 23707128.
16. James ER. The etiology of steroid cataract. *Journal of ocular pharmacology and therapeutics : the official journal of the Association for Ocular Pharmacology and Therapeutics*. 2007 Oct;23(5):403-20. PubMed PMID: 17900234.
17. Franssen L, Taberner J, Coppens JE, van den Berg TJ. Pupil size and retinal straylight in the normal eye. *Investigative ophthalmology & visual science*. 2007 May;48(5):2375-82. PubMed PMID: 17460305.
18. Congdon N, Yan X, Friedman DS, Foster PJ, van den Berg TJ, Peng M, et al. Visual symptoms and retinal straylight after laser peripheral iridotomy: the Zhongshan Angle-Closure Prevention Trial. *Ophthalmology*. 2012 Jul;119(7):1375-82. PubMed PMID: 22424576.
19. Ortiz C, Esteve-Taboada JJ, Belda-Salmeron L, Monsalvez-Romin D, Dominguez-Vicent A. Effect of Decentration on the Optical Quality of Two Intraocular Lenses. *Optometry and vision science : official publication of the American Academy of Optometry*. 2016 Dec;93(12):1552-9. PubMed PMID: 27776082.

20. Maurino V, Allan BD, Rubin GS, Bunce C, Xing W, Findl O, et al. Quality of vision after bilateral multifocal intraocular lens implantation: a randomized trial--AT LISA 809M versus AcrySof ReSTOR SN6AD1. *Ophthalmology*. 2015 Apr;122(4):700-10. PubMed PMID: 25537197.
21. Geneva, II, Henderson BA. The Complexities of Negative Dysphotopsia. *Asia-Pacific journal of ophthalmology*. 2017 Jul-Aug;6(4):364-71. PubMed PMID: 28726357.
22. Safran SG. Negative dysphotopsia: A persistent problem. *Journal of cataract and refractive surgery*. 2017 Feb;43(2):300-1. PubMed PMID: 28366382.
23. Wormstone IM, Wang L, Liu CS. Posterior capsule opacification. *Experimental eye research*. 2009 Feb;88(2):257-69. PubMed PMID: 19013456.

## Posterior Segment Possibilities

M. Tariq Bhatti, MD  
Duke Eye Center and Duke University Medical Center  
Durham, North Carolina

### LEARNING OBJECTIVES

1. The audience will be able to list the various clinical examination findings that differentiate an optic neuropathy from a maculopathy
2. The audience will be able to describe the clinical and paraclinical manifestations of a variety of retinal disorders that can present with a normal or near normal fundus examination
3. The audience will be able to understand and interpret the various ancillary tests to identify retinal dysfunction

### CME QUESTIONS

1. Ocular lipofuscin is derived from which of the following retinal cells?
  - a. Müller
  - b. Photoreceptor
  - c. Ganglion
  - d. Retinal pigment epithelium
2. What percentage of patients develops macular edema due to fingolimod?
  - a. 0.5
  - b. 1.5
  - c. 5
  - d. 10
3. Which of the following processes is the presumed pathogenesis of acute macular neuroretinopathy?
  - a. Vascular
  - b. Inflammatory
  - c. Infectious
  - d. Traumatic

### KEYWORDS (5 Max)

1. Unexplained visual loss
2. Fundus autofluorescence
3. Acute macular neuroretinopathy
4. Macular edema
5. Autoimmune retinopathy

### HIGHLIGHTS

Unexplained visual loss or visual loss in the setting of a normal fundus examination is a frequent clinical dilemma faced by the ophthalmologist. Often it is believed by the referring physician that the cause of the visual loss is due to a retrobulbar optic neuropathy prompting referral to a neuro-ophthalmologist. Some of these patients may have been previously seen by a retina specialist expressing the opinion that

there is no maculopathy or retinopathy, without performing the appropriate clinical and paraclinical testing or appreciating subtle clinical findings. This presentation will focus on retinal-macular causes of visual loss that present with a “normal fundus examination”, specifically, autoimmune retinopathy (AIR), acute macular neuroretinopathy (AMNR) and macular edema; with a special emphasis-- using a case based approach-- on the results and interpretation of ancillary tests that may not be part of the routine neuro-ophthalmic examination and unfamiliar to the neuro-ophthalmologist.

## SUMMARY

As tabled by Zacks and D’Amico a variety of retinal diseases can mimic optic neuropathies including vitreomacular traction syndrome, macular edema, macular holes, retinal dystrophies and degenerations, inflammatory choroidopathies, and autoimmune retinopathies.<sup>1</sup> It is important to appreciate that these diseases may not be apparent on a routine neuro-ophthalmic examination requiring additional testing and a focused examination of the macula. For example, a prolonged photostress test suggests a maculopathy<sup>2</sup> or a positive Watzke-Allen sign-- performed by shining a straight light beam onto the fovea region--suggests an anatomical disruption of the macula.<sup>3</sup> In terms of paraclinical testing, spectral domain-optical coherence tomography (SD-OCT) of the macula can provide valuable information regarding the anatomical status of the various layers of the retina and vitreous-retina interface.<sup>4</sup> Fundus autofluorescence, which relies on the accumulation of lipofuscin within the retinal pigment epithelial cells from the outer segments of the photoreceptor cells, can be very helpful in demonstrating retinal disease that otherwise may not be apparent on fundoscopic examination.<sup>5</sup> Electrophysiological testing with either full field electroretinogram (ERG) or multifocal ERG can provide objective evidence of retinal dysfunction.<sup>6,7</sup> Intravenous fluorescein angiography (IVFA) can expose retinal vascular abnormalities.<sup>8,9</sup>

## AUTOIMMUNE RETINOPATHY

Due to its rarity, clinical heterogeneity, absence of definitive clinical criteria and non-standardized laboratory testing AIR can be very challenging to diagnose.<sup>10</sup> AIR is divided into paraneoplastic (pAIR) and non-paraneoplastic (npAIR) depending on whether there is an underlying malignancy or not. AIR is believed to be an inflammatory disorder due to autoantibody induced apoptosis involving the caspase 3-dependent pathway.<sup>11</sup> Based on multiparametric flow cytometry results, there appears to be a faulty maturation process of B cells resulting in a higher population of naïve B cells and a lower frequency of switched memory B cells and plasmablasts in AIR patients.<sup>12</sup> A variety of antiretinal antibodies have been associated with AIR.<sup>13,14</sup> The presence of antiretinal antibodies does not confirm the diagnosis of AIR because they can be found in healthy individuals and in other inflammatory and degenerative retinal disorders.<sup>13,15</sup> In addition, there is no standardized system to detect these antibodies. In a study comparing the results between two different laboratories, the concordance rate of detecting antibodies was only 36%.<sup>16</sup> The only clinical laboratory improvement amendments (CLIA)- certified laboratory that performs testing for antiretinal antibodies is at the Ocular Immunology Laboratory at the Casey Eye Institute at the Oregon Health & Science University (<http://www.ohsu.edu/xd/health/services/casey-eye/diagnostic-services/ocular-immunology-lab/index.cfm>). Most experts recommend a 2-tier assay system that includes Western blot, immunohistochemistry or enzyme-linked immunosorbent assay with confirmation by a second laboratory.<sup>14,17</sup> The clinical presentation of AIR can be variable but in general patient presents with painless, rapid, progressive, bilateral visual dysfunction (visual loss and visual field deficits), photopsias and hemeralopia, nyctalopia or both.<sup>18</sup> Based on a consensus from an expert panel of 17 specialists, the five essential diagnostic criteria are<sup>17</sup>:

1. No apparent cause of visual loss from another disease
2. Abnormal ERG

3. Presence of antiretinal antibodies
4. No fundus lesions, retinal degeneration or retinal dystrophy to explain visual loss
5. No uveitis

The treatment of AIR is very challenging and unfortunately to date there have been no randomized controlled trials executed. Corticosteroids and “conventional” immunosuppressive agents are first line treatment modalities.<sup>17</sup> A recently published prospective, interventional case series showed modest positive results with rituximab. Of the 28 eyes (16 patients) treated, 4 eyes (14%) improved, 19 eyes (63%) stabilized and 7 eyes (23%) worsened. The 4 eyes that improved received either rituximab alone or rituximab with mycophenolate mofetil with an interval time from diagnosis to treatment of 4 and 7 months.<sup>19</sup>

### **ACUTE MACULAR NEURORETINOPATHY**

AMNR is a rare retinal disorder presumed to be vascular in etiology involving the deep retinal capillary plexus. Bhavsar et al performed a comprehensive review of the literature involving 156 eyes in 101 patients in which some common themes emerged in terms of cause, demographics, clinical characteristics, multimodality imaging findings and visual outcomes.<sup>20</sup> AMNR preferentially affects woman with a mean age of presentation of 29 years. In nearly half of cases, a flu-like illness or fever has been reported. The most common medication associated with AMNR are vasopressors such as epinephrine or ephedrine. Visual loss is bilateral in just over 50% of cases with nearly 75% of patients experiencing a visual scotoma (corresponding to a paracentral scotoma on formal visual field testing). Clinically, the characteristic macular findings have been described as reddish-brown or orange in color, wedge-shaped lesions with the apex pointing toward the fovea. IVFA is often normal. Multifocal ERG is more sensitive than full field ERG in detecting electrophysiological changes. SD-OCT demonstrates abnormalities of the outer retinal layers (e.g. ellipsoid zone, outer nuclear layer and outer plexiform layer).

Paracentral acute middle maculopathy (PAMM) is either a variant of AMNR or a distinct disease from AMNR with overlapping features.<sup>21,22</sup> First described in 2013, PAMM lesions are more superficially (at the junction of the outer plexiform and outer nuclear layers) located compared to AMNR lesions. On OCT the hyperreflective signal changes are seen as a band at the level of the inner nuclear layer, sparing the outer retina.<sup>22</sup> A retrospective observational case series of 9 patients suggests retinal vascular ischemia occurs either at the level of the superficial capillary plexus or deep capillary plexus, resulting in lesions appearing in the inner or outer portions of the inner nuclear layer, respectively.<sup>21</sup>

### **MACULAR EDEMA**

Macular edema is a very common ophthalmic problem frequently seen in the setting of intraocular surgery, retinal vascular disease, infections, systemic disease, uveitis and medications.<sup>23,24</sup> Macular edema is often managed by the retina specialist but with the approval of fingolimod (Gilenya™, Novartis Pharma AG, Stein, Switzerland) in 2010 for relapsing forms of multiple sclerosis (MS); neuro-ophthalmologist need to be more aware of the clinical features of macular edema. All patients are required to undergo a baseline eye examination with a follow-up examination 3 to 4 months after initiating therapy.<sup>25</sup>

Macular edema occurs from a disruption in the blood-ocular barrier involving the retinal capillary system resulting in the collection of extracellular fluid within the outer plexiform and inner nuclear layers.<sup>24,26</sup>



The diagnosis can often be made with a focused clinical examination of the macula but in mild situations SD-OCT or IVFA may be required.

Approximately 0.5% of patients taking 0.5 mg daily of fingolimod will develop macular edema. Interestingly in the package insert, the frequency of macular edema in MS patients not taking fingolimod was 0.4% (<https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/gilenya.pdf>). In the FTY720 Research Evaluating Effects of Daily Oral Therapy in MS (FREEDOMS) 2 trial, macular edema was seen in 3 (1%) patients in the 0.5 mg fingolimod group and 2 (1%) patients in the placebo group.<sup>27</sup>

The vast majority of fingolimod associated macular edema cases resolve with discontinuation of the medication.<sup>28</sup> However, several case reports have described successful treatment of the macular edema with intravitreal or sub-Tenon steroid injections, topical non-steroidal anti-inflammatory drugs, and acetazolamide.<sup>29-32</sup>

### CME ANSWERS

1. B
2. A
3. A

### REFERENCES

1. Zacks DN, D'Amico DJ. Maculopathies that resemble optic neuropathies. *Int Ophthalmol Clin* 2001; **41**(1): 61-71.
2. Glaser JS, Savino PJ, Summers KD, McDonald SA, Knighton RW. The photostress recovery test in the clinical assessment of visual function. *Am J Ophthalmol* 1977; **83**(2): 255-60.
3. Watzke RC, Allen L. Subjective slitbeam sign for macular disease. *Am J Ophthalmol* 1969; **68**(3): 449-53.
4. Wolf S, Wolf-Schnurrbusch U. Spectral-domain optical coherence tomography use in macular diseases: a review. *Ophthalmologica* 2010; **224**(6): 333-40.
5. Yung M, Klufas MA, Sarraf D. Clinical applications of fundus autofluorescence in retinal disease. *Int J Retina Vitreous* 2016; **2**: 12.
6. Hedges TR, 3rd, Quireza ML. Multifocal visual evoked potential, multifocal electroretinography, and optical coherence tomography in the diagnosis of subclinical loss of vision. *Ophthalmol Clin North Am* 2004; **17**(1): 89-105.
7. Yap GH, Chen LY, Png R, et al. Clinical value of electrophysiology in determining the diagnosis of visual dysfunction in neuro-ophthalmology patients. *Doc Ophthalmol* 2015; **131**(3): 189-96.
8. Yannuzzi LA, Ober MD, Slakter JS, et al. Ophthalmic fundus imaging: today and beyond. *Am J Ophthalmol* 2004; **137**(3): 511-24.
9. Rizzo JF, 3rd. Occult retinal and choroidal vascular disease. The value of timed and directed fluorescein angiography. *Ophthalmology* 1993; **100**(9): 1407-16.
10. Rahimy E, Sarraf D. Paraneoplastic and non-paraneoplastic retinopathy and optic neuropathy: evaluation and management. *Surv Ophthalmol* 2013; **58**(5): 430-58.
11. Adamus G. Autoantibody-induced apoptosis as a possible mechanism of autoimmune retinopathy. *Autoimmun Rev* 2003; **2**(2): 63-8.
12. Stansky E, Biancotto A, Dagur PK, et al. B Cell Anomalies in Autoimmune Retinopathy (AIR). *Invest Ophthalmol Vis Sci* 2017; **58**(9): 3600-7.

13. Grange L, Dalal M, Nussenblatt RB, Sen HN. Autoimmune retinopathy. *Am J Ophthalmol* 2014; **157**(2): 266-72 e1.
14. Grewal DS, Fishman GA, Jampol LM. Autoimmune retinopathy and antiretinal antibodies: a review. *Retina* 2014; **34**(5): 827-45.
15. Shimazaki K, Jirawuthiworavong GV, Heckenlively JR, Gordon LK. Frequency of anti-retinal antibodies in normal human serum. *J Neuroophthalmol* 2008; **28**(1): 5-11.
16. Faez S, Loewenstein JI, Sobrin L. Detection of antiretinal autoantibodies in serum by Western blotting--reply. *JAMA Ophthalmol* 2013; **131**(10): 1371-2.
17. Fox AR, Gordon LK, Heckenlively JR, et al. Consensus on the Diagnosis and Management of Nonparaneoplastic Autoimmune Retinopathy Using a Modified Delphi Approach. *Am J Ophthalmol* 2016; **168**: 183-90.
18. Braithwaite T, Holder GE, Lee RW, Plant GT, Tufail A. Diagnostic features of the autoimmune retinopathies. *Autoimmun Rev* 2014; **13**(4-5): 534-8.
19. Davoudi S, Ebrahimiadib N, Yasa C, et al. Outcomes in Autoimmune Retinopathy Patients Treated With Rituximab. *Am J Ophthalmol* 2017.
20. Bhavsar KV, Lin S, Rahimy E, et al. Acute macular neuroretinopathy: A comprehensive review of the literature. *Surv Ophthalmol* 2016; **61**(5): 538-65.
21. Sarraf D, Rahimy E, Fawzi AA, et al. Paracentral acute middle maculopathy: a new variant of acute macular neuroretinopathy associated with retinal capillary ischemia. *JAMA Ophthalmol* 2013; **131**(10): 1275-87.
22. Rahimy E, Kuehlewein L, Sadda SR, Sarraf D. Paracentral Acute Middle Maculopathy: What We Knew Then and What We Know Now. *Retina* 2015; **35**(10): 1921-30.
23. Makri OE, Georgalas I, Georgakopoulos CD. Drug-induced macular edema. *Drugs* 2013; **73**(8): 789-802.
24. Scholl S, Kirchhof J, Augustin AJ. Pathophysiology of macular edema. *Ophthalmologica* 2010; **224** **Suppl 1**: 8-15.
25. Jain N, Bhatti MT. Fingolimod-associated macular edema: incidence, detection, and management. *Neurology* 2012; **78**(9): 672-80.
26. Hosoya K, Tomi M. Advances in the cell biology of transport via the inner blood-retinal barrier: establishment of cell lines and transport functions. *Biol Pharm Bull* 2005; **28**(1): 1-8.
27. Calabresi PA, Radue EW, Goodin D, et al. Safety and efficacy of fingolimod in patients with relapsing-remitting multiple sclerosis (FREEDOMS II): a double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet Neurol* 2014; **13**(6): 545-56.
28. Zarbin MA, Jampol LM, Jager RD, et al. Ophthalmic evaluations in clinical studies of fingolimod (FTY720) in multiple sclerosis. *Ophthalmology* 2013; **120**(7): 1432-9.
29. Thoo S, Cugati S, Lee A, Chen C. Successful treatment of fingolimod-associated macular edema with intravitreal triamcinolone with continued fingolimod use. *Mult Scler* 2015; **21**(2): 249-51.
30. Minuk A, Belliveau MJ, Almeida DR, Dorrepaal SJ, Gale JS. Fingolimod-associated macular edema: resolution by sub-tenon injection of triamcinolone with continued fingolimod use. *JAMA Ophthalmol* 2013; **131**(6): 802-4.
31. Chui J, Herkes GK, Chang A. Management of fingolimod-associated macular edema. *JAMA Ophthalmol* 2013; **131**(5): 694-6.
32. Schroder K, Finis D, Harmel J, et al. Acetazolamide therapy in a case of fingolimod-associated macular edema: early benefits and long-term limitations. *Mult Scler Relat Disord* 2015; **4**(5): 406-8.

## NEUROLOGICAL VISUAL NUANCES

Jonathan Trobe, MD  
University of Michigan  
Ann Arbor, MI

### LEARNING OBJECTIVES:

1. Become acquainted with unexplained causes of retrobulbar vision loss.
2. Become acquainted with MRI-negative causes of retrobulbar vision loss.
3. Become acquainted with diagnostic and therapeutic management of these entities.

### CME QUESTIONS:

1. What is the likelihood that high quality MRI will show no pertinent abnormalities of the optic nerve in acute optic neuritis?
2. Can patients with hypoxic ischemic encephalopathy (HIE) have cortical vision loss without other neurologic deficits?
3. Can patients with HIE have normal MRI when the study is performed within 1 week of clinical onset?

### KEY WORDS:

1. Homonymous hemianopia
2. Unexplained retrobulbar vision loss
3. MRI

### SUMMARY:

Neuro-ophthalmologists are often confronted with patients who have subnormal visual function, yet they have normal pupillary reactions and no structural abnormalities on ophthalmoscopy or ocular imaging. Is there a retrobulbar lesion or is this psychogenic vision loss? To make this distinction, we depend mightily on retrobulbar imaging—especially MRI. It will not often fail us. But there are 12 conditions in which it might...

1. Optic neuritis. In active optic neuritis, we expect enhancement within the affected optic nerve. With high quality MRI, sensitivity has been 94% (1), 96% (2) and 97% (3). But an unpublished series from the University of Michigan showed only 84% sensitivity. So MRI in this situation is very good, but not perfect! If the optic neuritis is over 1 month old, the affected optic nerve may not show enhancement, but it should show (sometimes subtle) high T2 signal, even if visual recovery has been clinically “complete.” An afferent pupil defect is a helpful clue, but it will not be present if both optic nerves have been affected equally. This issue becomes more trenchant when a patient previously afflicted with optic neuritis in one eye returns later with new vision loss in the contralateral eye. The afferent pupil defect from the previous event is still present. Does the patient have new contralateral optic neuritis, even if MRI fails to show enhancement? Or is this psychogenic vision loss?
2. Optic tract lesions. Imaging abnormalities here may be subtle and frequently overlooked—even by experienced neuroradiologists. Why? Because the optic tract is a relatively small white matter structure wedged between two parenchymal structures--the temporal lobe and the midbrain. It is not outlined by spinal fluid, which limits its conspicuity. It travels obliquely in and out of the standard axial, coronal, or sagittal planes of MR imaging, so only a tiny segment is

ever visualized. One study (4) showed that two experienced neuroradiologists independently reviewing MRIs, and notified that the patients had optic tract lesions, uniformly failed to identify abnormally high or low intrinsic T2/ FLAIR signal, thinning, thickening, or enhancement. The causative lesions were mostly inflammation, trauma, and stroke. I vividly recall a patient who had developed a complete homonymous hemianopia after head injury in a motorcycle accident. Initial review of the brain MRI was declared “negative.” I diagnosed malingering. But a second review disclosed thinning of the affected optic tract, which is prone to contusion in traumatic brain injury (5). (The afferent pupil defect, usually present in complete homonymous hemianopia of optic tract origin, would have been a clinical clue to an optic tract lesion.)

3. Lateral geniculate body (LGB) lesions. Lesions here are extremely rare. Usually bilateral, they occur in pre-eclampsia, systemic hypotension, viral encephalitis, and rapid electrolyte correction (“osmotic demyelination,” “myelinolysis”)(6, 7). MRI typically shows signal abnormalities consistent with hemorrhagic infarction or demyelination. The layering of white and gray matter in the LGB, which resembles the anatomy of the pons, may render it vulnerable to disorders that also affect the pons.
4. Hypoxic-ischemic encephalopathy (HIE) affecting visual cortex. A 16 year old boy in a car crash suffered asystole and systemic hypotension. Three days after cardiac resuscitation, he regained consciousness and declared “I cannot see.” Visual acuity was 20/20 in each eye. Six days later, Humphrey visual fields were severely constricted without clear hemianopic features. Brain MRI performed 11 days after the accident showed no pertinent abnormalities (8). He recovered all neurologic function but the visual fields remained constricted. Was this psychogenic? At 6 months after the event, MRI finally demonstrated brain volume loss in primary visual cortex! I have subsequently encountered several patients with HIE who have had clinical and imaging abnormalities limited to visual cortex. In some, the imaging abnormalities have been absent at outset, appearing only months later as atrophy (9). Thus, HIE is unlike vaso-occlusive stroke of the visual cortex, which always shows obvious MRI abnormalities at outset. The ischemia in HIE is evidently mild enough to cause marked functional loss but not enough structural loss to produce restricted diffusion or high T2/FLAIR abnormalities. Volume loss appears later.
5. Visual variant Alzheimer disease (AD). In this variant of AD, visuospatial and even visual recognition deficits are well recognized. But there is also ample documentation of retrogeniculate visual field loss, sometimes affecting one hemifield much more than the other, suggesting a homonymous hemianopia (10). Patients may appear cognitively intact, so the diagnosis is delayed. MRI often shows posterior hemispheric volume loss, but sometimes it is subtle or obscured by generalized volume loss. Positron emission tomography confirms the diagnosis by showing reduced uptake in occipital regions.
6. Heidenhain variant of Creutzfeldt-Jakob disease. In this variant of prion disease, cortical visual field defects are present, sometimes as isolated manifestations. As the field defects are often bilateral, localization may not be apparent. Visual acuity may be degraded. MRI shows diffuse cerebral cortical (and sometimes basal ganglionic) restricted diffusion--but not always, and not obviously (11). The relatively pathognomonic electroencephalographic periodic sharp waves are not always present early.
7. Ictal and post-ictal cortical vision loss. Cortical vision loss occurs rarely during and after seizures, more in children than adults. Positive phenomena are much more likely, often underlying a

persistent homonymous hemianopia associated with a structural lesion visible on MRI. Temporary cortical blindness without positive phenomena has also been reported in partial occipital seizures with a normal brain CT (12). I have encountered a case in which high definition MRI was normal. Clinical clues to ictal blindness may be contralateral head and eye deviation, as well as contralateral tonic/clonic movements. Without these clues, diagnosis may be elusive, as performing EEG during the episodes is rarely feasible. Post-ictal blindness, like Todd's paralysis, lasts no more than a few hours. Whether undiagnosed or uncontrolled persistent visual cortical seizures leads to permanent blindness is unsettled.

8. Non-ketotic hyperglycemic (hyperosmolar) visual cortex dysfunction. This phenomenon is rare (I have seen only one case). The visual field loss is a unilateral or bilateral homonymous hemianopia (13). The idea is that the hyperglycemia draws water out of the visual cortical cells, rendering them nonfunctional. MRI may be normal or show subtle low T2/FLAIR signal in the affected cortex, reflecting intracellular dehydration. Vision loss rapidly reverses with correction of hyperglycemia.
9. Status migrainosus. This entity reflects continuous migraine, lasting hours to days. When visual cortex is affected, the patient experiences continuous scintillations, which block vision. Treatment involves intravenous propranolol or valproate.
10. Concussive head trauma. Concussive head trauma can cause temporary retrogeniculate blindness with normal MRI, especially in children and young adults. It is probably a variant of post-concussive migraine (14).
11. Focal visual cortical encephalitis. Focal visual cortical encephalitis (aka "cerebritis"), often idiopathic or associated with connective tissue disease, can produce homonymous hemianopia. The MRI findings-- enhancement and high T2/FLAIR abnormalities—are often subtle and evanescent. I will show an example.
12. Delayed visual maturation. This term applies to children in the first year of life who appear to have progressed normally in brain function but cannot see. They have no clinical signs of ocular or anterior visual pathway disorders or any contributory systemic disorders. Brain MRI is normal. By definition, they eventually develop normal vision. One study (15) disclosed normal visual evoked potentials, giving rise to the theory that the problem is extrastriate, perhaps an attentional or visuospatial deficit. The young children I have examined with retrogeniculate vision impairment have all had profound global cerebral cognitive deficits. If delayed visual maturation exists as an isolated cortical maturational impairment, it must be extremely rare.

#### **CME ANSWERS:**

1. Reports give a range of 5% to 30%. The higher number may derive from including patients with inflammation confined to the prelaminar optic disc (papillitis) or those whose scans are technically subpar.
2. Yes. HIE can cause isolated, or relatively isolated, damage to the primary visual cortex, as evidenced clinically and on MRI.
3. Yes. Even in the presence of substantial cortical vision loss, MRI performed within one week of clinical onset may not show any abnormalities, even on diffusion-weighted imaging. Proof that the visual cortex is the site of vision loss may be delayed for several weeks until gyral atrophy

appears on follow-up MRI. Radiologists, even neuroradiologists, do not usually look closely at the primary visual cortex area in cases of HIE because it is not considered a traditional "watershed zone"--but it should be!

#### REFERENCES:

1. Kupersmith MJ, Alban T, Zeiffer B, et al. Contrast-enhanced MRI in acute optic neuritis: relationship to visual performance. *Brain*. 2002; 125:812–822.
2. Hickman SJ, Toozy AT, Miszkial KA et al. Visual recovery following acute optic neuritis: a clinical, electrophysiological and magnetic resonance imaging study. *J Neurol*. 2004; 251:996-1005.
3. Rizzo JF, Andreoli CM and Rabinov JD. Use of magnetic resonance imaging to differentiate optic neuritis and nonarteritic anterior ischemic optic neuropathy. *Ophthalmology*. 2002; 109:1679-1684.
4. Kowal KM, Rivas Rodriguez FF, Srinivasan A, et al. Spectrum of magnetic resonance imaging features in unilateral optic tract dysfunction. *J Neuroophthalmol*. 2017;37:17-23.
5. Lindenbergh R, Walsh FB, Sacks J. *Neuropathology of Vision: An Atlas*. Philadelphia, Lea & Febiger, 1973.
6. Breker DA, Stacey AW, Srinivasan A, et al. Vision Loss Caused by Retinal and Lateral Geniculate Nucleus Infarction in H1N1 Influenza. *J Neuroophthalmol*. 2015;35:265-269.
7. Stem MS, Fahim A, Trobe JD, et al. Lateral geniculate lesions causing reversible blindness in a pre-eclamptic patient with a variant of posterior reversible encephalopathy syndrome. *J Neuroophthalmol*. 2014;34:372-376.
8. Margolin E, Gujar SK, Trobe JD. Isolated cortical visual loss with subtle brain MRI abnormalities in a case of hypoxic-ischemic encephalopathy. *J Neuroophthalmology* 2007;27:292-296.
9. Parmar HA, Trobe JD. Hypoxic-ischemic encephalopathy with clinical and imaging abnormalities limited to occipital lobe. *J Neuroophthalmol*. Jun 10 2016 [Epub ahead of print]. <http://dx.doi.org/10.1097/wno.0000000000000380>
10. Lee AG, Martin CO. Neuro-ophthalmic findings in the visual variant of Alzheimer disease. *Ophthalmology*. 2004;111:376-380.
11. Kropp S, Schulz-Schaeffer WJ, Finkenstaedt M, et al. The Heidenhain variant of Creutzfeldt-Jakob disease. *Arch Neurol*. 1999; 56:55-61.
12. Aldrich MS, Vanderzant CW, Alessi AG, et al. Ictal cortical blindness with permanent visual loss. *Epilepsia*. 1989;30:116-20.
13. Lavin PJ. Hyperglycemic hemianopia: A reversible complication of nonketotic hyperglycemia. *Neurology*. 2005;65:616–619.
14. Harrison DW, Walls RM. Blindness following minor head trauma in children: a report of two cases with a review of the literature. *J Emerg Med*. 1990;8:21-24.
15. Harris CM, Kriss A, Shawkat F, et al. Delayed visual maturation in infants: a disorder of figure—ground separation? *Brain Research Bull*. 1996;40:365-369.

## ORBITAL DISORDERS

Joseph L. Demer, MD, PhD  
Stein Eye Institute and Department of Neurology  
University of California, Los Angeles

### LEARNING OBJECTIVES

1. The attendee will be able to describe the way in which orbital connective tissue degeneration can pathologically induce oblique pulling directions for the rectus extraocular muscles.
2. The attendee will be able to distinguish the clinical findings and mechanism of age-related distance esotropia in sagging eye syndrome, from abducens palsy.
3. The attendee will be able to describe mechanisms and clinical presentations of compartmental lateral rectus and superior oblique muscle palsies.

### CME QUESTIONS

1. Which extraocular muscle(s) are NOT known to exhibit differential compartmental function and susceptibility to pathological denervation? (There may be more than one answer.)
  - a. Inferior rectus
  - b. Lateral rectus
  - c. Medial rectus
  - d. Superior oblique
  - e. Superior rectus
2. A middle-aged patient presents with gradually progressive esotropia and hypotropia in a unilateral, highly myopic eye, but has no other evidence of thyroid ophthalmopathy. Which statement(s) about orbital imaging features is correct in distinguishing an orbital connective tissue cause of this strabismus from a neuropathic cause? (There may be more than one answer.)
  - a. Atrophy of extraocular muscles indicates chronic denervation.
  - b. Inferior and nasal displacement of the lateral rectus muscle suggests heavy eye syndrome.
  - c. Hypertrophy of the LR-SR band ligament muscle suggests sagging eye syndrome.
  - d. Lateral and inferior displacement of the lateral rectus muscle is typical of sagging eye syndrome.
3. Which statement about acquired vertical strabismus in adults is true?
  - a. The three-step test is highly specific for superior oblique palsy.
  - b. The three-step test is highly sensitive for superior oblique palsy.
  - c. The hypertropic eye in sagging eye syndrome is usually also excyclotropic.
  - d. The hypertropic eye in unilateral superior oblique palsy is usually also excyclotropic.

### KEYWORDS

1. Age-related distance esotropia
2. Compartmental extraocular muscle palsy
3. Heavy eye syndrome
4. Sagging eye syndrome

## HIGHLIGHTS

Connective tissue structures called pulleys determine the pulling directions of the extraocular muscles (EOMs). While the horizontal rectus pulley suspensions “sag” inferiorly by a modest amount as a part of normal aging, accelerated degeneration or rupture of the LR-SR band ligament can gradually or suddenly imbalance lateral rectus (LR) muscle action by inferiorly and laterally displacing LR path and pulling direction. This is called the sagging eye syndrome (SES).” When LR sag is symmetrical, age-related distance esotropia (ARDE) results in horizontal diplopia for far viewing only. When asymmetrical, there is often cyclovertical strabismus causing vertical diplopia. Neither of these common forms of acquired diplopia has a neurological origin, and this mechanical cause of diplopia can readily be suspected based upon typical adnexal features of tissue laxity, including aponeurotic blepharoptosis, superior sulcus defect, floppy lids, and history of blepharoplasty. Excyclotropia is typically greater in the hypotropic eye in SES, in contrast the hypertropic eye in superior oblique (SO) palsy. Further etiological workup may be omitted when these features are present in an older adult, absent specific alternative signs such as saccade slowing, fluctuation of ptosis or alignment, proptosis, orbital congestion, or neurological signs. Strabismus in SES may be treated using spectacle prisms or strabismus surgery. An augmented dose of medial rectus recession is necessary to treat ARDE since EOMs are elongated in this condition.

Heavy eye syndrome (HES) consists of large angle esotropia and ipsilateral hypotropia with axial high myopia. While the LR-SR band ligament is degenerated in HES, the LR path shifts inferonasally as the entire globe shifts superotemporally in the orbit. HES requires unconventional surgical correction.

Most extraocular muscles (EOMs) consist of two mechanically independent, transverse compartments with separate peripheral innervation and separate functional behaviors demonstrable by functional MRI. Not uncommonly, lesions of the ocular motor cranial nerves predominantly or exclusively impair only one compartment of an individual EOM. The SO has medial and lateral compartments specialized for incycloadduction and infraduction, respectively, and innervated by separate trochlear nerve branches. Compartmental SO palsy is common and may underlie the heterogeneity of clinical presentation. The LR superior compartment is more vulnerable to neuropathic denervation than the inferior compartment, which is often relatively spared in LR paresis. Recognition of possible selective compartmental EOM pathology in paralytic strabismus can clarify diagnoses and provide a rational basis for selective strabismus surgical treatments of diplopia.

## SUMMARY

Acquired diplopia may be due to non-neurological connective tissue degeneration altering EOM pulling directions, or to neuropathic weakness of only a portion of an individual EOM.

## CME ANSWERS

1. E
2. A, B, and D
3. D

## REFERENCES

1. Demer, J. L. Current concepts of mechanical and neural factors in ocular motility. *Cur. Opin. Neurol.* 19: 4-13, 2006.
2. Chaudhuri, Z. and Demer, J. L. Sagging eye syndrome: Connective tissue involution causes horizontal and vertical strabismus in older patients. *JAMA Ophthalmol.* 131: 619-625, 2013.
3. Peragallo, J. H., Pineles, S. L., and Demer, J. L. Recent advances clarifying the etiologies of strabismus. *J. Neuroophthalmol.* 35: 198-193, 2015.



4. Clark, R. A. and Demer, J. L. Lateral rectus superior compartment palsy. *Am. J. Ophthalmol.* 157: 479-487, 2014.
5. Shin, S. Y. and Demer, J. L. Superior oblique extraocular muscle shape in superior oblique palsy. *Am. J. Ophthalmol.* 159: 1169-1179, 2015.
6. Le, A., Poukens, V., Ying, H., Rootman, D., Goldberg, R. A., and Demer, J. L. Compartmental innervation of the superior oblique muscle in mammals. *Invest. Ophthalm. Vis. Sci.* 56: 6237-6246, 2015.
7. Tan, R. J. and Demer, J. L. Heavy eye syndrome versus sagging eye syndrome in high myopia. *J. AAPOS*, 19: 500-506, 2015.
8. Le, A., Poukens, V., Ying, H., Rootman, D., Goldberg, R. A., and Demer, J. L. Compartmental innervation of the superior oblique muscle in mammals. *Invest. Ophthalm. Vis. Sci.* 56: 6237-6246, 2015.
9. Suh, S. Y., Clark, R. A., Le, A., and Demer, J. L. Extraocular muscle compartments in superior oblique palsy. *Invest. Ophthalmol. Vis. Sci.* 57: 5535-5540, 2016.

## **BRAINSTEM DISORDERS**

**Daniel Gold, DO**

**Division of Neuro-Visual & Vestibular Disorders**

**Assistant Professor of Neurology, Ophthalmology, Neurosurgery, Otolaryngology - Head & Neck Surgery**

**Director, Vestibular & Ocular Motor Oto-Neurology Fellowship**

**Director, Urgent Neurology**

**The Johns Hopkins Hospital**

**Baltimore, MD**

### **LEARNING OBJECTIVES**

1. The attendee will be able to correctly perform bedside maneuvers to elicit different types of brainstem related ocular motor disorders.
2. The attendee will be able to localize various patterns of eye movement disorders to particular parts of the brainstem
3. The attendee will be able to know which drugs might be used to treat different types of brainstem ocular motor disorders.

### **CME QUESTIONS**

1. A patient presents with acute prolonged vertigo, and is found to have a right Horner's syndrome, and ocular lateropulsion to the right – which of the following associated signs are most likely to be seen?
  - a. Left hypertropia ; ocular counterroll towards the left ear ; right head tilt
  - b. Left hypotropia ; ocular counterroll towards the left ear ; left head tilt
  - c. Left hypertropia ; ocular counterroll towards the right ear ; right head tilt
  - d. Left hypotropia ; ocular counterroll towards the right ear ; left head tilt
2. With an acute right medial longitudinal fasciculus lesion, which is the most common pattern of nystagmus?
  - a. Torsional nystagmus beating towards the right ear; upbeat nystagmus mainly in the left eye
  - b. Torsional nystagmus beating towards the right ear ; downbeat nystagmus mainly in the right eye
  - c. Torsional nystagmus beating towards the left ear ; upbeat nystagmus mainly in the right eye
  - d. Torsional nystagmus beating towards the left ear ; downbeat nystagmus mainly in the left eye
3. What is the typical pattern of head impulse testing in a right medial longitudinal fasciculus lesion?
  - a. Abnormal HIT in the planes of the right posterior and anterior canals
  - b. Abnormal HIT in the planes of the right posterior and horizontal canals
  - c. Abnormal HIT in the planes of the left posterior and horizontal canals
  - d. Abnormal HIT in the plane of the left posterior canal only

## KEYWORDS

1. Nystagmus
2. Medulla
3. Medial longitudinal fasciculus
4. Ocular tilt reaction
5. Saccadic dysmetria

## HIGHLIGHTS

### Brainstem

- 1) The anatomy – Key anatomy that will be discussed: lateral medulla including vestibular nucleus and inferior cerebellar peduncle ; inferior olive and central tegmental tract ; medial longitudinal fasciculus
- 2) The physiology – *lateral medulla* – will discuss the circuitry involved in ipsilesional ocular lateropulsion and saccadic dysmetria in the lateral medullary syndrome, and the physiology underlying the ipsiversive ocular tilt reaction in the lateral medullary syndrome ; *medial longitudinal fasciculus* – will discuss the vestibular pathways (semicircular canal and utricular-ocular motor) that, when damaged, cause characteristic patterns of dissociated vertical-torsional nystagmus and contraversive ocular tilt reaction
- 3) The clinical disorders – the lateral medullary (Wallenberg) syndrome – ipsilesional ocular lateropulsion and saccadic hypermetria and contralesional saccadic hypometria, contra- > ipsilesional spontaneous nystagmus and ipsiversive ocular tilt reaction ; MLF syndrome – contraversive ocular tilt reaction, ipsiversive torsional nystagmus with contralesional upbeat nystagmus (most common pattern)

## CME ANSWERS

1. C
2. A
3. D

## REFERENCES

Leigh, RJ, Zee, DS, The Neurology of Eye Movements, Edition 5, Oxford University Press, 2015

## CEREBELLAR DISORDERS:DIAGNOSIS AND TREATMENT

David S. Zee, MD  
Johns Hopkins School of Medicine  
Baltimore, MD

### LEARNING OBJECTIVES

1. The attendee will be able to correctly perform bedside maneuvers to elicit different types of cerebellar related ocular motor disorders.
2. The attendee will be able to localize various patterns of eye movement disorders to particular parts of the cerebellum
3. The attendee will be able to know which drugs might be used to treat different types of cerebellar ocular motor disorders.

### CME QUESTIONS

1. The combination of gaze-evoked, rebound and downbeat nystagmus most likely points to a lesion in the
  - a. Cerebellar nodulus
  - b. Cerebellar uvula
  - c. Cerebellar vermis
  - d. Cerebellar flocculus/paraflocculus
2. If a patient has impaired pursuit but normal VOR suppression one can assume that the head impulse test will show a (an)
  - a. Increased response
  - b. Decreased response
  - c. Normal response
  - d. Not able to tell
3. Impaired tilt suppression in a patient with an acute vestibular syndrome points to a
  - a. Peripheral lesion
  - b. Central lesion
  - c. Is of no help as could be either
  - d. Shortened VOR time constant when the body is rotated with the head upright

### KEYWORDS

1. Nystagmus
2. Flocculus
3. Dorsal vermis
4. Nodulus
5. Fastigial oculomotor region

## **SUMMARY**

### **Cerebellum**

- 1) The anatomy -- Three key areas: flocculus/paraflocculus (tonsil); nodulus/ventral uvula; dorsal vermis/posterior fastigial nucleus (FOR, fastigial oculomotor region);
- 2) The physiology – flocculus/paraflocculus – primarily image stabilization on fovea so pursuit and VOR suppression, and holding gaze steady; control amplitude and direction of high-frequency (head impulse) VOR responses; nodulus/ventral uvula – for vestibular responses especially duration of vestibular responses (low-frequency responses); dorsal vermis/FOR – saccade accuracy.
- 3) The clinical disorders – flocculus/paraflocculus – impaired gaze holding including gaze-evoked, rebound and downbeat nystagmus, impaired pursuit and vor suppression; nodulus/ventral uvula – prolonged VOR responses, impaired tilt suppression of post-rotatory nystagmus, periodic alternating nystagmus, abnormal positional nystagmus (downbeat, apogeotropic direction-changing horizontal nystagmus, pure torsional)
- 4) The treatments: 4-aminopyridine and baclofen

## **CME ANSWERS**

1. D
2. B
3. B

## **REFERENCES**

Leigh, RJ, Zee, DS, The Neurology of Eye Movements, Edition 5, Oxford University Press, 2015

# SOCIAL FUNCTIONS

## SATURDAY, MARCH 3

### Opening Reception – Lanai

6:00 pm - 7:30 pm

Please join us for the Opening Reception out on the lanai! All are welcome to attend the opening reception, which features complimentary cocktails and hors d'oeuvres.

## SUNDAY, MARCH 4

### Members-in-Training Reception – Lanai

6:00 pm - 7:00 pm

New to Neuro-Ophthalmology? All students, residents and fellows-in-training are encouraged to attend!

## TUESDAY, MARCH 6

### Afternoon Excursions

**\*Prior registration required for all excursions except for the Dolphin Quest. Dolphin Quest Registration is subject to availability.**



### Whale Watching

#### **(Pre-Meeting Registration Required)**

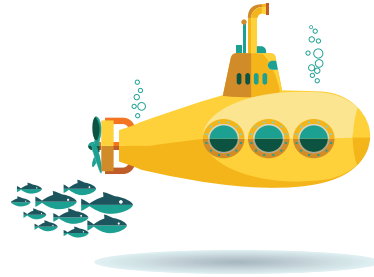
This is the experience of a lifetime. Each winter the Pacific Humpback whales migrate long distance from polar waters to tropical winter breeding grounds near Hawaiian Islands for mating and to bear their young. After the calf is born, the mother will remain close to shore, resting and nursing her young. An underwater hydrophone will allow you to hear the whales as they sing and the on board marine naturalists can answer any questions.

**Tour Includes:** Round trip transfer, 2 hour cruise, open bar, appetizers, delicatessen style lunch buffet, tropical juices and soft drinks, and Whale Naturalist.

Notes: Wear casual boat attire, sensible shoes, a light weight jacket and hat. Please note guest will get wet up to their knees -shorts are advised. Bring your camera.

#### **Timing:**

1:30 pm - Hotel pick up at Hilton Lower Lobby  
2:30 pm - 4:30 pm - Whale Watch Catamaran Sail Departures  
A-Bay & Mauna Lani Bay -- Boats will meet up on tour.  
5:00 pm - Estimated Return to Hotel



### Submarine Tour

#### **(Pre-Meeting Registration Required)**

The journey aboard the high-tech Atlantis submarine will travel 100 feet below the surface for a captivating experience through Kona's natural undersea world of endemic fish and coral reefs. As featured in National Geographic television specials, guests will explore a 25-acre natural coral reef! The spacious, air-conditioned submarine offers extra-large viewing ports to easily observe the changes as you descend. The viewing adventure continues as you rise to the surface and shuttle back to Kailua Pier.

**Tour Includes:** Shuttle boat ride from the pier to the submarine site, plus ferry transfer to submarine, which is 10 minutes each way. Actual underwater tour time is 45 minutes.

Notes: Bring sunglasses, sunscreen, camera & a light jacket. Close toe walking shoes & long pants are advised.

**\*\*Restrictions:** Passengers must be physically capable of ascending and descending a near vertical ladder unassisted in order to ride the sub. Children must be 36" or taller to ride the submarine.

#### **Timing:**

12:30 pm - Hotel pick up  
1:30 pm - Drop off at Kailua Pier  
2:00 pm - Check in Time at King Kamehameha Hotel (30 minutes before tour time)  
2:30 - 3:30 pm - Submarine Tour  
3:45 pm - Depart Kona  
4:45 pm - Hotel Return

### Shuttle To Kona

#### **(Pre-Meeting Registration Required)**

Not interested in a tour but want to get out and about?

Hop on a shuttle to Kailua Town! The shuttle will pick you up at the Hilton Waikoloa Village at 12:00 pm and drop you off at Kailua Town to explore on your own, then board the return shuttle to be back to the hotel by 5:00 pm for the Poster Reception.



## WEDNESDAY, MARCH 7

### Annual NANOS Reception and Banquet

6:30 pm – 12:00 am

Join colleagues for a fun, casual evening of socializing, dining and a little hula at the NANOS Annual Banquet! Dinner will take place in the Grand Promenade/Lanai, and the dance will proceed in the Kohala Ballroom. This event is complimentary for registered attendees; guests must purchase tickets for \$100 per person.

## FRIDAY, MARCH 9

### Friday Excursions



#### Volcano Tour

##### *(Pre-Meeting Registration Required)*

During this Volcano National Park tour, our guide will reveal the highlights of Hawaii Volcanoes National Park as you discover rare flora and fauna through the short and leisurely hikes in the rainforest and Thurston Lava Tube. We will also visit Kilauea Iki Lookout, steam vents, historic Jaggar Museum, and witness the explosive power of Halemaumau Crater.

**Tour Includes:** Round-trip Kohala Coast hotel transportation, all admission/entrance fees and expert narration. Time is included for a no-host lunch stop at The Crater Rim Restaurant for the guest to purchase lunch on own.

**Notes:** Bring your own water bottle! Wear sturdy, closed-toe shoes as this tour traverses sharp, uneven lava surfaces. Fumes (volcanic gasses) are hazardous to everyone's health. We discourage visitors with heart or breathing problems and infants, young children, and pregnant women are especially at risk and should avoid being in areas where fumes persist. All passengers are required to sign a waiver.

##### Timing:

- 8:30 am - Hotel pick up
- 8:30 - 10:30 am - Drive to Volcano National Park
- 10:30 - 11:00 am - Visitor Center
- 11:15 - 12:15 pm - Kilauea Iki Crater & Thurston Lava Tube
- 12:30 - 1:30 pm - No-Host Lunch at Crater Rim
- 1:45 - 2:30 pm - Jaggar Museum
- 2:30 - 4:30 pm - Drive back to Hotel
- 4:30 pm - Hotel return

#### Snorkeling Tour

##### *(Pre-Meeting Registration Required)*

This luxury catamaran departs from 'Aeāho'omalū Bay which is located at the Waikoloa Resort or from Kawaihae Harbor depending on weather. 'Aeāho'omalū Bay departures board on the beach through the surf and guests may get wet up to their knees. This Snorkel Adventure Sail will take you to the BEST pristine reefs on the coast (we have more than a dozen sites to choose from). You will start with an onboard marine life briefing and snorkel lesson.

**Tour Includes:** 3.5 hr sail includes round trip transfer, yogurt, pastries, Hawaiian juices, deli style lunch spread with salads, chips/salsa, and cookies, all snorkel gear with instruction and alcoholic beverages after snorkeling. The boats are equipped with Marine rest rooms.

**Notes:** Guests should wear swim suit under shorts and shirt, bring towels, sunglasses, sunscreen and cameras. Shoes will be left on the beach.

##### Timing:

- 9:55 am - Hotel pick up
- 10:00 am - Check in Time
- 10:30 am - 2:00 pm - Tour
- 2:15 pm - Hotel Return



#### Dolphin Quest

##### *Based on availability*

Space is limited, email Tulia Ferguson at [ferguson@dolphinquest.com](mailto:ferguson@dolphinquest.com) or call her at 808-647-4774. Her office hours are Monday-Friday, 8:30AM-4:30PM HST.

**Dolphin Encounter** - \$218.75 This 30-minute Dolphin Encounter program is designed for guests ten (10) years of age and older (guests 10 and younger to be accompanied by a paying parent or guardian 18 years of age or older). You'll love this intimate dolphin swim full of your favorite dolphin touch, feed and play activities. Swim alongside dolphins and enjoy above-water and below water views. Each encounter is unique, fun and always extraordinary. You will interact in small groups of no more than 6 guests and your trainer.



**Encounter Deluxe** - \$276.04 This 45-minute Dolphin Encounter Deluxe program is designed for guests five (5) years of age and older. Looking for a premium dolphin adventure that features maximum togetherness and fun? You'll fall in love at first sight with amazing dolphins in this combination shallow and deep-water dolphin swim experience, where touching a dolphin will touch your heart forever. This intimate swim supreme is full of dolphin touch, feed and play activities. Each encounter is unique, fun and always extraordinary. You will interact in small groups of no more than 6 guests and your trainer.





# Save the Dates

## FUTURE NANOS MEETINGS:



2019

45TH ANNUAL MEETING

# NANOS

Red Rock Casino, Resort & Spa,  
Las Vegas, Nevada



March 16-21,  
2019

See You There!



2020

46TH ANNUAL MEETING

# NANOS

Omni Hotels & Resorts,  
Amelia Island, Florida



March 7-12,  
2020

Don't Miss It!

For More Information:

[www.nanosweb.org](http://www.nanosweb.org)

