Pediatric Ophthalmology 2015

Golden Nuggets of Knowledge

Program Directors
Daniel E Neely MD and R Michael Siatkowski MD

In conjunction with the American Association for Pediatric Ophthalmology and Strabismus and the American Academy of Pediatrics

Sands Expo/Venetian
Las Vegas, Nevada
Saturday, Nov. 14, 2015

Presented by:
The American Academy of Ophthalmology
2015 Pediatric Ophthalmology
Subspecialty Day Planning Group

On behalf of the American Academy of Ophthalmology, the American Association for Pediatric Ophthalmology and Strabismus (AAPOS), and the American Academy of Pediatrics (AAP), it is our pleasure to welcome you to Las Vegas and Pediatric Ophthalmology 2015: Golden Nuggets of Knowledge.

Daniel E Neely MD
Program Director
Infacare Pharmaceuticals: C
Orbis International: C

R Michael Siatkowski MD
Program Director
National Eye Institute: S

Oscar A Cruz MD
None

Jane C Edmond MD
Alcon Laboratories, Inc.: L

Daniel J Karr MD
None

Sean P Donahue MD
Retrophin Inc.: C

Laura B Enyedi MD
Pediatric Eye Disease Investigator Group: S
Research to Prevent Blindness: S

David A Plager MD
Alcon Laboratories, Inc.: S
Bausch + Lomb: S
Omeros Corp.: C, S
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CME Credit

Academy’s CME Mission Statement
The purpose of the American Academy of Ophthalmology’s Continuing Medical Education (CME) program is to present ophthalmologists with the highest quality lifelong learning opportunities that promote improvement and change in physician practices, performance, or competence, thus enabling such physicians to maintain or improve the competence and professional performance needed to provide the best possible eye care for their patients.

2015 Pediatric Ophthalmology Subspecialty Day Meeting Learning Objectives
Upon completion of this activity, participants should be able to:
- Evaluate new disease entities, practices, technologies, and treatment that may change current practice
- Plan the surgical treatment of complex strabismus in adults and children
- Prepare for unexpected surgical outcomes and learn how to successfully manage them when they occur
- Apply current treatment strategies for retinoblastoma that increasingly emphasize preservation of vision
- Assess and correctly diagnose challenging ocular motility cases through pattern recognition
- Recognize the controversy surrounding the roles of telemedicine and anti-VEGF agents in ROP management

2015 Pediatric Ophthalmology Subspecialty Day Meeting Target Audience
The intended target audience for this program is pediatric ophthalmologists, comprehensive ophthalmologists, medical professionals, visual physiologists, and orthoptists who are involved in maintaining high-quality health care for the pediatric and strabismus populations.

2015 Pediatric Ophthalmology Subspecialty Day Meeting CME Credit
The American Academy of Ophthalmology is accredited by the Accreditation Council for Continuing Medical Education to provide CME for physicians.

The American Academy of Ophthalmology designates this live activity for a maximum of 7 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Teaching at a Live Activity
Teaching instruction courses or delivering a scientific paper or poster is not an AMA PRA Category 1 Credit™ activity and should not be included when calculating your total AMA PRA Category 1 Credits™. Presenters may claim AMA PRA Category 1 Credits™ through the American Medical Association.

Please contact the AMA to obtain an application form at www.ama-assn.org.

Scientific Integrity and Disclosure of Financial Interest
The American Academy of Ophthalmology is committed to ensuring that all CME information is based on the application of research findings and the implementation of evidence-based medicine. It seeks to promote balance, objectivity, and absence of commercial bias in its content. All persons in a position to control the content of this activity must disclose any and all financial interest. The Academy has mechanisms in place to resolve all conflicts of interest prior to an educational activity being delivered to the learners.

The Academy requires all presenters to disclose on their first slide whether they have any financial interests from the past 12 months. Presenters are required to verbally disclose any financial interests that specifically pertain to their presentation.

Attendance Verification for CME Reporting
Before processing your requests for CME credit, the Academy must verify your attendance at Subspecialty Day and/or AAO 2015. In order to be verified for CME or auditing purposes, you must either:
- Register in advance, receive materials in the mail, and turn in the Final Program and/or Subspecialty Day Syllabus exchange voucher(s) onsite;
- Register in advance and pick up your badge onsite if materials did not arrive before you traveled to the meeting;
- Register onsite; or
- Scan the barcode on your badge as you enter an AAO 2015 course or session room.

CME Credit Reporting
Level 2: Academy Resource Center, Hall B – Booth 2632
Attendees whose attendance has been verified (see above) at AAO 2015 can claim their CME credit online during the meeting. Registrants will receive an email during the meeting with the link and instructions on how to claim credit.

Onsite, you may report credits earned during Subspecialty Day and/or AAO 2015 at the CME Credit Reporting booth. The Academy transcript cannot list individual course attendance. It will list only the overall credits spent in educational activities at Subspecialty Day and/or AAO 2015.

NOTE: CME credits must be reported by Jan. 13, 2016. After AAO 2015, credits can be claimed at www.aao.org.

Academy Members: The Academy transcript cannot list individual course attendance. It will list only the overall credits spent in educational activities at Subspecialty Day and/or AAO 2015.

Nonmembers: The Academy will provide nonmembers with verification of credits earned and reported for a single Academy-
sponsored CME activity, but it does not provide CME credit transcripts. To obtain a printed record of your credits, you must report your CME credits onsite at the CME Credit Reporting booths.

**Proof of Attendance**

The following types of attendance verification will be available during AAO 2015 and Subspecialty Day for those who need it for reimbursement or hospital privileges, or for nonmembers who need it to report CME credit:

- CME credit reporting/proof-of-attendance letters
- Onsite registration receipt
- Instruction course and session verification

Visit www.aao.org for detailed CME reporting information.
Faculty

David H Abramson MD FACS
New York, NY
Chief, Ophthalmic Oncology Service
Memorial Sloan Kettering Cancer Center
Professor of Ophthalmology
Weill Cornell University

Michael C Brodsky MD
Rochester, MN
Professor of Ophthalmology and Neurology
Mayo Clinic

Antonio Capone Jr MD
Royal Oak, MI
Professor of Ophthalmology
William Beaumont Hospital - Oakland
University School of Medicine
Copresident / Partner / Owner
Associated Retinal Consultants

Mark S Borchert MD
Los Angeles, CA
Associate Director
The Vision Center at Children’s Hospital Los Angeles
Associate Professor of Ophthalmology
Keck School of Medicine
University of Southern California

Edward G Buckley MD
Durham, NC
Banks Anderson Sr. Professor of Ophthalmology and Pediatrics
Duke University
Vice Dean for Education
Duke School of Medicine

Yasmin Bradfield MD
Madison, WI
Associate Professor
Department of Ophthalmology and Visual Sciences
University of Wisconsin

Keith D Carter MD FACS
Iowa City, IA

R V Paul Chan MD
Chicago, IL
Professor and Vice Chair of Ophthalmology
Illinois Eye and Ear Infirmary
University of Illinois at Chicago

Hilda Capo MD
Miami, FL
Professor of Clinical Ophthalmology
Bascom Palmer Eye Institute
University of Miami Miller School of Medicine
Kenneth Paul Cheng MD
Wexford, PA
Clinical Instructor of Ophthalmology
University of Pittsburgh School of Medicine

Alex Christoff CO
Towson, MD
Assistant Professor of Ophthalmology
The Wilmer Eye Institute at Johns Hopkins Hospital
Certified Orthoptist
American Association of Certified Orthoptists

Monte A Del Monte MD
Ann Arbor, MI
Skillman Professor of Pediatric Ophthalmology
Professor of Pediatrics
University of Michigan
Director of Pediatric Ophthalmology and Adult Strabismus
W K Kellogg Eye Center and Mott Children’s Hospital

Michael F Chiang MD
Portland, OR
Knowles Professor of Ophthalmology & Medical Informatics
Oregon Health & Science University

David K Coats MD
Houston, TX
Professor of Ophthalmology and Pediatrics
Baylor College of Medicine
Department Chief
Pediatric Ophthalmology
Texas Children’s Hospital

Sean P Donahue MD PhD
Nashville, TN
Professor of Ophthalmology, Neurology, and Pediatrics
Vanderbilt University Medical Center
Chief of Pediatric Ophthalmology
Vanderbilt Children’s Hospital

Stephen P Christiansen MD
Boston, MA
Professor of Ophthalmology and Pediatrics
Chairman, Department of Ophthalmology
Boston University School of Medicine

Oscar Alfredo Cruz MD
Saint Louis, MO
Anwar Shah Endowed Chair, Professor, and Chairman
Department of Ophthalmology
Saint Louis University

Jane C Edmond MD
Houston, TX
Associate Professor
Department of Ophthalmology and Pediatrics
Baylor College of Medicine
Mays A El-Dairi MD  
Durham, NC  
Assistant Professor  
Duke Eye Center  

Laura B Enyedi MD  
Durham, NC  
Associate Professor of Ophthalmology and Pediatrics  
Duke University Medical Center  

K David Epley MD  
Kirkland, WA  
Consultant, Swedish Hospital and Medical Centers  
Consultant, Evergreen Health  

Sonal R Farzavandi FRCS  
Singapore, Singapore  
Senior Consultant  
Singapore National Eye Centre  
Former Head  
Pediatric Ophthalmology and Strabismus Service  
National University Hospital, Singapore  

Brenda L Gallie MD  
Toronto, ON, Canada  
Professor of Ophthalmology  
University of Toronto  
Head, Retinoblastoma Program  
Hospital for Sick Children, Toronto  

Rosario Gomez De Liaño MD  
Madrid, Spain  
Professor, Universidad Complutense de Madrid  
MD, Hospital Clinico San Carlos  

David B Granet MD  
La Jolla, CA  
Anne Ratner Professor of Ophthalmology & Pediatrics  
University of California, San Diego  
Director of Pediatric Ophthalmology & Strabismus Services  
Ratner Children’s Eye Center & Shiley Eye Center  
University of California, San Diego  

Mary Elizabeth Hartnett MD FACS  
Salt Lake City, UT  
Professor of Ophthalmology  
University of Utah  
Director of Pediatric Retina  
Moran Eye Center  

Gena Heidary MD  
Cambridge, MA  
Director, Pediatric Neuro-Ophthalmology Service  
Boston Children’s Hospital  
Assistant Professor in Ophthalmology  
Harvard Medical School
David G Hunter MD PhD  
Boston, MA  
Ophthalmologist-in-Chief  
Boston Children’s Hospital  
Professor of Ophthalmology  
Harvard Medical School

Grant T Liu MD  
Philadelphia, PA  
Neuro-Ophthalmology Service  
Division of Ophthalmology  
Children’s Hospital of Philadelphia  
Division of Neuro-Ophthalmology  
Department of Neurology  
Hospital of the University of Pennsylvania

Daniel E Neely MD  
Indianapolis, IN  
Professor of Ophthalmology  
Indiana University School of Medicine  
Senior Medical Advisor to Cybersight  
Orbis International

Daniel J Karr MD  
Portland, OR  
Professor, Ophthalmology and Pediatrics  
Oregon Health and Science University

Giovanni B Marcon MD  
Bassano Del Grappa, Italy  
Director, Strabismological Center

Kanwal K Nischal MBBS  
Pittsburgh, PA  
Professor of Ophthalmology  
University of Pittsburgh  
Director, Pediatric Ophthalmology, Strabismus and Adult Motility  
UPMC Eye Center and Children’s Hospital of Pittsburgh

Katherine A Lee MD PhD  
Boise, ID  
Pediatric Ophthalmologist  
St. Luke’s Children’s Hospital, Ophthalmology

Christie L Morse MD  
Concord, NH

Scott E Olitsky MD  
Kansas City, MO  
Chief of Ophthalmology  
Children’s Mercy Hospitals and Clinics  
Professor of Ophthalmology  
University of Missouri – Kansas City  
School of Medicine
Evelyn A Paysse MD  
Houston, TX  
Professor of Ophthalmology and Pediatrics  
Baylor College of Medicine

Stacy L Pineles MD  
Los Angeles, CA  
Assistant Professor of Ophthalmology  
University of California, Los Angeles

Ron W Pelton MD PhD  
Colorado Springs, CO  
Section Chief, Ophthalmology  
Memorial Hospital

David A Plager MD  
Indianapolis, IN  
Professor of Ophthalmology  
Director of Pediatric Ophthalmology and Strabismus  
Indiana University Medical Center

Paul H Phillips MD  
Little Rock, AR  
Professor of Ophthalmology  
University of Arkansas for Medical Sciences  
Chief of Staff  
Department of Ophthalmology  
Arkansas Children’s Hospital

Carol L Shields MD  
Philadelphia, PA  
Codirector, Ocular Oncology Service  
Wills Eye Hospital  
Professor of Ophthalmology  
Thomas Jefferson University Hospital

R Michael Siatkowski MD  
Oklahoma City, OK  
Professor of Ophthalmology  
Vice Chair for Academic Affairs  
Dean A McGee Eye Institute / University of Oklahoma

Carla J Siegfried MD  
Saint Louis, MO  
Professor of Ophthalmology and Visual Sciences  
Washington University School of Medicine

Mark L Silverberg MD  
Santa Barbara, CA
Lois E H Smith MD PhD
Boston, MA
Senior Associate in Ophthalmology
Boston Children’s Hospital
Professor of Ophthalmology
Harvard Medical School

Cynthia A Toth MD
Durham, NC
Professor of Ophthalmology
Duke University Medical Center
Professor of Biomedical Engineering
Pratt School of Engineering, Duke University

Constance E West MD
Cincinnati, OH
Associate Professor of Ophthalmology
Department of Ophthalmology
University of Cincinnati College of Medicine
Pediatric Ophthalmologist
Cincinnati Children’s Hospital Medical Center

Donny Won Suh MD
Omaha, NE
Chief of Pediatric Ophthalmology
Children’s Hospital and Medical Center
Associate Professor
University of Nebraska Medical Center

David K Wallace MD MPH
Durham, NC
Professor of Ophthalmology and Pediatrics
Duke Eye Center

Matthew W Wilson MD
Memphis, TN
Professor of Ophthalmology
Hamilton Eye Institute / University of Tennessee Health Science Center
# Pediatric Ophthalmology and Strabismus 2015: Golden Nuggets of Knowledge

In conjunction with the American Association for Pediatric Ophthalmology and Strabismus and the American Academy of Pediatrics

**SATURDAY, NOV. 14**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
<th>Presenter(s)</th>
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<tbody>
<tr>
<td>7:00 AM</td>
<td>CONTINENTAL BREAKFAST</td>
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<tr>
<td>8:00 AM</td>
<td>Welcome and Introductions</td>
<td>Daniel E Neely MD* R Michael Siatkowski MD*</td>
</tr>
<tr>
<td></td>
<td>Section I: <em>My Toughest Case—Strabismus</em></td>
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<tr>
<td>8:02 AM</td>
<td>Introduction</td>
<td>Oscar Alfredo Cruz MD</td>
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<tr>
<td>8:03 AM</td>
<td>Crisscross Poker</td>
<td>Hilda Capo MD</td>
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<tr>
<td>8:12 AM</td>
<td>It’s All in the Spin</td>
<td>Stephen P Christiansen MD*</td>
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<tr>
<td>8:21 AM</td>
<td>Little Things Mean a Lot</td>
<td>David K Coats MD</td>
</tr>
<tr>
<td>8:30 AM</td>
<td>Croupier’s Challenge: A Woman With Spinning, Skewing Strabismus</td>
<td>David G Hunter MD PhD*</td>
</tr>
<tr>
<td>8:39 AM</td>
<td>Know When to Hold 'Em and When to Fold 'Em: Replacing the Lost Force</td>
<td>Monte A Del Monte MD</td>
</tr>
<tr>
<td>8:48 AM</td>
<td>Never Give In, Never Give Up</td>
<td>Scott E Olitsky MD</td>
</tr>
<tr>
<td>8:57 AM</td>
<td>Conclusion</td>
<td>Oscar Alfredo Cruz MD</td>
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<tr>
<td></td>
<td>Section II: <em>Retinoblastoma Management 2015—Boxcars or Snake Eyes?</em></td>
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<tr>
<td>8:58 AM</td>
<td>Introduction</td>
<td>David A Plager MD*</td>
</tr>
<tr>
<td>8:59 AM</td>
<td>Who Needs Intra-arterial Chemotherapy?</td>
<td>David H Abramson MD FACS</td>
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<tr>
<td>9:17 AM</td>
<td>Who Needs Intravitreal Chemotherapy?</td>
<td>Carol L Shields MD</td>
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<tr>
<td>9:26 AM</td>
<td>Who Needs Genetic Testing?</td>
<td>Brenda L Gallie MD*</td>
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<tr>
<td>9:35 AM</td>
<td>Case Presentations and Discussion</td>
<td></td>
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<tr>
<td>9:57 AM</td>
<td>Conclusion</td>
<td>David A Plager MD*</td>
</tr>
<tr>
<td>9:58 AM</td>
<td>REFRESHMENT BREAK and AAO 2015 EXHIBITS</td>
<td></td>
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<tr>
<td></td>
<td>Section III: <em>High Stakes in ROP</em></td>
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<tr>
<td>10:38 AM</td>
<td>Introduction</td>
<td>Laura B Enyedi MD*</td>
</tr>
<tr>
<td>10:39 AM</td>
<td>The ROP Show: Featuring Vessels and Neural Tissue on OCT</td>
<td>Cynthia A Toth MD*</td>
</tr>
<tr>
<td>10:47 AM</td>
<td>ROP Treatment: Round 2</td>
<td>Antonio Capone Jr MD*</td>
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<tr>
<td>10:55 AM</td>
<td>ROP: A Global Perspective</td>
<td>R V Paul Chan MD*</td>
</tr>
<tr>
<td>11:03 AM</td>
<td>Prospects for Prevention</td>
<td>Lois E H Smith MD PhD*</td>
</tr>
</tbody>
</table>

* Indicates that the presenter has financial interest.
No asterisk indicates that the presenter has no financial interest.
11:11 AM  Mechanisms of Anti-VEGF and Prospects for Future Treatments  Mary Elizabeth Hartnett MD FACS*  24
11:19 AM  Telemedicine in the United States: Ready for Prime Time?  Michael F Chiang MD*  27
11:27 AM  The SUPPORT Study Controversy  David K Wallace MD MPH*  29
11:35 AM  Conclusion  Laura B Enyedi MD*

**Section IV:**  Surgical Surprises—The Morning After  
Moderator: Daniel E Neely MD*

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<tr>
<td>11:36 AM</td>
<td>Introduction</td>
<td>Daniel E Neely MD*</td>
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<tr>
<td>11:37 AM</td>
<td>Graves Disease: One Minute You’re Up, the Next You’re Down (or Vice Versa)</td>
<td>Mark I Silverberg MD*</td>
<td></td>
</tr>
<tr>
<td>11:46 AM</td>
<td>Doc, I Think You Did Surgery on the Wrong Eye!</td>
<td>Donny Won Suh MD</td>
<td>33</td>
</tr>
<tr>
<td>11:55 AM</td>
<td>You Really Irritate Me!</td>
<td>Yasmin Bradfield MD</td>
<td>34</td>
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<tr>
<td>12:04 PM</td>
<td>Botox Gone Bad</td>
<td>K David Epley MD</td>
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<tr>
<td>12:13 PM</td>
<td>E.T. Go Home</td>
<td>Evelyn A Paysse MD</td>
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<tr>
<td>12:22 PM</td>
<td>Double Bubble Trouble</td>
<td>Kanwal K Nischal MBBS</td>
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</tr>
<tr>
<td>12:31 PM</td>
<td>Conclusion</td>
<td>Daniel E Neely MD*</td>
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<tr>
<td>12:32 PM</td>
<td>LUNCH and AAO 2015 EXHIBITS</td>
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**Section V:**  Know When to Hold ‘Em, Know When to Fold ‘Em—Ethics and Your Practice  
Moderator: Daniel J Karr MD

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<th>Time</th>
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<tbody>
<tr>
<td>1:40 PM</td>
<td>Advocating for Patients</td>
<td>Kenneth Paul Cheng MD</td>
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<tr>
<td>1:45 PM</td>
<td>Introduction</td>
<td>Daniel J Karr MD</td>
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<tr>
<td>1:46 PM</td>
<td>Stop, Look, and Listen: Ethical No-Fly Zones</td>
<td>Christie L Morse MD*</td>
<td>41</td>
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<tr>
<td>1:56 PM</td>
<td>So You Think You Are an Expert: Ethical Expert Witness Testimony</td>
<td>Ron W Pelton MD PhD*</td>
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<tr>
<td>2:06 PM</td>
<td>Anti-VEGF for Pediatric Retina: A Game of Roulette, or Standard of Care?</td>
<td>R V Paul Chan MD*</td>
<td>41</td>
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<tr>
<td>2:16 PM</td>
<td>Protect Their Data, Protect Yourself: HIPAA and the Risks of Digital Media</td>
<td>Keith D Carter MD FACS</td>
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<tr>
<td>2:26 PM</td>
<td>Don’t Touch My Baby: The Ethics of Pediatric Research and Institutional Review Board Requirements</td>
<td>Carla J Siegfried MD*</td>
<td>41</td>
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<tr>
<td>2:36 PM</td>
<td>Summary</td>
<td>Christie L Morse MD*</td>
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<tr>
<td>2:39 PM</td>
<td>Conclusion</td>
<td>Daniel J Karr MD</td>
<td></td>
</tr>
<tr>
<td>2:40 PM</td>
<td>REFRESHMENT BREAK and AAO 2015 EXHIBITS</td>
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**Section VI:**  True Confessions from the Experts—What I Never Knew  
Moderator: R Michael Siatkowski MD*

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<th>Time</th>
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<tr>
<td>3:20 PM</td>
<td>Introduction</td>
<td>R Michael Siatkowski MD*</td>
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<tr>
<td>3:21 PM</td>
<td>A Better E-Nuclear Weapon: A Novel Use of the Tonsil Snare</td>
<td>Edward G Buckley MD</td>
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<tr>
<td>3:29 PM</td>
<td>CT, X-Rated: The Bad News in Cerebrotendinous Xanthosis</td>
<td>Sean P Donahue MD PhD*</td>
<td>44</td>
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<tr>
<td>3:37 PM</td>
<td>Turn the Lights On and Keep Two Feet on the Floor: Improving Your History-Taking and Physical Examination</td>
<td>Constance E West MD*</td>
<td>45</td>
</tr>
<tr>
<td>3:45 PM</td>
<td>Stripping With Bad Hairs: Superior Oblique Surgery and Ciliopathies</td>
<td>David B Granet MD</td>
<td>46</td>
</tr>
</tbody>
</table>

* Indicates that the presenter has financial interest.  
No asterisk indicates that the presenter has no financial interest.
<table>
<thead>
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<th>Time</th>
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<tbody>
<tr>
<td>3:53 PM</td>
<td>(Ig) Gee, That’s News to Me: IgG4 Disease and Other Stuff</td>
<td>Stacy L Pineles MD</td>
<td>47</td>
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<tr>
<td>4:01 PM</td>
<td>When in Doubt, Don’t Try Anything: The Value of Retesting and</td>
<td>Alex Christoff CO</td>
<td>48</td>
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<tr>
<td></td>
<td>Prism Adaptation Pearls</td>
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<tr>
<td>4:09 PM</td>
<td>Patience for Patients: Views From the Other Side</td>
<td>Katherine A Lee MD PhD</td>
<td>49</td>
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<tr>
<td>4:17 PM</td>
<td>Conclusion</td>
<td>R Michael Siatkowski MD*</td>
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</table>

**Section VII: Wild Cards! Menacing and Remarkable Video Presentations in Pediatric Neuro-Ophthalmology**

Moderator: Jane C Edmond MD*

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<tbody>
<tr>
<td>4:18 PM</td>
<td>Introduction</td>
<td>Jane C Edmond MD*</td>
<td></td>
</tr>
<tr>
<td>4:19 PM</td>
<td>Craps!</td>
<td>Grant T Liu MD</td>
<td>52, 56</td>
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<tr>
<td>4:25 PM</td>
<td>Up the Ante!</td>
<td>Sonal R Farzavandi FRCS</td>
<td>52, 56</td>
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<tr>
<td>4:31 PM</td>
<td>Losing Your Poker Face</td>
<td>Paul H Phillips MD</td>
<td>52, 57</td>
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<tr>
<td>4:37 PM</td>
<td>Stuck!</td>
<td>Gena Heidary MD</td>
<td>52, 58</td>
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<tr>
<td>4:43 PM</td>
<td>Nystagmus in a Happy Waif</td>
<td>Michael C Brodsky MD</td>
<td>53, 59</td>
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<td>4:49 PM</td>
<td>Bluff!</td>
<td>Mays A El-Dairi MD*</td>
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<tr>
<td>4:55 PM</td>
<td>Anisocoria in Motion</td>
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* Indicates that the presenter has financial interest.
No asterisk indicates that the presenter has no financial interest.
Crisscross Poker

Hilda Capo MD

I. History
A. 25-year-old female graduate student presented with headaches and was subsequently found to have hydrocephalus and a mass in the pineal region.
B. The patient underwent surgical excision of the pineal mass, which was later diagnosed as a schwannoma.
C. Postoperatively, the patient developed constant binocular diplopia.
D. Prisms did not alleviate diplopia.
E. Used a MIN occlusion lens over the right eye

II. Examination
A. Ocular motility demonstrated mild underaction of both superior oblique muscles, with no overaction of the inferior oblique muscles. Versions were otherwise full.
B. In primary position she had an esotropia that measured 2-4 PD.
C. Folder test: Positive. Patient reported that when viewing a folder below eye level, the upper edge of the folder appeared to “scissor” into 2 images.
D. Double Maddox rod: Primary position O.D. 15 degrees excyclotorsion, O.S. 5 degrees excyclotorsion

III. Surgical Treatment Options
A. Superior oblique muscle surgery
B. Inferior oblique muscle surgery
C. Horizontal rectus muscle surgery
D. Vertical rectus muscle surgery: Novel approach

IV. Surgical Outcome
A. Patient no longer uses MIN occlusion lens.
B. Residual diplopia only in extreme downgaze
C. Orthotropic in primary position, 4 PD of esotropia in downgaze

V. Take Home Points
It’s All in The Spin

Stephen P Christiansen MD

A young woman presented with a horizontally incomitant left hypertropia, a severe left eye depression deficit, incyclotorsion, and a large left face turn. She had a history of left eye trauma as a child. Surgical exploration revealed irretrievable avulsion of both the inferior rectus and inferior oblique muscles. When both the primary and secondary excyclorotary muscles are lost, how should the surgeon approach the torsion and the incomitant vertical strabismus? This presentation, with discussion from the panel, will discuss management options along with possible salutary and deleterious outcomes to be aware of. It’s all in the spin … Or is it?
Little Things Mean a Lot

David K Coats MD

A woman with a prior history of multiple strabismus operations as a child presents with a history of a progressive vertical deviation. There is limited upgaze in the right eye, and proptosis is noted. The patient desires additional surgery, which is performed.
Croupier’s Challenge: A Woman With Spinning, Skewing Strabismus

David G Hunter MD PhD

CASE

Case History

53-year-old woman with chief complaint of double vision.

- Three years previously developed meningoencephalitis, slowly, which progressed over the course of a year
- Inflammation involved brain stem and cerebellum.
- Two years previously suffered a cerebrovascular accident with left-sided paresis
- Eyes were fixed in various directions of gaze at different times over the weeks.
- Rhythmic oscillations of the eyes also noted

The patient has now recovered much of her strength but is still wheelchair-bound with left-sided weakness. She is frustrated by persistent diplopia.

Examination

- Corrected visual acuity: RE 20/25, LE 20/20
- End-gaze nystagmus plus large, episodic, torsional movements of both eyes with extorsion of right eye and intorsion of left eye
- Motility
  - RE: −2 limitation of elevation
  - LE: −3 limitation of depression; bilateral abduction limitation
- Deviations
  - Distance with correction: exotropia 30, left hypertropia 25
  - Near with correction: exotropia 40, left hypertropia 30
  - No change when patient supine
- Dilated fundus: Variable torsion
  - Sometimes negative
  - Every 15-30 seconds: RE +2 extorsion; LE +2 intorsion

Discussion

What to do?

Selected Readings

Know When to Hold ’Em and When to Fold ’Em: Replacing the Lost Force

Monte A Del Monte MD

“Only the names have been changed to protect the innocent.”

I. History
   A. 40-year-old woman presents with abnormal eye movements.
   B. She reports waking up in the a.m. with her right eye “rolled up and out.” Also complains of loss of vision in the right eye.
   C. No recent falls or trauma
   D. Recent headache, but no changes in speech or motor symptoms
   E. MRI of brain and orbits: normal
   F. Past ocular history: ? amblyopia of right eye
   G. Past medical history: anxiety, depression, oral herpetic ulcers; no diabetes or hypertension
   H. Meds: Klonopin, Paxil, Valtrex, Ambien
   I. Family history: noncontributory

II. Examination
   A. BCVA: 20/150 O.D., 20/25 O.S.
   B. Pupils: 4.5 → 3.0 O.D. +APD and 4.0 → 2.5 O.S.
   C. WRx: -4.50 +3.50 x 27 O.D., -3.25 +3.25 x 132 O.S.
   D. Motility: 60-90 PD right exotropia and 30 PD right hypertropia in primary gaze
   E. Ductions and versions: -5 adduction O.D. with ↑ “swooping” elevation on adduction

III. Diagnostic Gaze Photos and Video
   For the panel: What is the diagnosis and treatment plan?

IV. Surgery and Result / Follow-up
   To be discussed with the panel.

V. Points for Discussion
   A. Don’t always trust the history.
   B. Importance of physical exam yourself
   C. Planning surgery for atypical/complex strabismus: Look at the full exam, motility, and measurements, then use what you have to replace and balance lost forces for the optimal result.

Selected Reading
Never Give In, Never Give Up
The Patient Who Would Not Give Up

Scott E Olitsky MD

CASE

A 56-year-old woman presented with a history of a meningioma that had been previously resected. Following her resection she noted the onset of double vision and was referred to a local ophthalmologist for evaluation and treatment. The local ophthalmologist diagnosed her with a third cranial nerve palsy of the right eye and suggested strabismus surgery. Due to continued diplopia she underwent a series of surgeries (see Table 1). Following her fourth surgery, she continued to experience double vision and was then referred for further evaluation and treatment.

Table 1. Patient’s Previous Strabismus Surgeries

1. Recession right lateral rectus / resection right medial rectus
2. Recession right inferior rectus
3. Resection right superior rectus
4. Re-resection right superior rectus

At the time of her examination, patient had 20/20 vision in both eyes. Her external examination was remarkable for a moderate ptosis of her right eye that did not occlude the visual axis. Her anterior segment examination was normal. Her motility examination was remarkable for a right exotropia of 5 PD, a right hypotropia of 4 PD and 15 degrees of excyclotorsion. She had minimal deficits of both abduction and adduction but was unable to elevate or depress her right eye beyond the midline. There was no apparent incyclotorsion of the right eye in attempted gaze down and to the left. She was able to see single with a 30 degree left head tilt.

A long discussion was had with the patient regarding her diagnosis and the limited options available to her. Based upon this discussion, a plan for further treatment was made. This would not be the last such conversation with this patient.
Who Needs Intra-arterial Chemotherapy?

David H Abramson MD FACS

I. History
A. 1940s
1. Reese used triethylene melamine injected into carotid artery.
2. 54 patients
3. Called “intra-arterial chemotherapy”
B. 1980s: Kaneko used balloon technique occluding internal carotid above take-off of ophthalmic artery, called “selective ophthalmic artery infusion of chemotherapy.”
C. 2006: Abramson/Gobin (Memorial Sloan Kettering Cancer Center) begin direct injection into the ophthalmic artery, called “ophthalmic artery chemosurgery (OAC).”

II. As of July 2015:
A. More than 100 publications in peer review literature
B. More infusions reported in the literature than total reports on laser, cryo, or episcleral plaques
C. > 50% of retinoblastoma centers worldwide use OAC as first-line therapy.
D. > 75% of centers using OAC use it as first-line therapy.
E. Only option (beside enucleation) for eyes that fail systemic chemotherapy with seeds
F. 41 countries worldwide doing it
G. > 3000 infusions worldwide
H. Used in almost every U.S. retinoblastoma center

III. Results
A. Kaneko reported 20-year follow-up on > 1469 infusions (Japan) using melphalan.
1. Successful cannulation rate: 98.8%
2. Mean number of treatments per eye: 3.69
3. Used in conjunction with radiation and intravitreal injections
4. No procedure deaths
5. No CNS procedure events
6. No transfusions or sepsis
7. No ports
8. Death rate same as prior (enucleation) experience
9. No increase in second cancers
B. Memorial Sloan Kettering Cancer Center experience using melphalan, carboplatin, and topotecan (1300 infusions); outpatient procedure; 1 hour
1. Successful cannulation: > 99%; 15% via external carotid
2. Mean number of treatments per eye: 3.8
3. Eliminated need for external beam radiation
4. No procedure deaths
5. One CNS event (transient)
6. Transfusions < 1% (all with melphalan dose > 0.4 mg/kg)
7. Sepsis < 1%
8. No ports
9. No deaths
10. No increase in second cancers
11. Complications: Few / New anesthesia reflex confirmed (18%)
12. Bilateral eyes treated (“tandem therapy”)
13. Young children (“bridge therapy”)
14. Used as primary treatment and for eyes that failed all prior therapies
15. Striking observations
   a. Could be curative with just 1 infusion (of 1 drug)
   b. ERG monitoring reveals rare toxicity of melphalan, carboplatin, or topotecan in naive eyes.
   c. No two orbits have the same vascular anatomy.
   d. Ophthalmic artery has laminar flow; infusion must be pulsed.
   e. Greatest blood flow of ophthalmic artery is not the eye, it is supratrochlear artery (therefore nasal phenylephrine used).
   f. Radiation exposure during procedure monitored in all cases: Minimal
   g. 40% of eyes with extinguished electroretinograms regain function.
   h. Retinal detachment resolves in > 80% of cases
   i. No cataracts
j. Eliminates need for external beam irradiation (and therefore will decrease second tumor incidence and prolong survival in patients)
k. Eliminates the need (and side effects) of systemic chemotherapy for all children > 3 months of age
l. Prevents the development of new intraocular tumors
m. Despite late staged ocular disease, no increase in orbital disease
n. Cures 75% of eyes with extensive vitreous seeds
o. Cured > 90% of eyes with subretinal seeds (which are rarely curable with radiation or systemic chemotherapy)
p. First treatment to salvage eyes that fail systemic chemotherapy and have significant recurrences (50%-65% of eyes saved)
q. If recurrence after OAC retreatment, salvages > 95% of eyes without vitreous seeding
r. Has been used for optic nerve disease and orbital disease

c. **Worldwide findings**
   1. Decreases need for enucleations (see Figure 1)
   2. **Learning curve:** Complications are directly related to experience.\textsuperscript{14}
   3. Eyes with retinal detachment do best.
   4. Best therapy for eyes with active tumor and vitreous seeds (role of intravitreal injections also important)\textsuperscript{15}
   5. Best/only therapy for eyes with subretinal seeds
   6. No increase in metastatic deaths
   7. Cheaper than intravenous chemotherapy

d. **Before-and-after examples (see Figure 2)**

![Figure 1. Enucleations per year (%); represents MSKCC experience.\textsuperscript{12,13}]
Figure 2. Examples before (left) and after OAC (right).
Selected Readings


Who Needs Systemic Chemotherapy?

Matthew W Wilson MD

There are 4 indications for the use of systemic chemotherapy in patients with retinoblastoma: (1) metastatic disease, (2) pinealoblastoma, (3) adjuvant therapy for high-risk pathology following enucleation, and (4) neoadjuvant therapy for the treatment of intraocular disease. The chemotherapeutics and the doses used differ based on indication.

I. Patients With Metastatic Retinoblastoma

A. Children’s Oncology Group Trial ARET0321
   1. Combination chemotherapy, autologous stem cell transplant, ± radiation
   2. Stratified treatment based on extent of disease

B. International Retinoblastoma Staging System (IRSS)
   1. Stage I: Eye enucleated, tumor completely resected on histopathology. No additional treatment
   2. Stage II: Eye enucleated, microscopic residual in the form of:
      a. Tumor invasion into extrascleral tissue
      b. Tumor invasion into cut end of optic nerve
      c. Adjuvant therapy: cisplatin, cyclophosphamide, vincristine and etoposide + external beam or proton beam radiation
   3. Stage III: Regional extension
      a. Overt orbital disease
      b. Preauricular or cervical lymph node disease
      c. Adjuvant therapy: cisplatin, cyclophosphamide, vincristine and etoposide + external beam or proton beam radiation
   4. Stage IV: Metastatic disease
      a. Bone, bone marrow and/or liver without CNS extension
         i. Single lesion
         ii. Multiple lesions
      b. CNS extension with or without any other site of regional or metastatic disease
         i. Prechiasmal involvement of the optic nerve
         ii. CNS mass
         iii. Leptomeningeal disease
      c. Adjuvant therapy: cisplatin, cyclophosphamide, vincristine and etoposide + high dose chemotherapy with autologous stem cell rescue ± external radiation

II. Trilateral Retinoblastoma

A. Treated similar to metastatic patients
B. Biopsy to confirm disease, ± resection
C. Cisplatin, cyclophosphamide, vincristine, and etoposide
D. High-dose chemotherapy with autologous stem cell rescue
E. External beam or proton beam radiation

III. Patients Undergoing Primary Enucleation

A. High-risk histopathology (HRH)
   1. Massive choroidal invasion
   2. Post-laminar optic nerve invasion
   3. Ciliary body invasion
   4. Iris invasion
   5. Anterior chamber seeding
   6. Scleral invasion
   7. Extraocular extension

B. Children’s Oncology Group Trial ARET0332
   1. No HRH features: Observation only
   2. Any single HRH or any degree of concomitant focal choroid and optic nerve involvement: adjuvant therapy with carboplatin, vincristine, etoposide (CVE) x 6 cycles

C. Risk stratified chemotherapy (RET5, SJCRH)

1. Low-risk histopathology
   a. No HRH
   b. Observation only

2. Intermediate risk histopathology
   a. Anterior chamber seeding, iris invasion, ciliary body invasion, massive choroidal invasion, post-laminar optic nerve invasion with concomitant choroidal invasion
   b. Adjuvant therapy: cyclophosphamide, vincristine, doxorubicin (CVD) x 4 cycles

3. High-risk histopathology
   a. Scleral invasion, microscopic extraocular extension or microscopic tumor at cut margin of optic nerve
   b. Alternate courses CVE and CVD for total of 6 cycles plus orbital radiation for extraocular disease
   c. Also could be treated per ARET321 IRSS Stage II
IV. Patients With Intraocular Retinoblastoma

A. Patient selection
1. Unilateral patients?
2. Bilateral patients?
3. International classification?
4. Potential for useful vision?

B. Chemoreduction of intraocular disease to facilitate focal consolidation in attempts to save the eye and vision while minimizing need for external beam radiation
1. Initial regimens derived from treatment of metastatic disease
   a. Carboplatin, vincristine and etoposide
   b. Variations
      i. Addition of cyclosporine to block multidrug resistance protein
      ii. Single agent carboplatin
      iii. Two-agent therapy carboplatin / vincristine (SJ RET3 and ARET0331)
      iv. Addition of subconjunctival carboplatin (ARET0231)
2. Newer regimens: carboplatin, vincristine, and topotecan
   a. RET5
   b. SJ RET6

C. Risks of neoadjuvant chemotherapy
1. Increases burden of care
2. Masks HRH, potentially down-staging disease and placing child at risk for metastatic disease if intended therapy is not completed
3. Prolongation of therapy increases incidence of HRH.
4. Associated treatment-related toxicities

V. Need for Novel Targeted Therapies

Selected Readings
5. Vincristine, carboplatin, and etoposide or observation only in treating patients who have undergone surgery for newly diagnosed retinoblastoma. ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT00335738.
Who Needs Intravitreal Chemotherapy?

Carol L Shields MD

Introduction to Retinoblastoma

Retinoblastoma is the most common primary eye malignancy worldwide.1-3 This tumor is generally detected in infants or young children under the age of 3 years and begins as a tiny intraretinal cancer that can grow to fill the eye, spread to the brain, and lead to remote metastasis in a matter of 1 to 2 years. The management of retinoblastoma is tedious, focused primarily on protection of the patient from metastatic disease, with secondary goals of saving the eye, protection from pineoblastoma, reduction in long-term second cancers, and, finally, protection of visual acuity.2-5

Several chemotherapy protocols from major retinoblastoma centers have lead to exciting alternatives for retinoblastoma management using intravenous chemotherapy (IVC), intra-arterial chemotherapy (IAC), periocular chemotherapy (POC), and intravitreal chemotherapy (IVitC).2-5 These developments have revolutionized the management of retinoblastoma and allowed thousands of children to maintain their eye(s) and enjoy a life with vision rather than blindness. Herein, we summarize the rationale for IVitC in the management of retinoblastoma.

Overview of Chemotherapy for Retinoblastoma

The management of retinoblastoma with chemotherapy is a complex science. This approach involves an in-depth understanding of the effectiveness of chemotherapy for specific manifestations of retinoblastoma, such as solid tumor, subretinal tumor, or vitreous tumor. There are other factors to consider as well, such as the estimated time to response and the clinical features of response. Other questions involve when to use combination chemotherapies, when to consolidate with thermotherapy, cryotherapy, or plaque radiotherapy, and understanding the possible exposures to the child from chemotherapy and multiple anesthesias as well as complications of chemotherapy in infants and young children. The management of retinoblastoma requires an appreciation of the precious balance of treatment efficacy and toxicity with salvage of life, globe, and vision.

When to Use Intravitreal Chemotherapy?

Intravitreal chemotherapy for retinoblastoma was explored in the 1960s using thiopeta and later meltxoetrexate, but lasting success was not uniformly achieved.6,7 Japanese investigators8 found melphalan to be most effective against retinoblastoma based on in vitro testing. Later, Japanese colleagues investigated intraviteal injection of 8-30 µg melphalan combined with ocular hyperthermia for vitreous tumor seeding in 41 eyes, and unpublished results revealed an eye preservation rate of nearly 51% (Presentation at the International Society of Ocular Oncology; Buenos Aires, Argentina; November 16, 2011).

The main indication for intravitreal chemotherapy includes patients with active vitreous seeds nonresponsive to standard therapy. Most clinicians use IVitC as a secondary therapy following failure of previous therapies to control vitreous seeding.9,12 The use as a primary therapy is interesting but perhaps not justifiable until adequate IVC or IAC is employed. The number of injections depends on response, and we generally propose 4-6 injections delivered on a weekly or biweekly schedule.

There is a cautious fear that tumor seeding can occur following IVitC. A review of published cases or series of IVitC from 1946 to 2013 by Smith and Smith found that a total of 1304 intravitreal injections were given in 315 eyes of 304 patients and only 1 patient developed metastatic disease.13 In a subset of 347 injections in 61 patients in which “safety-enhancing” techniques were used, there was no report of tumor spread. They concluded that proper technique led to no increased risk of tumor spread.

Munier and colleagues studied 23 patients with heavily treated retinoblastoma with recurrent vitreous seeds, using 20-30 µg melphalan on a weekly basis, and found 83% success at 15 months.10 Ghassemi and Shields evaluated 12 eyes treated with intravitreal melphalan for recurrent vitreous seeding and defined proper dosing.9 They identified that low-dose melphalan (8–10 µg) showed less control and minimal side effects, whereas high-dose melphalan (30–50 µg) showed excellent control but the 50-µg dose was toxic, with possible hypotonia and phthisis bulbi. Shields and colleagues subsequently reviewed an additional 55 injections for recurrent vitreous seeding in 16 retinoblastoma cases that led to globe salvage in all cases (100%).11 Complications were minor retinal pigment epithelial mottling at the site of injection and extra-axial cataract. There was no case of extraocular tumor extension.

The addition of topotecan to melphalan has been evaluated in rabbits and found to reach bioavailable levels with minimal toxicity. Ghassemi and colleagues studied the addition of intravitreal topotecan with melphalan in humans and noted that this led to complete vitreous seed control with a remarkable 1 or 2 injections, without the need for the standard 6 injections.12 In an analysis of 8 eyes that came to enucleation following IVitC, there was no evidence of retinoblastoma invading the needle tract.

Summary

Several therapies, such as enucleation, radiotherapy, intravenous chemotherapy, and intra-arterial chemotherapy, can control vitreous seeding from retinoblastoma. Intravitreal chemotherapy is particularly beneficial for vitreous seeding, targeting the vitreous cavity and eradicating active disease in > 90% of cases. Intravitreal chemotherapy is reserved for vitreous seed recurrence and generally is given on a weekly or monthly basis for 3 to 6 consecutive injections.

References


Who Needs Genetic Testing?

Brenda L Gallie MD
Case Presentations and Discussion
The ROP Show: Featuring Vessels and Neural Tissue on OCT

Cynthia A Toth MD, Sharon Freedman MD, Mays El-Dairi MD, Shwetha Mangalesh MD, Lejla Vajzovic MD

I. Ocular Sequelae of Prematurity

Premature birth and the sequelae of preterm birth such as ROP and treatment of ROP affect ocular tissues in predictable patterns. Ophthalmologists have long recognized the optic nerve, vitreous, and retinal findings on conventional fundus examination of infants in the intensive care nursery. While some abnormal developments are transient and not persisting into childhood, others produce residual fundus abnormalities present throughout childhood. Thus either during ROP examinations or later in childhood, the ophthalmologist may observe the following:

A. Optic nerve cupping
B. Optic nerve pallor
C. Optic nerve hypoplasia
D. Poor foveal reflex or lack of reflex
E. Tortuous vessels and plus disease
F. Active and regressed neovascular / fibrovascular tissue of ROP
G. Retinal dragging with straightened retinal vessels
H. Vitreous and retinal hemorrhages
I. Retinal folds
J. Pigmentary changes of retinal pigment epithelium and choroid
K. Retinal detachment

II. OCT Findings

OCT retinal imaging in ROP reveals specific patterns of retinal anatomy in cross-section that correlate with some of the above findings. This presentation will focus on both vascular structures and the neural tissue of the retina:

A. OCT findings that correlate to the above retinal findings in preterm infants
B. Persisting inner retinal layers at the foveal center
C. Epiretinal membrane
D. Vitreoretinal attachment
E. Retinal schisis
F. Optic nerve cupping or nerve elevation
G. Retinal nerve fiber layer thinning
H. Changes of the retinal pigment epithelium

III. Unique OCT Findings

Unique OCT findings that will be reviewed include the following:

A. Macular edema
B. Swept source OCT imaging (faster scans)
C. OCT angiography, which reveals vascular patterns without any dye injection
D. Pediatric-specific imaging

IV. Neurodevelopment

The microanatomy of the optic nerve and retina appear to reflect neurodevelopment. Since up to 70% of very preterm infants have abnormal neurodevelopment, the ophthalmologist may have an even greater role in future partnership with neonatologists in determining infants at risk for poor neurodevelopment.

V. Limitations in OCT Imaging of ROP

There are limitations in current spectral domain OCT imaging of ROP. These include the following:

A. Limited imaging of intraretinal hemorrhages
B. Limited widefield viewing preventing imaging of peripheral retina
C. Time and alignment required to capture images in infants and young children

VI. Developments in OCT Imaging

OCT imaging has progressed from the low-resolution and slower time-domain systems of the 1990s to much faster and higher resolution systems available in 2015. With the increase in speed of imaging and portability, this imaging is more amenable to aiding in the evaluation and monitoring of pediatric disease. Exciting developments in OCT imaging that may be useful in future ROP clinical evaluation, research, and in pediatric follow-up include the following:

A. Limited imaging of intraretinal hemorrhages
B. OCT angiography, which reveals vascular patterns without any dye injection
C. Pediatric-specific imaging

VII. Summary

Recognizing the unique early OCT findings of ROP and the late sequelae visible on OCT is important to pediatric ophthalmologists who will need to distinguish the effects of ROP and preterm birth from the findings of other pediatric retinal diseases.
Selected Readings


ROP Treatment: Round 2
What to Do When Primary Treatment Fails

*Antonio Capone Jr MD*

I. Introduction
   A. Peripheral laser retinopexy
   B. Pharmacotherapy
   C. Features/circumstances associated with treatment failure

II. Definitions
   A. Failure
      1. Persistent plus disease
      2. Reactivation of plus disease
      3. Retinal detachment
   B. Persistent avascular peripheral retina

III. Features
   A. Persistent plus disease
      1. Post-retinopexy
      2. Post-pharmacotherapy
   B. Reactivation
      1. Post-retinopexy
      2. Post-pharmacotherapy
   C. Retinal detachment
      1. Post-retinopexy
      2. Post-pharmacotherapy

IV. Management
   A. Reactivation
      1. Post-retinopexy
      2. Post-pharmacotherapy
   B. Retinal detachment
      1. Post-retinopexy
      2. Post-pharmacotherapy

V. Conclusions
   A. Unique clinical features
   B. Management considerations
ROP: A Global Perspective

R V Paul Chan MD

I. The Third Epidemic of ROP—What Is It?
A. Countries with middle-income economies where intensive neonatal care is being introduced or expanded are experiencing increasing survival of low birth weight and larger preterm babies, leading to intermediate infant mortality rates (10-60 per 1000).
B. Countries with intermediate infant mortality rates have the highest incidence of ROP and the highest proportion of childhood blindness attributed to ROP—termed “the third epidemic of ROP.”

II. Factors Contributing to the Third Epidemic of ROP in the Developing World
A. Middle-income countries have sufficiently advanced medical facilities to increase infant survival, while at the same time they may lack appropriate resources to screen and manage ROP.
B. In regions where neonatal intensive care is just being introduced, pediatricians rather than trained neonatologists are often providing care.
C. Babies are routinely given supplemental oxygen, but facilities to monitor blood gas levels are commonly not available.
D. Screening measures currently in place are inconsistently implemented or inadequately designed for proper detection and evaluation of at-risk babies.
E. A substantial dearth in appropriately trained professionals to perform ROP diagnosis and treatment contributes to the epidemic.

III. Development of Telemedicine Screening Programs Demonstrates Potential to Improve Access to Care
A. Properly timed screening and treatment for ROP is of upmost importance for effectively reducing blindness and results in significant government cost savings.
B. Telemedicine programs have potential to overcome barriers to effective screening programs, such as complexity of coordination of care, shortage of specialists trained to diagnose ROP, and the time required to perform ROP examination.
C. Telemedicine using digital color fundus photography can improve diagnostic accuracy and reliability compared to the somewhat subjective traditional dilated indirect ophthalmoscopy examination, and it may be more cost-effective.

IV. Tele-education systems to train physicians and nonphysician medical providers can help ensure quality and standard of care.
A. Current methods of training medical personnel internationally confront issues of sustainability and high costs of travel.
B. Increased availability and decreasing costs of Internet access in middle-income countries clear the way for implementation of tele-education systems for trainees in developing countries.
C. Telemedicine may use nonphysician personnel trained via tele-education systems to diagnose ROP.
D. Concerns about insufficient training due to limited experience with ROP cases during residency can be addressed using tele-education.
E. The digital images collected for tele-education systems could serve as a repository for future educational use and research.

V. Intravitreal Anti-VEGF Injection for the Treatment of ROP
A. Ablation of the peripheral avascular retina with laser photocoagulation or cryotherapy has long been the standard of care for treatment-requiring ROP.
B. The effectiveness of intravitreal anti-VEGF therapy has been proven in the treatment of other neovascular diseases, and its use in ROP is becoming more common.
C. While preliminary trials have shown the effectiveness of anti-VEGF therapy for treatment-requiring ROP, the lack of long-term studies leaves open the question of what the potential long-term adverse effects could be.
D. VEGF is essential to normal development of the neonate, and anti-VEGF drugs that escape into the system may disrupt development.
E. Anti-VEGF therapy may change ROP from a disease with a relatively predictable course and finite follow-up period to one with a potentially indefinite follow-up period that can lead to late complications.
F. There is still much to learn about the timing, dose, choice of drug, and long-term safety of intravitreal anti-VEGF therapy for ROP.


Prospects for Prevention

Lois E H Smith MD PhD

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Introduction

Retinopathy of prematurity (ROP) is a major cause of blindness in children in both the developing world and the developed world because of increasing survival of preterm infants. Today there is improved understanding of the initiating factors causing ROP, giving rise to novel preventative treatment possibilities that will likely help to reduce the number of sight-threatening complications from late-stage ROP.

Pathogenesis

ROP has two postnatal phases. In Phase 1 retinal vascularization is inhibited due to hyperoxia and loss of nutrients and growth factors provided through the maternal-fetal interface. Blood vessel growth stops, and as the retina matures and metabolic demand increases, hypoxia results. Hypoxia stimulates expression of oxygen-regulated factors such as erythropoietin (EPO) and vascular endothelial growth factor (VEGF), which stimulate retinal neovascularization (Phase 2). Insulin-like growth factor 1 (IGF-1) concentrations increase slowly from extremely low levels after preterm birth to concentrations high enough to allow activation of VEGF pathways. This hypoxic Phase 2 of ROP can lead to retinal detachment and blindness. Prevention measures are necessary starting immediately after preterm birth to more closely reflect the in utero environment to prevent Phase 1 of ROP, which will then prevent the destructive sequelae of Phase 2.

Insulin-like growth factor

IGF-I, which is suppressed during starvation, is essential for muscle, bone, neural, and vascular growth during fetal life and for growth and remodeling postnatally, mediated mainly through the IGF-I receptor (IGF-IR). IGF-I serum levels fall rapidly after preterm birth, due to loss of the maternal-fetal interaction. IGF-I is required for maximum VEGF activation of vascular endothelial cell proliferation and survival pathways. Replacement of IGF-I to in utero levels in preterm infants may restore normal retinal neurovascularization and prevent Phase 1 (and thereby prevent Phase 2) of ROP. In addition, IGF-I is also an important inducer of overall systemic growth and development. The effect of IGF-I on postnatal systemic growth might be important to both ROP and the development of other organs, such as brain and lung. Increasing systemic IGF-I to levels that would be normal during that developmental window could therefore have a beneficial effect on overall postnatal growth and improve the general health and development of a preterm infant, with associated beneficial effects on his or her ROP risk. At present, a Phase 2 study of IGF-I replacement is under way (www.clinicaltrials.gov#NCT01096784).

ω-3 Polysaturated fatty acids

Polyunsaturated fatty acids (PUFAs), both ω-3 and ω-6, are essential fatty acids, and deficient levels are important in the development of ROP. Like IGF-I, ω-3 PUFA is depleted in preterm infants, who miss the normal massive transfer of PUFAs in the third trimester from mother to infant. It is not found in most parenteral nutrition formulas given to preterm infants. Omega-3 fatty acids can reduce Phase 1 and Phase 2 in animal models and in human infants.

The suppressive effects of ω-3 PUFA supplementation on the development of ROP has been demonstrated to be comparable to the effects of anti-VEGF therapy in the mouse model of oxygen-induced retinopathy, offering a promising new therapy for the prevention of ROP.

Oxygen

In the 1950s, early excess oxygen treatment was identified as an important risk factor for ROP. Fluctuations in oxygen concentrations during the first few weeks of life are also associated with increased risk of ROP. Additionally, fluctuating intermittent hypoxia during the first 8 weeks of life is associated with later severe disease. Control of oxygen tension in preterm babies helps prevent Phase 1 of ROP, although this must be balanced against adequate oxygen delivery to the brain to prevent death and cerebral palsy.

As we better understand the normal retinal physiology and the pathophysiology of the ROP, new medical approaches to prevent ROP with IGF-I supplementation, optimal control of supplemental oxygen, and restoration of normal in utero levels of essential fatty acids may help prevent ROP.

References


Mechanisms of Anti-VEGF and Prospects for Future Treatments

Mary Elizabeth Hartnett MD FACS

I. Why to Consider Inhibiting VEGF in Severe ROP

A. VEGF is an angiogenic factor and also increases permeability of capillaries and vessels.

B. Angiogenesis includes endothelial cell migration, proliferation, chemotaxis (migration of cells toward the source of a gradient), and survival.

C. ROP is a disease associated with aberrant angiogenesis in which normal developmental angiogenesis is affected and vessels instead grow into the vitreous.

D. In severe ROP, there is also dilation and tortuosity of vessels and leaky vessels, and this is affected by increased VEGF signaling.

II. Clinical Studies of VEGF Levels in Infants With ROP

A. Vitreous VEGF increased in stage 4 ROP: vascularly active \((n = 12; 3454 \text{pg/mL median})\), vascularly inactive \((n = 10; 316 \text{pg/mL})\), control cataract surgery \((n = 5, 59 \text{pg/mL})\). Stromal derived factor-1 \((\text{SDF-1alpha})\) was 1029 pg/mL, vascularly active; 609 pg/mL, vascularly inactive; and 327 pg/mL, control; \(P < .001\) vs. control.

B. Vitreous VEGF increased in active stage 4 ROP compared to stage 5 ROP; VEGF receptors found in retrolental membranes.

III. Dilemma of Inhibiting VEGF in Preterm Infants

A. VEGF is involved in pathologic aberrant angiogenesis but is also involved in physiologic retinal vascularization.

B. Preterm infant eye, brain, lungs, and kidneys may all require VEGF during some time in development. VEGF is also important for adult tissue health. Therefore, inhibiting VEGF may harm other organ systems in the developing infant regardless of developmental age when administered.

C. Relative volume of vitreous to the volume of blood in the preterm infant is much greater than in the adult, causing the concentration of drug in the blood stream to be greater in the infant than in the adult.

D. Difficulty in assessing safety of intravitreal anti-VEGF in preterm infants who often have other complications from extreme prematurity

IV. Models of Oxygen-Induced Retinopathy (OIR)

Used to study ROP because unsafe to experiment on human preterm infant eyes

A. Mouse OIR model

1. High oxygen induces capillary dropout of newly developed capillaries.

2. Intravitreal neovascular buds develop after pups returned to room air.

3. Benefit of using transgenic animals

B. Rat OIR model

1. Most representative of human ROP today based on arterial oxygen fluctuations, extrauterine growth restriction, and appearance.

2. Delayed retinal vascular development leads to hypoxia-induced intravitreal neovascularization at junctions of vascular / avascular retina.

C. Beagle OIR model

Some features of mouse and rat OIR with benefit of larger eye size in puppy compared to rodent pup to assess pharmacologic approaches for human eyes

V. Preclinical Studies on Angiogenesis, Intravitreal Neovascularization, and Intraretinal Vascularization

A. Intravitreal neutralizing antibody to VEGF reduced intravitreal neovascularization without apparent increase in avascular retina.

B. VEGF-Trap at certain doses caused persistent avascular retina and decreased electroretinography amplitudes.

VI. What is the evidence currently?

A. Efficacy

1. Numerous case series show that intravitreal bevacizumab or ranibizumab can reduce severe ROP and may limit the development of high myopia.

2. Current clinical trials

a. Bevacizumab reduced Stage 3 ROP (IVNV) and facilitated physiologic retinal vascular development compared to laser for Stage 3+ ROP.

b. Refractive errors (Anti-VEGF associated with less high myopia in some studies.)

i. Five years after BEAT-ROP, a cohort of 28 patients (54 eyes). Eleven patients (22 eyes) had intravitreal bevacizumab; 17 patients (32 eyes) had laser. Intravitreal bevacizumab-treated eyes had recurrence in 3 eyes, retinal detachment or straightening of vessels in 0, average refractive error of \(-2.4 \text{D at 22.4 months postgestational age. Laser-treated eyes had 1 recurrence, retinal detachment in 1 eye, and macular ectopia in 3 eyes, and average of \(-5.3 \text{D at 37.1 months postgestational age.} \)
ii. High myopia after intravitreal bevacizumab and laser compared to intravitreal bevacizumab alone was not due to increased axial length.

iii. In a study of type 1 ROP in 37 patients, bevacizumab (0.625 mg/mL) caused myopia of −5 D or more in 6 eyes whereas ranibizumab (0.25 mg/mL) caused −5 D or more myopia in 0 eyes. No eye had recurrent neovascularization.

B. Safety

1. Reduced serum VEGF and persistent levels of drug in serum; intravitreal injection of 0.625-mg bevacizumab remained detectable in serum for 8 weeks after injection and correlated with reduced serum VEGF (8 patients with type 1 ROP).

2. Reactivation of ROP

a. Persistent peripheral avascular retina and recurrent neovascularization with stage 5 ROP reported 1 year after bevacizumab

b. Reactivation of ROP in 5/6 eyes treated with intravitreal 0.25 mg/mL ranibizumab compared to 0 with 0.625 mg/mL bevacizumab

VII. Conclusions

A. VEGF is important in development and pathologic neovascularization in ROP.

B. Preclinical studies show importance of dose, especially in potent VEGF neutralizers (eg, VEGF-Trap).

C. Safety of VEGF inhibition of ROP still unknown

1. Need to know what “normal” levels of VEGF are in the premature infant

2. What are the levels of VEGF after laser?

D. Refractive errors vary and may depend on many variables: duration of follow-up, size and postgestational ages of infants when administered anti-VEGF, variation in laser treatment.

E. Future treatments

1. Regulation of VEGF signaling

2. Promote physiologic retinal vascular development

a. Inositol: Essential nutrient required by human cells in culture for growth and survival. When given as repeated doses, reduced death and stage 3 or greater ROP in 4 studies in Cochrane review.

b. Erythropoietin’s nonerythroid effects include angiogenesis and neuroprotection. Previous studies found associations between severe ROP and use of erythropoietin for anemia of prematurity. However, later preclinical and clinical studies suggest timing of treatment may make a difference.

c. Insulin-like growth factor: Ongoing studies

References


Telemedicine in the United States: Ready for Prime Time?

Michael F Chiang MD

I. Background

A. AAP-AAO-AAPOS guidelines (2001): ROP exam “should be performed using indirect ophthalmoscopy,” documentation with hand-drawn sketches.

B. Practical challenges

1. Time intensive: travel, coordination
2. Exam: difficult, imprecise, subjective
3. Medicolegal liability
4. More infants at risk (survival)
5. Fewer ophthalmologists willing to perform exams: Limited access to care

C. Training challenges

1. Limited accuracy of trainees
2. Half of U.S. examiners are not fellowship trained in pediatric ophthalmology or retina.

II. Telemedicine Approach

A. Design

1. Imaging by trained nurses or other personnel
2. Remote diagnosis
3. Referral for in-person exam in cases of severe disease, poor images, etc.

B. Potential benefits: quality, cost, accessibility, objectivity

III. Validation: Is the diagnosis accurate?

A. Over 20 published studies

B. AAO technology assessment

1. Seven level I study cohorts (458 infants): high sensitivity for diagnosis of clinically significant disease
2. Three level III study cohorts (1462 infants): high sensitivity and specificity for diagnosis of clinically significant disease

C. Large-scale trial

1. 1257 infants: High sensitivity for “referral-warranted disease”
2. Reading center model with trained and certified nonexpert readers

IV. Validation: What is the correct diagnosis?

A. What is the gold standard, and is ophthalmoscopy inherently better?

B. Intraphysician agreement of telemedicine vs. ophthalmoscopic exams: 86% intraphysician agreement, 14% discrepancies; rationale for telemedicine being more accurate in many discrepancies

V. Validation: Cost-effectiveness and Speed

A. Cost-utility model: Telemedicine at $3193/QALY vs. ophthalmoscopy at $5617/QALY

B. Time-motion analysis: Telemedicine at 1-2 minutes/exam vs. ophthalmoscopy at 4-6 minutes/exam

VI. Where are we now?

A. Major real-world programs

B. Revised AAP-AAO-AAPOS guidelines (2013): “Digital remote interpretation is a developing approach to ROP screening. At minimum, programs that employ this method should comply with recommendations outlined here.”


D. Lesson: Evolution from clinical need → research → real-world technology adoption

References


The SUPPORT Study Controversy

David K Wallace MD MPH

I. The Study

A. SUPPORT = Surfactant, Positive Pressure, and Oxygenation Randomized Trial

B. Study question: Will a lower oxygen saturation target range (85%-89%) reduce ROP without increasing adverse events?

C. Methods

1. Randomized trial comparing target ranges of oxygen saturation: 85%-89% vs. 91%-95%

2. 1316 infants born between 24 and < 28 weeks

3. Primary outcome = Composite of severe ROP (threshold, laser, or bevacizumab), death before discharge from the hospital, or both

D. Conceived in 2003, initiated in 2005, and completed in 2009

E. Trials addressing the same clinical question were initiated in 2006 in the United Kingdom, Australia, and New Zealand: Benefits of Oxygen Saturation Targeting (BOOST II)

II. The Results

Table 1. Results of SUPPORT Study

<table>
<thead>
<tr>
<th></th>
<th>Severe ROP or Death</th>
<th>Death before Discharge</th>
<th>ROP Among Survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower saturation</td>
<td>28.3%</td>
<td>19.9%</td>
<td>8.6%</td>
</tr>
<tr>
<td>Higher saturation</td>
<td>32.1</td>
<td>16.2</td>
<td>17.9</td>
</tr>
<tr>
<td>P-value</td>
<td>.21</td>
<td>.04</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

III. The Controversy

A. Office for Human Research Protections (OHRP)

1. Branch of the U.S. Department of Health and Human Services (HHS)

2. Mission: Provides leadership in the protection of the rights, welfare, and well-being of subjects involved in research conducted or supported by HHS

B. It was alleged that informed consent for SUPPORT was inadequate.

C. In 2011, OHRP began investigating the informed consent process of SUPPORT.

IV. The Investigation

A. Letter of determination sent to lead center (UAB) on 3.7.13: “It was alleged, and we determine, that the IRB [institutional review board] approved informed consent documents for this study failed to include or adequately address the following basic element required by HHS [Health and Human Services] regulations at 45 CFR 46.116(a): Section 46.116(a) (2): A description of any reasonably foreseeable risks and discomforts.” OHRP requested actions on the part of UAB to prevent future violations.

B. Consent form notes the higher risk of ROP associated with prolonged exposure to supplemental oxygen but states that “the benefit of higher versus lower levels of oxygenation in infants, especially for premature infants, is not known” and “babies in the lower range group will have a target saturation of 85%–89%, while the babies in the higher range group will have a target saturation of 91%–95%. All of these saturations are considered normal ranges for premature infants.”

C. OHRP judged the consent form section on risks to be inadequate because:

1. It did not include information about prior research looking at the relationship between oxygen and ROP and examining whether changing the oxygen range might affect whether an infant develops ROP.

2. It did not include information about the prior research looking at the relationship between oxygen and morbidity / mortality (except ROP).

3. It did not identify any specific risk to randomizing infants to a high or low range of oxygen.

D. Other findings by OHRP

1. The consent suggested that this was a low-risk study, noting that all of the treatments in the study were “standard of care” and that there was “no predictable increase in risk for your baby.”

2. It would have been appropriate for the consent to explain that the study involves substantial risks, and that the level of oxygen provided to an infant can have an important effect on many outcomes, including blindness, brain injury, and death.

V. The Response

A. Many published letters supporting the SUPPORT study and its investigators, including letters from the NIH and numerous bioethicists and neonatologists, argued that:

1. Before the study the evidence suggested that oxygen saturations of 70% to 90% were associated with less retinopathy without an increase in mortality.
2. Infants in both treatment groups had lower rates of death before discharge (16.2% in the higher-oxygen-saturation group and 19.9% in the lower-oxygen-saturation group) than did those who were not enrolled (24.1%) and historical controls (23.1%).

3. Consent forms were conscientiously drafted, and parents were provided with the best information known at the time.

4. OHRP confused risks of the clinical treatment with the risks of the randomization; there are risks involving oxygen administration to premature infants, but there was no evidence that randomization increased that risk.

B. In response to public outcry, OHRP withdrew the request for compliance actions.

VI. The Effect

A. Data safety and monitoring boards in the United Kingdom and Australia did joint safety analyses, pooling data from the SUPPORT study with 2315 infants in the UK, Australia, and New Zealand trials. They found a statistically significant survival advantage for the high-oxygen group, so both the UK and Australia trials were terminated early.

B. One letter alleged that OHRP investigation has had the effect of damaging the reputation of the investigators and casting a pall over the conduct of clinical research to answer important questions in daily practice.

C. In a letter to the New England Journal of Medicine, representatives from the NIH opined: “This controversy has alarmed some of the parents of infants who were in the study, confused the biomedical research community, and befuddled IRBs. Several other studies seeking new insights to improve care for these vulnerable infants have been put on hold as the field tries to understand the OHRP findings.”

D. Class action lawsuit was filed in federal court against UAB providers and IRB members on behalf of infants enrolled in the SUPPORT study (through their parents).

VII. Lessons Learned

A. Reminder of good clinical practices required when consenting subjects for studies

1. Carefully explain the possible risks of all possible treatments in the study, even when both treatments are considered usual care, as in comparative effectiveness research.

2. Emphasize that participation is optional, and that it is not necessary to receive excellent care.

B. Value of registries

1. Investigators were able to use registry data from the Neonatal Research Network to show that study subjects were safer than comparable babies who were not in the study.

2. Prospective randomized trials and registry data are complimentary; registries allow estimates of outcomes for patients whose treatment is subject to variation common in the “real world.”

3. Advances in medical informatics will hopefully make it easier to include EHRs to analyze outcomes.

C. Those individuals tasked with oversight of human-subjects research, such as members of IRBs and the OHRP, must protect participants while being mindful of the value of important research; any measures that impede the conduct of this research must offer substantive protection to participants.

VIII. Future Directions

A. OHRP has drafted guidelines on disclosing reasonably foreseeable risks and posted it for comments.

B. Changes in OHRP processes described by representatives from the NIH: “The community will benefit from an explicit description of the process the OHRP follows for investigating complaints. For example, when questions are raised about reasonably foreseeable risks and the state of the science relevant to a particular clinical trial, appropriate independent experts might need to be consulted…. [T]he DHHS plans to ensure that investigators and IRBs will have a fair and transparent process for appealing OHRP findings and compliance actions, in those situations in which reasonable people disagree about the actions taken.”

C. Comparison of outcomes between patients in research studies and similar patients receiving conventional therapy will allow measurement of the risks of research (ie, is it riskier for patients to be enrolled in clinical trials or to receive treatment based on the physician’s clinical judgment?).

D. If it is safer to be in a study than to not be in a study, then the ethical requirements of informed consent will make it essential to inform potential study subjects of this fact—a notion that will no doubt produce controversy!

Selected Readings


13. HHS. About the draft guidance on risk disclosure in research evaluating standards of care (OHRP draft guidelines). Available at: www.hhs.gov/ohrp/newsroom/rfc/draftstandarqseach.html.
Graves Disease: One Minute You’re Up, the Next You’re Down (or Vice Versa)

Mark L Silverberg MD

History of Present Illness
C.B. is 64-year-old woman with vertical diplopia.

Past Medical History
Graves disease, anxiety, HTN. Underwent radioactive thyroid treatment.

Past Ocular History
Tried acupuncture and various homeopathic remedies—no help.

Meds
Losartan (Cozar), metoprolol

Eye Exam
- Visual acuity, spectacle corrected = 20/30 O.U. Slit lamp and fundus unremarkable.
- Motility shows limited elevation L eye >> R eye
- Left hypotropia (primary) = 30 PD. Increases to 50 PD in upgaze. Decreases to 8 PD in downgaze.
- Double Maddox rod = 10 degrees left excycl

Assessment
64-year-old woman with Graves and left hypotropia

Plan
Strabismus surgery: recess left inferior rectus
Doc, I Think You Did Surgery on the Wrong Eye!

Donny Won Suh MD

Objectives
Objectives of study are to determine the prevalence of and contributing factors for wrong-site strabismus surgery in pediatric ophthalmology.

Methods
Approximately 1000 members of a pediatric ophthalmology Listserv were contacted to complete a survey from June to July 2015. It was composed of 20 questions to determine the frequency of wrong-site surgeries and to assess the risk factors contributing to the errors in strabismus surgery.

Results
One hundred fifty strabismus surgeons responded the survey. We are currently collecting data that will be shared at the 2015 AAO meeting in Las Vegas. Contributing factors to these errors will be discussed in detail.

Conclusions
In concordance with the previous reports, self-reported error in strabismus surgery is not uncommon. An emphasis on efficiency, less contact time with patients, and unfamiliarity with EMR are possibly increasing the incidence of wrong-site surgeries in pediatric ophthalmology.

Reducing errors in strabismus surgery may involve directly addressing some of these contributing factors.
You Really Irritate Me!

Yasmin Bradfield MD

A 34-year-old healthy male presented for strabismus surgery for long-standing right superior oblique palsy. He underwent uneventful surgery consisting of a right medial rectus recession and right inferior oblique recession. He presents postoperatively with increasing chemosis, eye pain, and worsening diplopia.

What next?
Botox Gone Bad
The Horror of Human Response to Toxins

K David Epley MD

I. My Very First Botox Patient: 13-Month-Old Baby
   A. Infantile esotropia (ET) of 30 PD
      1. Microsoft family: fully researched the available treatments and settled on Botox after articles by McNeer and Ing
      2. Refused conventional surgery
   B. Surgery day
      1. Brought to the OR, anesthesia administered
      2. 7.5 units Botox given into each medial rectus with EMG guidance
   C. Results
      1. One week: 45 exotropia (XT)
      2. One month: 45 XT
      3. Three months: 40 XT (Oh crap! What have I done!)
      4. Five months: Ortho distance and near!
      5. Five years
         a. Ortho distance and near
         b. 40 arc seconds stereo!
      6. Fifteen years
         a. Ortho distance and near
         b. 40 arc seconds stereo!
         c. Wow!
   D. Where’s the “gone bad”? It’s in the middle.
   E. Would have been better to quit while I was ahead...

II. Flash Forward: Five-Year-Old Girl
   A. Left esotropic Duane syndrome (type 1)
      1. Head turn increasing to around 20 degrees to fuse
      2. Developing amblyopia
      3. Parents want to avoid surgery.
   B. Botox: 7.5 units injected into the left medial rectus with sedation
   C. Results
      1. One week: 35 XT
      2. One month: 40 XT!!
      3. Three months
         a. 40 XT
         b. No sweat, right? It will come back.
      4. Six months
         a. 35 XT
         b. Amblyopia worsening despite patching
         c. What the heck!
   5. What now?
      a. Strabismus surgery: left lateral recession 10 mm
      b. One week: Essentially no effect from a 10-mm recession!
      c. One month
         i. No longer fusing with head turn
         ii. Still 25 XT
   D. What do I do now?
      1. Consult the masses
      2. Discussed on peds Listserv and with a couple local peds docs
      3. Consensus: Y-split the lateral, Botox lateral, and resect medial
   E. Surgery #3
      1. Detach and Y-split the lateral, Botox 7.5 units into muscle under direct visualization
      2. Did not resect medial
      3. One week
         a. Fusing in right gaze again
         b. Expecting the ET from the Botox, right?
         c. −5 abduction and −4 adduction
   F. What now?
      Refer to a “super-specialist” in another state!
   G. Surgery #4
      1. Super-specialist cleans up the mess: lysis of adhesions around lateral rectus and inferior oblique
      2. Now fusing in primary with minimal head turn
      3. Amblyopia resolving with patching

III. Flash Forward: 83-Year-Old Retired Ophthalmologist
   A. You can guess the story from here.
      1. Small angle ET of 6 PD, stable but uncomfortable in prisms
      2. Has multifocal IOLs and wants to get rid of glasses
      3. Wants to do Botox over conventional surgery for small angle
B. Botox
   1. 3.75 units Botox injected into the medial rectus
   2. Discussed ptosis, overcorrection, vertical deviations prior to injection

C. Results
   1. One month
      a. 25 XT, 12 right hypertropia (RHT)
      b. Okay, expected some overcorrection, but not this much with only 3.75 units
      c. On the positive side, no ptosis!
   2. Two months: XT 10, RHT 8
   3. Three months: 2 RH(T)

IV. Conclusions
   A. Botox requires patience.
      1. It’s important to prepare your patient/parent for the long haul: 4-6 month “recovery” period for alignment.
   2. Every person’s response is different.
      a. Some have large initial overcorrections.
      b. Some have undercorrections due to lack of response.
   B. Choose your Botox patients carefully.
      1. Augmenting conventional strabismus surgery for large angles
      2. Primary treatment for infantile ET
      3. Sixth nerve palsy
      4. Augmenting Knapp transpositions
      5. Caution for small angles (< 10)
      6. Caution with vertical deviations
      7. Avoid Duane syndrome
Six-year-old boy woke up 3 days after uneventful bilateral lateral rectus recession surgery with a large esotropia, left abduction deficit, and hemorrhagic chemosis temporally in the left eye. What in the world happened?
Dislocated lenses can be managed conservatively or surgically. Vitreoretinal surgeons often argue that such lenses should be removed via a posterior approach to prevent retinal detachment complications. This author prefers an anterior approach.

The main issue is to avoid aspiration of any vitreous during vitreolensectomy. Clues to the presence of vitreous in the area of vitreolensectomy when only lens aspiration is being conducted include a fluttering movement of the iris or capsular bag. Sometimes if the surgeon anticipates a particularly unstable lens, strategies can be employed to stabilize the lens. Some of these techniques are demonstrated in this video.
2015 Advocating for Patients

Kenneth P Cheng MD

Ophthalmology’s goal in protecting quality patient eye care remains a key priority for the Academy. All ophthalmologists should consider their contributions to the following three funds as (a) part of their costs of doing business and (b) their individual responsibility in advocating for patients and their profession:

- Surgical Scope Fund (SSF)
- OPHTHPAC® Fund
- State Eye PAC

Your ophthalmologist colleagues serving on Academy committees—the Surgical Scope Fund Committee and the Secretariat for State Affairs and OPHTHPAC Committee—are committing many hours on your behalf. The Secretariat for State Affairs is collaborating closely with state ophthalmology society leaders to protect Surgery by Surgeons at the state level. Meanwhile, the OPHTHPAC Committee is hard at work identifying congressional advocates in each state to maintain close relationships with federal legislators in order to advance ophthalmology and patient causes. Both groups’ ultimate goals are to ensure robust funds for both the SSF and the OPHTHPAC Fund so that they are able to (a) protect quality patient eye care, (b) protect ophthalmology practices from payment cuts, (c) reduce burdensome regulations, and (d) advance the profession by promoting funding for vision research and expanded inclusion of ophthalmology in public and private programs.

These committed ophthalmologists serving on your behalf have a simple message to convey:

“We also need you!”

- We need you to contribute to each of these three funds.
- We need you to establish relationships with state and federal legislators.
- We need you to help us protect quality patient eye care and the profession.

Surgical Scope Fund

The Surgical Scope Fund (SSF) provides grants to state ophthalmology societies to support their legislative, regulatory, and public education efforts to derail optometric surgery proposals that pose a threat to patient safety, quality of surgical care, and surgical standards. Since its inception, the Surgery by Surgeons campaign—in partnership with state ophthalmology societies and with support from the SSF—has helped 32 state/territorial ophthalmology societies reject optometric surgery proposals.

As of July 1, 2015, the Secretariat for State Affairs, in collaboration with the California Academy of Eye Physicians and Surgeons (CAEPS) and the California Medical Society, continues to battle an onerous optometric surgery scope of practice bill (SB 622) in the Golden State. The Secretariat has reached out to all ophthalmology subspecialty society partners to help in this effort, and several have stepped up to the plate. In addition, ophthalmology leaders at California academic institutions have played a critical role by voicing their concerns about the California surgery bill and the impact it would have on quality eye care for patients. A June 24 op-ed in the San Francisco Examiner aptly focused on these leaders’ concerns with its headline “Quality surgical eye care ensured through training.” CAEPS has benefited from contributions to the SSF, having received significant support from the fund.

Other state ophthalmology societies have also benefitted from SSF distributions in 2015 and were able to successfully implement patient safety advocacy campaigns to defeat attempts by optometry to expand its scope of practice to include surgery. The Texas Ophthalmological Association was successful in its patient advocacy and public education efforts to defeat three different optometric-backed surgical scope expansion bills in the Texas state legislature.

In addition, the Academy supported the Alaska Society of Eye Physicians and Surgeons in opposing optometric surgery scope legislation that posed a threat to patient surgical care. If enacted, the optometric surgery bill would have authorized optometrists in Alaska to perform surgery with lasers, scalpels, and needles, and to perform other surgical procedures. The legislation would also have allowed optometrists to perform all injections except intravitreal and to prescribe any controlled substances. Thanks to an effective Surgery by Surgeons advocacy campaign, with support from the SSF, this legislation died in committee. The Alaska state legislature adjourned for the year on April 27.

The Academy relies not only on the financial contributions to the SSF from individual ophthalmologists and their business practices, but also on the contributions made by ophthalmic state, subspecialty, and specialized interest societies. The American Association for Pediatric Ophthalmology and Strabismus (AAPOS) contributed to the Surgical Scope Fund in 2014, and the Academy recognizes its leadership for their support.

OPHTHPAC® Fund

OPHTHPAC is a crucial part of the Academy’s strategy to protect and advance ophthalmology’s interests in key areas including physician payments from Medicare as well as protecting ophthalmology from federal scope of practice threats. Established in 1985, OPHTHPAC is one of the oldest, largest, and most successful political action committees in the physician community and is very successful in representing your profession to the U.S. Congress. As one election cycle ends, a new one starts. OPHTHPAC is always under financial pressure to support our incumbent friends as well as to make new friends with candidates. These relationships allow us to have a seat at the table and legislators willing to work on issues important to us and our patients. Among the significant achievements of OPHTHPAC are the following:

- Repealed the flawed Sustainable Growth Rate (SGR) formula
- Blocked the unbundling of the Medicare global surgery fee period
- Removed a provision in fraud and abuse legislation that targeted eyelid surgery
- Protected your ability to perform in-office ancillary services
• Working to reduce the burdens from Medicare’s existing quality improvement programs such as the Electronic Health Record Meaningful Use program
• Working in collaboration with subspecialty societies to preserve access to compounded and repackaged drugs such as bevacizumab

Leaders of the AAPOS and the American Academy of Pediatrics (AAP), Section on Ophthalmology, are part of the American Academy of Ophthalmology’s Ophthalmic Advocacy Leadership Group (OALG), which has met every January for the past eight years in the Washington D.C. area to provide critical input and to discuss and collaborate on the Academy’s advocacy agenda. The topics discussed at the 2015 OALG meeting included collaborative efforts on the IRIS Registry and quality reporting under Medicare. As 2015 Congressional Advocacy Day (CAD) partners, the AAPOS and the AAP’s Section on Ophthalmology ensured a strong presence of pediatric ophthalmologists to support ophthalmology’s priorities as nearly 400 Eye M.D.s had scheduled CAD visits to members of Congress in conjunction with the Academy’s 2015 Mid-Year Forum in Washington, D.C. The AAPOS and the AAP’s Section on Ophthalmology remain crucial partners with the Academy in its ongoing federal and state advocacy initiatives.

State Eye PAC
It is also important for all ophthalmologists to support our respective State Eye PACs because state ophthalmology societies cannot count on the Academy’s SSF alone. The presence of a strong State Eye PAC providing financial support for campaign contributions and legislative education to elect ophthalmology-friendly candidates to the state legislature is also critical. The Secretariat for State Affairs strategizes with state ophthalmology societies on target goals for State Eye PAC levels.

**ACTION REQUESTED: ADVOCATE FOR YOUR PATIENTS!!**

Academy Surgical Scope Fund contributions are used to support the infrastructure necessary in state legislative / regulatory battles and for public education. PAC contributions are necessary at the state and federal level to help elect officials who will support the interests of our patients. Contributions to each of these three funds are necessary and should be considered the costs of doing business. SSF contributions are completely confidential and may be made with corporate checks or credit cards, unlike PAC contributions, which must be made by individuals and which are subject to reporting requirements.

Please respond to your Academy colleagues who are volunteering their time on your behalf to serve on the OPHTHPAC* and Surgical Scope Fund** Committees, as well as your state ophthalmology society leaders, when they call on you and your subspecialty society to contribute. Advocate for your patients now!

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Stop, Look, and Listen: Ethical No-Fly Zones

Christie L Morse MD, Ron W Pelton MD PhD, RV Paul Chan MD, Keith D Carter MD, Carla J Siegfried MD

Introduction: Christie L Morse MD

Ethics in medicine is usually thought to refer to issues such as euthanasia, end-of-life, abortion, and transplant waiting lists. However, ethics affects every aspect of medicine, including patient encounters, informed consent, contracts with others, speaking engagements, expert witness testimony, digital media, and research. Declining reimbursement, increased regulatory oversight, new patient and parental demands, and the uncertain impact of health care reform all threaten the professional satisfaction we seek, yet it remains imperative that we continue to practice in an ethical manner. This ethics session will first review the history of the American Academy of Ophthalmology’s Code of Ethics (Code), leading up to the Academy being the only professional organization to receive approval of its Code by the Federal Trade Commission. The structure of the Code, with attention paid to the 17 specific enforceable rules and the available sanctions for violating the Code, will be discussed. Tips to avoid unethical behavior will be highlighted.

Expert Witness Testimony: Ron W Pelton MD PhD

Compliance with the Academy’s Code of Ethics can turn a good litigation defense into a great one. Rule 16 of the Code states, “Expert testimony should be provided in an objective manner using medical knowledge to form expert medical opinions. Non-medical factors (such as solicitation of business from attorneys, competition with other physicians, and personal bias unrelated to professional expertise) should not bias testimony. It is unethical for a physician to accept compensation that is contingent upon the outcome of litigation. False, deceptive or misleading expert testimony is unethical.” Expert witness testimony that is compliant with this rule will be discussed.

Surgical Treatment: RV Paul Chan MD

As new technology and treatments emerge, there are certain ethical considerations for their use. Adequate informed consent, adequate pretreatment assessment, and appropriate postoperative care in the use of anti-VEGF treatments are required in order to comply with the Code of Ethics. Principles 1 and 7 of the Code serve as aspirational reminders to act in the best interest of the patient. The Informed Consent Rule 2 states, “The performance of medical or surgical procedures shall be preceded by appropriate informed consent.” These pertinent principles and rules will be discussed as they relate to the use of anti-VEGF treatment for ROP. Rule 3, on Pretreatment Assessment, states, “Treatment shall be recommended only after a careful consideration of the patient’s physical, social, emotional and occupational needs. The ophthalmologist must evaluate the patient and assure that the evaluation accurately documents the ophthalmic findings and the indications for treatment. Recommendation of unnecessary treatment or withholding of necessary treatment is unethical.” Rule 8, on Postoperative Care, states, “The providing of postoperative eye care until the patient has recovered is integral to patient management. The operating ophthalmologist should provide those aspects of postoperative eye care within the unique competence of the ophthalmologist (which do not include those permitted by law to be performed by auxiliaries). Otherwise, the operating ophthalmologist must make arrangements before surgery for referral of the patient to another ophthalmologist, with the patient’s approval and that of the other ophthalmologist. The operating ophthalmologist may make different arrangements for the provision of those aspects of postoperative eye care within the unique competence of the ophthalmologist in special circumstances, such as emergencies or when no ophthalmologist is available, so long as the patient’s welfare and rights are the primary considerations. Fees should reflect postoperative eye care arrangements with advance disclosure to the patient.”

Privacy: Keith D Carter MD

This presentation will define federal privacy mandates and relevant ethical practices: the HIPAA Privacy and Security Rules that protect the privacy of individually identifiable health information. Also featured will be attendees’ responsibilities under federal law, proper use of various mobile devices, encryption strategies, the multiple password conundrum, email authorizations, patient use of social media for communication of health issues, and the relevant ethical issues. Code of Ethics Rule 17, on Confidentiality, states, “An ophthalmologist shall respect the confidential physician-patient relationship and safeguard confidential information consistent with the law.”

Research: Carla J Siegfried MD

This presentation will define “research,” how/what to submit to institutional review boards (IRBs), and applicability of research rules/regulations. Discussion topics will include existing guidelines/regulations for research in all settings, types of IRB review (full, expedited, exempt), institutional vs. private review boards, statutory authority of the Office for Human Research Protections (OHRP), specific regulations impacting all human research (prospective and retrospective), and special informed consent required by research. Via a case study, real-life obstacles in interactions with IRBs, including prolonged turnaround times impacting grant/study timelines and multiple IRB submissions on one project with potentially different reviewing bodies, will be highlighted. The potential consequences of not following ethical practices in IRB submission will be discussed. Rule 3 of the Code states, “Research and innovation shall be approved by appropriate review mechanisms to protect patients from being subjected to or potentially affected by inappropriate, ill-considered, or fraudulent basic science or patient-oriented research. Basic science and clinical research are conducted to develop adequate information on which to base prognostic or therapeutic decisions or to determine etiology or pathogenesis, in circumstances in which insufficient information exists. Appropriate informed consent for research and innovative procedures must recognize their special nature and ramifications. In emerging areas of ophthalmic treatment where recognized guidelines do not exist,
the ophthalmologist should exercise careful judgment and take appropriate precautions to safeguard patient welfare.”

Selected Resources


A Better E-nuclear Weapon: A Novel Use of the Tonsil Snare

Edward G Buckley MD

Introduction

Enucleation is often recommended when all else fails and the eye contains a malignancy, becomes painful, or looks ugly. The surgical technique has been pretty standard for many years and involves detaching the extraocular muscles, cutting the optic nerve, and releasing orbital connections to the globe.

One of the least controlled portions of the procedure is severing the optic nerve. This requires passing a curved scissor into the deep orbit and identifying the optic nerve by “feel.” Once the nerve is cut, arterial bleeding often occurs, which requires packing the orbit and waiting for it to stop. Quite a bit of bleeding can occur in a very short span, creating a mess until it’s stopped. This occurrence is quite common when performing enucleations for malignancy, where removing a long segment of optic nerve is important to address possible subsequent tumor spread. Normally a hemostat can be used to clamp the artery before cutting, but this makes getting a long nerve segment difficult in retinoblastoma patients and decreases available space for the scissors in children.

Using a Tonsil Snare for Enucleation

The ENT doctors have to deal with a similar bleeding problem in the throat. The tonsils are a very vascular structure, and the technique for removal has to incorporate a way to remove an appended structure at its base while controlling subsequent bleeding risk. A wire snare was used for many years as a primary tool for completing this task. Since it was difficult to cut all the way around the tonsil, the snare simplified that portion of the procedure. Today more advanced techniques to control bleeding are popular, but when compared, the “cold steel and snare” approach is still very successful.

Myers reported excellent results using the snare for enucleation 65 years ago, noting that the snare crushes rather than cuts the central retinal artery and vein, which results in excellent hemostasis. Schiedler and colleagues reported several advantages, including excellent hemostasis, long optic nerve stump, and minimal “crush” artifact at the cut nerve ending.

Surgical Technique

The initial portion of the procedure is the same. The extraocular muscles are isolated on sutures and detached from the globe. While not absolutely required, the placement of the snare is greatly facilitated by removing the oblique muscles as well. In order to prevent the rectus muscles from getting caught up in the closing snare, their sutures should be secured to the drape so they are on some tension and out of the way. The loop is placed around the globe, which is on tension to proptose it. This facilitates getting the wire loop behind the globe. A hemostat is used to grasp the loop 180 degrees from the handle to aid in pushing the wire behind the globe. Once in place, the wire is tightened around a spool. There is a ratchet to prevent unwinding, so care must be made because you can’t “back up.” Once the loop gets small, the hemostat is removed and the loop is pulled completely into the barrel, severing the nerve and vessels. No blood, and the globe is easily freed from the remaining tissues.

References

CT, X-Rated: The Bad News in Cerebrotendinous Xanthomatosis
A Rare Cause of Developmental Cataracts

Sean P Donahue MD PhD

I. Cerebrotendinous Xanthomatosis (CTX)
A. A lipid storage disease
B. Symptom onset in infancy
C. Cataracts in adolescence
D. Treatment available

II. Symptoms
A. Chronic diarrhea from infancy
B. Cataracts: first to second decade
C. Xanthomatosis on tendons
   1. Achilles tendon
   2. Extensor tendons of hands and elbow
   3. Patellar tendon
   4. Neck tendon
D. Intellectual impairment
   1. Begins around puberty
   2. Dementia begins in early 20s
   3. Neuropsychiatric symptoms
   4. Pyramidal and cerebellar signs (20s - 30s)

III. Biochemistry / Testing
A. High plasma and tissue cholestanol
B. Decreased chenodeoxycholic acid
C. Increased bile alcohols
D. CSF increased cholestanol and apolipoprotein B

IV. Gene Testing
A. CYP27A1 mutation
B. Autosomal recessive inheritance

V. Management
A. Treatment with chenodeoxycholic acid
B. HMG-CoA reductase inhibitors

Selected Readings
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brotendinous xanthomatosis: 11-year treatment with chenodeoxy-
Turn the Lights On and Keep Two Feet on the Floor: Improving Your History Taking and Physical Examination

Constance E West MD

Overview
It pays to look at patients with the lights on; subtle physical findings are easier to detect. And, don’t be in a hurry to leave. The last thing the patient/parent says is usually the most important!

Discussion
An ever-tighter clinic schedule can lead to a history and examination that is so problem-focused that the ophthalmologist’s attention is directed only to the eyes and visual system. Much of the ophthalmic encounter occurs in dim illumination with the patient seated, making it easy to miss subtle exam findings essential to the patient’s health. In the dark, it is easy to miss polydactyly with perfectly formed extra digits, a subtle patch of abnormal skin pigmentation, a subtle ptosis or facial palsy, or abnormal dentition. Take the time to turn the lights on, and be sure to take note of the patient’s skin, hands, teeth, and ears. Pay particular attention to the side of the face opposite to the refraction desk, especially if there is poor lighting or shadows.

As residents, we are taught to record the ophthalmic examination as a series of numbers: acuity as a fraction, the grade of an afferent pupillary defect, the angle of misalignment in prism diopters, and refraction in spherocylindrical notation. The history and discussion of findings/plan with the patient and family can be similarly mechanical and programmed. Patients need to take time to absorb and process the information and to ask questions about the information presented to them. As Jane Orient, author of Sapira’s Art and Science of Bedside Diagnosis, noted, “Patients often say very important things to you as you are leaving the room.” And Stephen King: “The most important things are the hardest to say…. That’s the worst, I think. When the secret stays locked within, not for want of a teller but for want of an understanding ear.”

After presenting the diagnosis and options to a patient, I try to make sure to remain seated and attentive; you’d be amazed what patients ask or say at the last moment.

References
The ciliopathies represent an emerging class of genetic disorders that I am really only learning about now. You may be too—so let’s learn this together.

Mutations that disrupt the assembly, structure, maintenance, or function of cilia (or basal bodies) result in a spectrum of diseases known as “ciliopathies.” These multisystemic disorders cause kidney disease, mental retardation, polydactyly, and retinal degeneration. With the realization that many conditions previously considered different from one another are a part of these disorders, there has been exploding interest in the function of cilia in developmental signaling and homeostasis.

All ciliopathies show a recessive mode of inheritance (either autosomal or X-linked), with strong evidence of genetic modifiers that determine expressivity—thus putting these conditions at the interface of simple and complex genetics. Ciliopathies can be subdivided into “motile ciliopathies” and “nonmotile ciliopathies.” Motile ciliopathies display situs inversus, for example. Nonmotile ciliopathies show mixed features in several organs, including the brain, kidney, and liver—as well as others like the eye and finger.

Ciliopathies range from largely organ-specific disorders, such as polycystic kidney disease, to cerebello-oculo-renal syndrome (CORS) and Jeune asphyxiating thoracic dystrophy.

Examples of ocular disorders associated with ciliopathies include: Joubert and Meckel-Gruber syndromes, Bardet-Biedl syndrome, Usher syndrome type 2A, and nephronophthisis in association with retinal degeneration is known as the Senior-Løken syndrome. Additionally, it is estimated that one-third of the genetic defects associated with inherited retinal dystrophies are located in genes that make ciliary proteins. Moreover, clinically different appearing ciliopathies can result from mutations in a single gene, suggesting very complex genetic interaction.

Our discussion topics will include available testing and possible therapies.

Superior Oblique Stripping for Brown Syndrome

In his original description, Brown (and over time others) agreed that “stripping” of the superior oblique was an unsuccessful approach to Brown syndrome.

Superior oblique sharpening, however, originally described by Paulo Horta-Barbosa to treat Brown syndrome (Horta-Barbosa P. La nueva técnica quirúrgica para el syndrome de Brown. In: Gómez de Liaño F, Ciancia AO, eds. Encuentro estrabológico iberoamericano. Madrid: ONCE; 1992:237-239), is a technique I only recently learned about. Others have replicated this work. Sharpening is described thusly: “The direct portion of the SO [is] sharpened by placing the eye downwards and outwards and releasing restriction until turning passive duction negative.” This is followed by steroid injection.

With this procedure, little overcorrection is reported and there is a high success of correction. So why the difference between stripping and sharpening?

Perhaps this is relates to what Wright in his AOS thesis noted, “Parks refers to the fascia around the superior oblique tendon distal to the trochlea as tendon capsule and describes the intervening connective tissue between the superior rectus and medial rectus muscles that envelopes the superior oblique tendon as intermuscular septum.” This description is in contrast to descriptions by Fink, “who termed the fascial tissue surrounding the tendon at and distal to the trochlea as the tendon sheath. This is an important concept, as ‘tendon sheath stripping’ procedures removed the fascia along the anterior aspect of the superior oblique tendon, namely, the tendon capsule and intermuscular septum, not the tendon sheath, as described by Parks.”

Video demonstration of the technique is planned, along with a review of the data.

Selected Readings

Ciliopathy

Brown Syndrome
(Ig) Gee, That’s News to Me: IgG4 Disease and Other Stuff

Stacy L. Pineles MD

I. Background
A. Immunoglobulin G4 (IgG4)-related disease has been gaining attention among clinicians within several medical subspecialties, including ophthalmology.
B. IgG4-related disease is a systemic inflammatory process with an unknown underlying etiology that manifests in most of the human organ systems.
C. There have been multiple case reports detailing orbital involvement in IgG4-related disease, with the lacrimal gland, infraorbital nerve, and extraocular muscles all reportedly at risk for involvement.1
D. Ophthalmic manifestations
1. Most patients initially present with painless eyelid swelling.
2. In the largest series of patients with IgG4-related orbitopathy, 89% of the 27 included subjects had extraocular muscle involvement. Most commonly, the lateral rectus was involved (71%), and the disease was bilateral in 88% of the patients.1
3. Coexistent lacrimal gland, infraorbital nerve, and paranasal sinus disease was present in the majority of patients, thereby helping to clinch the diagnosis in this difficult disease.
4. Interestingly, the propensity to affect the lateral rectus may be quite useful to clinicians attempting to differentiate IgG4 disease from thyroid eye disease.

II. Pathogenesis and Diagnosis
A. The pathogenesis of IgG4-related disease has not been fully elucidated.
B. It is characterized by lymphoplasmacytic infiltrates with large numbers of IgG4-positive cells.
C. It was originally recognized in Japan in a group of patients with autoimmune pancreatitis and since then has been described in various organs, including the biliary tree, retroperitoneum, salivary glands, orbit, lymph nodes, kidney, lungs, meninges, aorta, breast, prostate, thyroid, pericardium, and skin.2,3
D. The diagnosis of IgG4-related disease is made based upon pathological criteria:
1. Dense lymphoplasmacytic infiltrates
2. Storiform fibrosis
3. Obliterative phlebitis
4. IgG4 plasma cell count
5. IgG4+ / IgG+ ratio
E. Recently cases previously described as “idiopathic orbital inflammatory syndrome” have been proven to be due to IgG4-related disease.

III. Evaluation and Management
A. Strabismus specialists should suspect IgG4-related disease in patients with acquired strabismus and coexistent:
1. Eyelid edema,
2. Lacrimal gland inflammation,
3. Atypical patterns of extraocular muscle enlargement.
B. If a clinician suspects IgG4 disease, workup should be coordinated with a rheumatologist.
1. A biopsy should be performed when possible.
2. Serum IgG4 levels should be evaluated; however, they are not very sensitive.
3. Systemic workup may consist of abdominal and chest imaging.
C. Treatment typically consists of steroids followed by steroid-sparing agents when necessary.

References
When in Doubt, Don’t Try Anything: The Value of Retesting and Prism Adaptation Pearls

Alex Christoff CO

I. When in Doubt, Retest
   A. Case 1: An 8-year-old girl with decreased acuity for age
   B. Case 2: A 6-year-old girl with decreased acuity for age

II. Prism Fitting Pearls
   In-office prism adaptation and how to accurately involve your patients in their own prism fitting
   A. Case 1: A 79-year-old woman with an incomitant exodeviation
   B. Case 2: A 79-year-old female with a large, long-standing, exodeviation measuring near greater than distance
   C. Case 3: An 80-year-old man with strabismus and diplopia due to untreated orbital fracture
Patience for Patients: View From the Other Side

Kathy Lee MD PhD

I. What didn’t I know mid-career?
A. I am not protected from bad luck.
B. Rare disease
   1. New to me
   2. And my new doc
C. Access to all my data
D. Doctor, patient, and curious

II. How did my access to my own data influence me as patient?
A. Directed my care
   1. I am my only patient with this disease.
   2. Positives and negatives
B. Data came unaltered, without buffer or interpretation.
   1. Data access greater than physician access
   2. Anxiety colored my view
   3. Often many steps ahead on the decision tree
C. Access to provider notes
   1. Read them like a good book
   2. Not too many surprises
   3. Some inaccuracies
D. My access to my own data was illegal.

III. Open Notes Initiative
A. The study
   One-year study in 3 primary care practices: Beth Deaconess, Harborview, Geisinger
   1. 105 primary care docs (143 declined), 19,000 patients, email notification that note was ready
   2. Analysis by survey before and after, email volume and portal use
B. The results
   1. Patients: 80% opened at least 1 note; 2/3 reported better understanding of care; 1%-8% were worried, confused, or offended; 20% shared note; 85% said note availability would influence choice of providers.
   2. Doctors: 3% spent more time answering questions outside of visits; 11% spent more time writing or editing notes; 20% changed how they wrote about cancer, obesity, substance abuse, and mental health.
C. Open Note health systems: www.myopennotes.org
   1. All VA medical centers
   2. Mayo and Cleveland Clinics, Dartmouth-Hitchcock Medical Center, MD Anderson Cancer Hospital, Kaiser Permanente Northwest, and Group Health Cooperative
   3. Pediatrics: Boston Children’s Hospital and Nationwide Children’s Hospital in Ohio
D. Who owns the note? Doctor or patient?

IV. What I do differently now?
A. Write my notes for the reader
B. Instructions!
C. Teamwork

Selected Readings
Section VII: Wild Cards!
Menacing and Remarkable Video Presentations in Pediatric Neuro-Ophthalmology
Cases: History and Exam
Section VII: Wild Cards! Menacing and Remarkable Video Presentations in Pediatric Neuro-Ophthalmology

Craps!
Grant T Liu MD

CASE

- A previously healthy 9-year-old girl was seen for ptosis and double vision that developed over days.
- Visual acuity: Normal
- Visual fields: Normal
- External exam: Ptosis right upper lid
- Pupils: Right pupil was slightly enlarged compared to the left, but both reacted to light and dilated normally.
- Motility: Right, limited abduction and adduction; left, mild limitation in adduction and elevation
- Neuro exam: Otherwise unremarkable

What is your differential diagnosis and recommended testing?

Up the Ante!
Sonal R Farzavandi FRCS

CASE

Presentation
A 26-year-old gentleman presented to an outside ophthalmologist with constant binocular vertical diplopia for past 18 months. This was associated with weakness of the right upper and lower limbs and right sided facial weakness.

Past Medical History
Hypertension, controlled

Exam
- Visual acuity: 6/6 O.D. and 6/12 O.S.
- Color vision: Normal each eye
- Motility: Left esotropia 18 and left hypotropia 12 by alternate cover testing. Limited elevation and abduction (left eye > right eye), reduced convergence, convergence retraction nystagmus on attempted upgaze
- Pupils: Poorly reactive to light, well reactive to near stimulus
- Confrontation visual fields: Normal each eye

Differential diagnosis and workup of esotropia, hypotropia, limited elevation and abduction, convergence retraction nystagmus and poor pupil reactivity to light?

Losing Your Poker Face
Paul H. Phillips MD

CASE

Presentation
A previously healthy 2 1/2 year old boy developed jerking of the limbs, poor balance with difficulty walking and abnormal eye movements. He had no previous febrile illness.

Stuck!
Gena Heidary MD

CASE

History
An 8-month-old baby boy was referred by pediatric neurology to the neuro-opthalmology clinic for bilateral blepharoptosis and limited eye movements. The parents have noted the eyelid position since birth but were unaware whether the eye movement abnormalities were also present.

Birth history
The baby was born full term from an uncomplicated pregnancy.

Maternal medical history
No known medical illnesses. Prenatal vitamins were used throughout the pregnancy.

Family history
No history of strabismus or ptosis. He has an older 8-year-old brother with no visual concerns.

Social history
Mother and father are from India. There is no history of consanguinity.

Exam
Vision: Preferential looking (PL) testing revealed 20/180 vision in each eye, with no fixation preference. Cycloplegic refraction was +5.00 sphere in each eye. The external exam was notable for a marked chin-up posture and bilateral blepharoptosis. Sensorimotor exam was notable for full horizontal eye movements with inability to elevate the eyes to midline even with an oculocephalic maneuver. Upon attempted elevation of the eyes, the eyes converged. No strabismus was noted in downgaze, which was the position of the eyes at presentation.

Pupillary examination was normal. Anterior segment examination was normal in each eye. A dilated fundus examination revealed normal appearance of the optic nerves and foveae.
Nystagmus in a Happy Waif!

Michael Brodsky MD

CASE

History
- A 7-month-old-boy with a 4-month history of weight loss and negative GI evaluation
- Two months ago he developed monocular horizontal nystagmus in the right eye

Examination
- Good responses to optokinetic nystagmus drum
- Brisk pupillary responses with no afferent pupillary defect
- Low amplitude-high frequency horizontal nystagmus O.D.
- Sees well with each eye in both hemifields
- Optic discs normal

Anisocoria in Motion

Giovanni B Marcon MD

CASE

History and Exam
Six-year-old girl presents with a 1-year history of anisocoria. The parents were certain the anisocoria was not present prior to this point.
Past medical history: Negative.

First consultation (December 2012)
- Visual acuity without correction: 20/20 each eye
- External exam: Normal, no ptosis, no apparent enophthal-mos.
- Slit lamp: Normal O.U.
- Pupils: Right 3 mm, left 5 mm; both well reactive to light, no afferent pupillary defect
- Motility: Orthotropia with normal motility O.U.
- Fundus: Normal O.U.

Differential diagnosis and workup for anisocoria?

Bluff!

Mays Antoine El-Dairi MD

CASE

Presentation
Twelve-year-old girl presents with 3-month history of intermittent diplopia. Episodes are painless and recur about 6 times a day. They can happen at any time of the day, and they last about 1 minute. Diplopia is binocular, but she is not sure if it is horizontal or vertical.

Past Medical History
She has had a partial resection of medulloblastoma 4 years ago and has received craniospinal radiation of 5580 cGy, along with chemotherapy: cisplatin, CCNU, and vincristine. She has been in remission since age 9 (3 years ago), and her last MRI, done 2 days prior to presentation, was unchanged.

On examination, vision, color vision, pupils, ductions, and versions were normal. Stereopsis was 40 arc seconds. Initial prism alternate cover testing was normal, but when performed repeatedly in right gaze for more than 30 seconds, her right eye developed a large adduction deficit and a large angle exotropia that lasted about 1 minute before resolving.

Diagnosis?

Keep Your Eyes on the Prize!

Mark Borchert MD

CASE

A 22-month-old boy presents with the parents complaining that he has “balance problems” and that his “eyes don’t move with the head.” He falls whenever he tries to walk. Since birth they have noted that his eyes frequently “go up” to one side or the other. He has global developmental delay. He is just starting to take steps and he has no speech, but appears to hear well. He smiles appropriately to visual targets. He has had no previous eye examination. He has no known non-neurological systemic problems. No neuroimaging or laboratory tests have been performed.

What is your differential diagnosis and recommended testing?
Snake Eyes!
Rosario Gómez de Liaño MD

CASE

History
A 47-year-old female complains of significant difficulties with reading for 2 years. As soon as she begins to read she develops blurred vision and diplopia as well as nonspecific symptoms, such as headache, ocular pain, and dizziness.

Examination
- VA: RE, LE: 20/25-30 each eye
- Near VA with +4.00 add: J1+ each eye (very poor without correction)
- Binocular near VA: Immediately she becomes diplopic with blurred vision.
- Cycloplegic refraction: RE +1.00 sph +0.50 x 105, LE +1.00 +0.50 x 85. Normal distance vision with full cycloplegic refraction and +4.00 add at near.
- Pupils: Miotic with small anisocoria
- External: Mild LE upper lid ptosis
- Motility: Normal retinal correspondence and fusion with 4 dot test. Stereopsis 240” arc (TNO test)
- Cover test: Primary position, distance 4 PD esophoria, near esophoria 2 PD. She develops esotropia and convergence spasm on attempted reading at near.
- Rotations: Upon successive rotations the patient develops progressive abduction limitation of the LE until she cannot pass midline. Also some degree of limitation of abduction is observed on the RE after several versions. The limitation of abduction improves occluding 1 eye. Also develops limitation of elevation and depression (less so).
- With a +4.00 add: Ocular versions are normal but the patient cannot read because of defocused image.
- After cycloplegia: Limitation of abduction disappears, but limitation of elevation still present.

This patient underwent a complete neurologic and psychiatric assessment. Examinations revealed peripheral neuropathic pain, treated with pregabalin (Lyrica), and anxiety.
Section VII: Wild Cards!
Menacing and Remarkable Video Presentations in Pediatric Neuro-Ophthalmology
Answer and Teaching Points
Section VII: Wild Cards! Menacing and Remarkable Video Presentations in Pediatric Neuro-Ophthalmology

Craps!
Video Presentation of Myasthenia Gravis
Grant T Liu MD

Learning Objectives
• To understand the differences and similarities between children and adults with ocular myasthenia gravis (OMG)

Similarities Between Children and Adults With OMG
• Juvenile and adult myasthenia gravis are both autoimmune disorders.
• Presentation with ptosis, strabismus, and/or ophthalmoplegia
• Diagnosis with acetylcholine receptor antibody testing
• Use of ice test or rest test
• Treatment options include pyridostigmine, prednisone, immunosuppression, and thymectomy.

Differences Between Children and Adults With OMG
• Other forms to consider in infancy: neonatal myasthenia gravis
• Use of the edrophonium test, repetitive stimulation, or single fiber electromyography may not be possible in some children because of lack of cooperation.
• Therefore when the acetylcholine receptor antibody testing is normal, the diagnosis of ocular myasthenia gravis in a child may lack confirmatory testing.
• Amblyopia due to ptosis (deprivational) and ocular misalignment (strabismic) makes aggressive treatment more of a priority.
• Thymectomy in younger children can be performed transthoracically rather than transcervically or transsternally.
• Thymoma rare
• In our series, the development of generalized symptoms (23%) was lower than early case series of pediatric OMG (36%-43%) and that of adult OMG (31%-49%).
• These rates corroborate the notion that development of generalized symptoms may be less common in pediatric OMG than in the adult population.

References

Up the Ante!
Sonal R Farzavandi FRCS

Differential Diagnosis of Clinical Signs
Elevation deficit
• Thyroid eye disease
• Myasthenia gravis
• Ocular myositis
• Infiltrative orbitopathies
• Orbital trauma
• Nuclear CN III palsy
• Parinaud syndrome
• Myopathies

Abduction deficit
• CN VI palsy (hydrocephalus, intracranial pathology—tumor, etc.)
• Orbital trauma
• Thyroid eye disease
• Myasthenia gravis
• Myopathies

Pupillary light near dissociation
• Adie pupil
• Argyll Robertson pupil
• Dorsal midbrain lesions / compression lesions

Convergence retraction nystagmus
• Congenital fibrosis of extraocular muscles causing convergence on attempted upgaze?
• Myasthenia gravis? The combination of bilateral elevation deficit and abduction deficit could be due to myasthenia gravis. However, the presence of pupillary involvement, convergence retraction nystagmus, and reduced convergence ruled out myasthenia gravis.
Parinaud Syndrome—The Leading Diagnosis

This constellation of findings prompted us to order urgent neuroimaging, which revealed an enhancing lesion involving the tectum and extending to the left thalamus, with massive adjacent meningeal enhancement and hydrocephalus. The brainstem involvement would have accounted for patient’s right-sided hemiparesis and right facial nerve palsy.

Clinical Course

The patient underwent a ventriculoperitoneal shunt and partial resection of a pineal gland tumor due to the brainstem involvement. Histology revealed germinoma of the pineal gland. Patient underwent chemotherapy and radiotherapy. The tumor responded well to chemotherapy and radiotherapy, with improvement in the hemiparesis and facial paresis.

However, despite all treatments, the diplopia persisted.

Parinaud Syndrome

Parinaud syndrome, also known as dorsal midbrain syndrome and pretectal or sylvian aqueduct syndrome, is characterized by paralysis of conjugated vertical eye movements. Depending on their etiology and extension, midbrain lesions resulting in disturbances of the voluntary saccadic ocular movements may also affect convergence, pupillary constriction, and accommodation.1-3

Most supranuclear disorders, such as Parinaud syndrome, affect both eyes equally and do not cause diplopia. However, certain supranuclear lesions can have asymmetric involvement, resulting in strabismus and symptomatic diplopia.4,5

Etiology

- Compression of the dorsal midbrain
  - In children due to congenital hydrocephalus
  - Later in life, often from midbrain or pineal gland tumors
- Demyelination
- Vascular
- Infection
- Mesencephalic hemorrhage
- Arteriovenous malformation
- Trauma

In patients with Parinaud syndrome, if the diplopia persists 6 months after a shunting procedure, the likelihood of complete resolution is small. In addition, the most incapacitating symptom is the limitation or inability to elevate the eyes, along with the spastic movements the eyes make when attempting elevation. To compensate for this, some patients have to adopt an uncomfortable compensatory head posture. Buckley and Holgado2 have shown that this can be relieved with bilateral inferior rectus resections, and the retraction nystagmus and convergence movements also markedly improved.

References


Losing Your Poker Face
Opsoclonus / Flutter
Paul H Phillips MD

I. Clinical Features

A. Involuntary, rapid, saccades (uncontrolled saccadic intrusions: saccadomania)
B. No intersaccadic interval
C. High frequency
D. Horizontal with ocular flutter
E. Multidirectional with opsoclonus
F. Flutter and opsoclonus may occur in the same patient.
G. May occur with ataxia, myoclonus (jerky, involuntary limb movements)

II. Etiology

Localizes to cerebellum or omnipause neurons of pons

A. Paraneoplastic from occult neuroblastoma in children (50% of children with opsoclonus)
B. Paraneoplastic from small cell lung carcinoma or breast/ovary cancer in adults??
C. Brainstem encephalitis
D. Metabolic/toxic: drugs, toxins, hyperosmolar coma
E. Multiple sclerosis
F. Idiopathic

III. Differential (Pitfall)

A. Transient in healthy neonates; resolves by 3 months of age
B. Voluntary nystagmus
  1. Unsustained (< 30 seconds)
  2. Occurs with convergence
  3. Facial grimacing
  4. Eyelid fluttering
  5. Absence of ataxia, myoclonus
IV. Workup
A. Neuroimaging to detect neuroblastoma/carcinoma
B. Positron emission tomography of body to identify neoplasm
C. Blood/cerebrospinal fluid tests for paraneoplastic etiologies
   1. Anti-Ri antibody for breast/ovary cancer
   2. Anti-Hu antibody for neuroblastoma
D. Urine HVA, VMA
E. Toxic/metabolic evaluation

V. Treatment: Underlying Disorder and Symptomatic
A. Steroids
B. Plasmapheresis
C. Intravenous immunoglobulin (IVIG)
D. Immunoabsorption therapy
E. Immunosuppressive drugs: azathioprine
F. Other: propranolol, verapamil, clonazepam, gabapentin, thiamine

Selected Readings

Stuck!
Gena Heidary MD

Clinical Course and Outcome
In the setting of congenital bilateral blepharoptosis and an upgaze paresis, genetic testing for the congenital fibrosis of the extraocular muscles type 1 or 3 (CFEOM 1 or CFEOM 3) was pursued. A mutation in the KIF21A gene was identified for the diagnosis of CFEOM 1. The child underwent sequential surgery, first to address the torticollis and then to address the ptosis.

To address the marked chin-up posture, bilateral superior oblique tenotomies, large inferior rectus recessions, and superior rectus plications were performed. Approximately 1 month following strabismus surgery, bilateral frontalis slings were placed.

Postoperatively, the patient has experienced a substantial improvement in the head posture, with no exposure keratopathy.

Final Diagnosis
Congenital, bilateral blepharoptosis and upgaze limitation in genetically confirmed CFEOM1

Teaching Points
Teaching Point 1
Congenital fibrosis of the extraocular muscles (CFEOM) refers to several rare strabismus disorders characterized by nonprogressive ophthalmoplegia that primarily affects the extraocular muscles innervated by the oculomotor and trochlear nerves. In children who present with features suggestive of CFEOM, genetic testing may be pursued to evaluate for the 3 primary CFEOM clinical phenotypes: CFEOM 1, CFEOM 2, and CFEOM 3.

Teaching Point 2
The surgical management of strabismus in these patients is difficult given the complexity of the disease process, and few reports in the literature exist regarding surgical approach and outcomes. Even with an aggressive surgical approach, the strabismus may be refractory to treatment, and patients should be counseled that multiple surgical procedures may be required.

Teaching Point 3
The frontalis suspension procedure is preferred to treat blepharoptosis in this condition as it can be better titrated to prevent exposure keratopathy in these patients.

Selected Readings
Nystagmus in a Happy Waif!
Michael Brodsky MD

Differential Diagnosis

Monocular nystagmus in children

I. Spasmus Nutans
   A. Horizontal or pendular disconjugate nystagmus
   B. Head nodding
   C. Head tilting

II. Red Flags (Chiasmal/Hypothalamic Glioma)
   A. A relative afferent pupillary defect
   B. Optic atrophy or disc swelling
   C. Large head size
   D. Café au lait spots
   E. Coexistent neurological dysfunction or emaciation
   F. Small optic discs

III. Heimann-Bielschowsky Phenomenon
   A. Monocular vertical nystagmus
   B. Coarse, slow pendular movements
   C. Eye with profound visual loss of long duration

Diagnosis

Russell diencephalic syndrome
- Profound emaciation in infancy
- Absence of subcutaneous adipose tissue
- Normal or only slightly diminished caloric intake
- Alert appearance with motor overactivity
- Euphoria
- Normal or accelerated linear growth

Selected Readings


Bluff!
Mays Antoine El-Dairi MD

AVS Question 1

Which of the following is true:
1. Given variable ocular motility, this patient needs to be checked for myasthenia gravis.
2. The eye movement abnormality is related to her history of brain tumor and radiation treatment.
3. The new eye movement abnormality is concerning for recurrence of her brain tumor that could not be detected on the recent MRI.
4. These are convergence spasms. No need for further workup.

Diagnosis

Ocular neuromyotonia.

Ocular neuromyotonia (ONM) is an eye movement abnormality characterized by paroxysmal involuntary contraction of one of the extraocular muscles, resulting in intermittent diplopia and ocular misalignment. The exact mechanism of ONM remains unknown, but it is believed to be caused by aberrant neuronal signaling by injured or demyelinated cell membranes (termed “ephatic transmission”). This would be similar to the pathophysiology of hemifacial spasm, peripheral neuropathy, and trigeminal neuralgia. Other hypotheses include aberrant regeneration, nuclear hyperexcitability due to cell membrane potassium channel dysfunction, and central synaptic reorganization after retrograde axonal degeneration. Findings on ocular motor recordings suggest that the cause is related to impairment of relaxation of the extraocular muscles supplied by one of the ocular motor cranial nerves due to unstable neuronal cell membranes.

The diplopia is induced by change in gaze and is caused by overaction of extraocular muscle resisting ipsilateral antagonist muscle (eye is “stuck”). The nerve to be most commonly involved is CN III, but CN VI and IV have also been described. Ocular neuromyotonia has been described mainly following radiation to the base of the skull, but it has also been reported in the setting of aneurysms, thyroid eye disease, myelography, and demyelinating or inflammatory disorders, and in some cases no cause was identified. The onset of symptoms is usually more than 2 months (and up to 18 years) after radiation treatment is finalized.

Differential diagnosis of ONM includes ocular myasthenia gravis, demyelinating disease, convergence / accommodative spasm, decompensated phoria, superior oblique myokymia, and cyclic third nerve palsy. ONM can be successfully treated with medications that are thought to act as neuronal cell membrane stabilizers such as carbamazepine.

AVS Question 2

Which of the following history elements is important when making a diagnosis of ocular neuromyotonia?
1. History of brain tumor
2. History of radiation to base of skull
3. Family history of abnormal eye movements
4. Intermittent ptosis
Selected Readings


Anisocoria in Motion

Giovanni B Marcon MD

Clinical Course and Outcome

Presumptive diagnoses
Physiologic anisocoria vs. Horner syndrome.
Pharmacological testing with apraclonidine 0.5%: Positive. Affected pupil more mydriatic than the contralateral. Diagnosis of Horner syndrome confirmed.

Ancillary testing
- Urine catecholamines (adrenaline and noradrenaline) were performed to rule out neuroblastoma: Negative.
- Imaging
  - Chest x-ray with 2 projections: Normal
  - MRI and MRA of the brain: Normal
  - Cervical MRI: Normal

December 2013: RE: development of mild ptosis and apparent enophthalmos and iris heterochromia.

Diagnosis
Congenital Horner syndrome

Teaching Points

Introduction
Horner syndrome results from the interruption of the sympathetic innervation to the eye and the face. This determines miosis, ptosis, and anhidrosis (loss of hemifacial sweating). Most of the time the classical triad (miosis, ptosis, and enophthalmos) is not complete, and frequently anisocoria is the only clinical manifestation of the sympathetic innervation damage.

Anatomy
Sympathetic innervation of the eye and the face consists of a 3-neuron arc. The first-order sympathetic fibers arise from the posterior hypothalamus, descend along the midbrain and the pons, and terminate in the ciliospinal center of Budge at the level of C8-T2 in the spinal cord.
Second-order preganglionic fibers exit the spinal cord through the ventral spinal roots at the level T1 and ascend the paravertebral sympathetic chain, being in close proximity to the lung apex and the subclavian artery. These fibers synapse in the superior cervical ganglion at the skull base at the C3 level, in close proximity to the bifurcation of the common carotid artery.

Third-order postganglionic fibers contain vasomotor and sudomotor fibers, pupillary fibers, and fibers for the Müller muscle. At the carotid bifurcation, vasomotor and sudomotor fibers run along the external carotid artery, while pupillary fibers run along the internal carotid artery. Pupillary fibers enter the cavernous sinus, join briefly the abducens nerve, and enter the orbit through the superior orbital fissure in the ophthalmic branch of the trigeminal nerve.

The nasociliary nerve and the long ciliary nerves innervate the iris dilator and the Müller muscle.

Pathophysiology
Horner syndrome may develop from lesions at any point along the sympathetic fiber pathway.
There are some abnormalities found in any patient regardless of the level of interruption:
- Superior lid ptosis caused by reduced contraction (denervation) of the Müller muscle
- Mild elevation of the inferior lid (denervation of the lower lid muscle)
- Miosis

Impaired flushing and sweating may be found ipsilaterally only in central and preganglionic lesions because vasomotor and sudomotor fibers branch off the sympathetic chain after the superior cervical ganglion. With postganglionic lesions, anhidrosis is either absent or limited to an area above the ipsilateral forehead.
Heterochromia (affected eye hypopigmented) may be seen in congenital Horner syndrome or in long-standing cases.

Main systemic clinical manifestations

Central Horner syndrome
Patients with central Horner syndrome can usually be identified by the presence of associated hypothalamic or brainstem signs or symptoms (eg, contralateral IV nerve palsy, diabetes insipidus, disturbed temperature or sleep regulation, meningeal signs, vertigo, anhidrosis of the body, etc.).

Preganglionic Horner syndrome
Patients with preganglionic Horner syndrome may have neck pain or arm pain, anhidrosis involving the face and the neck, brachial plexopathy, vocal cord paralysis, or phrenic nerve palsy.

Postganglionic Horner syndrome
Patients with postganglionic Horner syndrome may have ipsilateral pain and other symptoms suggestive of cluster headaches (eg, tearing, facial flushing, rhinorrhea).

Main ocular clinical findings
- Ipsilateral mild ptosis
- “Upside-down ptosis”
- Apparent enophthalmos
- Anisocoria due to ipsilateral miosis
- Dilation lag (slow dilation after lights are dimmed)
- Increased accommodative amplitude
- Transient ocular hypotony and conjunctival hyperemia
- Variable ipsilateral facial anhidrosis
- Heterochromia of the iris
Etiology
Horner syndrome may be congenital, acquired, or iatrogenic.

Congenital
Congenital Horner syndrome may be caused by lesions to the:
- Carotid sympathetic plexus (obstetric perinatal forceps)
- Presumed superior cervical ganglion lesions
- Surgical or obstetric trauma to the preganglionic pathway

Acquired and iatrogenic Horner syndrome
Central Horner syndrome: Neoplasm, infection, demyelination, inflammation, trauma, ischemia, or infarction
Preganglionic Horner syndrome: Neoplasm, mediastinal or neck lymphadenopathy, cervicothorax abnormalities, neck, brachial plexus, or lung trauma or surgery, thoracic aneurysms, infection, or inflammation
Postganglionic Horner syndrome: Cavernous sinus lesions (neoplasm, infection, inflammation, aneurysms), headache syndromes, inflammatory lesions of adjacent structures (otitis media, petrositis), infection, neoplasm, trauma including surgery (basilar skull fracture, orbital fractures, middle ear surgery), vascular abnormalities of the internal carotid artery (aneurysms, dissection)

Evaluation
The evaluation of a Horner syndrome includes three stages:
1. Recognition of the clinical syndrome
2. Confirmation and localization by pharmacological testing
3. Systemic tests and imaging

Pharmacological testings are very helpful to confirm the diagnosis and to identify the level of involvement. Three main drugs may be used, all administered in drops: cocaine 2%-10%, apraclonidine 0.5%, and hydroxyamphetamine 1%

Cocaine inhibits the reuptake of norepinephrine from the sympathetic cleft at the nerve ending.

The test is performed by instilling cocaine solution 2%-4% in each eye. A sympathetically denervated pupil dilates poorly to cocaine, and the anisocoria increases. Post-cocaine anisocoria greater than 0.8 mm is sufficient to confirm Horner syndrome.

The apraclonidine 0.5% test is a practical and reliable test alternative to the cocaine test. It is currently the test of choice.

Apaclonidin is a weak alpha 1 agonist and a strong alpha 2 agonist. In Horner syndrome upregulation of alpha 1 receptors increases apraclonidine sensitivity and causes denervation supersensitivity of the dilator muscle. This supersensitivity results in pupillary dilation and lid elevation on the affected side and practically no response in the normal side. The test is more obvious under high-ambient illumination

Hydroxyamphetamine 0.5% stimulates the release of stored endogenous norepinephrine from the postganglionic axons into the neuromuscular junctions at the iris dilator muscle. So if the postganglionic fibers are intact, the affected pupil will dilate to an equal or greater extent than the normal pupil. If the postganglionic fibers are damaged, the affected pupil will not dilate as the normal pupil.

This test allows the examiner to localize the lesion in a preganglionic or postganglionic level. Localizing the lesion is important because preganglionic lesions are associated with a higher incidence of malignancy that requires extensive examinations.

Systemic tests and imaging
In general, laboratory studies do not play a significant role in the diagnosis and management of Horner syndrome. However, depending on the localization and suspected etiology, certain laboratory tests may be considered—in particular, urine test (ie, vanillylmandelic acid [VMA] and homovanillic acid [HVA]) to rule out neuroblastoma.

Imaging studies may be ordered in conjunction with appropriate medical or surgical consultation, depending on the localization and suspected etiology. A chest radiograph should always be obtained; apical bronchogenic carcinoma is the most common cause of Horner syndrome. Painful Horner syndrome should alert the physician to the possibility of carotid artery dissection, and the patient should undergo further testing (ie, MRI/magnetic resonance angiography of the brain and neck) to exclude this possibility. Internal carotid artery dissection is life-threatening and carries a risk that the patient will experience a disabling stroke.

Still unclear is whether the imaging workup should include the entire oculosympathetic pathway or should be more targeted. There are treatable causes, including malignancies, in children presenting with Horner syndrome, which justify imaging workup of the entire oculosympathetic pathway, unless the lesion level can be determined clinically.

Treatment
In general, appropriate treatment of Horner syndrome depends on the underlying cause. The goal of treatment is to eradicate the underlying disease process. In many cases, however, no effective treatment is known. Prompt recognition of the syndrome and expedient referral to appropriate specialists are vital.

Selected Readings
Keep Your Eyes on the Prize!
Mark Borchert MD

Diagnosis
Ocular motor apraxia

Teaching Points

Learning objectives
Recognize the difference between benign congenital ocular motor apraxia (OMA) and ocular motor apraxia due to neurodegenerative disease

Distinguishing features of OMA
- Inability to generate volitional saccades
- Normal pursuit and random saccades
- Tonic deviation with optokineti (OKN) stimulus
- Saccades initiated by head thrust or blink
- Delayed walking; delayed fine motor skills and reading

Differences between congenital and acquired OMA
- Congenital OMA is always confined to horizontal saccades; acquired may be horizontal and/or vertical.
- Congenital OMA may present in infancy as apparent poor vision before child has developed smooth pursuit or adequate head control to redirect gaze.
- Congenital OMA has steady progress in motor skills and eye movements. Eye movement deficiencies may be very subtle after age 8-10 years. Slight “clumsiness” may persist through life.
- Acquired OMA may be associated with progressive ataxia, if due to ataxia telangiectasia or Joubert disease.
- If associated with dilated conjunctival vessels, the diagnosis is ataxia telangiectasia; get genetics consultation (ATM gene mutations).
- If associated with see-saw nystagmus, the diagnosis is Joubert disease until proven otherwise. Get MRI of brainstem looking for hypoplasia of cerebellar vermis. Monitor vision and retina exam. Consider genetic testing for ataxia with oculomotor apraxia (AOA1 [GRID2]; AOA2 [SETX]; AOA3 [PIK3R5]).
- Acquired OMA may be associated with organomegaly, spasticity, and cognitive decline if associated with Gaucher disease. Get leukocyte glucocerebrosidase assay.

Selected Readings

Snake Eyes!
Rosario Gómez de Liaño MD

Diagnosis
Spasm of the near reflex (accommodative spasm)
- Is characterized by a triad of accommodative spasm, miosis, and attacks of variable esotropia that usually are transient
- Complaints of episodic blurred vision, diplopia, and ocular discomfort on attempt to read or near fixation
- In severe cases, symptoms may persist for many months or even years.

Etiology
- Functional/nonorganic is most frequent, often associated with anxiety, emotional and specific personality types. Hysterical cases have been reported.
- Organic causes: midbrain and posterior fossa lesions due to stroke, tumors, trauma, multiple sclerosis, Arnold-Chiari malformation, encephalopathies
- Hyperopia unable to relax, sometimes in presbyopia patients

Examination
- Imaging and neuropsychiatric consultation
- Pupils: marked miosis (variable) that increases with near fixation and with ocular rotations
- Visual acuity and refraction: fluctuating vision and pseudomyopia
- Esotropia that is variable, increasing after a brief reading period and may be associated with limitation of abduction of one or both eyes (asymmetric and variable on different examinations). The limitation of abduction also may appear on successive ocular rotations, and after cycloplegia.
- Cover test is difficult to perform, inaccurate, with many refixations.
- Sometimes brief occlusion of 1 eye improves the transient ET.
- Occlusion of 1 eye improves the convergence spasm and limitation of abduction on ocular rotations.
- Cycloplegia usually improves the convergence spasm.

Differential Diagnosis
- Decompensated esophoria/tropia
- CN VI palsy, divergence insufficiency, horizontal gaze palsy
- Myasthenia gravis
- Accommodative or convergence spasm
- Blockage nystagmus syndrome

Treatment Options
- Reassurance improves some patients but severe cases may need psychiatric counseling.
- Anxiolytics such as benzodiazepines (frequently already tried)
- Cyclopentolate + reading glasses (bifocal)
- Some authors report good results with Botulinum toxin injected into the medial rectus. (In our small experience the spasm recurred when MR recovered function.)
- Occlusion of 1 eye

**Selected Readings**

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Sonal R Farzavandi FRCS
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Melanie Rafaty  
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Debra Rosencrance  
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Beth Wilson  
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Disclosures current as of 10/9/2015  
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