NON-INFECTIOUS UVEITIS

Lana Rifkin, MD
MODERATOR

Fina Barouch, MD
PROGRAM COMMITTEE COORDINATOR

UPDATE ON MANAGEMENT OF MACULAR DEGENERATION

with Taylor Smith Oration

Andre Witkin, MD
MODERATOR

Shlomit Schaal, MD
PROGRAM COMMITTEE COORDINATOR

HECHT POSTER CONTEST

Donna Siracuse-Lee, MD
MODERATOR

MAY 31, 2019

Back Bay Event Center
180 Berkeley Street | Boston, MA 02110
NON-INFECTIONOUS UVEITIS
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Accreditation:
Accreditation: The New England Ophthalmological Society 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.

The New England Ophthalmological Society is accredited by the Massachusetts Medical Society to provide continuing medical education for physicians.
Welcome to the 775th meeting of the New England Ophthalmological Society and our final meeting of the 2018-2019 academic year. As usual, we will begin at 7:30 am in the Freedom Room with Grand Rounds, presented this time by residents and fellows from the Yale University Department of Ophthalmology. Immediately following Grand Rounds please join us for our morning session, “Non-Infectious Uveitis” which features Guest of Honor Debra Goldstein, MD, Director of the Uveitis Fellowship Program at Northwestern University. Throughout the morning, please make sure to visit the hall downstairs to peruse our resident/fellow/trainee posters. NEOS is proud to hold the Hecht Poster Contest once yearly courtesy of a generous gift to the Educational Endowment Fund by the late Sanford Hecht, MD.

In the afternoon, we will switch to “Update on the Management of Macular Degeneration”, with Guest of Honor Allen C. Ho, MD, FACS, Director of Retina Research at Wills Eye Hospital. The Taylor Smith Oration is a much-anticipated part of our afternoon retina session. This year the Taylor Smith lecture will be given by Dr. Allen Ho and is titled Cell Therapy for Atrophic Age-related Macular Degeneration. Thank you to Dr. Michael Bradbury for introducing the lecture.

NEOS was founded in 1884, the very year that Susan B. Anthony addressed the United States House Judiciary Committee arguing for an amendment to the U.S. Constitution granting women the right to vote. Much has changed in the world and in the field of ophthalmology since 1884. The American Academy of Ophthalmology admitted its first woman member in 1904. Today fully one-half of ophthalmology residents are women and about 34% of practicing U.S. ophthalmologists are women. An increasing number of women and minorities are assuming leadership positions in our societies and academic departments. I believe this bodes well overall for our profession, for future trainees and most importantly for our patients.

I want to thank you for the opportunity to serve as president this year and congratulate Mary Daly our incoming president. Thanks to Judy Cerone Keenan, Michael Bradbury, our Executive Board and our membership for your continued steadfast dedication to this remarkable society.

Sincerely,
Laura C. Fine, MD
President
ALLEN C. HO, MD, FACS

Allen C. Ho MD, FACS is Attending Surgeon and Director of Retina Research of Wills Eye Hospital and Professor of Ophthalmology at Thomas Jefferson University. He maintains special interests in macular diseases, diabetic retinopathy, surgical retinal diseases and clinical trials investigating new treatments for vitreoretinal diseases and new surgical drug delivery devices and techniques. His experience includes collaborative translational and clinical trial clinical research with expertise in study design, methodological testing, data analyses, surgical instrumentation and procedure development, execution and communication of these studies and their study results.

Through the Wills Eye Hospital Retina Fellowship, he has mentored over 60 retina fellows and international research trainees. He has been Study Chair, Steering Committee Member or Principal Investigator of over 50 clinical trials. Dr. Ho has served on the US FDA Ophthalmic Device Panel, AAO Ophthalmic Retina Technology Assessment Committee, AAO Retina Measures Group, AAO IRIS Registry Committee and is past Chair of the AAO Retina Subspecialty Days and Vail Vitrectomy meetings. He serves as Vice President of the Retina Society.

Dr. Ho has authored over 200 peer reviewed publications and several textbooks including Age Related Macular Degeneration Diagnosis and Treatment, The Wills Eye Hospital Color Atlas and Synopsis of Retinal Disease and is Editor-in-Chief of Current Opinion in Ophthalmology and Chief Medical Editor of Retina Today. He has received the American Society of Retina Specialists’ Crystal Apple Award, AAO Secretariat Award, AAO Lifetime Achievement Award, AAO Senior Achievement Award, ASRS Senior Honor Award, Retina Hall of Fame Charter Member, American Diabetic Association 75th Anniversary Distinguished Physician Award and been named to Castle Connolly Best Doctors in America, Philadelphia Magazine’s Top Doctors and The Ophthalmologist’s 100 Most Influential Ophthalmologists in the World. He serves as board member of the American Diabetes Association Greater Philadelphia and participates in AAO EyeCare America serving underinsured Americans.
Past Recipients of the Taylor Smith Medal

1985     Lorenz E. Zimmerman, MD
1986     David G. Cogan, MD
1987     Charles L. Schepens, MD
1987     Mrs. Taylor Smith
1988     Carl Kupfer, MD
1989     Frederick C. Blodi, MD
1990     Eliot L. Berson, MD
1993     John E. Dowling, PhD
1995     David Shepro, PhD
2000     Thomas A. Aaberg Sr., MD
2004     Daniel M. Albert, MD, MS
2008     Donald J. D’Amico, MD
2010     Carmen Puliafito, MD
2013     Stanley Chang, MD
2017     Allen Kreiger, MD
DEBRA A. GOLDSTEIN, MD

Dr. Debra A. Goldstein is Magerstadt Professor of Ophthalmology, Director of Uveitis Service, and the Director of the Uveitis Fellowship Program at Northwestern University in Chicago, IL, where she has been since 2012. She was born and trained in Canada, completing her medical school, residency and first uveitis fellowship at McGill University in Montreal. She then moved to Chicago and completed a second uveitis fellowship at the University of Illinois in Chicago under Dr. Howard Tessler. She remained at UIC for seventeen years, where countless medical students, residents, and fellows were fortunate enough to train under her tutelage.

Dr. Goldstein’s early academic achievements earned her a designation as not only the top 5% of entering students but also the top 10% of all McGill students and the top 5% of the Faculty of Science. Her merits continued, earning her various prestigious research awards, as well as several designations for best paper and/or best poster. As a renowned teacher and lecturer, Dr. Goldstein has amassed a myriad of honors, including the Golden Apple Award for Best Teacher in Ophthalmology, more than once. She has served as the American Uveitis Society liaison for Education and been selected as an author of the top papers in uveitis, multiple years running.

The American Academy of Ophthalmology awarded Dr. Goldstein with a Lifetime Achievement Award in 2018. She is an active member of the International Uveitis Study Group, American Uveitis Society, and the International Ocular Inflammation Society.

Dr. Goldstein has authored or co-authored over 160 peer-reviewed publications, written over 40 book chapters, and been involved in nearly 30 clinical trials. She has traveled the world as an Invited Speaker on various uveitis topics over 270 times and taught nearly 75 courses. Her contributions to the uveitis literature are unparalleled.

As a dedicated clinician, Dr. Goldstein has been selected as Chicago’s Top Doc, Chicago’s Super Doctor, and Best Doctor in America from 2001 - 2018, all years inclusive.

Dr. Goldstein has trained two to three uveitis fellows per year for decades, and is proud that they now work as distinguished uveitis specialists all over the world.
NON-INFECTIOUS UVEITIS

Lana Rifkin, MD, Moderator
Fina Barouch, MD, Program Committee Coordinator

Professional Practice Gaps:
Feedback from NEOS members and Program committee review identified that the diagnosis of uveitis, particularly potentially associated systemic disorders, is challenging for our members. In particular, there is a need for strategies of diagnosing non-infectious etiologies.

Program Objectives:
The content and format of this educational activity has been specifically designed to fill the practice gaps in the audience’s current potential scope of professional activities by:

1. Helping clinicians identify potential systemic associations of non-infectious uveitis.
2. Providing an update on the diagnosis and management of scleritis and non-infectious anterior, intermediate, and posterior uveitis.

7:00 am  Registration/Exhibits
7:30  Best of the NEOS Hal Freeman Video Library ........................................ Main Hall
7:30-8:15  Grand Rounds .................................................................................. Freedom Room
8:30  Introduction .......................................................................................... Lana Rifkin, MD
8:35  Scleritis – The Painful Red Eye .................................................... Priya Janardhana, MD
8:45  Acute Anterior Uveitis: Beyond HLAB27 ................................. Ninani Kombo, MD
8:55  Recurrent Unilateral Iritis – Is it Really Non-infectious?................. George Papaliodis, MD
9:05  Drug-induced Uveitis ................................................................. Peter Chang, MD
9:15  Introduction of Guest of Honor .................................................. Lana Rifkin, MD
9:20  Pediatric Anterior Uveitis – Part 1 ........................................ Debra Goldstein, MD
9:42  Intermediate Uveitis Essentials................................................ Paul Gaudio, MD
9:52  Sarcoid Uveitis.............................................................................. Nicholas Butler, MD
10:02  Business Meeting
10:12  Refreshment Break / Exhibits
10:42  Birdshot Chorioretinopathy – Local vs Systemic Management ................................ Lucia Sobrin, MD
10:52  Pediatric Anterior Uveitis – Part 2 ........................................ Debra Goldstein, MD
11:14  Questions and Panel Discussion ................................. Lana Rifkin, MD, Moderator
Nicholas Butler, MD  Debra Goldstein, MD  George Papaliodis, MD
Peter Chang, MD  Priya Janardhana, MD  Lucia Sobrin, MD
Paul Gaudio, MD  Ninani Kombo, MD
11:45  **LUNCHEON SEMINARS**

I. Uveitis Cases: Diagnostic and Treatment Challenges  
   Dr. Goldstein, Patriot Room

II. Surgical Pearls from 25 Years of Retinal Surgery  
    Dr. Ho, Freedom Room

III. Pearls for Selecting and Building a Practice  
     Young Ophthalmologists  
     Main Hall – NO FEE – NO CME - MUST BE PREREGISTERED

**BE SURE TO SCAN IN AT REGISTRATION BEFORE GOING TO LUNCHEON SEMINAR TO RECEIVE CREDIT**
UPDATE ON MANAGEMENT OF AGE-RELATED MACULAR DEGENERATION (AMD)

Moderator: Andre Witkin, MD
Program Committee Coordinator: Shlomit Schaal, MD

Educational Gaps:
Feedback from EOS members and program committee review identified the need to inform attendees how to diagnose AMD, risk factors for AMD, use of imaging to diagnose AMD, update on current treatments of AMD.

NEOS Program Objectives:
1. Improve competence in diagnosis of dry and wet age-related macular degeneration.
2. Increase understanding of current treatment options for dry and wet age-related macular degeneration.
3. Increase understanding of possible upcoming treatments for dry and wet age-related macular degeneration.

1:00 Introduction..............................................................Andre Witkin, MD
1:05 Risk Factors and Genetic Testing...............................Deeba Husain, MD
1:15 Diagnosis of AMD and Masqueraders......................Archana Seethala, MD
1:25 OCT Angiography of Choroidal Neovascularization (CNV)..........................Caroline Baumal, MD
1:35 Current Anti-VEGF Treatment for Wet AMD..............Brian Kim, MD
1:45 Introduction Taylor Smith Orator............................Michael Bradbury, MD
1:50 Introduction of Guest of Honor..............................Andre Witkin, MD
1:55 Cell Therapy for Atrophic Age-related Macular Degeneration..................Allen Ho, MD, FACS
2:15 Refreshment Break and Exhibits
2:45 Anti-VEGF Non-responders in Wet AMD........................Jorge Arroyo, MD
2:55 On-going Phase 3 Clinical Trials in Wet and Dry AMD....Gregory Blaha, MD
3:05 Prevention and Home Monitoring of AMD....................Chirag Shah, MD
3:15 Gene Therapy for Neovascular AMD..........................Allen Ho, MD, FACS
3:35 AMD Cases and Panel Discussion............................Andre Witkin, MD, Moderator
Jorge Arroyo, MD  Allen Ho, MD  Brian Kim, MD
Caroline Baumal, MD  Deeba Husain, MD  Archana Seethala, MD
Gregory Blaha, MD   Chirag Shah, MD
SCLERITIS - THE PAINFUL RED EYE

Priya Janardhana, MD
UMASS MEDICAL CENTER, CHESTNUT HILL, MA

Objective: Early Detection, Diagnostic Work-up and Treatment of Scleritis.

Scleritis is a visually threatening disease which can often be associated with a systemic disease or infection. The timely recognition, diagnostic work-up and treatment of scleritis can be both visually and life saving for the patient. The goal of this talk is to go over features of recognizing scleritis and to categorize the types of scleritis. We will discuss the common diseases associated with scleritis and the laboratory work-up necessary to diagnose these associated diseases. Finally, we will discuss current treatment options for scleritis.
Objective: Review non-infectious causes of anterior uveitis.

HLA B27 is the most common identifiable cause of non infectious anterior uveitis in the adult population in the United States however there are other causes of uveitis anterior non infectious that must be considered.

These include:

Idiopathic, Ulcerative Colitis, Inflammatory bowel disease, other genetic predisposition (NOD-2), rebound inflammation/immune reconstitution and medications.
RECURRENT UNILATERAL IRIritis - IS IT REALLY NON-INFECTIOUS?

George N. Papaliodis, MD
MASSACHUSETTS EYE AND EAR INFIRMARY, BOSTON, MA

Objective: Review laterality as a diagnostic method suggestive of herpes virus.

Systemic inflammatory disorders can manifest as uveitis, and in theory, both eyes should be equally susceptible. The development of recurrent unilateral iritis raises suspicion about the possibility of an underlying viral etiology as these entities (and specifically the Herpes viruses) establish latency within anatomic structures that would predispose to recurrences within the same eye (ie. trigeminal ganglion, ciliary ganglion, corneal endothelium, vascular endothelium). Aside from laterality, the Herpes viruses often have other ocular findings that may alert the clinician to the presumed diagnosis including: raised intraocular pressure (38-90% of eyes), corneal scars and/or opacities (33% of eyes), patchy or sectoral iris atrophy (10-88% of eyes), posterior synechiae (38% of eyes). Although the laterality of recurrent inflammatory events may be suggestive of a viral condition, this factor alone is not diagnostic. Rosenbaum et al reported a series of patients with HLA-B27 associated uveitis. The initial event occurred in the right eye in 52.5% of patients and in the left 44% of patients, but the difference between involvement right versus left was not statistically significant. Interestingly, 69.4% of subsequent episodes occurred in the same eye affected previously. In summary, laterality along with other associated clinical features may suggest a viral diagnosis, but the manifestation of recurrent, monocular iritis does not exclude the possibility of an autoimmune disorder.

Objective: To review systemic, topical, and intraocular medications associated with uveitis. Characteristic findings of uveitis associated with each of these medication will be discussed:

Systemic: biphosphonate, cidofovir, fluoroquinolones, rifabutin, sulfonamides, TNF-alpha inhibitors, immune checkpoint inhibitors (pembrolizumab, ipilimumab, nivolumab), MEK inhibitors and BRAF inhibitors

Topical: brimonidine, metipranolol, prostaglandin analogues

Intraocular: anti-VEGF, triamcinolone acetonide

Vaccines: BCG, influenza, MMR, Hepatitis B, HPV, varicella

Drug-induced tubulointerstitial nephritis and uveitis (TINU) syndrome: flubiprofen, Goreisan (a Chinese herb), paracetamol, codeine phosphate, lamotrigine, smoking synthetic cannabinoid


Objective: To understand the clinical presentation, differential diagnosis, risks for and treatment of pediatric anterior uveitis.

Pediatric anterior uveitis - Pearls for diagnosis and management.

Classification of uveitis based on location, timing, laterality, clinical features, associated systemic findings.

Location: Anterior, Intermediate, Posterior, Panuveitis

Onset and duration: Sudden or insidious onset, short or long duration, Unilateral or bilateral, Granulomatous or non-granulomatous


**infectious vs non-infectious

Common diagnoses:


TINU. Tubulointerstitial nephritis and uveitis syndrome. Classically presents as bilateral acute anterior uveitis. Often with preceding systemic illness. Posterior segment findings may be under-reported. Often need systemic immunomodulatory therapy

HLA-B27 associated. Typically recurrent acute anterior uveitis, one eye at a time. First episode may be bilateral. May be severe and fibrinous, with hypopyon. Ask about low back pain and stiffness, worse with inactivity.

Granulomatous uveitis. Think of sarcoidosis, Blau syndrome, TB.


INTERMEDIATE UVEITIS ESSENTIALS
Paul A. Gaudio, MD
EYE DISEASE CONSULTANTS, WEST HARTFORD, CT

Objective: Essentials of intermediate uveitis.
Define intermediate uveitis.
Case-based discussion of pars planitis: demographics, symptoms, exam findings, angiography/OCT findings. Additional studies. Treatment.
Case based discussion of non-pars planitis intermediate uveitis, attention to key examination points and imaging findings.
SARCOID UVEITIS

Nicholas Butler, MD
VA BOSTON HEALTHCARE SYSTEM, JAMAICA PLAIN, MA

Objective: To provide an update on the epidemiology, clinical features, diagnosis, and treatment of sarcoidosis-associated uveitis.

Sarcoidosis, a multisystem inflammatory disorder of unknown etiology, may present with ocular involvement in a significant proportion of patients. Numerous exam findings increase the suspicion for sarcoid uveitis—mutton-fat keratic precipitates, iris nodules, vitreous snowballs, retinal periphlebitis, peripheral chorioretinal white spots, and choroidal granulomas—but none is pathognomonic. Definitive diagnosis may be elusive and requires histologic examination of involved tissue, demonstrating non-caseating granulomas. In the absence of available tissue, various serum and ocular fluid profiles can provide additional support for the diagnosis. Numerous treatment strategies have demonstrated efficacy in sarcoidosis-associated uveitis, from local steroid therapy to systemic biologics. Therapeutic decisions are informed by the disease severity, in the eyes as well as other end-organ systems, and often require multidisciplinary collaboration.


**BIRDSHOT CHORIORETINOPIATHY - LOCAL VS. SYSTEMIC MANAGEMENT**

*Lucia Sobrin, MD, MPH*

**MASSACHUSETTS EYE AND EAR INFIRMARY, BOSTON, MA**

**Objective:** To delineate the indications for local vs. systemic treatments in birdshot chorioretinopathy.

Birdshot chorioretinopathy is a chronic, non-infectious posterior uveitic disease without systemic manifestations. It is associated very strongly with HLA-A29. There is a spectrum of disease severity. In the moderate to severe cases, there can be profound vision loss if it is not appropriately managed. There are multiple treatment options including local treatments, primarily periocular and intraocular corticosteroids, as well as systemic treatments, including traditional immunosuppressant medications and biologics. The indication for local corticosteroid treatment is primarily for the short-term management of vitritis and cystoid macular edema. Systemic medications are necessary in a majority of patients to avoid ongoing damage from inflammation flares and avoid complications of repeated corticosteroid injections. For patients who cannot refractory or intolerant to systemic medications, longer acting local corticosteroid implants are sometimes necessary. Systemic corticosteroid-sparing medications are the mainstay of treatment and can induce long term remission, whereas local corticosteroids should be used for short term control of inflammation.
PEDIATRIC ANTERIOR UVEITIS- PART 2

Debra Goldstein, MD

NORTHWESTERN UNIVERSITY, CHICAGO, IL

See page 14.
Objective: Learn about the known risk factors of AMD and genetic testing in age related macular degeneration.

Age-related macular degeneration AMD is the leading cause of blindness in people over the age of 50 years of age in the developed world and third leading cause worldwide. About 196 million are projected to have AMD globally by 2020 and 288 million by 2040. AMD is a multifactorial disease, where genetics and other non-genetic factors have been shown to play a role. The pathogenesis of AMD is not fully understood, and this has led to lack of treatments for the dry forms of this disease.

Some of the risk factors are better understood than others and there is ongoing research to evaluate the role of these risk factors. Age appears to be the most important risk factor; the chance of developing AMD increases significantly as a person gets older. Smoking is another established risk factor for age-related macular degeneration. Other factors that may increase the risk of this condition include race, sex, high blood pressure, heart disease, diet, level of activity and exposure to ultraviolet (UV) rays from sunlight. Researchers have considered changes in many genes as possible risk factors for age-related macular degeneration. A large AMD consortium study has shown that genome wide search revealed 34 loci and genes with rare variant burden for AMD. However, studies evaluating the role of these genetic factors in causation of AMD, progression of disease and response to treatment have had conflicting results. In this talk I will present what we know about the nongenetic & genetic risk factors and role of genetic testing in AMD.


DIAGNOSIS OF AMD AND MASQUERADERS

Archana Seethala, MD
HARVARD VANGUARD MEDICAL ASSOCIATES, ATRIUS HEALTH, BOSTON, MA

Objective: To discuss key elements in diagnosing macular degeneration, as well as how to differentiate it from common masqueraders.

While macular degeneration is one of the most common causes of vision loss in the elderly, the diagnosis is not always straightforward. Many conditions can mimic and masquerade as macular degeneration, both on clinical manifestation as well as symptoms.

These conditions include central serous chorioretinopathy, macular telangiectasia, myopic degeneration, pattern dystrophy, as well as inherited dystrophy such as rod cone dystrophy, vitelliform dystrophy.

In some of these conditions, differentiating between the actual diagnosis and macular degeneration can mean a significant change in treatment plan for the patient, thus is crucial.

We will review clinical characteristics on exam and imaging, as well as patient symptoms to aid in making a targeted diagnosis.

Optical Coherence Tomography Angiography (OCTA) produces high-resolution, 3-dimensional segmented images of the choroidal and retinal microvasculature. Advantages of OCTA compared to fluorescein angiography (FA) include lack of intravenous dye injection, increased efficiency and reduced procedure time. OCTA has found utility for non-invasive imaging of choroidal neovascularization (CNV) in various disorders including AMD, myopia, CSCR and multifocal choroiditis. It has been efficacious to demonstrate subclinical CNV in non-exudative AMD. OCTA may eventually prove to be an endpoint for monitoring of CNV therapeutic response. The diagnostic OCTA features of CNV will be presented, supported by clinical cases.

CURRENT ANTI-VEGF TREATMENT FOR WET AGE-RELATED MACULAR DEGENERATION

Brian Y. Kim, MD
UNIVERSITY OF VERMONT MEDICAL CENTER, BURLINGTON, VT

Objective: To discuss the current regimens for treatment of wet macular degeneration, including findings from recently completed Phase 3 clinical trials.

Previously a blinding disease with poor treatment options, wet age-related macular degeneration now has many powerful therapeutic options available. Specifically, anti-vascular endothelial growth factor agents have played a central role in greatly diminishing the visual impact of this disease. Clinical trials have estimated that by using agents such as bevacizumab, ranibizumab and aflibercept, greater than 90% of patients lose less than 15 ETDRS letters after one year. However, despite the successes of these agents, durability and sustainability of these treatments remain problematic for both patients and their providers. Promising results from recent phase 3 trials gives hope that new agents such as brolucizumab and abicipar may help address some of the current short comings in current therapy.

CELL THERAPY FOR ATROPHIC AGE-RELATED MACULAR DEGENERATION

Allen C. Ho, MD, FACS
WILLS EYE HOSPITAL, PHILADELPHIA, PA

Objective: Prevention of growth of atrophy and vision loss due to atrophic AMD.

Clinical trials are in progress for atrophic age-related macular degeneration and there are a spectrum of therapeutic strategies. Immune modulation therapies (complement pathway) have demonstrated mixed results - although some continue into phase 3 clinical trials and new phase 1 trials are starting. Most cell-based therapies currently utilize hESC derived human RPE cells delivered to the subretinal space in subjects with atrophic AMD; one clinical trial utilizing umbilical cord derived cells delivered to the subretinal space did not demonstrate a reduction in progression of geographic atrophy. Safety issues have been generated from “stem cell clinics” injecting lipid derived autologous cells into the vitreous cavity. Independent data monitoring is important for patient safety.

Surgical delivery of hESC derived human RPE cell suspensions have shown early promise in independent trials with potential engraftment of RPE cells noted at the border of geographic atrophy. More data and further refinement of surgical delivery of cell suspensions are required since epiretinal membrane formation has been observed and may be related to cell egress through a retinotomy. An ab externo surgical approach to the subretinal space via a suprachoroidal microcatheter obviates the need for a vitrectomy or retinotomy and may improve dosing precision and reduce epiretinal membrane formation.

A composite sheet of hESC derived human RPE cells on an ultrathin polymer has been surgically implanted into the subretinal space in areas of atrophy and has been well tolerated in an early phase clinical trial. There may be potential for improved visual function over this RPE transplant.


ANTI-VEGF NONRESPONDERS IN WET AGE-RELATED MACULAR DEGENERATION

Jorge Arroyo, MD
BETH ISRAEL DEACONESS MEDICAL CENTER-HMS, BOSTON, MA

Objective: To present a pathophysiologic framework that will help the clinician better understand and treat wet AMD anti-VEGF non-responders.

Age-related macular degeneration (AMD) is a leading cause of irreversible vision impairment worldwide. The current standard-of-care for patients with wet AMD typically includes regular intravitreal injections of anti-VEGF drugs which result in decreased subretinal exudation and stable or improved vision.1 Unfortunately, there still remains a small set of patients who either do not experience a reduction or experience an increase in subretinal exudation, either early (never demonstrate a response to treatment) or late (initial response to treatment with recurrence of subretinal exudation).2,3 We will present a pharmacokinetic and pathophysiologic framework upon which to better understand these challenging cases and more rationally consider other therapeutic options.


ON GOING PHASE 3 CLINICAL TRIALS IN WED AND DRY AGE-RELATED MACULAR DEGENERATION

Gregory Blaha, MD, PhD
LAHEY MEDICAL CENTER, PEABODY, MA

Objective: To discuss on-going Phase 3 clinical trials in wet and dry age-related macular degeneration (AMD).

Treatment for wet AMD underwent a profound shift with the development of anti-vascular endothelial growth factor (anti-VEGF) medicines. However, there has not been a new medicine approved for wet AMD since aflibercept in 2011 and there is still no treatment for dry AMD. This talk will discuss current Phase 3 clinical trials for wet AMD including novel anti-VEGFs, drug delivery systems, anti-ang2 compounds, modified antibodies, and biosimilars. Phase 3 trials for dry AMD will also be presented including complement inhibitors and visual cycle modulators. In addition, there will be a brief summary of recently completed, unsuccessful Phase 3 trials for E10030 (Fovista) and Lampalizumab.


PREVENTION AND HOME MONITORING OF AGE-RELATED MACULAR DEGENERATION

Chirag Shah, MD, MPH
OPHTHALMIC CONSULTANTS OF BOSTON, BOSTON, MA

Objective: To discuss current research in the prevention of dry and wet AMD. To update the audience about recent technology aimed at home monitoring and early detection of wet AMD.

AREDS and AREDS 2 vitamins still remain the standard of care in decreasing the risk of intermediate dry AMD from progressing to wet AMD1. There are still no proven treatments to halt, slow, or prevent progression to atrophic AMD. Studies are evaluating several pathways to slow progression of atrophic AMD, mostly focused on the complement pathway. Parallel phase III studies evaluating lampalizumab, Chroma and Spectri, found no benefit2. A recent study evaluating subthreshold laser for prevention of dry AMD progression found no benefit. A post hoc analysis found dry AMD progression slowed by 20% in eyes without reticular pseudodrusen; this finding warrants further study3. For wet AMD, the PROCON study tested the hypothesis that quarterly aflibercept injections in eyes with high risk drusen might prevent (or treat subclinically) conversion to wet AMD. This study found no benefit of preventative aflibercept4. The CATT study found that earlier detection and treatment of wet AMD resulted in better visual acuity outcomes5. Notal Vision developed the Foresee Home device to detect conversion to wet AMD earlier than would be detected with Amsler grid testing. They found that 87% of eyes converting to wet AMD earlier than would be detected with Amsler grid6. SightSentry is a home OCT device to monitor anatomy, rather than symptoms.


**GENE THERAPY FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION**

*Allen C. Ho, MD, FACS*

**WILLS EYE HOSPITAL, PHILADELPHIA, PA**

**Objective:** To establish a safe effective and durable anti VEGF therapy for neovascular AMD.

Gene therapy delivering a transgene for an anti-VEGF protein has the potential for continuous anti-VEGF therapy after a one-time subretinal administration. The RGX-314 Phase I/IIa study is underway to evaluate the safety and signals of efficacy of an AAV8 vector encoding for a soluble anti-VEGF Fab protein, in previously-treated for nAMD subjects.

**Methods:** Phase I/IIa trial is evaluating five doses of RGX-314 (3 x 10^9, 1 x 10^10, 6 x 10^10, 1.6 x 10^11, and 2.5 x 10^11 genome copies/eye) administered via subretinal delivery. Assessments of safety and efficacy are being conducted with the Primary Endpoints at week 26 and continued assessments to week 106. Measurements include: ocular and systemic adverse events, RGX-314 aqueous protein level, vision, central retinal thickness (CRT), and additional anti-VEGF injections needed post-RGX-314.

**Results:** Twenty-four nAMD subjects (Cohort 1 to 4) have been enrolled into the dose-escalation trial. To date, RGX-314 has been well tolerated with no drug-related adverse events or drug-related serious adverse events. Dose dependent protein production was observed in cohorts 1-3. Cohort 3 showed sustain RGX-314 protein production from one month to six months with stability in vision and anatomy despite few to no injections. Cohort 3 (6 x 10^10 GC/eye) had three subjects (50%) which have not needed any additional anti-VEGF injections in nine months with anatomic stability (CRT -37 um) and improved vision (+13 ETDRS letters) from baseline through nine months. The first six subjects in Cohort 4 had a 1 month mean aqueous protein level higher than Cohort 3.

**Conclusion:** Subretinal administration of RGX-314 in 24 nAMD subjects has been tolerated and initial results show potential for the treatment of nAMD requiring continued therapy.
NEOS SCIENTIFIC POSTER PROGRAM

Residents and fellows from all the New England ophthalmologic teaching programs have submitted abstracts for our annual scientific poster presentation contest being conducted today. Posters will be judged on originality and scientific merit. Awards will be made for the first prize $500.00, second prize $300.00, third prize $200.00 and three honorable mentions of $50.00 each. Funding for the awards is derived from a gift to the NEOS Education Endowment Fund honoring the late Sanford Hecht, MD.

Please take some time to stop by these interesting posters in the lower lobby.

NEOS thanks

Donna Siracuse-Lee, MD, *the Moderator of the Poster Contest*

AND THIS YEAR’S JUDGES

Manishi Desai, MD, Michelle Liang, MD, and Erin Salcone MD
ANTI-VEGF NON-RESPONDERS ARE OFTEN SHORT-TERM RESPONDERS

Saghar Bagheri, MD
MASSACHUSETTS EYE AND EAR, HARVARD MEDICAL SCHOOL, BOSTON, MA

Objective: To investigate the duration of anti-VEGF treatment effect in patients with nvAMD, DME and RVO, and to determine if non- or poor-responders at the standard 4-week interval actually demonstrate a treatment response at an earlier time point.

Purpose: The purpose of our study was to investigate the duration of anti-VEGF treatment effect in patients with neovascular age-related macular degeneration (nvAMD), diabetic macular edema (DME) and retinal vein occlusion, and to determine if non- or poor-responders at the standard 4-week interval actually demonstrate a treatment response at an earlier time point.

Methods: This study is a prospective multi-center trial with patients recruited from the Eye Clinic of the University Hospital of Heraklion and from the OMMA Eye Institute in Athens, Greece. Patients received intravitreal anti-VEGF (0.5 mg ranibizumab) injections and subsequently were assessed weekly for a total period of 4-6 weeks by spectral-domain optical coherence tomography (SD-OCT) for reduction in central retinal thickness (CRT) and the presence of intra- and subretinal fluid. Data collected included age, sex, visual acuity, past ocular history, total retinal volume, axial length and lens status.

Results: 52 eyes of 52 patients (mean age 67.8 years, 59.6% female, 54% treatment naive) were assessed. More than half of the eyes (51.5 %) presented with maximal CRT reduction on SD-OCT two-weeks post- injection and almost all had significantly increased CRT at week 4 compared to week 3 or week 2. Eyes that showed no to minimal CRT reduction at week 4 and would have been classified as non-responders in the usual clinical evaluation were found to have CRT reduction at weeks 2 or 3 post-injection. Furthermore, we found a higher proportion of non- and poor responders at week 4 in DME (7 of 12, 58%) compared to nvAMD (6 of 25, 24%) eyes (chi-square 4.194, p=0.0406). The time to maximal CRT reduction was not related to axial length, age, lens status or prior history of injections.

Conclusions: Our study suggests that almost all non-responders or poor responders to anti-VEGF therapy are responders if assessed at an earlier time point such as at week 2 or 3 post-injection. Our study assesses for anti-VEGF treatment response by weekly CRT measurements with SD-OCT and is the first study to describe the treatment response in previously considered non-responders. Further large, prospective studies are needed to optimize dosing intervals and to evaluate whether more frequent anti-VEGF treatment might preserve visual function in this cohort of short-term responders.
Objective: Prior OCTA studies of the choriocapillaris (CC) in dry AMD have focused on individual lesions and surrounding areas, with limited work on global analysis and staging. This study analyzed CC perfusion throughout the macula in all stages of dry AMD.

This study aimed to investigate (1) whether dry AMD stage has an independent association with macular CC perfusion, and (2) how this association (if any) varies by region. 3x3 mm and 6x6 mm swept-source OCTA images from eyes with early, intermediate, and advanced dry AMD (61 eyes from 44 patients) were analyzed using an algorithm to account for drusen shadowing followed by binarization and particle analysis to assess global and regional flow deficit metrics (flow deficit %, average flow deficit size). Analyzed regions were defined by concentric areas centered on the fovea: a 1 mm diameter circle, 1.5 mm diameter ring, 2.5 mm diameter circle, 2.5 mm diameter ring, and whole image (3x3 mm images); a 1 mm diameter circle, 3 mm diameter ring, 5 mm diameter circle, 5 mm diameter ring, and whole image (6x6 mm images). Data were analyzed using the Generalized Estimating Equations (GEE) approach, which can account for correlation among fellow eyes.

The independent association of stage with flow deficit metrics was statistically significant (p < .05) only in more peripheral regions of the macula: 5 mm ring (flow deficit %); 3 mm ring, 5 mm circle, 5 mm ring, and whole 6x6 mm area (average flow deficit size). The association of age with flow deficit metrics was significant in all regions at both image sizes, except for average flow deficit size in 3x3 mm images (only the 1.5 mm ring showed significance). There was no significant association of eye side with flow deficit metrics in any region of analysis.

To address the central questions of this study: (1) there seems to be an independent association between dry AMD stage and macular CC perfusion; (2) this association is most prominent in more peripheral regions of the macula.


Zheng F, Zhang Q, Shi Y, et al. Age-Dependent Changes in the Ma
Monoclonal Antibody Therapy for Neuromyelitis Optica: A Systematic Review and Meta-Analysis

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Objective: Due to the absence of randomized controlled trials, we sought to gain a greater understanding of the efficacy and safety of rituximab, eculizumab and tocilizumab in the treatment of neuromyelitis optica patients.

Purpose: Neuromyelitis optica (NMO) is a rare autoimmune disorder that follows a relapsing/remitting course and often leaves patients severely disabled, despite aggressive treatment with traditional immunosuppressive medication. While off-label monoclonal antibody therapy has shown efficacy in treating NMO, no large randomized control trials (RCTs) exist. In lieu of such trials, we performed a systematic review and meta-analysis to assess the efficacy and safety of rituximab, eculizumab and tocilizumab in NMO patients.

Methods: We searched MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL) and Embase from January 1, 2006 through November 15, 2018 for prospective studies using rituximab, eculizumab or tocilizumab in NMO patients and reporting annual relapse rate (ARR) and Extended Disability Status Scale Score (EDSS) before and after monoclonal therapy. Endpoints were pooled using traditional random effects meta-analysis methods, producing mean differences and 95% confidence intervals (CI).

Results: Fifteen studies involving 324 patients were included in the systematic review and meta-analysis. Monoclonal therapy resulted in a statistically significant mean reduction in ARR of 1.77 (95% CI, 1.37 to 2.17) (Figure 1) and a statistically significant mean reduction in EDSS of 1.14 (95% CI, 0.87 to 1.41) (Figure 2). Severe adverse effects were reported in 7% (23/324) of patients. Specifically, 12 patients (3.7%) had a reactivation of or primary infection, 5 patients (1.5%) had persistent leukopenia, 3 patients (0.9%) experienced an infusion-related reaction/allergic response, 1 patient (0.3%) developed cancer, 1 patient (0.3%) developed atrial fibrillation and 1 patient (0.3%) died.

Conclusions: This systematic review and meta-analysis provides evidence that monoclonal antibodies, specifically rituximab, eculizumab and tocilizumab, have a reasonable efficacy and safety profile in the treatment of NMO patients. Treatment with monoclonal antibodies was shown to reduce the frequency of NMO relapses and improve neurological disability in affected individuals. However, large RCTs are needed to definitively demonstrate their effectiveness and safety.
EVALUATION OF CLINICAL PRACTICE GUIDELINES FOR MANAGEMENT OF DRY EYE

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Objective: We evaluated three guidelines for the management of dry eyes using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument.

Purpose: Clinical practice guidelines (CPGs) are often published to provide clinicians with up to date, evidence-based recommendations. We evaluated clinical practice guidelines (CPG) distributed by the Tear Film and Ocular Surface Society (TFOS), the Cornea External Disease and Refractive Society, and the American Academy of Ophthalmology (AAO) for the management of dry eyes. The evaluation was performed using the Appraisal of Guidelines for Research and Evaluation (AGREE) II Instrument.

Methods: We conducted a literature search of CPGs of dry eye available to ophthalmologists and selected three. Four evaluators then independently appraised the CPGs with the AGREE II Instrument. The scores were presented on a 7-point scale. Score were averaged under six domains (Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity of Presentation, Applicability and Editorial Independence). We calculated standardized scores for each domain and overall quality as well as intraclass correlation coefficients to assess agreement between evaluators.

Results: Domain averages for the AAO guideline ranged between 51% to 89%; the CEDARS guideline between 42% and 93%; and 38% and 80% for the TFOS guideline. The intraclass correlation coefficients of the reliability of the score averages were AAO: 0.70 [0.39 – 0.88], CEDARS: 0.89 [0.76 – 0.95], and TFOS: 0.82 [0.63 – 0.93]. Overall, the three guidelines scored well on Scope and Purpose and Clarity of Presentation, and presented weaker in the domains of Stakeholder, Rigor of Development, and Applicability.

Conclusions: Dry eye management clinical practice guidelines could benefit from improvement in the domains of Stakeholder, Rigor of Development and Applicability.
Objective: Our goal is to elicit the perspectives of ocularists regarding communication with ophthalmic plastic surgeons, patient education, implant size, eyelid position at time of referral and selection of surgical materials and techniques. Ocular implants can improve the quality of life of patients who have experienced globe loss. While expert opinion has suggested that collaboration between ophthalmic plastic surgeons and ocularists is important to optimize patient outcomes, we are presenting the first survey-based investigation of this important relationship. We distributed an electronic survey to 208 practicing and retired members of the American Society of Ocularists regarding collaboration with ophthalmic plastic surgeons. Our goal was to elicit their perspectives regarding communication with surgeons, patient education, implant size, eyelid position at time of referral and selection of surgical materials and techniques. We had an 18% response rate (38/208). 98% of respondents worked in USA/Canada, 60% had 30 years or more of experience and 75% received referrals from 5 or more ophthalmic plastic surgeons. 87% reported that collaboration with ophthalmic plastic surgeons was critical to successful patient outcomes, while only 68% reported that collaboration was “always” or “often” adequate. 47% stated that patient education prior to referral for first visit was inadequate, 34% reported difficulty contacting referring surgeon, and 10% reported that their concerns were not taken seriously by the surgeon. Regarding size of implant, 55% reported problems with size of implant, with 37% reporting too large, 25% too small, and 37% variable. 50% reported problems with lower lid laxity or upper lid ptosis upon initial evaluation. Ocularists identified “good surgical technique” as the most important factor in technical success. They preferred acrylic, bio-integrated, and porous materials. Pegging was the least desirable technique. Our data suggest that while the majority of ocularists are satisfied with the level of collaboration, there remain opportunities for improvement in ease and quality of communication, patient education prior to referral, as well as improved selection of surgical materials and techniques. We suggest future research is needed to improve the quality of care we offer to patients who have experienced globe loss.

Objective: The aim of this study was to provide a comprehensive review of the underlying embryology, anatomy, and clinical presentation of punctal agenesis and to review existing management strategies and outcomes.

Punctal agenesis is defined as the absence of the punctum occurring secondary to a failure of embryogenesis. This review synthesizes existing data on the embryology, anatomy, clinical presentation, symptomatology, management options and treatment outcomes of punctal agenesis. A foundational knowledge of the underlying embryologic and anatomical abnormalities is fundamental to understanding its clinical presentation and assists in choosing an appropriate management strategy. Existing outcomes data is generally favorable and suggests management with a step-wise approach can alleviate symptoms in patients across a spectrum of disease.


DIFFERENTIAL ASSOCIATION OF MACULAR SUPERFICIAL VERSUS DEEP VASCULAR DENSITY WITH MICROANEURYSMS AND NONPERFUSION IN DIABETIC RETINOPATHY

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Objective: To understand the association between macular vessel density (VD) measurements and retinal nonperfusion (NP) and microaneurysm counts (MA#) in diabetic eyes.

Methods: Same day optical coherence tomography angiography (OCTA) and ultrawide field fluorescein angiography (UWFFA) images were obtained from eyes of diabetic patients. Global NP and NP index (NPI), and specific posterior pole (PP, central 10mm diameter zone), mid-periphery (MP, 10-15mm) and far periphery (FP, >15mm) zones were evaluated. Retinal MA were manually annotated and quantified on UWFFA. OCTA 3x3 mm images were processed with projection artifact removal software (Angiovue ver 2017.1.0.151). Automated segmentation of superficial (SCP) and deep (DCP) capillary plexuses provided VD for the whole image and parafoveal macular quadrants.

Results: A total of 54 eyes of 34 patients with mean±SD age 48.4±14.2 years, HbA1c 8.1±0.6%, diabetes duration 25.3±10.0 years, with 48.1% female, and 57.4% type 1 diabetes were imaged. DR distribution was mild 5 (9.3%), moderate 16 (29.6%), and severe 17 (31.5%) nonproliferative DR and proliferative DR 16 (29.6%). MA# and NPI increased with increasing DR severity (p PP (r=0.77, p global SCP VD and MA# or NPI. However, temporal (T) and inferior (I) SCP VD was correlated with PP NPI (T: r=-0.46, p MP MA# (MP: r=-0.49, p=0.003) and FP NPI (r=-0.34, p=0.01). All DCP quadrants correlated with PP MA#. DCP-S, PP and MP while DCP-S correlated with FP MA#. DCP T and I VD were correlated with PP NPI (T: r=-0.41, p=0.003) and T VD correlated with MP and FP NPI (r=-0.43, p=0.002 and r=0.37, p=0.007).

Conclusions: These findings suggest that macular superficial versus deep vascular plexuses have differential associations with posterior versus peripheral MAs and nonperfusion in diabetes. Correlation with peripheral retinal pathology also varies between macular plexus quadrants. Further studies may provide further insight into how specific zones within OCTA macular scans reflect or predict disease activity beyond the posterior pole.


COLLAGEN CROSS-LINKING IN COLLAGEN XII DEFICIENT MICE WITH RIBOFLAVIN AND UVA LIGHT

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Objective: 1. To understand the role of collagen XII in collagen cross-linking with riboflavin and UVA light. 2. To determine if collagen XII participates in interfibrillar bonds which may affect stromal hydration. 3. To determine if collagen XII participates in cross-linking of normal aging.

Murine eyes were harvested from WT C57 mice and Col12a1 deficient mice and de-epithelialized using 35% ethanol. In the first experiment, 0.136% riboflavin in 25% dextran solution was applied to P60 eyes every 5 minutes for 35 minutes while exposed to UVA light at 3 mW/cm². In the second, P60 eyes were soaked in balanced salt solution for 30 minutes. In the third, eyes at P210 were soaked in balanced salt solution. All eyes were fixed and imaged with transmission electron microscopy. Fibrils in the anterior stroma were then quantified using ImageJ software as the number of fibrils per 0.04 um² area.

12 images from 1 to 2 eyes were analyzed per experimental group. With riboflavin and UVA light, the average number of fibrils per 0.04 um² area in WT C57 was 21.50 versus 9.83 in Col12a1 deficient mice (p

This preliminary data suggests collagen XII may affect fibril spacing after riboflavin and UVA treatment, but its impact on fibril organization during hydration appears minimal. Repeat trials are needed. Future studies with uniform epithelial removal and alternative analysis may better reveal the role of collagen XII in collagen cross-linking.
RISK FACTORS IN PERSISTENT INFLAMMATION POST-LPI IN PATIENT WITH NARROW ANGLES

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Objective: The intent of this study is to retrospectively investigate patients with persistent inflammation post-LPI and define any risk factors or common factors for this persistent post-LPI inflammation.

Methods: We analyzed retrospectively about 84 patients who had LPI in 2018 at Boston Medical Center who had LPI for narrow angles. Fisher exact test and t-test was used for statistical analysis of the data.

Results: Total of 84 patients who underwent LPI included in the study. Total number of patients with inflammation were 11 and 73 patients were with no inflammation. Comparing patient with persistent inflammation to patients with no inflammation, race was not statistically significant with a p value of 0.8767. Type of laser (Argon and Yag vs Yag alone) was close to statistically significance with a p-value of 0.058. Moreover, gender, location of LPI, surgeon experience was not found to contribute to persistent inflammation post-LPI.

Conclusions: Our results did not find location of LPI, race, type of laser, surgeon experience to contribute to persistent inflammation post-LPI. Pending further evaluation of more patient to include from prior years, the use of both Argon and Yag might contribute to persistent inflammation given how close the p value was to statistical significance. Pending further evaluation of more patient, the current data suggests past intraocular inflammation and intraocular surgical history might contribute to persistent inflammation post-LPI.
Objective: To present a case of vision loss in a pediatric patient with cerebral venous sinus thrombosis with special attention to workup and management.

Methods: Case Report.

Results: An 11-year-old male patient with past medical history of chronic headaches and recent head trauma while playing hockey, presented to neurology with complaint of worsening headache. His initial exam was notable for bilateral disc edema, prompting referral to the Emergency Department and urgent Ophthalmology Consult. Family history was significant for multiple family members with thrombosis, early cardiac events and/or death. On exam, he was noted to have prominent veins on the forehead. Visual acuity was 20/20 OU, IOP was normal, and an APD OS was present. Slit lamp biomicroscopy was notable only for mild diffuse conjunctival injection. On dilated fundus exam, significant bilateral disc edema was confirmed (Figures 1). Visual field testing revealed dense scotomas in both eyes, left worse than right. MRI demonstrated optic nerve findings consistent bilateral optic nerve edema (Figure 2). MRV revealed extensive but non-occlusive venous sinus thrombosis (Figure 3). Extensive hypercoagulable workup was performed (Figure 4). Notably, lipoprotein (A) was found to be elevated. The patient was started on heparin and acetazolamide. He underwent multiple lumbar punctures with elevated opening pressures; each required periprocedural suspension of anticoagulation. He also developed metabolic acidosis, a known adverse effect of acetazolamide. Despite treatment, there was minimal improvement in clinical exam. He had continued severe bilateral optic nerve edema and visual field defects. His central vision in the left eye declined to 20/30. Neurosurgery was consulted, and an LP shunt was placed. Post-operative course was complicated by low pressure headaches and cerebellar tonsillar herniation. Optic nerve edema improved following LP shunt placement. Final visual acuity has stabilized at 20/20 OD and 20/70 OS. Repeat MRV 3 months later shows persistent and large clot burden despite continued anticoagulation therapy.

Conclusion: Cerebral venous sinus thrombosis (CSVT) is a life-threatening condition with the potential for permanent vision loss. Given the often non-specific presenting symptoms, a high index of suspicion is needed in order to establish a diagnosis and initiate treatment early. Elevated lipoprotein (A) has been identified as a new risk factor of CVST.1,2 Despite early treatment, CVST remains difficult to manage.
Appearance of right and left fundus at symptom onset.

Figure 2. T2-Weighted MRI with fat suppression revealed symmetric dilation of the optic nerve sheaths with fluid, flattening of the posterior globes, and anterior bowing of the optic nerves.
MRV revealed extensive but non-occlusive thrombosis of the distal superior sagittal sinus, right transverse and sigmoid sinuses. Findings of slow flow in the left transverse sinus with small nonocclusive thrombus at the junction of the left transverse and sigmoid sinuses.

Figure 4. Hypercoagulability Workup

<table>
<thead>
<tr>
<th>Abnormal</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR</td>
<td>92 (0.00 - 15 mm/h)</td>
</tr>
<tr>
<td>CRP</td>
<td>26.4 (0.00 - 10.00 mg/L)</td>
</tr>
<tr>
<td>PT</td>
<td>14.2 (10.2 - 12.0 sec)</td>
</tr>
<tr>
<td>INR</td>
<td>1.3 (0.8 - 1.2)</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>540 (154 - 448mg/dL)</td>
</tr>
<tr>
<td>Factor VIII Activity</td>
<td>150 (53 - 131)</td>
</tr>
<tr>
<td>Lupus Anticoagulant</td>
<td>1.31 (&lt; 1.21)</td>
</tr>
<tr>
<td>Fecal calprotectin</td>
<td>283.7 (0.0 - 49.9 mg/kg)</td>
</tr>
<tr>
<td>Lipoprotein (A)</td>
<td>57 (&lt;/= 30mg/dL)</td>
</tr>
</tbody>
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CORRELATION OF THREE-DIMENSIONAL NEURORETINAL RIM THICKNESS AND VISUAL FIELDS IN GLAUCOMA: A BROKEN STICK MODEL

Wendy Liu, MD, PhD
BOSTON, MA

Objective: To determine the minimum distance band (MDB) neuroretinal rim thickness at which visual field (VF) damage becomes detectable and associated with structural loss.

Purpose: To determine the minimum distance band (MDB) neuroretinal rim thickness at which visual field (VF) damage becomes detectable and associated with structural loss.

Design: Retrospective cross-sectional study.

Participants: 57 healthy and 101 glaucoma subjects (one eye per subject) were recruited from an academic institution.

Methods: All patients had VF examinations (Swedish Interactive Threshold Algorithm 24-2 test of the Humphrey visual field analyzer 750i; Carl Zeiss Meditec, Dublin, CA) and spectral domain optical coherence tomography volumetric scans (Spectralis, Heidelberg Engineering, Heidelberg, Germany). Comparison of MDB thickness values with VF mean deviation values showed a plateau of VF mean deviation values followed by a sharp decline at lower MDB neuroretinal rim thickness values. A broken stick statistical analysis was utilized to estimate the tipping point at which MDB neuroretinal rim thickness values are associated with initial VF defects. The slope was computed for data below the tipping point.

Main Outcome Measures: Point at which VF loss becomes associated with MDB neuroretinal rim thickness values.

Results: 158 subjects were recruited for the study (57 healthy and 101 open angle glaucoma patients). 55% of the subjects were female, and 65% were Caucasian. Of the OAG patients, 67 had primary OAG, 14 had pseudoexfoliation glaucoma, 8 had pigmentary glaucoma, and 12 had normal tension glaucoma. The mean MDB thickness was 313 microns for healthy subjects and 175 microns for glaucoma subjects. The mean global MDB value associated with VF loss was 227 um, which is a 25.8% loss from the mean normal value.

Conclusions: In open angle glaucoma, substantial MDB neuroretinal rim thickness loss occurs before functional visual field defects become detectable.
SECOND EYE INVOLVEMENT AND RETINAL DETACHMENT IN EYES WITH CYTOMEGALOVIRUS RETINITIS TREATED WITH INTRAVITREAL GANCICLOVIR: A PROSPECTIVE INTERVENTIONAL COHORT STUDY

Louisa Lu, BA
YALE SCHOOL OF MEDICINE, CT

Objective: To report the incidence of, and to estimate the risk factors associated with, the development of second eye involvement and retinal detachment in a cohort of HIV-infected patients with CMV retinitis receiving treatment with intravitreal ganciclovir.

Purpose: The purpose of this study was to report the incidence of, and to estimate the risk factors associated with, the development of second eye involvement and retinal detachment in a cohort of HIV-infected patients with cytomegalovirus (CMV) retinitis receiving treatment with intravitreal ganciclovir.

Design: Prospective interventional cohort study.

Participants: This study included HIV-infected patients with newly-diagnosed cytomegalovirus retinitis who presented to the ophthalmology clinic at Maharaj Nakorn Hospital in Chiang Mai, Thailand between May 2013 and March 2016.

Methods: Patients with CMV retinitis underwent dilated fundus examinations and received treatment with intravitreal ganciclovir according to a standardized schedule for 12 months. The incidence of second eye involvement of CMV retinitis and new-onset retinal detachment were assessed and baseline risk factors for both outcomes were analyzed using a Cox proportional hazards model, adjusted for the patient’s CD4 count and treatment with highly-active antiretroviral therapy (HAART).

Main Outcome Measures: Two main outcomes were pre-specified: (1) contralateral CMV retinitis in participants with initially unilateral disease (second eye involvement), and (2) new onset of retinal detachment.

Results: A total of 111 eyes with CMV retinitis from 76 HIV-infected patients were included in the cohort study. Of the 49 participants with unilateral CMV retinitis at enrollment, 7 developed second eye involvement over the first 3 months of follow-up (incidence 4.8 per 100 person-months, 95% CI 1.9 to 9.8). None of the person-level or eye-level baseline characteristics were predictive of subsequent second eye involvement at 3 months. Of the 105 eyes without a retinal detachment at the time of initial diagnosis, 6 eyes from 6 people developed a retinal detachment over the first 3 months of follow-up (eye-level incidence: 2.0 per 100 eye-months, 95% CI 0.7 to 4.3; person-level incidence: 2.9 per 100 person-months, 95% CI 1.0 to 6.2). None of the person-level or eye-level baseline covariates had a significant association with subsequent retinal detachment.
Conclusions: The incidence rates of retinal detachment among patients in this cohort study receiving intravitreal ganciclovir injections were similar to rates among other studied populations in the HAART era, suggesting that intravitreal anti-CMV therapy does not substantially increase retinal detachment risk. In addition, the development of contralateral eye involvement of CMV retinitis was still relatively common, highlighting the necessity for more affordable systemic anti-CMV therapy to narrow treatment disparities and effectively treat the global burden of CMV retinitis.


PROJECTION OF VISUAL OUTCOME AFTER CONVERTING TO AFLIBERCEPT FOR REFRACTORY NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

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BOSTON, MA

Objective: Determine what is best predictor of 3-year visual acuity outcomes in patients with nAMD.

Purpose: To determine factors that predict 3-year visual acuity (VA) outcomes in patients converted to intravitreal aflibercept (IVA) from intravitreal bevacizumab (IVB) or intravitreal ranibizumab (IVR) for treatment refractory neovascular age related macular degeneration (nAMD).

Methods: 43 eyes from 40 patients treated with IVB/IVR and converted to IVA during a 3-year course. Visual acuity data was collected at baseline, the first 3 loading doses, and at 3-year follow-up.

Results: Good visual acuity (VA), defined as >=70 letters (20/40 Snellen equivalent), at the 4th loading dose of anti-VEGF was the best predictor of 3-year VA outcome (OR 7.44; 95% CI, 1.85-29.96; P=0.005). Good baseline VA, absolute change in VA from baseline, time to first grading of the choroidal neovascular lesion as inactive, and rate of VA change did not predict 3-year VA outcome.

Conclusion: Achieving good VA (>=70 letters; Snellen equivalent, 20/40) by the 4th injection is a useful marker to predict 3-year visual acuity outcome in treatment refractory nAMD.


Objective: We performed a retrospective chart review of patients who were treated with checkpoint inhibitors to assess for risk factors for severe vision loss after uveitis.

Purpose: There have been several reports in the literature of uveitic entities developing in patients undergoing treatment with checkpoint inhibitors. We performed a retrospective chart review of patients who were treated with these powerful agents to assess for risk factors for severe vision loss after uveitis.

Methods: A retrospective chart review was performed. Patients treated with checkpoint inhibitors were identified and their charts analyzed to determine if any risk factors existed among patients taking these medications who developed uveitis. Ophthalmic and personal history was assessed as were types of uveitis, responsiveness to treatment, and visual outcomes.

Results: Age and sex was found to be evenly distributed among patients that developed poor visual outcomes after being treated with checkpoint inhibitors. Patients with good visual outcomes were more often non-smokers and overwhelmingly carried a diagnosis of cutaneous metastatic melanoma compared to those with poor visual outcomes that were more likely to have unknown primary or non-cutaneous melanoma primary. Multiple systemic immune-related adverse events from the medications were associated with poor visual outcomes. Uveitis that proved challenging to control requiring multiple treatment modalities was also associated with poorer visual outcomes.

Conclusions: Patients treated with checkpoint inhibitors who developed uveitis were more likely to experience multiple systemic immune-related adverse events. Patients found to have severe uveitis were more likely to have poor visual outcomes.
Objective: To evaluate whether anterior segment optical coherence tomography (AS-OCT), en face OCT, and AS-OCT angiography (AS-OCTA) can aid in the diagnosis of malignant versus benign ocular surface lesions (OSL).

Methods: We performed a retrospective review of patients with biopsy-confirmed OSL and used Avanti XR (Optovue Inc., Freemont, CA) AS-OCT, en face OCT, and AS-OCTA imaging to assess morphological features and vasculature of the lesion. Two masked graders performed measurements of total lesion thickness, epithelial thickness, area at OSL base, and vessel diameter and depth entering the OSL.

Results: A total of 20 eyes with OSL from 18 patients, with biopsy-confirmation in clinically suspected lesions, were analyzed (4 nevi, 5 pingueculae, 2 conjunctival intraepithelial neoplasias (CIN), 2 squamous cell carcinomas, 2 lymphomas and 2 melanomas). There was no statistical difference of age and gender between benign and malignant groups (p>0.05). We compared benign lesions such as nevi and pingueculae with malignant lesions such as conjunctival intraepithelial neoplasia, squamous cell carcinoma, lymphoma, and melanoma. Malignant lesions did not have a statistically significant difference in total lesion thickness or area when compared with benign lesions. The CIN and squamous cell carcinoma cases demonstrated a characteristic hyper-reflective and thickened epithelium. Malignant lesions had a statistically greater epithelial thickness of 82.2 ± 34 µm compared to benign lesions, which had an average epithelial thickness of 60.5 ± 20 µm (p=0.012). Dilated feeder vessels were another hallmark feature that was readily visualized by AS-OCTA in malignant lesions. The identified malignant feeder vessels were larger in diameter measuring at 70.7 ± 20 µm compared to vessels found in benign lesions which measured 43.3 ± 9 µm (p=0.001). In addition, the vessel depth of malignant lesions were deeper at 336.9 ± 81 µm compared to vessels of benign lesions which had an average depth of 191.1 ± 38 µm (p<0.001).

Conclusion: Multimodal OCT imaging is non-invasive and could be a useful quantitative tool in the diagnosis and management of OSL.


ENDOPHTHALMITIS: IS ANTIBIOTIC RESISTANCE A THREAT

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Objective: To characterize the nature of infectious endophthalmitis cases at an academic referral center and determine the rate of antibiotic resistance among culture-proven cases of endophthalmitis.

Purpose: Endophthalmitis is a rare but potentially devastating intraocular infection. Aqueous or vitreous tap and intravitreal injection of antibiotics are the mainstay of treatment. Antibiotic resistance has increased in recent years, yet the majority of tap and inject procedures for endophthalmitis utilize a limited number of antibiotics. This study seeks to characterize the rates of antibiotic resistance among isolates from culture-proven endophthalmitis cases.

Methods: Retrospective review of all inpatient and emergency dept. consultations at a tertiary care hospital for cases of suspected endophthalmitis over an 8-year period (2010-2018). Records were reviewed to identify cases of culture-proven endophthalmitis with documented culture sensitivities.

Results: We identified 79 cases of presumed endophthalmitis, resulting in 62 tap and inject procedures and 20 positive cultures with an identified organism and sensitivities. In total, 98 samples were obtained, including 63 aqueous (64.3%) and 35 vitreous (35.7%) samples. 16 of 63 aqueous samples resulted in a positive culture (25.4%) and 9 of 35 vitreous samples were positive (25.7%). There was no significant difference in the rate of culture positivity between aqueous and vitreous samples.

Positive cultures included 8 strep species (40%), 5 staph species (25%) and 7 others (35%) including Serratia, Klebsiella and Fungi. Resistance to ceftazidime was most commonly encountered, affecting up to 50% of staph and serratia species (figure 1). Vancomycin and ceftazidime were the most commonly used antibiotics, given in 88.7% and 80.7% of injections respectively. Empiric coverage was appropriate in 95% of cases, with the identified organism being susceptible to one or both of the antimicrobial agents being used. There were no cases of MRSA or vancomycin resistance identified in this cohort.

Conclusions: Real world culture yield from aqueous and vitreous tap for endophthalmitis are poor, with approximately one quarter of samples positive in this series. Empiric use of vancomycin and ceftazidime continues to provide excellent coverage for the majority of cases of bacterial endophthalmitis despite resistance to ceftazidime.


THE USE OF AUTOMATED PUPILLOMETRY IN THE TREATMENT OF OPIOID ADDICTION

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BOSTON MEDICAL CENTER, BOSTON, MA

Objective: To determine whether more precise measurements of pupil size and reactivity, obtained using automated infrared pupillometry, might aid in the dosing of opioid agonist therapy.

Introduction: The goal of opioid agonist therapy in addiction treatment is to control a patient’s withdrawal symptoms without causing excess sedation. Tolerance to opioid medication is variable and dosage decisions are based on a combination of a patient’s reported symptoms and clinically observed signs of withdrawal, including a rough estimate of pupil size that is prone to interobserver variability. The goal of this study was to determine whether more precise measurements of pupil size and reactivity, obtained using automated infrared pupillometry, might aid in the dosing of opioid agonist therapy.

Method: A prospective study of inpatients at an urban academic hospital between the age of 18 and 50 seeking treatment for opioid addiction. Patients on opiate agonist therapy (methadone or buprenorphine/naloxone) consented to have pupil size and several reactivity variables measured - once before and at several time points after medication dosage - using a NeuroOptics NPi-200 pupillometer. Withdrawal symptoms and signs were also assessed using the Clinical Opioid Withdrawal Scale (COWS), the current standard for dosing opioid agonist therapy. Additionally, a survey measuring patient satisfaction with withdrawal symptom control was administered following dosing.

Results: We enrolled 20 patients (70% male, average age 33.2 years) in the study. There was a statistically significant decrease in pupil size (both light and dark) and dilation velocity when comparing pre-dosing measurements to those obtained at 30 and 60 minutes post-dosing. There was no significant change in constriction velocity, percent constriction, or latency time.

Conclusions: We report a significant change in pupil size and dilation velocity following administration of opioid agonist therapy. With a larger patient cohort, we hope to identify an average change in these parameters corresponding to optimal control of opioid withdrawal symptoms. We hope that this will provide a more objective tool in the initial dosing of opioid replacement therapy and help to prevent relapse.
EFFECT OF INFERIOR OBLIQUE MYECTOMY ON PRIMARY POSITION HORIZONTAL ALIGNMENT IN PATIENTS WITH EXOTROPIA

Christina Scelfò, MD
Maan Alkharashi, MD
BOSTON MEDICAL CENTER, BOSTON, MA

Objective: We aim to evaluate the surgical success and need for adjustment due to overcorrection in patients who undergo inferior oblique myectomy (IOM) combined with lateral rectus recession (LRc) for exotropia in the setting of inferior oblique overaction.

Introduction: We aim to evaluate the surgical success and need for adjustment due to overcorrection in patients who undergo inferior oblique myectomy (IOM) combined with lateral rectus recession (LRc) for exotropia in the setting of inferior oblique overaction.

Methods: We conducted a retrospective chart review of patients with exotropia who underwent LRc using adjustable sutures alone versus LRc combined with IOM from January 2010 to present at our institution. Binocular alignment was recorded before and within one week of surgery. We evaluated post-operative alignment, surgical success (distance alignment of ?10PD), and need for post-operative adjustment due to overcorrection.

Results: The chart review identified 48 patients. Twenty-four underwent LRc alone and 24 underwent LRc combined with IOM. Surgical success was significantly higher in the lateral rectus recession alone group (91.6%) compared to the IOM group (62.5%) (P=0.036). The need for post-operative adjustment due to overcorrection was also significantly higher in the IOM group (20.8%) compared to the LRc alone group (0%) (P=0.049).

Discussion: In this study, more patients needed adjustment for overcorrection when undergoing LRc combined with IOM compared with LRc alone. Since the tertiary action of the inferior oblique is abduction, it is possible that in patients with inferior oblique overaction, weakening the inferior oblique surgically causes more esodeviation and overcorrection.

Conclusion: Surgical correction of exotropia and inferior oblique overaction with LRc combined with IOM may lead to overcorrection and increased need for post-operative adjustment.


Objective: To investigate how atrophic lesions secondary to Stargardt disease enlarge over time in untreated eyes.

Purpose: Controversy exists regarding the natural history of atrophic lesion secondary to recessive Stargardt disease (STGD1) with the reported growth rates of lesion area varying widely across clinical trials. We performed a study- and individual-level analysis to investigate how the lesions grow over time in untreated eyes.

Methods: We searched in MEDLINE, Embase, Web of Science, clinicaltrials.gov, Pubmed, and Google Scholar up to November 20, 2018 for studies that monitored atrophic lesions progression by fundus autofluorescence (FAF) in untreated eyes with STGD1 for ≥6 months. We analyzed both study- and individual-level data from the included studies using three models: the area linear model (ALM), radius linear model (RLM), and area exponential model (AEM), in which the area, radius, and natural log-transformed area changes linearly with time, respectively. A horizontal translation factor was added to shift each dataset to correct for differences in subjects’ entry time into the studies [1-3]. The best model was determined by the predicted age of lesion onset and dependence of growth rates on baseline lesion sizes. The risk of bias was assessed using the Newcastle-Ottawa Scale.

Results: Of 1503 articles screened, 7 studies (564 eyes) met our inclusion criteria. Cumulative study- and individual-level datasets fit along a straight line in the RLM after introducing horizontal translation factors to correct for different entry times (r² = 0.99 and 0.93, respectively). The growth rate of effective lesion radius was 0.104 mm/year (95% Confidence Interval = 0.086-0.123 mm/year). The age of atrophy onset predicted by the RLM (22.7±5.0 years) is remarkably similar to the reported age of onset of symptoms (22.1±3.1 years); in contrast, the predictions by the ALM and AEM deviate from this number by >5 years. Based on the individual-level data, the effective radius growth rate was independent of the baseline lesion size (r = 0.06); in comparison, the growth rates of area and natural log-transformed area were significantly dependent on the baseline lesion size (r = 0.47 and -0.33, respectively).

Conclusions: The progression of STGD1 lesions followed the RLM in both study- and individual-level data. The effective radius growth rate of atrophic lesions could serve as a reliable outcome measure to monitor STGD1 progression.

References: Shen L, Liu F, Grossetta Nardini H, Del Priore LV. Natural History of Geographic Atrophy in Untreated Eyes with Nonexudative Age-Related Macular


Objective: To evaluate superior oblique anomalies in CFEOM (including prevalence, implications on pathophysiology, and role in surgical management).

Introduction: Congenital fibrosis of the extraocular muscles (CFEOM) is a rare genetic syndrome characterized by non-progressive ophthalmoplegia and ptosis. Mutations in axonal proteins have been identified in CFEOM and correlate with abnormal embryonic development of the oculomotor nucleus and its innervated muscles. Patients often require strabismus surgery to prevent functional limitations from anomalous compensatory head postures. We noticed abnormal superior oblique (SO) muscles intraoperatively in several children with CFEOM and wished to investigate this further.

Methods: Retrospective chart review of patients evaluated for CFEOM at a teaching hospital between January 2010 and July 2018.

Results: Of 24 patients identified (ages 1 month-62 years), 10 (42%) had genetically-confirmed CFEOM. Twenty-two underwent strabismus surgery, 14 (64%) involving the SO muscle. Of these, 13 (93%) had a documented SO abnormality, including absent, thin, or anomalously inserted tendons in 9 (most commonly attached nasal to the superior rectus muscle), and tight muscles in 4.

Discussion: Almost all CFEOM patients who underwent SO surgery had abnormal SO muscles, a finding mentioned (though not well-characterized) in two previous reports to our knowledge. The high incidence of tendon misplacement may be under-appreciated given that tenotomies are often performed in the superonasal fornix, away from the tendon’s insertion on the globe.

Conclusion: CFEOM patients often have tight SO muscles or anomalously placed tendon insertions, suggesting that abnormal SO innervation is another feature of the disease process in these patients. Surgeons should expect to find such variants and should therefore plan to exclusively approach the SO tendon using a superonasal rather than superotemporal approach.

References:
OUTCOMES OF CYANOACRYLATE TISSUE ADHESIVE APPLICATION IN CORNEAL THINNING AND PERFORATION

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Objective: To report the outcomes of cyanoacrylate tissue adhesive (CTA) application in corneal thinning and perforation.

Methods: A chart review of 10,052 patients treated for corneal thinning, perforation or descemetocele at Massachusetts Eye and Ear from January 2006 to January 2018 was performed. The data from 137 patients treated with Cyanoacrylate glue was recorded and analyzed.

Results: Median age of the cohort was 63 years and 69 (50%) were female. One hundred fifteen patients (84%) had at least one systemic condition, 46 (34%) had autoimmune diseases. Eighty-nine eyes (64%) presented with perforation while 51 (36%) with thinning. The perforation/thinning was central/paracentral in 82 eyes (59%) and peripheral in 57 eyes (41%). The median size of perforation was 3.1 mm². Causes of perforation and thinning were a microbial infection in 75 (55%), sterile melt in 49 (35%), laceration in 10 and keratoprosthesis melt in 8 eyes. Median glue retention was 58 days. The success rate of glue application (defined as an intact globe without surgical intervention) was 72%, 61% and 46% at 10, 30 and 90 days post-glue application, respectively. The larger size of perforation/thinning, perforation (vs. thinning) and single glue application (vs. multiple) were correlated with a higher failure rate. Systemic conditions, use of topical corticosteroid, etiologies and location of perforation/thinning were not significantly correlated with glue failure.

Conclusion: CTA application was moderately effective in stabilizing corneal perforation and thinning in the very short-term. Multiple applications are often required. Maintenance of globe integrity after glue application decreases with time and the need for surgical intervention remains high.


LEUKEMIC INFILTRATION OF THE OPTIC NERVE: A CASE REPORT

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Objective: Leukemic optic nerve infiltration is a rare complication of acute lymphoblastic leukemia (ALL) and can occur despite central nerve system prophylaxis. Herein, we report a case of leukemic infiltration of the optic nerve in a 24-year-old male.

Methods: Case Report.

Results: A 24 year-old-male with pre-B cell ALL (diagnosed 9 months prior) was referred to our clinic with new onset blurry vision OD. He had previously undergone standard pediatric four-drug induction and was on a maintenance chemotherapy regimen. On examination, vision was 20/30 OD and 20/20 OS with normal IOP and no APD. Slit-lamp biomicroscopy revealed no anterior chamber abnormality and no anterior vitreous cell. On DFE, the right optic nerve exhibited a white, elevated infiltrate with associated peripapillary hemorrhage. The left optic nerve was normal with an otherwise stable retinal exam (Figures 1). Fluorescein angiography revealed late disc leakage of the right eye; left eye was unremarkable (Figure 2). MRI orbits showed no retrobulbar enhancement; CSF and bone marrow studies were negative for blasts. Vitreous biopsy revealed no blasts or immunoglobulin gene rearrangements. Evaluation by ocular oncology at MEEI confirmed leukemic nerve infiltrate and the patient was treated with systemic (cytarabine, asparaginase) and intrathecal (methotrexate, cytarabine, hydrocortisone) chemotherapy as well as optic nerve irradiation OU (800cGy total). Two months after treatment, vision was 20/20 OU without APD or color vision loss. DFE revealed nearly complete regression of nerve infiltrate and peripapillary hemorrhages (Figure 3). The patient is scheduled for bone marrow transplant.

Conclusion: A multidisciplinary approach is crucial in management of ALL patients. Frequent DFEs should be considered standard of care in all patients as many exhibit ocular manifestations of the disorder. In the setting of optic nerve involvement, emergent orbital radiation is warranted to decrease morbidity and mortality.

n/a **Figures available upon request (unable to upload through website)
INTRAOCULAR PRESSURE IN RESPONSE TO CONVERSION FROM BEVACIZUMAB OR RANIBIZUMAB TO AFLIBERCEPT IN PATIENTS WITH NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

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TUFTS UNIVERSITY SCHOOL OF MEDICINE, BOSTON, MA

Objective: To investigate longitudinal intraocular pressure changes associated with intravitreal injection of agents directed against vascular endothelial growth factor in patients with neovascular age-related macular degeneration with and without comorbid glaucoma.

Purpose: To understand the safety profile of intravitreal injections of agents directed against vascular endothelial growth factor in patients with neovascular age-related macular degeneration (nAMD) with and without coexisting glaucoma.

Methods: Retrospective single center (teaching hospital) interventional case series of 62 eyes (58 patients) with nAMD that received ≥3 IVB and/or IVR injections prior to ≥3 IVA injections. Charts were reviewed to identify patients with any degree of primary open angle glaucoma (POAG), pseudoexfoliative glaucoma, and/or narrow angle glaucoma. Secondary types of glaucoma, e.g. steroid or trauma induced, were not included. Intraocular pressure (IOP) data was collected as the average of three visits for the following time points: baseline, following 3 loading doses of IVB/IVR, for the 3 visits before and after the switch to IVA, and for the 3 visits at the end of the follow-up period (EOF).

Results: 19 patients had glaucoma compared to 43 without glaucoma. Baseline IOP was similar for glaucoma and non-glaucoma patients. No change in IOP followed the loading doses of IVB/IVR for glaucoma or non-glaucoma patients; however, a significant rise in IOP was noted in patients with glaucoma by the final IVB/IVR injections (1.61±0.52 mmHg, p

Conclusion: IOP in subjects with glaucoma appears to be more sensitive to intravitreal injections, rising with IVB/IVR, and declining following the switch to IVA. IVA may be safer for patients with glaucoma compared to IVB/IVR.

Objective: To describe an open, ab-externo method of XEN gel stent implantation and discuss early surgical results of this technique.

The XEN is a gelatin stent that bypasses the eye’s natural drainage pathway create a bleb. One of the challenges of XEN implantation is ensuring subconjunctival placement and avoiding entanglement in tenon’s capsule. The rates of bleb needlings postoperatively are high, with most estimates in published literature ranging from 30% to 40%. There has been interest in utilizing ab externo surgical methods to improve XEN placement. A retrospective case series was performed to compare surgical outcomes of patients who had XEN implantation with the traditional ab interno, closed conjunctiva method compared to an ab externo, open conjunctiva method. Early results suggest that the ab externo, open method is associated with less medication use post-operatively, as well as a lower needling rate, when compared to the ab interno, closed method.


n/a **Figures available upon request (unable to upload through website)**
DOXYCYCLINE ASSOCIATED CONJUNCTIVAL CYSTS

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Objective: To report a case of doxycycline associated pigmented lesions of the conjunctiva in a patient with severe dry eye disease.

Hyperpigmentation of the skin and teeth associated with chronic doxycycline is well recognized and there are several prior reports of conjunctival pigmented lesions associated with other tetracycline class antibiotics. Conjunctival hyperpigmentation associated with doxycycline, however, has not been well described.

An 85-year-old woman was found to have pigmented lesions of the tarsal conjunctiva. Histopathology revealed variably sized subepithelial cysts with PAS positive laminated and globular concretions that stained negatively for iron, calcium, and melanin. The microscopic characteristics of the cysts were nearly identical to those described in prior reports of tetracycline-minocycline associated conjunctival pigmentation.

Chronic use of oral doxycycline may result in pigmented lesions of the conjunctiva similar to those associated with other tetracycline antibiotics. Doxycycline use should be included in the differential diagnosis of pigmented conjunctival lesions.


Objective: To ascertain demographic factors associated with vision screening results

The UCLA Preschool Vision Program (UPVP) is a community outreach program that travels throughout Los Angeles County to provide free vision care for children 3-5 years old. Information collected during the vision screening visits can inform us on the vision status of children residing in different Los Angeles County Supervisorial Districts. This study aimed to provide insights into whether gender, ethnicity, language background, as well as residential neighborhood are associated with vision screening outcomes. We found that there were no gender differences in failed rates; however, being Latino, self-identifying as primary Spanish speaker, and being in District 1 was associated with higher fail rates during screening. The information provided by this study can help public health officials identify unmet needs for children's vision care in the various Los Angeles County Supervisorial Districts.

References:
Objective: Given that floaters are a common vision complaint and are frequently searched on YouTube, we sought to analyze the most watched “floater” videos.

Purpose: YouTube is an internet-based video-sharing website which allows users to upload, view, share, like or dislike various kinds of videos including medical educational videos. Informational videos can be uploaded by anyone and are of varied quality and accuracy. Given, that floaters are a common vision complaint and are viewed heavily on Youtube, we sought to analyze the most watched “floater” videos.

Methods: To analyze videos available on YouTube in October 2018, we used the following search terms: “floater eye” and “floater vision.” Selection criteria included videos in English with over 50,000 views. We excluded duplicate and irrelevant videos. Two independent ophthalmology residents graded videos using established CRAAP criteria (Current, Relevant, Accurate, Authority, Purpose), and classified them as excellent, satisfactory, or poor. Videos were additionally graded based on audiovisual quality and on 5 floater specific questions which, contributed to accuracy and comprehensiveness scores. Total video scores were based on overall presentation, quality, and floater specific questions.

Results: There were a total of 19,065,336 views ranging from 52,224 to 10,898,050 per video. 37% of all videos were made by medical providers including ophthalmologists, optometrists and chiropractors. Patients, companies, institutions, and unknown uploaders created 24%, 20%,14%, and 4% of videos respectively. 63% of videos had primary or secondary educational aims, while 41% focused on advertising. 25% of the videos described alternative and unproven treatment options for floaters, while 18% of the videos showed YAG vitreolysis or vitrectomies by medical providers. Audiovisual quality was excellent in 47% and poor in 37% of videos. Comprehensiveness was excellent in 20% and poor in 53%, and accuracy was excellent in 43%, and poor in 41% of videos. With regards to addressing 5 floater specific questions, 14%, 27%, and 59% scored excellent, satisfactory, and poor, respectively. 18%, 37%, and 45% of videos were ultimately considered excellent, satisfactory, and poor, respectively. There was small positive correlation between presentation, video quality, FSQs and total video score to like-to-dislike ratio.

Conclusions: Floaters are a common chief complaint and are heavily searched and viewed on YouTube. This study suggests that the information on YouTube regarding floaters is largely unreliable and in many cases misleading to viewers.


Objective: The purpose of this study was to describe retinal manifestations in paraprotein-related diseases. We present a series of cases involving retinal changes secondary to lymphoplasmacytic lymphoma, MGUS, and multiple myeloma.

Retinal findings in lymphoplasmacytic and myeloid disorders are not well characterized. The purpose of this study was to describe retinal manifestations in paraprotein-related diseases. We present a series of cases involving retinal changes secondary to lymphoplasmacytic lymphoma, monoclonal gammopathy of undetermined significance (MGUS), and multiple myeloma. Methods: Medical records were reviewed from 4 patients treated from 2009-2018 at the Boston VA healthcare system in Boston, VA. Dilated ocular exam findings (DFE) and imaging studies were assessed. Case 1: 57 yo male with dyspnea, renal failure, and severe anemia presented with diffuse cotton wool spots and retinal hemorrhages. Sub-retinal and sub-retinal pigment epithelium (RPE) deposits were present along the arcades and macula. Increased serum kappa LC were present with associated glomerulosclerosis. The patient was diagnosed with B-cell lymphoma and concurrent LC disease with ocular involvement. He maintained good visual acuity with stable diffuse RPE deposits throughout the fundus bilaterally. Case 2: 55 yo male presented with diffuse bilateral cotton wool spots. FA showed extensive nonperfusion in the setting of monoclonal gammopathy of undetermined significance (MGUS) with elevated serum IgA and kappa LC. He was referred to hematology for bone marrow (BM) biopsy. Case 3: 64 yo male with hx of MGUS presented with unilateral vitreous hemorrhage. His clinical course was marked by progressive retinal ischemia bilaterally. FA showed macular ischemia with hyperfluorescence and late leakage. He was treated with intravitreal anti-VEGF and laser. Serum studies showed increased lambda LC and a diagnosis of myeloma was made. Case 4: 69 yo male referred for maculopathy evaluation. DFE was significant for scattered RPE changes and tortuous vessels. FA showed numerous areas of hyperfluorescence that leaked over time without ischemia. OCT showed central RPE level hyperreflectivity, mild SRF, and RPE detachments. BM biopsy showed plasma cell dyscrasia with lambda restricted plasma cells. Conclusion: We present a case series of 4 patients with light chain paraprotein disease with ocular manifestations. Common ocular manifestations among our patients include severe ischemic retinopathy, intra- or sub-retinal fluid, and RPE level deposition disease with variable effects on acuity. Findings were identified in the absence of serum hyperviscosity. Larger cases series are needed to better delineate the spectrum of disease and pathomechanism of intraocular findings of these disorders.
Objective: To examine the correlation of normal tension glaucoma with a reduction in corneal endothelial cell density in a single center with a predominant African-American and Hispanic population.

Purpose: Normal tension glaucoma (NTG) is a subset of open-angle glaucoma that is less dependent on intraocular pressure (IOP), making screening difficult. Although increased IOP has been associated with decreased corneal endothelial cell (CEC) density, two previous studies correlating a reduction in CEC density and NTG reported conflicting results. We performed an observational cross-sectional study to examine the correlation of NTG with a reduction in corneal endothelial cell (CEC) density.

Methods: 24 NTG patients and 26 age-matched controls were examined at the eye clinic in Boston Medical Center between January 2016 - November 2018. Exclusion criteria included those with a documented IOP above 21mmHg, prior eye surgery, lasers, ocular trauma, corneal diseases, uveitis or inflammation. CECs were imaged using a noncontact specular microscope. In patients with bilateral disease, the right eye was analyzed unless met with exclusion criteria in which case the left eye was analyzed. Outcome measures included CEC density, size and shape, and differences between NTG eyes and controls were analyzed using the Student’s t-test.

Results: Baseline characteristics including age, sex, and ethnicity were homogenous between the 24 NTG and 26 control subjects. The average CEC density in NTG eyes (2307 ± 514.7) was significantly reduced (p = 0.0440) compared to controls eyes (2570 ± 276.4). The average CEC size in NTG eyes (458.3 ± 94.82) was significantly larger (p = 0.0042) compared to control eyes (384.0 ± 57.41). The coefficient of variance in NTG eyes (43.75 ± 14.82) was not significantly greater (p = 0.9564) compared to control eyes (43.58 ± 6.178).

Conclusion: There was a significant decrease in CEC density in NTG eyes compared to normal eyes. NTG eyes had significantly increased polymegathism but no significant increase in pleomorphism compared to normal eyes. Thus, there may be a mechanism for decreased CECs in glaucomatous eyes other than elevated IOP. These findings may offer an additional risk factor to consider in screening for NTG, and may instigate further work in analyzing the relationship between CECs and trabecular meshwork cells, which arise from a common neural crest lineage.

References:
FRACTAL DIMENSIONAL ANALYSIS OF
CHOROIDAL VASCULATURE USING WIDE
FIELD INDOCYANINE GREEN ANGIOGRAPHY

Benjamin Young, MD, MS
YALE UNIVERSITY DEPARTMENT OF OPHTHALMOLOGY AND VISUAL SCIENCES, NEW HAVEN, CT

Objective: Describe the fractal analysis of the choroidal vasculature, and its implications on embryology and pathology

Purpose: While the retinal vasculature has had its fractal dimension well studied, similar analysis of the choroidal vasculature has never been evaluated. This observational study evaluates the fractal dimension of choroidal vasculature using wide field ICG angiography. While retinal vasculature follows the model of diffusion limited aggregation, we hypothesize that choroidal vasculature more closely follows the percolation model.

Methods: Both wide-field indocyanine green (ICG) angiography and fluorescein angiography (FA) were retrospectively reviewed in 27 eyes. Both types of images were binarized using the NIH’s ImageJ software, then evaluated for fractal dimension using the box counting method in an automated fashion, centered at the optic disc, from the temporal edge of the macula to an equivalent distance nasally, using the FracLac application for ImageJ. These values were then compared using a Student’s T test.

Results: The average fractal dimension of choroidal vasculature by ICG was 1.847. The fractal dimension of retinal vasculature by FA with these techniques was on average 1.703, in close agreement with previous literature, and statistically significantly different from the fractal dimension of ICG (p < 0.05).

Conclusions: While the fractal dimension of the retinal vasculature observed here closely agrees with the model for diffusion limited aggregation, which theoretically approaches 1.7, the high fractal dimension of the choroidal vasculature more closely agrees with the percolation model, with or without trapping, with predicted values of 1.82 and 1.89, respectively. Regardless, this analysis fits with the previously understood model that embryologic choroidal development follows the spreading pigmentation of in the retinal pigment epithelium, which may fit with a percolation model, in contrast to retinal vascular development that may be induced by local metabolic needs, fitting with the aggregation model.
OBJECTIVE: To investigate the incidence, clinicopathologic features, and survival of ocular adnexal lymphoma (OAL) in the pediatric population and compare these data with adults.

Design: Retrospective cohort study.

Participants: The Surveillance, Epidemiology, and End Results database was accessed to identify individuals with OAL less than or equal to 18 years of age, diagnosed between 1973 and 2015. OAL located in the eyelid, conjunctiva, lacrimal apparatus, and orbit were included. An adult cohort was queried for comparison.

Methods: Age-adjusted incidence rates (AIRs) and descriptive statistics were calculated for comparison of clinicopathologic characteristics. Overall (OS) and cancer-specific (CS) survival were evaluated with Kaplan-Meier curves and compared among subgroups using the log-rank test.

Main Outcome Measures: AIRs per 1,000,000 population at risk, descriptive statistics of clinicopathologic features, OS and CS

Results: The AIR of pediatric OAL was 0.13 (95% confidence interval [CI], 0.09-0.17) per 1,000,000. OAL AIRs showed a higher trend towards pediatric males and Blacks: males 0.17 (95% CI, 0.12-0.25), females 0.08 (95% CI, 0.04-0.13), Whites 0.11 (95% CI, 0.06-0.15), Blacks 0.26 (95% CI 0.14-0.44), Hispanics 0.12 (95% CI, 0.06-0.20), and Asians 0.03 (95% CI, 0.00-0.17). The conjunctiva was the most common site (45.0%), as opposed to adult OAL which originated primarily in the orbit (58.7%). The majority of pediatric OAL were categorized as localized SEER stage (66.7%) at the time of diagnosis. T-cell and lymphoblastic lymphoma comprised 5.0% and 15.0% of pediatric OAL, but only 0.2% and 0% of adult OAL, respectively. Advanced SEER stage, orbital involvement, diffuse-large-B-cell lymphoma, and anaplastic-large-cell lymphoma subtype were associated with increased mortality. In the pediatric cohort, the 5-year OS and CS was 91.0% (95% CI, 79.6%-96.2%) and 92.6% (95% CI, 81.4%-97.2%), respectively. The final OS and CS was 85.7% (95% CI, 71.9%-93.1%) and 89.6% (95% CI, 76.3%-95.7%), respectively. Both OS (p<0.001) and CS (p=0.02) were superior in pediatric individuals compared to adults.

Conclusions: Compared with adults, OAL in the pediatric population is characterized by significant clinicopathologic differences and better OS and CS. These results can assist clinicians in predicting long-term outcomes and in educating patients and their families.
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Baumal, Caroline:

Fees for Non-CME Services Received Directly from Commercial Interest or their Agents - Genentech
Speaker Bureau: Zeiss

Bradbury, Michael:

Ownership Interest: Regeneron, Chase and Associates, Inc (Iviews imaging system)

Dagianis, John

Fees for Non-CME Services Received Directly from Commercial Interest or their Agents: Lumenis, Speaker Bureau

Heier, Jeffrey:

Consulting Fees: 4D Molecular Technologies, Adverum, Aerie, Aerpio, Allegro, Apellis, Asclepix, Bayer, BVI, Coda Therapeutics, Corcept, Daiichi-Sankyo, Genentech/Roche, Heidelberg, Hemera, Janssen R&D, Kanghong, Kodiak, Neurotech, Notal Vision, Novatis, Ocular Therapeutix, Quark, Ra Pharmaceuticals, Regeneron, Regenxbio, Scifluor, Shire, Stealth Biotherapeutics, Thrombogenics, TLC, Tyrogenex

Contracted Research: Aerpio, Apellis, Astellas, Corcept, Daiichi Sankyo, Genentech/Roche, Genzyme, Hemera, Janssen R&D, Ophthotech, Optovue, Regeneron, Regenxbio, Scifluor, TLC, Tyrogenex

Ownership Interest - Ocular Therapeutix, Adverum
Goldstein, Debra

**Consulting Fees:** Abbvie Pharma; Allergan; B&L; Clearside Biomedical; Santen; XOMA; pSivida

**Fees for Non-CME services:** AbbVie; XOMA

**Contracted Research:** Clearside; pSivida

**Ownership Interest:** Husband is invested in his IVF lab

Ho, Allen:

**Consulting Fees:** Genentech, Janssen, BioTime, Orbit Biomedical, RegenexBio

**Contracted Research:** Genentech, Janssen, BioTime, Orbit Biomedical, RegenexBio, Apellis

Husain, Deeba:

**Consulting Fees:** Allergan, Genentech

**Other Types:** Lions Vision Gift Grant Commonwealth Grant

Neecker, Robert

**Consulting Fees:** Allergan, Alcon, Inotek, Aerie, Ocular Therapeutics, Kateena, BVI, Iridex, Quantel, Santen, Glaukos, Shire, Sun, Polyactiva, Diopsys, Ethis Communications, SOLX

**Fees for Non-CME Services Received Directly from Commercial Interest or their Agents:** Allergan, Alcon, Inotek, Aerie, Ocular Therapeutics, Kateena, BVI, Iridex, Santen, Iridex, Glaukos, Diopsys

**Contracted Research:** Allergan, Glaukos, Santen

**Ownership Interest:** Ocular Therapeutics

Rizzo, Joseph

**Receipt of Intellectual Property Rights/Patent Holder:** Bionic Eye Technologies

**Consulting Fees:** GenSight

**Ownership Interest:** Bionic Eye Technologies

Shah, Chirag:

**Contracted Research:** I am a sub-investigator for studies with the following sponsors: Genentech, Regeneron, Ellex, Novartis, NIH

**NO FINANCIAL INTEREST**

None of the other individuals in a position to control the content of this activity, including planners, CME Review Committee members, faculty presenters, moderators, panelists and reviewers have any relevant financial relationship with an ACCME-defined commercial interest to disclose.
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The following candidate has submitted application for membership and letters of support have been received by sponsors:

CANDIDATE
Desai Shilpa, MD
Boston, MA

SPONSOR
Michelle Liang, MD
Boston, MA

SPONSOR
Andre Witkin, MD
Boston, MA

FUTURE NEOS MEETINGS

THEME: FUTURE NEOS MEETINGS
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<td>September 6</td>
<td>Future of Ophthalmology</td>
<td>Carolyn Kloek, MD</td>
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<td>Ethics and Risk Management</td>
<td>Alice Lorch, MD</td>
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<td>November 1</td>
<td>Glaucoma (with Simmons Lecture)</td>
<td>Christopher Teng, MD</td>
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<td>Cataract</td>
<td>Joseph Williams, MD</td>
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<td>March 13</td>
<td>Cornea</td>
<td>Nicoletta Fynn-Thompson, MD</td>
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<td>Innovations in Ophthalmology</td>
<td>Deborah Jacobs, MD</td>
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<td>April 24</td>
<td>New Drugs in Ophthalmology</td>
<td>Lucia Sobrin, MD</td>
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<td>Retina</td>
<td>Peter Chang, MD</td>
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<td>June 5</td>
<td>Ocular Trauma</td>
<td>Magdalena Krzystalik, MD</td>
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<td>Subday: Neuro-ophthalmology</td>
<td>Crandall Peeler, MD</td>
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<td>Uveitis</td>
<td>Ninani Kombo, MD</td>
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<td>Strabismus</td>
<td>Oren Weisberg, MD</td>
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