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Review of Nutritional Supplementation Options for the Anterior Segment: An Evidence Based Approach

Allan Slomovic, MD, FRCSC
Manokamna Agarwal, MD

Introduction

The anterior segment of the eye is a metabolically active system, which includes the ocular surface of the eye and extends posteriorly to the crystalline lens.[1] Ocular surface diseases often disrupt the complex interplay of cornea, conjunctiva, meibomian glands, eyelids, and the lacrimal system, leading to diminished visual acuity and discomfort, and occasionally to frank pain. This can negatively impact the patient's quality of life. Other anterior segment diseases including keratoconus, glaucoma, and cataract may also affect visual acuity. Oxidative stress and inflammation have been investigated in pathogenesis of these diseases.[2] There has been an increase in the number of studies investigating various nutritional supplements benefiting the anterior segment structures. This review discusses the role of these supplements with supported clinical evidence.

Treatment Modalities for Ocular Surface Diseases

Autologous Serum Tears

Autologous serum tears have garnered significant interest within the realm of ocular surface health, emerging as a promising intervention for addressing various eye pathologies. Derived from the patient's own

blood, these unique tears contain a rich assortment of essential growth factors and bioactive compounds crucial for the regeneration and rejuvenation of compromised ocular tissues.[3] Clinical applications have explored different concentrations of serum, including 20%, 40%, and 50%. Hussain *et al.*[4] concluded that at 50%, serum tears are safe and effective for the long-term treatment of dry eye disease (DED). Encouragingly, multiple studies have demonstrated positive outcomes, affirming the effectiveness of autologous serum tears in mitigating discomfort associated with dry eye syndrome and various other ocular surface disorders. In a cross-over study, severe DED patients were randomized to receive 3 months of treatment with autologous serum eye drops 50% and 3 months with conventional therapy, and vice versa; symptoms and impression cytology of conjunctival epithelial cells improved significantly after treatment with autologous serum tears.[5-7] While systematic reviews and meta-analyses of randomized controlled trials (RCTs) indicate some benefits for patients with DED compared to artificial tears, further large-scale RCTs are warranted to validate these findings.[8]

Platelet Rich Plasma Eye Drops

Autologous platelet rich plasma (PRP) eye drops have been shown to be beneficial in various ocular surface disorders, including severe DED, neuropathic ulcers, LASIK-induced dry eye, recurrent corneal erosions, acute corneal chemical injury, and persistent epithelial defects.[9-13] Platelets play an important role in tissue regeneration and wound healing.[14] Metheetrairut *et al* have shown that PRP contains higher concentration of epitheliotropic factors like fibronectin, transforming growth factor-beta1(TGF- β1) and epidermal growth factor in PRP eye drops when compared to autologous serum drops.[15]

Recently, a meta-analysis and systematic review concluded that platelet-rich plasma significantly reduces the signs and symptoms of DED. This meta-analysis included 19 studies from different parts of the world including Spain, Italy, Egypt, India, and Columbia. Both evaporative and aqueous tear deficient dry eye were treated with PRP eye drops and improvement in tear quality, tear quantity and corneal staining, along with symptomatic improvement, was noted.[16]

Plasma Rich in Growth Factors (PRGF) Eye Drops

Plasma rich in growth factors has also been used for the treatment of DED. This technology activates the PRP using calcium chloride, which allows the release of biologically active proteins from platelets. In 2007, Rocha *et al* successfully used PRGF eye drops for neurotrophic ulcer following LASIK surgery.[17] Corneal healing with PRGF drops was reported by Lopez-Plandolit *et al.* in patients who were refractory to other medical treatments such as topical corticosteroids, autologous serum drops or amniotic membrane.[18] Successful treatment of rapidly progressive corneal melt with PRGF has also been noted in an isolated case report.[19] PRGF was noted to be effective and safe in refractory DED and neurotrophic keratitis stages 2 and 3 showing poor response to traditional treatments, with improvement in ocular symptomatology and signs of inflammation.[20-22]

Albumin, Fresh Frozen Plasma (FFP) and Heparin Eye Drops

Albumin eye drops can also be used for dry eyes as an alternative to serum eye drops. The compounded drops are available as human albumin 5% infusion solution.[23] Unlike autologous blood drops, these drops do not require individual extraction or centrifugation. Serum albumin is abundantly present in human serum and carries many physiologic roles. In therapeutic models, it has shown to rescue epithelial cells from apoptosis in dry eyes.[24] A clinical study conducted by Seki *et al.* showed statistically significant improvement in symptoms of keratoconjunctivitis sicca with the use of human albumin eye drops. The human albumin drops were well tolerated in 95% of the patients in their study with no adverse reactions.[25] Both FFP and heparin are used topically in treating ligneous conjunctivitis.[26,27]

Amniotic Membrane Extract Eye Drops (AMEED)

Similar to cryopreserved amniotic membrane, amniotic membrane extract also contains a high concentration of growth factors and inhibitory proteases that prevent inflammation, scarring, and angiogenesis.[28] AMEED can be prepared by different methods yielding different concentrations of bioactive components.[29] Studies conducted by

Perez *et al.* and Sabater-Cruz *et al.* show promising results in severe ocular surface pathologies including limbal stem cell deficiency, neuropathic ulcer, and DED.[30,31]

Vitamin A

Limited clinical evidence exists in the literature on the efficacy of topical Vitamin A. Kim *et al.* compared the efficacy of Vitamin A and cyclosporine A 0.05% eye drops in DED and found both treatments to be effective.[32] Another study compared Vitamin A to placebo and found Vitamin A ophthalmic solution (500 IU/mL) was safe and effective for the treatment of patients with dry eye.[33] The role of Vitamin A has also been studied in corneal healing. A study by Chelala *et al.* concluded that Vitamin A eye ointment did not affect re-epithelialization time, postoperative pain, corneal haze formation, or visual outcomes following PRK.[34]

Vitamin B

No direct study has evaluated the role of Vitamin B12 supplementation to treat neuropathic pain. However, Ozen *et al.* did find that Vitamin B12 deficiency was related to neuropathic ocular pain in DED patients.[35]

Compounded Testosterone, Lactoferrin and Selenoprotein P

There is limited evidence in the literature to support the benefits of topical testosterone in improving the quality of meibum in patients with meibomian gland disease.[36] Clinical evidence is limited for use of oral lactoferrin and selenoprotein P in DED.[37,38]

Omega-3 Fatty Acid Supplementation

Oral omega-3 fatty acids, often derived from fish oil, have become quite popular as a nutritional supplement in patients with dry eye. There are different formulations available, with a particular focus on the ratio of docosahexaenoic acid (DHA) to eicosapentaenoic acid (EPA). A large, multicentre, prospective, and double-masked clinical trial (DREAM study) was conducted to assess the efficacy and safety of 3000 mg of oral omega-3 fatty acid supplementation (2000 mg EPA, 1000 mg DHA) vs olive oil (1000 mg) as placebo for the treatment of dry eye, and did not show any difference in either of the groups.[39] We believe olive oil may not have been the best choice for a placebo as polyphenols found in the olive oil can reduce the risk of cardiovascular diseases, and omega-9 oleic acid is an anti-inflammatory agent.[40] An updated systematic review and meta-analysis indicates that omega-3 supplementation helps in improving the symptoms of DED. In contrast to the DREAM study, this review included studies with other sources of omega-3 such as krill and flaxseed oil. Also, the placebo included wheat germ oil, safflower oil and sunflower oil in addition to olive oil.[41] In addition, to reduce the risk of coronary vascular disease, the American Heart Association recommends a daily intake of 3 grams of omega-3 fatty acids in healthy adults and 1 gram in patients with documented coronary heart disease.[42]

Cataracts and Nutritional Supplements

Many recent RCTs that have studied the role of nutritional supplements show no significant results in preventing or halting cataract development.[43-46]

Glaucoma and Nutritional Supplements

Although there is much evidence supporting the role of oxidative stress in glaucoma, the meta-analysis done by Ramdass *et al.* did not show strong evidence to support the role of nutritional supplements in preventing glaucoma.[47]

Vitamin D

The association of Vitamin D with anterior segment disorders have been explored. It has been noted that patients with DED and keratoconus have lower levels of Vitamin D.[48-50] Although the evidence is still a work in progress, Gorimanipalli *et al.* offer valuable insights into the existing evidence and practical guidelines for incorporating Vitamin D into the management of keratoconus and dry eyes.[51]

Conclusion

The focus of this paper was to review the current evidence for nutritional supplementation in the management of anterior segment diseases. Our conclusions are that, while there is evidence suggesting a role for nutritional supplements in managing anterior segment disorders of the eye, especially for DED, further research is warranted to solidify these findings. Studies with larger sample sizes and more prospective, double-blinded RCTs are essential to enhance the evidence base and provide clearer guidance for healthcare professionals and patients alike. As our understanding of the relationship between nutrition and eye health continues to evolve, continued investigation into the efficacy and

safety of nutritional supplements will be crucial in optimizing treatment strategies and improving outcomes for individuals affected by anterior segment disorders.

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Endothelial Corneal Dystrophy

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Introduction

Fuchs endothelial corneal dystrophy (FECD) was first described by Ernst Fuchs in 1910. It is a bilateral corneal endothelial dystrophy characterized by progressive loss of corneal endothelial cells and formation of excrescences at the level of Descemet's membrane called guttae. The diseased endothelium leads to corneal edema and loss of corneal clarity. FECD typically manifests in the fifth and sixth decade of life coinciding with the development of cataracts. Careful preoperative evaluation and surgical technique allows for selection of patients who can safely undergo cataract surgery alone. Some patients, however, would benefit from both cataract surgery and endothelial transplantation (EK). This can be done as a staged surgery (cataract surgery then EK or vice versa) or in combination as a single procedure. This review evaluates the management strategies for individuals with cataract and FECD to help guide surgical decision-making and planning.

Pre-operative Assessment

Patient History

Clinical history should aim to differentiate if symptoms are related to cataract, FECD, or both. Symptoms such as glare, blurry vision and decreased contrast sensitivity overlap between FECD and cataracts. FECD patients may experience blurry vision upon awakening which gradually improves throughout the day. They may also report a foreign body sensation and pain if bullae are present.[1,2] Cataracts are more likely to cause a significant myopic shift.

Slit Lamp Exam & Diagnostic Testing

Slit lamp examination should assess the presence and distribution of guttae, typically described as a beaten bronze appearance. Guttata in FECD tend to be central and slowly become more prominent peripherally. By contrast, Hassall-Henle bodies represent peripheral guttata that are not associated with corneal edema and are seen as a normal change in the cornea with advancing age. Signs of manifest corneal edema, such as epithelial or stromal edema, Descemet's folds, or posterior fibrosis, should be evaluated. Most patients seen in clinical practice have Stage I or II disease (**Table 1**). When evaluating the cataract, it is important to assess cataract density and depth of the anterior chamber. A denser lens and shallow anterior chamber indicate higher risk of increased cumulative dissipated energy (CDE) near the corneal endothelium and a higher risk of corneal decompensation with surgery.

Diagnostic Testing

Slit lamp examination does not account for the presence of subclinical edema, an important indicator for the risk of corneal decompensation following cataract surgery. Diagnostic testing plays a role in evaluating FECD patients with subclinical edema and identifying eyes at a higher risk for post-operative corneal decompensation following cataract surgery.

Historically, central corneal thickness (CCT) >640 µm measured with pachymetry was used as a marker to predict risk of corneal edema following cataract surgery. CCT is now understood to be a weak predictor of prognosis, especially without previous measurements to compare to which may indicate progressive corneal edema.

Specular microscopy provides information on endothelial cell density (ECD); variable enlargement (polymegethism), loss of hexagonal shape (pleomorphism), guttae variation, and CCT. Risk factors for persistent post-operative corneal edema include endothelial cell count below 1000 cells/mm^2, high pleomorphism (>50% of non-hexagonal cells), and high polymegethism (>0.4 coefficient of variation).[3] When significant cell dropout has occurred, specular microscopy decreases in accuracy given that the guttae cannot easily be measured, characterized, and counted. Confocal biomicroscopy has shown promise for measuring corneal transparency and assessing backscatter, an objective measurement

Stage	Vision loss	Symptoms	Clinical Findings
I	None	Rare glare Mild colour vision deficit	• Non-confluent central guttae • Pigment deposition on posterior surface • Grayish thickened Descemet membrane
II	Mild	Diurnal glare	• Confluent central guttae with peripheral spread • Transient stromal edema
III	Moderate	Painful hydrops	• Persistent stromal edema • Epithelial and subepithelial microcysts and bullae
IV	Severe	Painless	• Peripheral neovascularization • Subepithelial pannus, scarring, and opacification

Table 1. Clinical stages of Fuchs endothelial corneal dystrophy; *adapted from Adamis AP et al. Fuchs endothelial dystrophy of the cornea. Surv Ophthalmol.1993;38:149–68.*

of corneal haze. Both specular and confocal microscopy can be operator-dependant and not easily accessible by all ophthalmologists.

Corneal tomography is emerging as a valuable tool for identifying subclinical edema in FECD. Three markers have been identified to indicate subclinical corneal edema and risk of decompensation following cataract surgery.[4] These include: **(1)** loss of regular isopachs; **(2)** displacement of the thinnest corneal point; and **(3)** focal posterior corneal surface depression.[4] The four-year cumulative risk of progression/intervention after uncomplicated cataract surgery was 0% when no features were present, 50% when one or two features were present, and 75% when all features were present.[5] Corneal tomography can guide ophthalmologists in deciding whether a combined procedure should be considered and assist with counselling patients regarding their risk of significant progression in subsequent years. Arnalich-Montiel *et al.* developed a pre-operative risk score with high sensitivity and specificity, predicting the risk of corneal decompensation using Pentacam indices, including anterior layer corneal backscatter and changes in CCT.[6]

Cataract Surgery Alone

Surgical planning

Once it has been determined that a patient has a visually significant cataract in the context of FECD, patients need to be informed regarding the risk of post-operative refractive error, delayed healing, corneal decompensation, and potential need for EK.

For patients exhibiting visually significant cataract without evidence of sub-clinical or manifest edema, standalone cataract surgery is recommended, preferably performed early to minimize the risk of increased ultrasound energy causing greater endothelial damage.[1] When mild subclinical edema is present, cataract surgery can also be performed when accompanied by detailed consent regarding the risk of EK post-operatively.

Intraocular Lens Selection

Intraocular lens (IOL) selection requires a detailed pre-operative discussion due to the risk of post-operative refractive error. A hydrophobic monofocal IOL is recommended due to the potential need for EK. Hydrophilic IOLs should be avoided due to the risk of calcification and opacification after EK.[1]

FECD is postulated to cause swelling of the posterior cornea leading to posterior corneal

flattening and a myopic shift. Thus, Wacker *et al.* suggested that surgeons should target myopia (-0.50 to -1.25) in eyes with FECD.[7] When both eyes require surgery, post-operative refractive shift in the first eye can be used as a reference in optimizing refractive outcomes in the second eye.[1]

In cases where the patient seeks spectacle independence, the consideration of a toric IOL is possible; however, meticulous preoperative evaluation and discussion with the patient are crucial to minimize the risk of dissatisfaction. The corneal edema associated with FECD causes flattening of the posterior cornea surface and a hyperopic shift. This resolves if the patient proceeds to receive a corneal transplant. In mild cases of FCED without significant corneal edema, toric IOLs can be considered when the astigmatism is regular, stable, and repeatable. Obtaining optical biometry and corneal tomography prior to the development of corneal edema can aid in determining the potential for astigmatism correction at the time of cataract surgery.[8] Biometry measurements become unpredictable as edema progresses, therefore caution should be used prior to selecting a toric IOL in advanced stages of disease. The use of multifocal IOLs is relatively contraindicated in patients with FECD. With time, patients with FECD experience reduced contrast sensitivity, glare, and decreased vision. This is compounded by the implantation of a multifocal IOL leading to compromised vision post-operatively, even when done following successful Descemet's membrane endothelial keratoplasty (DMEK).[9] If a patient is keen for astigmatic correction or spectacle independence but also requires a corneal transplant, a staged procedure is recommended as discussed below.

Future directions of IOL options may include a light adjustable lens (LAL). The LAL is made of a photosensitive silicone material and allows post-operative adjustments using targeted UV light exposure. This would be especially helpful to fine tune the refractive target following the resolution of corneal edema after cataract surgery or when done in combination with EK.[10]

Surgical Technique

In general, surgeons should utilize techniques that minimize the time of surgery and CDE. Torsional emulsification mode, lower bottle height, higher vacuum, and a phaco-chop technique where nucleus disassembly occurs within the capsular bag have been shown to minimize CDE. However, it is important to utilize the safest technique that each surgeon is most comfortable with. Ophthalmic viscosurgical devices (OVDs) are essential in cataract surgery to protect the endothelium. Generous amounts of cohesive OVDs should be used to protect the endothelium. Aliquots of cohesive OVD can be reapplied through surgery to ensure adequate coverage of the endothelium during nucleus disassembly and lens insertion. A soft-shell technique whereby a dispersive viscoelastic is used to coat the endothelium and is then followed by a cohesive OVD to deepen the anterior chamber and push the dispersive OVD upwards towards the cornea has also been shown to minimize cell loss.[11] At the conclusion of the case, excessive or forceful wound should be avoided to minimize the risk of Descemet's detachment.

Post-operative Care and Complications

Post-operative care following cataract surgery for patients with FECD is similar to that of standard procedures. Full visual recovery may be delayed if post-operative edema is present. Corneal clarity can take up to three months; hypertonic saline can be added when corneal edema persists. It has been shown that cases with intra-operative complications were 6 times more likely to develop post-operative corneal edema compared to those without intraoperative complications.[12] If a posterior capsular tear occurs during surgery, anterior chamber IOLs should be avoided; instead plan for a secondary scleral sutured or sulcus fixated IOL. If posterior capsular opacification occurs, Nd:YAG capsulotomy should also be delayed due to risk of posterior lens dislocation during EK if transplantation is required in the future.

Cataract Surgery Combined with EK in Patients with FECD

For patients with both a visually significant cataract and FECD with manifest corneal edema, both cataract surgery and EK are required. DMEK is now the most common and preferred surgery for FECD. Cataract surgery can be performed before (Phaco-DMEK), after (DMEK-Phaco) or combined as a single procedure. The decision to perform a staged or combined procedure depends on multiple variables. A meta-analysis of staged surgeries found no statistical difference between staged (Phaco-DMEK) or combined procedures regarding corrected distance visual acuity

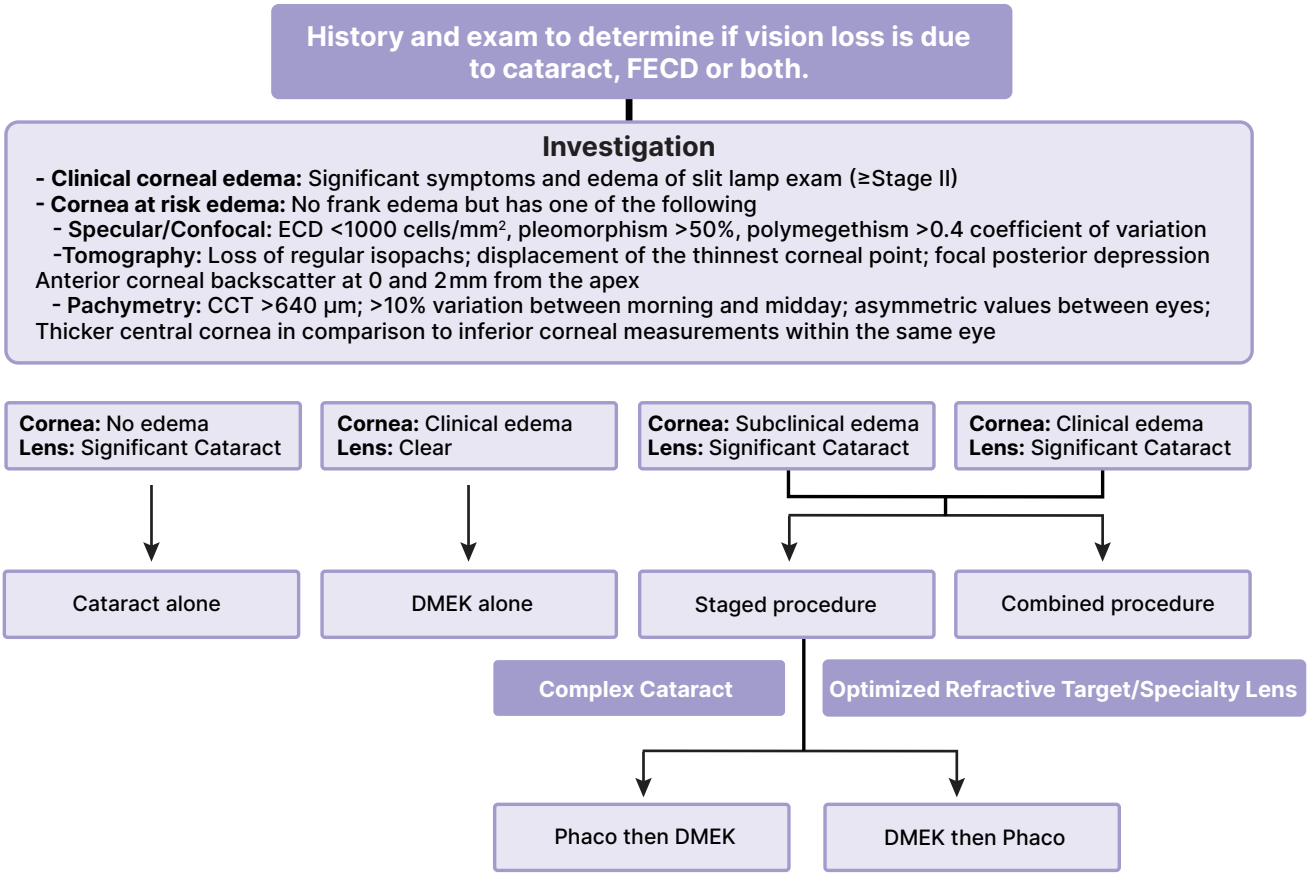

Figure 1. Algorithm describing authors approach to Fuchs endothelial corneal dystrophy (FECD) with cataract; *adapted from Ali M et al.*

improvement, post-operative ECD, re-bubbling, and primary graft failure rate.[13] Combined surgery offers the advantage of faster visual recovery and reduced risks and costs compared to undergoing two separate procedures. Cataract surgery before DMEK can be used in young patients to preserve accommodation, or in complex eyes with higher risk of complication during surgery. DMEK followed by cataract surgery is increasingly being used to optimize refractive outcomes for patients with FECD. In these cases, DMEK is performed followed by cataract surgery 3–5 months later once optical biometry has stabilized. Ultimately, the decision to opt for a staged or combined procedure should be guided by the surgeon's expertise and patient preference.[1]

Conclusion

Managing cataracts in individuals with FECD poses unique challenges for both the attending ophthalmologist and the patient. A comprehensive evaluation of the patient's medical history, slit lamp examination and diagnostic tests to detect subclinical edema are imperative. Tailoring the management approach to each patient is essential, considering the stage of the disease, cataract density, and surgeon and patient preferences (**Figure 1**). Careful surgical technique can allow for cataract surgery to be performed alone; however, some patients would benefit from both cataract surgery and EK. The choice of a combined surgery vs staged surgery is dependent on surgeon preferences and the patient's expectations regarding refractive outcome. As with any surgery, a thorough discussion with the patient is paramount to ensure satisfaction.

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Rookaya Mather, MD, FRCSC (moderator)

Dr. Rookaya Mather is Associate Professor of Ophthalmology at the Schulich School of Medicine, Western University in London, Ontario. Her subspecialty practice is in medical and surgical cornea and external disease. She completed her fellowship training in Cornea & External Disease at the Proctor Foundation, UCSF in San Francisco, California. Dr. Mather is actively engaged in research and has published in various peer-reviewed journals. She is passionate about raising awareness about ergonomic optimization in ophthalmology.

Samuel Masket, MD

Dr. Samuel Masket recently retired as a Clinical Professor of Ophthalmology at the Geffen School of Medicine, UCLA and founding partner of Advanced Vision Care in Los Angeles. He is a past president of the American Society of Cataract and Refractive Surgery. Dr. Masket has published more than 150 peer-reviewed articles and two textbooks. Currently, Dr. Masket is the Chair of American Academy of Ophthalmology's Senior Ophthalmologist Committee.

ABOUT THE PANELISTS

Terry Zavitz

Terry Zavitz is the Senior Vice-President of Zavitz Insurance and Wealth: A HUB International Company, focusing on insurance protection and specializing in disability insurance. Terry has handled hundreds of disability claims for physicians, business owners, and their employees. She was the Chair of the Women's Healthcare Campaign with London Health Sciences Centre, and plays an active role in many associations, including the YMCA, the London Health Sciences Centre, St. Joseph's Health Care, and various other local organizations.

Deepinder Dhaliwal, MD

Dr. Deepinder Dhaliwal is a Professor of Ophthalmology and Vice Chair of Wellness and Communications at the Department of Ophthalmology at the University of Pittsburgh. She is also the Director of Refractive Surgery and the Cornea Service at the University of Pittsburgh Medical Center (UPMC) Eye Center. Dr. Dhaliwal also serves as the Director of the UPMC Vision Institute's Laser Vision Center and the Associate Medical Director of the Campbell Ophthalmic Microbiology Laboratory.

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Musculoskeletal Injuries and Ophthalmologists: Prevention Requires a System-Level Approach

A Roundtable Discussion

Rookaya Mather, MD, FRCSC (moderator)
Samuel Masket, MD
Terry Zavitz
Deepinder Dhaliwal, MD

Musculoskeletal injuries make up about 15% of physicians' insurance claims. These injuries lead to patient care disruptions, cancelled surgeries, significant disability, and early retirement. Dr. Rookaya Mather sat down with three fellow advocates for physician wellness and WMSD prevention, including two fellow ophthalmologists and a disability insurance expert. They discussed the factors that contribute to injury – from the culture of medicine to suboptimal ergonomic design of examination and surgical equipment – and the role that insurance companies, practising ophthalmologists, academic institutions, and manufacturers can play in preventing injury.

Rookaya Mather: This topic is a very personal for me. I recently had a work-related injury that required a brief disability leave. In researching what I could do to prevent further injury, I quickly realized injury prevention requires a system-level approach. As ophthalmologists, we focus our attention and efforts on delivering great care to patients. We don't recognize that our work places us at risk for developing work-related musculoskeletal disorders. How common and problematic are work-related musculoskeletal injuries among physicians?

Terry Zavitz: Physicians are always taken aback when they become injured and can't work. No one thinks a debilitating injury will happen to them. These injuries are physically painful and challenging on many levels. It's not easy for doctors to take time off work and seek treatment since physicians feel a deep sense of obligation to their patients and colleagues. The role that I play is to help physicians get the support they need from their insurance company so they can recover and return to the profession when they're ready.

Samuel Masket: When I trained, which was a long time ago, we were not (or no one was) having discussions about how we can use instruments like slit lamps and operating microscopes in a way that protects and preserves our own bodies. Approximately 15% of ophthalmologists retire early because of musculoskeletal disorders. This is a significant workforce issue, particularly with the aging population. In the United States, ophthalmologists are retiring at a faster rate than new ophthalmologists are entering the workforce. I retired during the pandemic because I developed numbness and tingling in my neck as a result of my surgical work.

Deepinder Dhaliwal: I also didn't have any training on how to properly use a

slit lamp or how to position myself at the microscope. The focus was on making the patient comfortable. In the past, I would have the patient sit back comfortably in the examination chair and I would have to lean forward awkwardly over them. I did this for many years until I had a fall in the operating room. I slipped and fell due to water on the floor of the operating room. I injured my back and my imaging revealed that I had a very large disc herniation. I had severe pain and weakness in my leg that continued to get worse until my physical therapist said I needed to stop working. I had to cancel all my patients' surgeries. It was devastating.

Fortunately, my recovery only took two weeks. Every day during those two weeks, I did physical therapy, acupuncture, or meditation. I consulted more than one physical therapist. The exercises recommended by the first two physical therapists didn't help but the third physical therapist, who I call the spine whisperer, used the type of spine manipulation that was ideal for my back. He took a personalized approach and taught me how to strengthen the multifidus muscle along the spine. The improved stability of my spine was key to my return to the operating room. One piece of advice I have, is to not give up and say, 'this treatment isn't working,' but to try different methods and different practitioners.

Unfortunately, many of us take the approach of "Just keep going" and we manage the pain with ibuprofen without seeking professional help. In my case, I had to hit rock bottom which was scary. It wasn't until I had severe nerve pain that medication didn't alleviate, that I decided to make changes in my life. I focused on healing myself so that I could go back to work stronger, with a completely different mindset.

RM: The word 'scary' sums it up. There is a perfect storm of a lack of awareness and education about injury prevention, the suboptimal ergonomics of our procedure and exam equipment, and then the culture in medicine, that we don't complain. In 2017, my colleagues and I conducted a survey of Canadian ophthalmologists. The vast majority said they dealt with musculoskeletal problems with rest and self-medication. Only 25% of those surveyed sought care from their physician for their injuries. How do we train our future ophthalmology workforce so they know how to prevent injury as well as seek the appropriate care afterwards?

SM: We need to have conversations at the highest academic level, as well as in specialty-focussed literature, as we're doing here. Ergonomic practices and wellness in general should become part of the curriculum and given as much weight as slit lamp training. This isn't just important for the individual, but also the workforce. We are going to be significantly understaffed in the foreseeable future if we don't focus on injury prevention.

TZ: The lack of awareness is especially acute when it comes to the importance of intervening early and not waiting until one is totally disabled. Some types of disability coverage aren't available until you're totally disabled, and you've been off work for 90 days with an injury. But there are ways to get support before an injury is debilitating. In Canada, most physicians have partial disability coverage. They're reimbursed based on the difference between their annual income prior to their partial disability and afterward. This allows physicians to take a short time off from work, or reduce their hours, before they have a more difficult-to-treat injury.

DD: We need a module in the Basic and Clinical Science Course (BCSC) on how to stay well as physicians. Universities have physiotherapists, physiatrists, and other extremely knowledgeable colleagues who could help us create this module for ophthalmologists. We should have a checklist that we run through when we're using the slit

lamp or the microscope so that we know we're adopting the right posture. We could also use stickers to put on equipment, that remind us of the correct posture. As an ophthalmology community, we can increase awareness with videos and social media posts as well. There are many ways to reach trainees all the way to our senior colleagues. It's never too late to incorporate body awareness and injury prevention into our daily practices.

SM: On an uplifting note, I'm aware of at least two institutions, the University of Michigan and Wills Eye Hospital, that have incorporated an ergonomic approach into the training of residents and fellows. In addition to physiotherapy, yoga, and other types of exercise are important to increasing our physical resilience when working with equipment that's not ideal from an ergonomic perspective.

We also need to engage ergonomic experts and manufacturers' associations. I have spoken with many people who work for equipment manufacturers, and they are aware of the problems of the slit lamp. We could create an ophthalmologist-led designation that indicates equipment has been ergonomically tested. Manufacturers might strive for the highest ergonomic rating. For too long, we've had to deal with one-size-fits-all slit lamps. This contributes to the fact that female ophthalmologists experience more musculoskeletal disorders than their male counterparts.

RM: I agree Sam, engaging with industry is vital, because we need system changes that go beyond what individual ophthalmologists and practices can do.

RM: I want to pivot now to the value of disability insurance coverage. How should ophthalmologists protect their careers financially from career-interrupting or -ending musculoskeletal disorders?

TZ: Every physician should have their disability insurance reviewed annually to make sure they have the right amount of coverage, not only to cover their own income, but also their office overhead, including rent, salaries, and fees. If you're 40, and you're earning $250,000, with 2.5% income inflation, you will earn $8.5 million over the next 25 years. This is significant value that you need to protect.

DD: When choosing disability insurance, "own occupation" is very important. If you're a cornea specialist and you have own occupation coverage, that means that if you can no longer be a cornea specialist, you'll be able to access your disability insurance, even if you were able to work in a lower-paying medical or non-medical role.

TZ: I agree that the "own occupation" definition of disability is vital in an insurance contract, as well as the ability to go on a partial disability claim. You also want options to increase your amount of coverage, regardless of your health status, so that you can ensure your coverage keeps pace with your income over the course of your career.

RM: Do you think the insurance industry has a role to play in physician injury prevention?

TZ: Insurance companies tend to be reactive. Most of the carriers will connect an injured physician with their rehabilitation departments or physical therapy to help them get back to work, but they're not proactive about preventing injury in the first place. This is changing, but right now, the preventative efforts of insurance companies are focused on mental illness; 57% of all physician complaints relate to mental health challenges.

SM: The data is pretty clear that physicians with musculoskeletal injuries are more likely to have mental health challenges, and vice versa. I think a committee that includes academic institutions could incentivize the insurance industry to promote injury prevention efforts, by demonstrating that investing in MSK injury prevention will cost insurance companies less money overall.

RM: Dr. Dhaliwal and Dr. Masket, I'd like to ask you how we can improve the ergonomics in our everyday practices right now.

DD: There are many low-cost or zero-cost changes that we can make. I ask patients to move towards the edge of the exam chair so I can remain in a good ergonomic posture for the entire slit lamp exam, that is, I sit with my ears over my shoulders and shoulders over my hips. When examining the retina, I try to adjust the patient's chair to the highest level so I'm not craning my neck. Every inch that we flex our neck forward increases the weight that the neck muscles need to support.

We can also take micro breaks in between patients and reverse the posture that we used for an exam. The otolaryngology literature has shown that stretching breaks in between surgeries are very effective at reducing pain and fatigue in surgical specialties. As ophthalmologists, we're lucky in that we can get up and stretch often. Patients may think we look funny, but it's vital that we stretch many times throughout the day.

There are many innovations that are happening as well. Industry is receptive. With the operating microscope, the heads-up display is exciting, though most heads-up displays require the specific angle set-up for each surgeon. I have also seen surgical stools, where the phaco and microscope pedals are on a platform, so they're always in a comfortable spot. There are also a number of different types of surgical chairs available with lumbar support.

SM: I photograph and take videos of my fellows at the microscope, so that I can raise their awareness about their posture and how they can adjust it. I also talk to them about the importance of exercise. The late Dr. Joel Shugar, who pioneered the intracameral use of a mydriatic and anesthetic combination and tragically passed away, used to do vigorous yoga to prepare himself for a day of surgery. We may not be Lebron James, but we perform physically as well as mentally. We need to prepare our minds and our bodies, and if that understanding can be incorporated into the training curriculum, then, going forward, we'll be in a much better place.

RM: Thank you for sharing your personal experiences and taking the learnings you've had from these experiences to outline several viable system-level opportunities to prevent work-related MSK injuries. We've uncovered valuable insights into ways to promote ergonomic optimization in our practices and we've talked about the critical role of different stakeholders such as the insurance industry, the COS, the AAO, and residency training programs. We can all agree that enhancing our wellbeing and our career longevity also enhances the care we deliver to our patients everyday. Thank you for coming together to have this vital discussion.

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T.Z.: None declared.

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Peripheral Retinal Diseases: Indications for Prophylactic Laser Treatment versus Observation

Ravi Dookeran, MD
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Peripheral retinal diseases encompass a spectrum of conditions that can affect multiple layers of the retina, posing potential risks to visual function if left untreated. This article provides an overview of common peripheral retinal diseases, discusses the indications for prophylactic laser treatment versus observation, and highlights the factors that influence clinical decision-making in managing these conditions. Understanding the appropriate timing for intervention is crucial in preventing vision-threatening complications and optimizing visual outcomes.

Introduction

Peripheral retinal diseases encompass a diverse group of conditions that can impact visual health and function. While some of these conditions are asymptomatic and may have a benign course, others can progress to potentially sight-threatening complications, such as retinal detachment, especially in the context of visual symptoms.[1] Careful clinical evaluation and timely intervention are essential in managing peripheral retinal diseases to prevent loss of visual acuity, particularly when predisposing risk factors are present. Obtaining a proper history may help

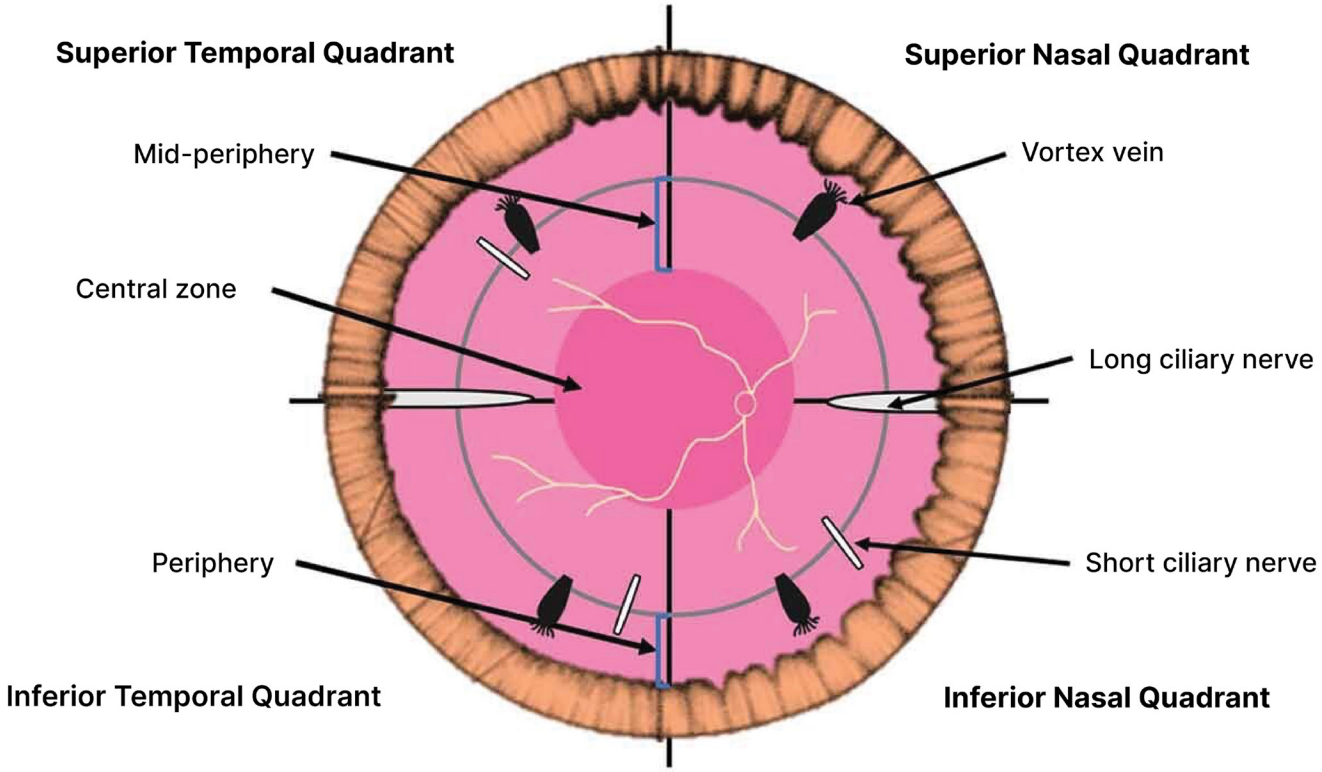

Figure 1. Four zones of the peripheral retina; *courtesy of Cheung R, Ly A, Katalinic P et al. Visualization of peripheral retinal degenerations and anomalies with ocular imaging. Seminars in Ophthalmology. 2022 Mar 7;37(5):554-82.*

identify some genetic conditions associated with higher incidence of retinal tears and detachment such as high myopia or Stickler syndrome. Other factors to consider include the new onset of symptoms of posterior vitreous detachment, prior history of trauma or relatively recent intraocular surgery such as cataract surgery, intravitreal injection or YAG capsulotomy.[2]

Retinal regions based on gross anatomy including vessels was defined in 1961 by Duke-Elder who categorized the peripheral retina into four zones: **1)** the near periphery, a 1.5 mm ring adjacent to the 6 mm diameter macula; **2)** the middle periphery, the next 1.5 mm ring; **3)** the far-periphery, measuring the next 9-10 mm on the temporal and 16 mm on the nasal side; **4)** the ora serrata or extreme periphery, measuring the additional 2.1 mm in the temporal and 0.7 mm on the nasal side (**Figure 1**).[3,4]

Peripheral degenerations can be divided into intraretinal, vitreoretinal and chorioretinal categories (**Table 1**).[3]

Peripheral Degeneration

A) Intraretinal

Degenerative Retinoschisis

Degenerative retinoschisis, also known as acquired or senile, is a rare eye disease characterized by the abnormal separation of the neurosensory retina layers due to microcystic degeneration, typically at the outer plexiform layer or inner nuclear layer (inner retinoschisis). Inner retinoschisis is more often seen in congenital retinoschisis (also called juvenile or X-linked retinoschisis).[5]

Retinoschisis is commonly associated with myopia with a prevalence that varies being cited as being found in 2–7% of the general population in one study[5] to 22% in another.[6] It is more common in patients 40 years and older and has no sex prediliction.[5] This lesion is a bullous elevation of the peripheral retina, found predominantly in the inferotemporal quadrant 72% and superotemporal 28%.[6] (**Figure 2a**). It is typically asymptomatic. The progression of a

Care Management	Management Options
Type of Lesion	**Treatment***
Acute symptomatic horseshoe tears	Treat promptly
Acute symptomatic operculated holes	Treatment may not be necessary
Acute symptomatic dialyses	Treat promptly
Traumatic retinal breaks	Usually treated
Asymptomatic horseshoe tears (without subclinical RD)	Consider treatment unless there are signs of chronicity
Asymptomatic operculated tears	Treatment is rarely recommended
Asymptomatic atrophic round holes	Treatment is rarely recommended
Asymptomatic lattice degeneration without holes	Not treated unless PVD causes a horseshoe tear
Asymptomatic lattice degeneration with holes	Usually does not require treatment
Asymptomatic dialyses	No consensus on treatment and insufficent evidence to guide management
Eyes with atrophic holes or lattice degeneration where the fellow eye has had a RD	No consensus on treatment and insufficient evidence to guide management

Table 1. Management options for peripheral retinal lesions; *adapted from American Academy of Ophthalmology. AAO PPP Retina/Vitreous Committee, Hoskins Center for Quality Eye Care. Preferred Practice Pattern: Posterior Vitreous Detachment, Retinal Breaks, and Lattice Degeneration PPP 2022.*

Abbreviations: PVD: posterior vitreous detachment, **RD:** retinal detachment

***There is insufficient evidence to recommend prophylaxis of asymptomatic retinal breaks for patients undergoing cataract surgery.

Figure 2a. Fundus photo showing temporal retinoschisis(RS) from 7:00 to 10:00 without identified inner, outer, or full-thickness retinal breaks extending into the temporal macula[7]; *photo courtesy of Ravi Dookeran, MD and Charbel Wahab, MD.*

schisis cavity is rare and patients typically don't become symptomatic until it reaches the arcades. Retinoschisis may demonstrate outer retinal breaks that may lead to detachment of the neurosensory retina. These are known as a schisis-detachment and can remain static and contained. Should there be an inner retinal break then communication with the vitreous can result in a rhegmatogenous detachment requiring surgical repair. Given the rarity of this type of progression there are no adequate case series guiding management and observation is usually recommended. If documented progression of a schisis cavity through clinical exam, fundus photography and/or OCT is present then it may be treated with argon laser photocoagulation notably if patients are increasingly symptomatic (**Figure 2b and 2c**).[6]

White Without Pressure

White without pressure presents as irregular, translucent areas in the retinal periphery, sometimes with a red-brown border (**Figure 3**).[9] Lesions are usually located beyond the equator, although changes may occur near the major retinal vascular arcades. WWOP is often bilateral, and is typically found in up to 30% of normal eyes and in young myopic patients. This degeneration can be mistaken for retinal detachment or retinoschisis. The exact etiology is still unknown; one perspective suggests that it is a result of traction on the peripheral vitreous, while another viewpoint holds that it is merely an abnormal light reflex originating from a structurally normal interface within the vitreoretinal system due to increased density of collagen bundles at the vitreous base. Optical coherence tomography (OCT) shows white areas that correspond to hyperreflective outer retinal layers and ellipsoid zone, with no vitreous traction.

There is no need for prophylactic laser as it has low risk for association with retinal detachment. Patients can be monitored with dilated fundus examinations every 1–2 years.

White With Pressure

White with pressure presents with a distinctive milky white or opalescent appearance of the peripheral retina observed in many normal eyes when examined with scleral depression. It is the term used to describe flat peripheral detachment without any retinal break (**Figure 4**).[9]

It must be carefully distinguished from a subclinical peripheral retinal detachment. The retina appears normal without scleral depression. It is a benign condition and is not associated with retinal breaks, thus no prophylactic treatment is needed.

Dark Without Pressure

Dark without pressure (DWOP) is defined as a hypopigmented lesion region with the border of DWOP corresponding to the site where the ellipsoid zone has faded or disappeared (**Figure 5**).[10] It is typically asymptomatic and benign, without need for prophylactic laser.

Peripheral Cystoid Degeneration

Peripheral cystoid degeneration, a common occurrence characterized by tiny cyst-like spaces observed in the layers from inner to outer plexiform layers, has been identified in approximately 87% of autopsy eyes across various age groups, and virtually 100% of eyes in older individuals as a result of aging (**Figure 6**).[11] Additionally, current research on preventing rhegmatogenous retinal detachment lacks substantial evidence to strongly advocate for preventive treatment of lesions beyond symptomatic flap tears.[11]

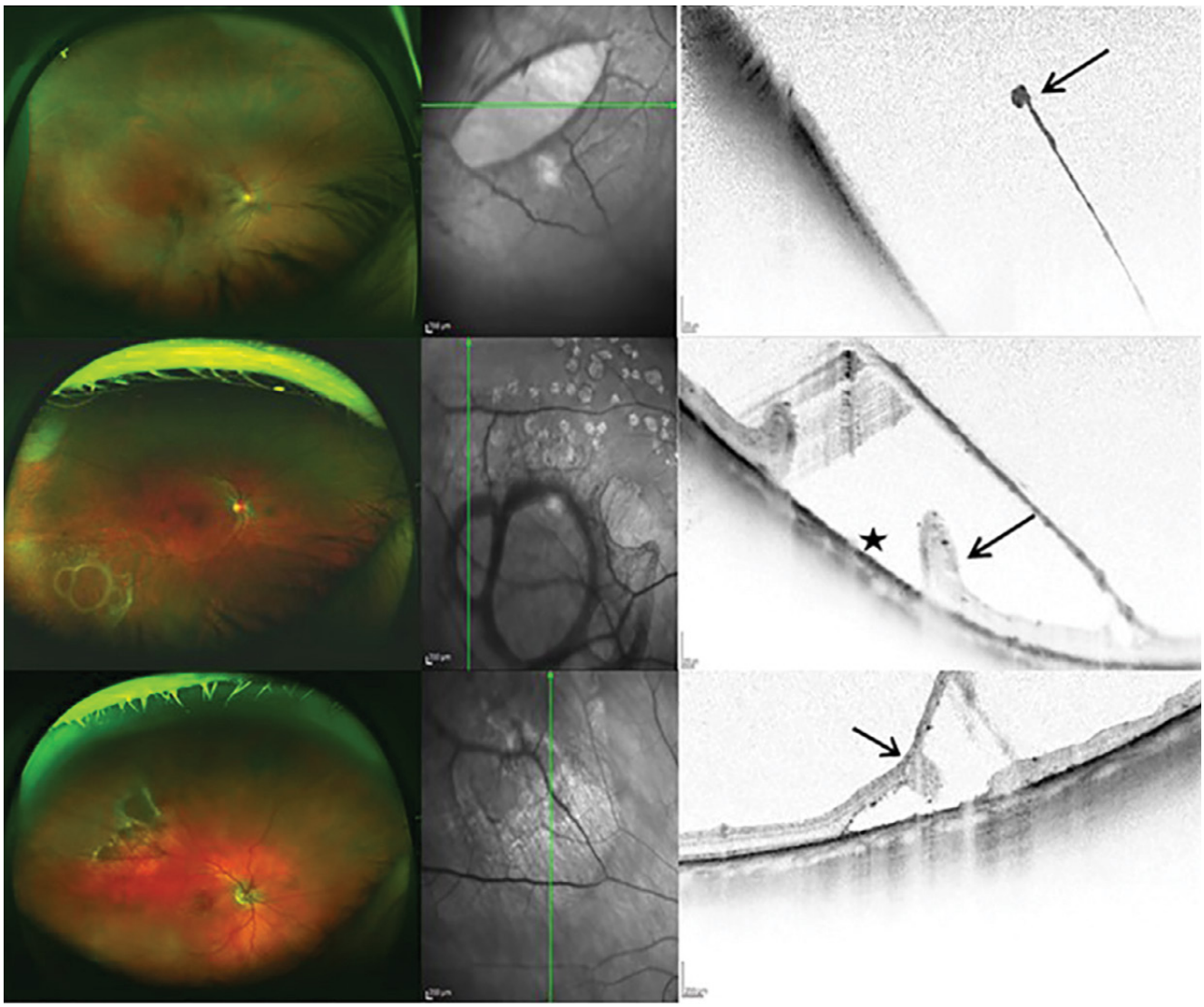

Figure 2b. Top row: The fundus photograph (left) of the right eye shows a superotemporal RS with inner-layer break (ILB). The horizontal green line of the infrared photograph (middle) indicates the exact location of the optical coherence tomography (OCT) scan of the ILB. The corresponding OCT scan (right) shows the interruption of the atrophic inner leaf (arrow).
Middle row: The fundus photograph (left) of the right eye shows an RS with multiple outer-layer (OL) breaks. The infrared photograph (middle) shows the exact location of the OCT scan of the OL breaks (vertical green line). The corresponding OCT scan (right) of the OL break shows the attached outer leaf with rolled-up edges (arrow) and the tissue retraction (star).
Bottom row: The fundus photograph (left) of the right eye pictures a superotemporal RS and an OL break. The vertical green line of the infrared photograph (middle) shows the exact location of the OCT scan (right), where a tissue retraction with a smooth edge and intraschisis pillar (arrow) is shown; *photo courtesy of Ravi Dookeran, MD and Charbel Wahab, MD.*

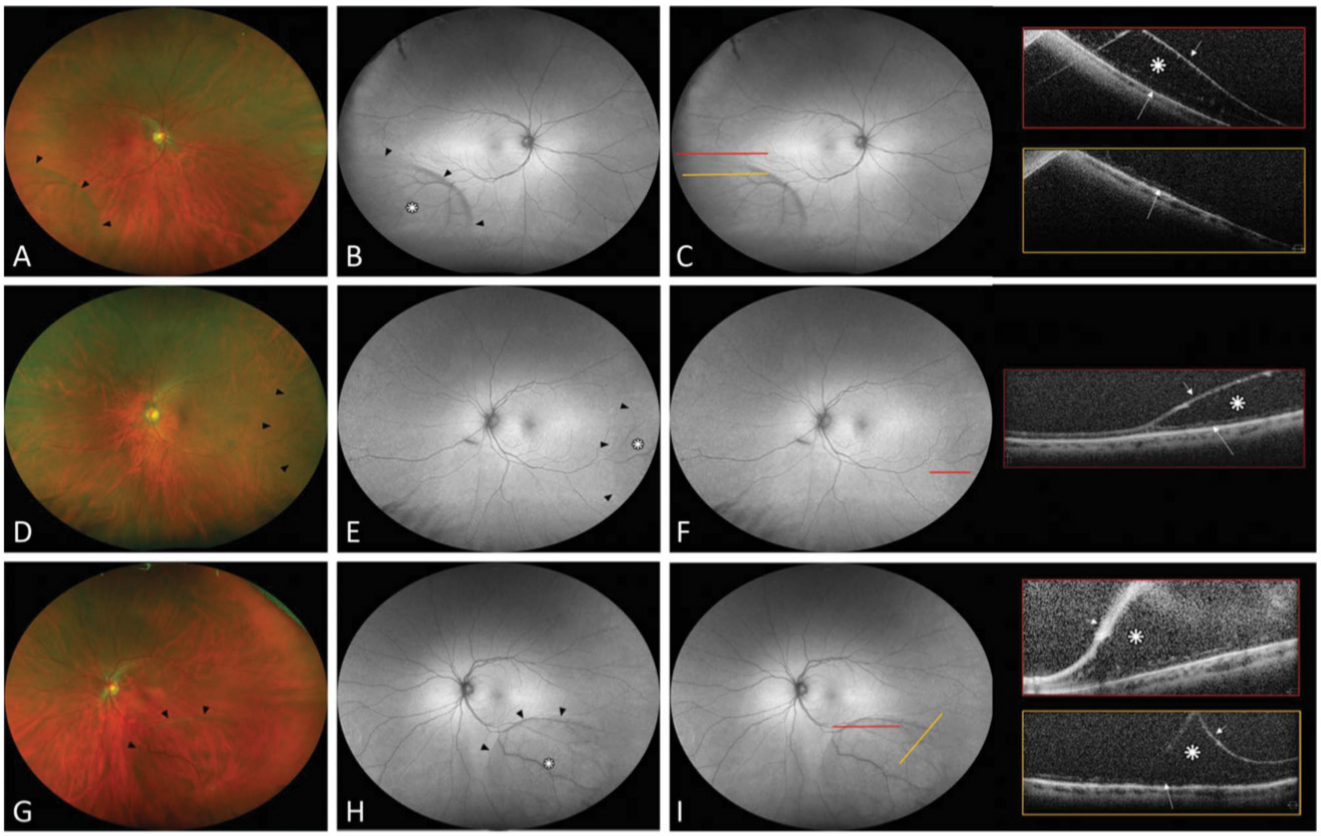

Figure 2c. Detection of Neurosensory Retinal Detachment Complicating Degenerative Retinoschisis by Ultra-Wide Field Fundus Autofluorescence Imaging. RETINA 2020; *courtesy of Francone et al.*

Ultra-widefield fundus autofluorescence and spectral domain OCT findings in degenerative RS without neurosensory retinal detachment. **Group B:** no hyperautofluorescence present. **A, D, and G:** Ultra-widefield color fundus photographs showing degenerative RS (black arrowheads). **B, E, and H:** Ultra-widefield fundus autofluorescence demonstrating the area of RS as isoautofluorescence (white asterisk) with a hypoautofluorescence line (black arrowhead) at the posterior edge. **C, F, and I:** Colored lines indicate the exact location through which the OCT scans were taken. Scans show splitting of neurosensory retina: the schisis cavity (white asterisk), the detached inner retinal layer (short white arrow), and a thin irregular band of moderately reflective tissue over the RPE hyperreflective band corresponding to the outer retinal layer (white large arrow).

Snowflake Degeneration

Snowflake degeneration manifests clinically with the emergence of minute crystalline deposits in the retina spanning from the ora serrata to the equator. Initially thought to be a form of retinitis pigmentosa, both clinical observations and genetic investigations affirm snowflake degeneration as a distinct disease entity (**Figure 7**).[8]

Some research studies recommend prophylactic laser while others do not.[8] It is generally recommended to observe unless other high-risk characteristics for retinal detachment coexist.

B) Vitreoretinal

Lattice Degeneration

Lattice degeneration is a common peripheral retinal finding characterized by areas of retinal thinning and lattice-like appearances.

Lattice degeneration manifests as thinning of the retina accompanied by the absence of the neurosensory layer, along with prominent vitreoretinal adhesion surrounding the affected area. It is prevalent in approximately 6–8% of the general population's eyes[12] and can have a variety of presentations. It can be oriented circumferentially midway between the ora serrata and equator or may present radially along vessels

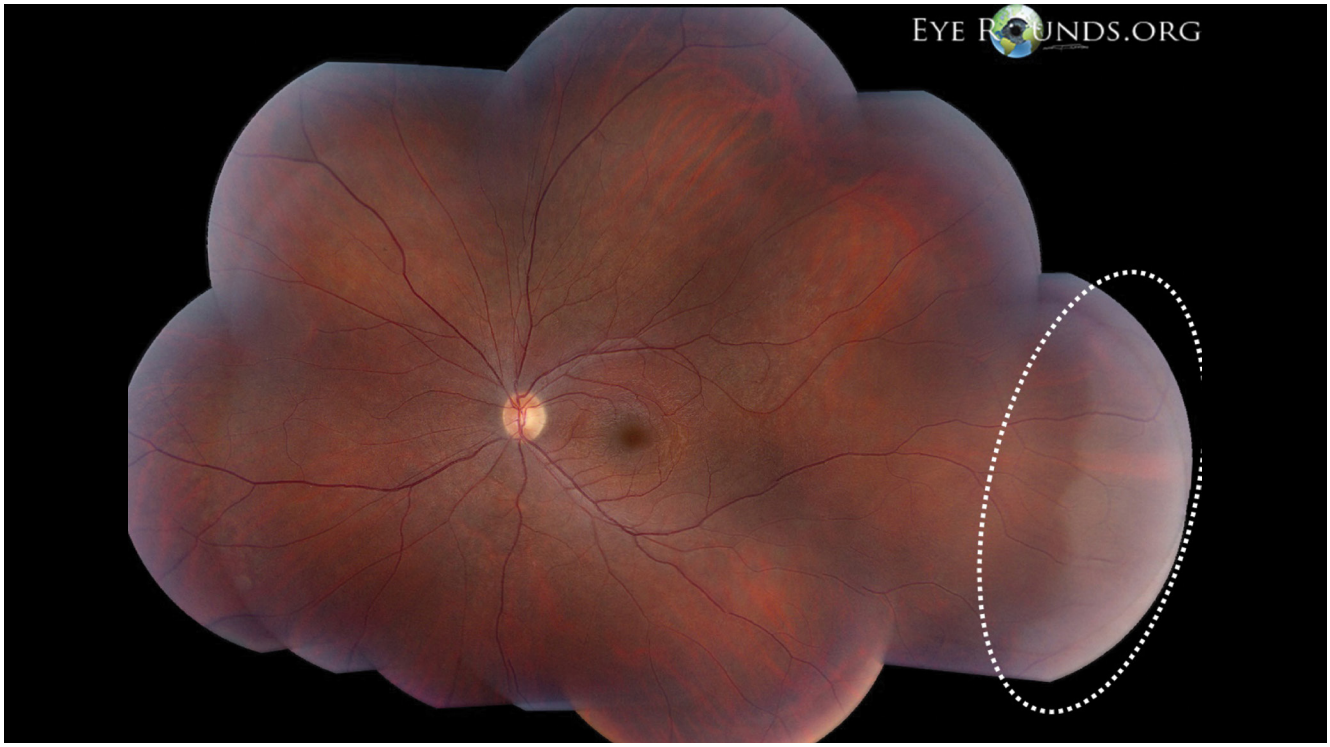

Figure 3. Wide field photo of the left eye showing white without pressure extending from 2 till 4 o'clock; *photo courtesy of Ravi Dookeran, MD and Charbel Wahab, MD.*

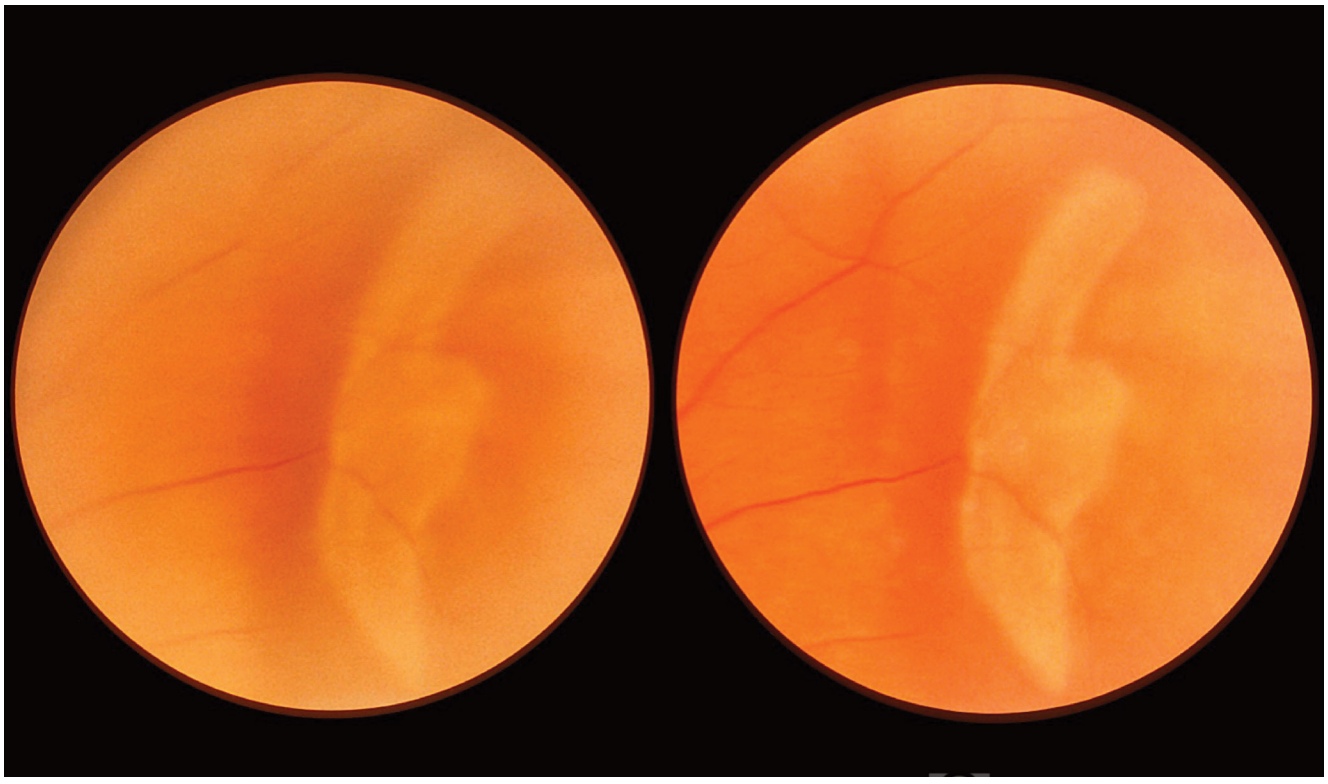

Figure 4. White with pressure observed during scleral depression; *photo courtesy of Ravi Dookeran, MD and Charbel Wahab, MD.*

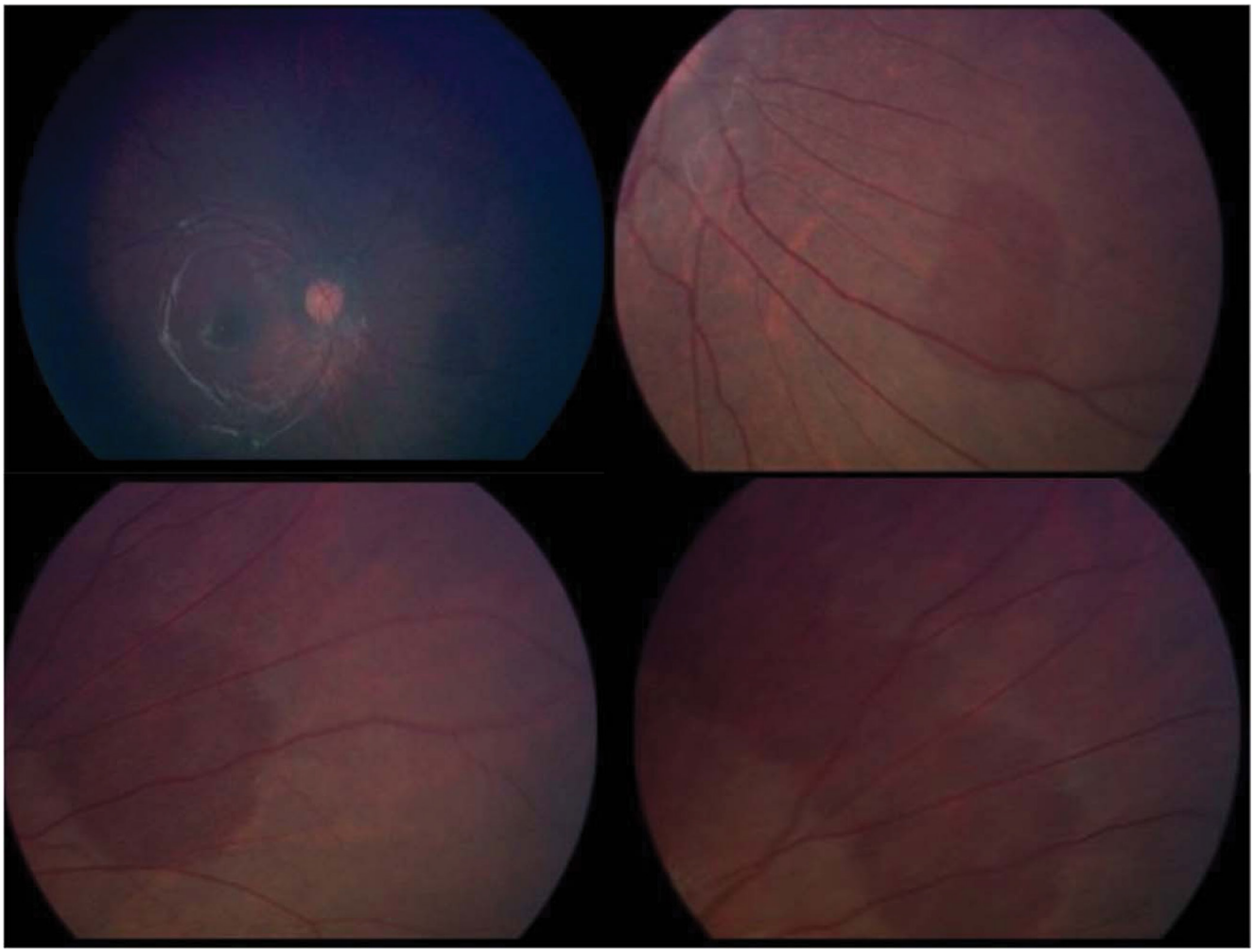

Figure 5. Color fundus images of the right eye showing multiple flat patches of reddish dark retina with well-defined scalloped edges nasal to the optic nerve head; *courtesy of Flores Pimentel, M.A., Duncan, J.L., de Alba Campomanes, A.G. et al. Dark without pressure retinal changes in a paediatric age group. Eye. 35, 1221–1227 (2021).*

(radial perivascular lattice). This condition impacts both the retina and vitreous, representing a significant peripheral vitreoretinal degeneration that heightens the risk of retinal tears and rhegmatogenous retinal detachment due to traction from the vitreous (**Figure 8**).[12]

While most cases of lattice degeneration are benign and do not require intervention, patients with associated retinal holes or tears are at increased risk of retinal detachment. Twenty to 30% of all detachments occur in eyes that have lattice degeneration but are not necessarily causative. The presence of lattice increases the relative risk of detachment from 0.01% to 0.3%–0.5%[13]. Prophylactic laser treatment may be indicated in individuals with high-risk features such as flap tears, pseudophakia or aphakia, previous retinal detachment in the fellow eye, or a strong family history of retinal detachments. The acute onset of new symptoms (floaters and/or photopsia) is a significant risk factor for developing a retinal detachment warranting laser retinopexy. Close observation is recommended for asymptomatic individuals with isolated lattice degeneration and no high-risk factors. High myopia (>6 diopters) with greater than 6 clock hours of lattice should also be observed.

Lattice as a Risk Factor for Retinal Detachment or Tear Following Cataract Surgery

With the evolution of microincisional cataract surgery the incidence of rhegmatogenous retinal detachment (RRD) and retinal tear (RT) have decreased. Prior to small incision

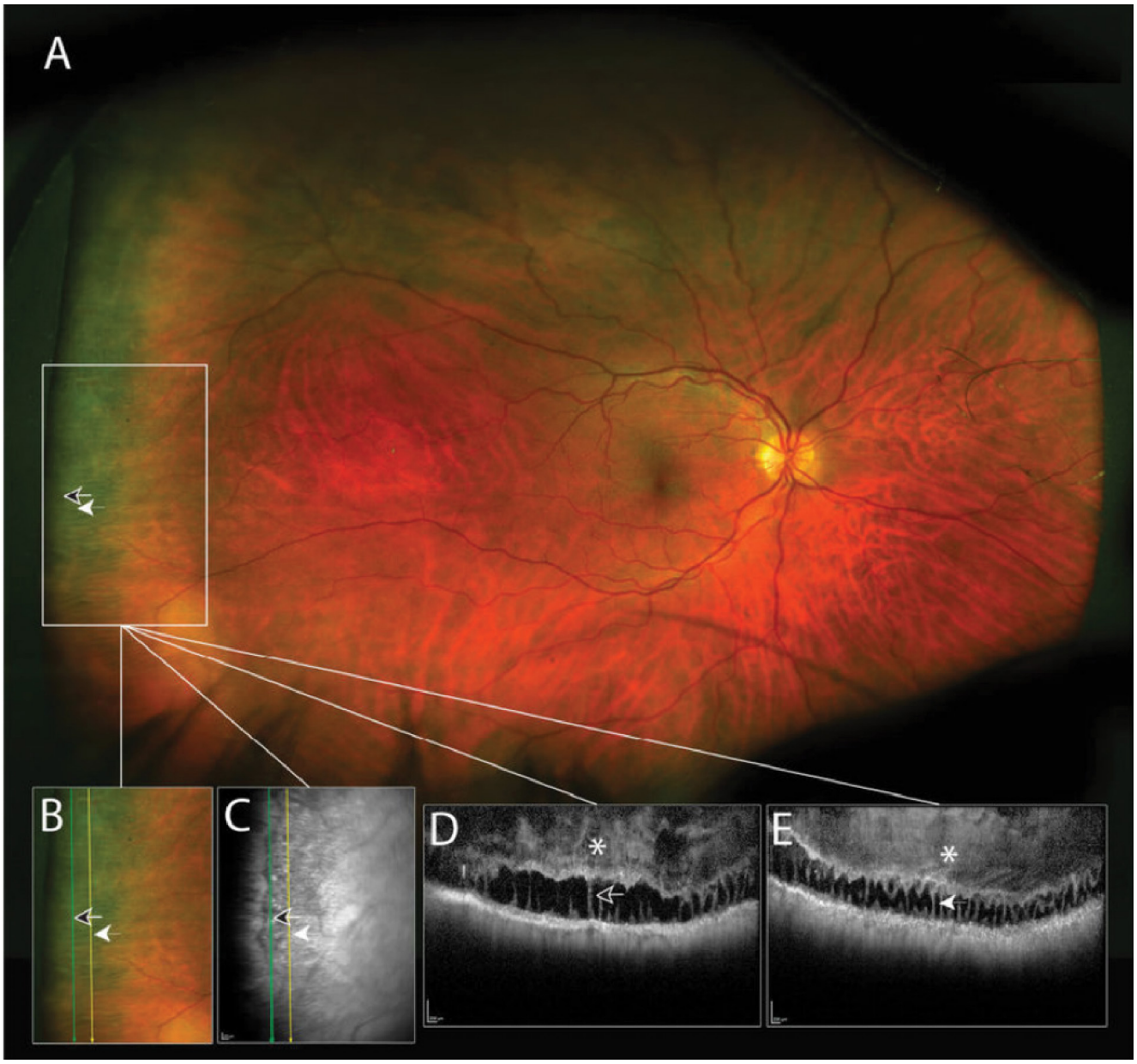

Figure 6. Wide field photo of the right eye with spectral domain OCT over the peripheral cystoid degeneration demonstrating saw-tooth patterns which are comprised of hyporeflective cystoid cavities and broad columns; *courtesy of Choudhry N, Golding J, Manry MW, Rao RC. Ultra-Widefield Steering-Based Spectral-Domain Optical Coherence Tomography Imaging of the Retinal Periphery. Ophthalmology. 2016 Jun;123(6):1368–74.*

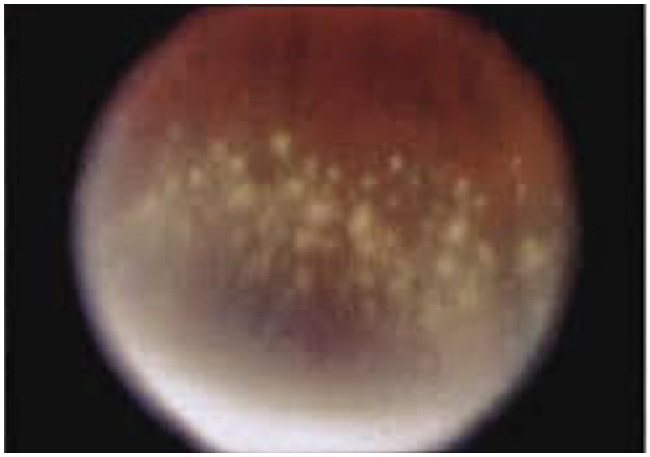

Figure 7. Snowflake degeneration; *courtesy of Robertson DM, Link TP, Rostvold JA. Snowflake Degeneration of the Retina. Ophthalmology. 1982 Dec;89(12):1513–7.*

surgery previous studies cited incidence of RRD at 0.6%–1.7%, whereas a study of greater than 3 million cataract surgeries performed in the US between 2014–2017 found the incidence reduced to 0.21% (roughly 1 in 500) in the first year.[14]

This study found the incidence of retinal tear to be 0.17% and found certain risk factors associated with RRD and RT. These include male, younger age (<70), lattice degeneration, high myopia, posterior vitreous detachment, mature cataract and complicated surgery (as identified by code). The greatest increased risk was with lattice degeneration at 1.44%. The odds ratio for RRD and RT with lattice was 10.53 and 43.86 respectively.[14] It is unclear whether this apparent increased risk confers some bias in detection post cataract surgery due to clearing of the opacity, but it acknowledges that further studies are needed to determine whether this risk can be reduced with early treatment to the lattice. The overall magnitude of the increased risk of RRD and RT, however, warrants careful evaluation to identify lattice degeneration and consideration of treatment versus close monitoring when counselling individual patients on the risks associated with cataract surgery.

Snail Track Degeneration

Snail track degeneration manifests as closely positioned shiny, crinkled or frosted bands within the retina, resembling the tracks left by a snail. These formations, comprised of pinpoint glistening white dots, are also clearly observable through red-free ultra-widefield imaging. On OCT, the lesions present as irregular thinning and a wrinkled curvilinear inner retinal surface, potentially lacking traction, or condensation of the overlying vitreous (**Figure 9**).[8]

Snail track lesions have not been associated with an increased risk of retinal breaks or retinal

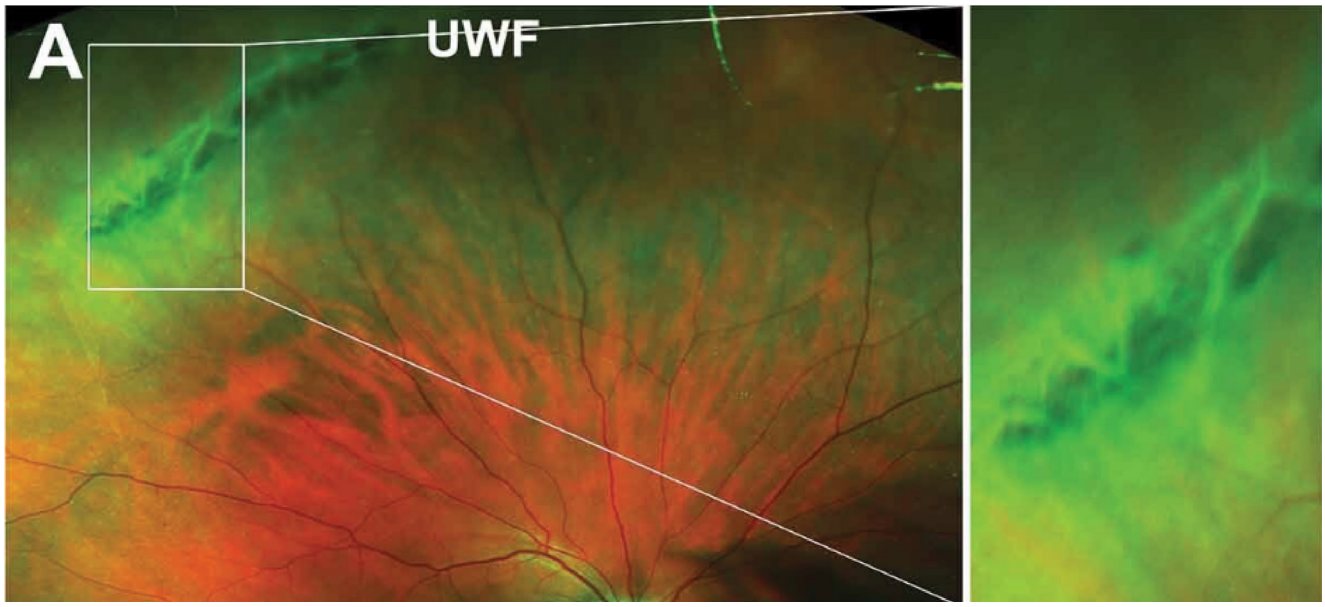

Figure 8a. Area of lattice degeneration at the periphery of the right eye in the supertemporal area; *courtesy of Cheung R, Ly A, Katalinic P, Minas Theodore Coroneo, Chang A, Kalloniatis M, et al. Visualisation of peripheral retinal degenerations and anomalies with ocular imaging. Seminars in Ophthalmology. 2022 Mar 7;37(5):554–82.*

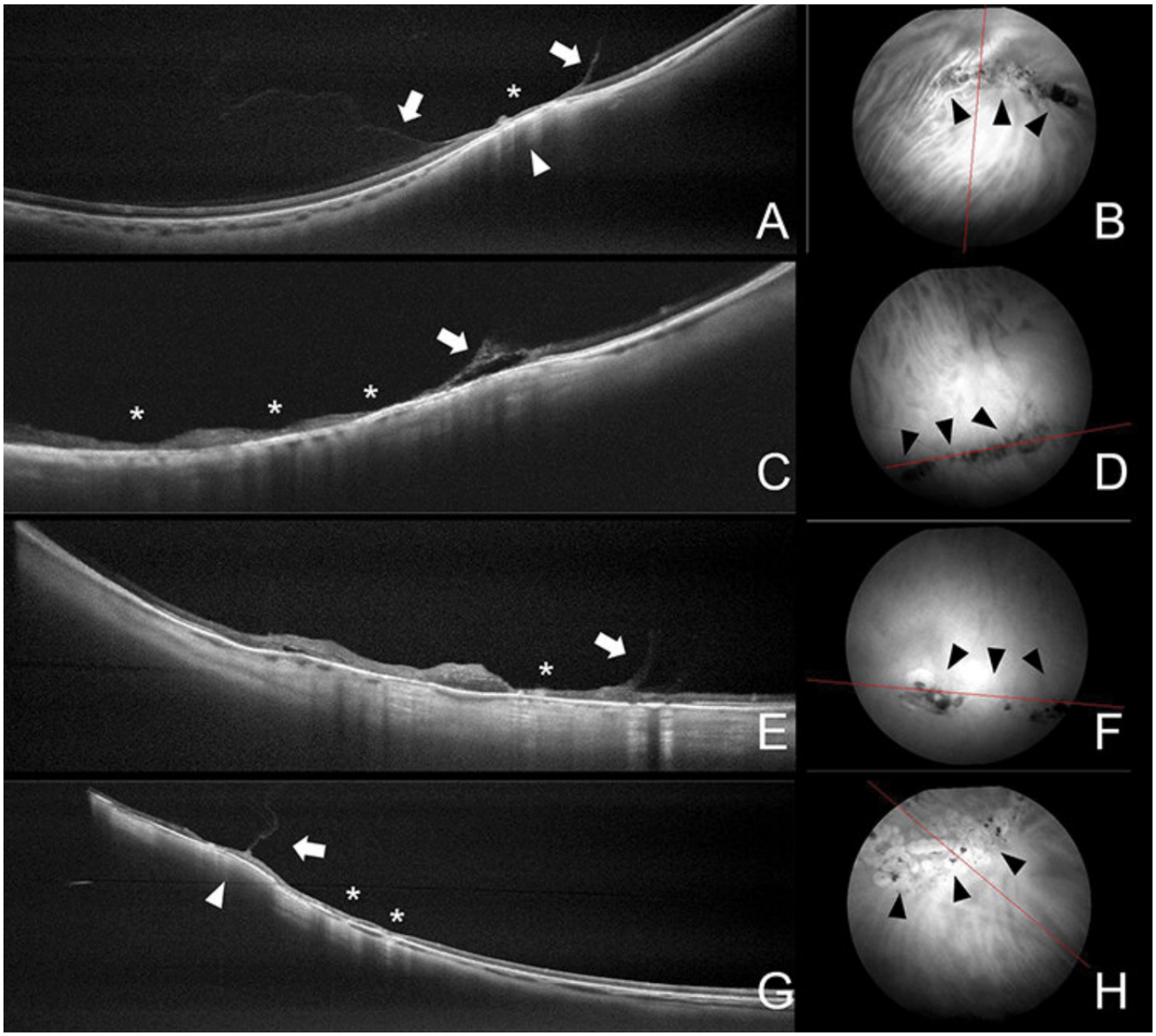

Figure 8b. Spotlight on Lattice Degeneration Imaging Techniques; *courtesy of Maltsev et al. Clinical Ophthalmology 2023:17 2383–2395.*

Optical coherence tomography findings in lattice degeneration. **(A)** Cross-sectional scan passing the lesion crosswise demonstrates U-shaped vitreous adhesion and liquification (arrows), retinal and choroidal thinning (asterisk), and dome-shaped scleral indentation (arrowhead). **(B)** Corresponding infrared image shows perivascular moderately pigmented lesion (black arrowheads) (position of the scan is indicated by the red line). **(C)** Cross-sectional scan passing along the lesion demonstrates retinal and choroidal thinning (asterisks) and retinal separation (arrow). **(D)** Corresponding infrared image shows concentrical highly pigmented lesion (black arrowheads) (position of the scan is indicated by the red line). **(E)** Cross-sectional scan passing along the lesion demonstrates retinal and choroidal thinning (asterisks) and vitreous traction (arrow). **(F)** Corresponding infrared image shows concentrical mildly pigmented lesion with chorioretinal atrophy (black arrowheads) (position of the scan is indicated by the red line). **(G)** Cross-sectional scan passing the lesion crosswise demonstrates chorioretinal scars after laser photocoagulation (asterisks), "blunted" vitreous traction (arrow), and dome-shaped scleral indentation (arrowhead). **(H)** Corresponding infrared image shows mildly pigmented lesion surrounded by chorioretinal scars after laser photocoagulation (black arrowheads) (position of the scan is indicated by the red line).

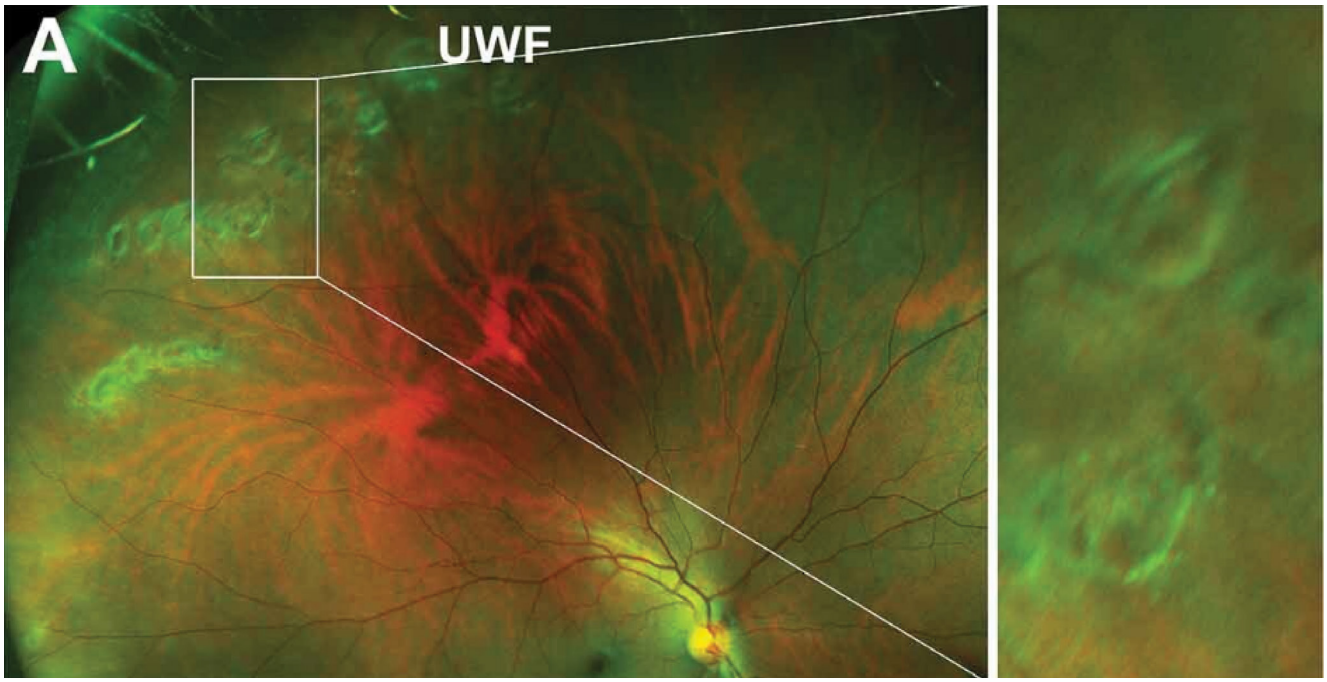

Figure 9. Snail track degeneration in the superotemporal peripheral retina of the right eye; *courtesy of Cheung R, Ly A, Katalinic P, Minas Theodore Coroneo, Chang A, Kalloniatis M, et al. Visualisation of peripheral retinal degenerations and anomalies with ocular imaging. Seminars in Ophthalmology. 2022 Mar 7;37(5):554–82.*

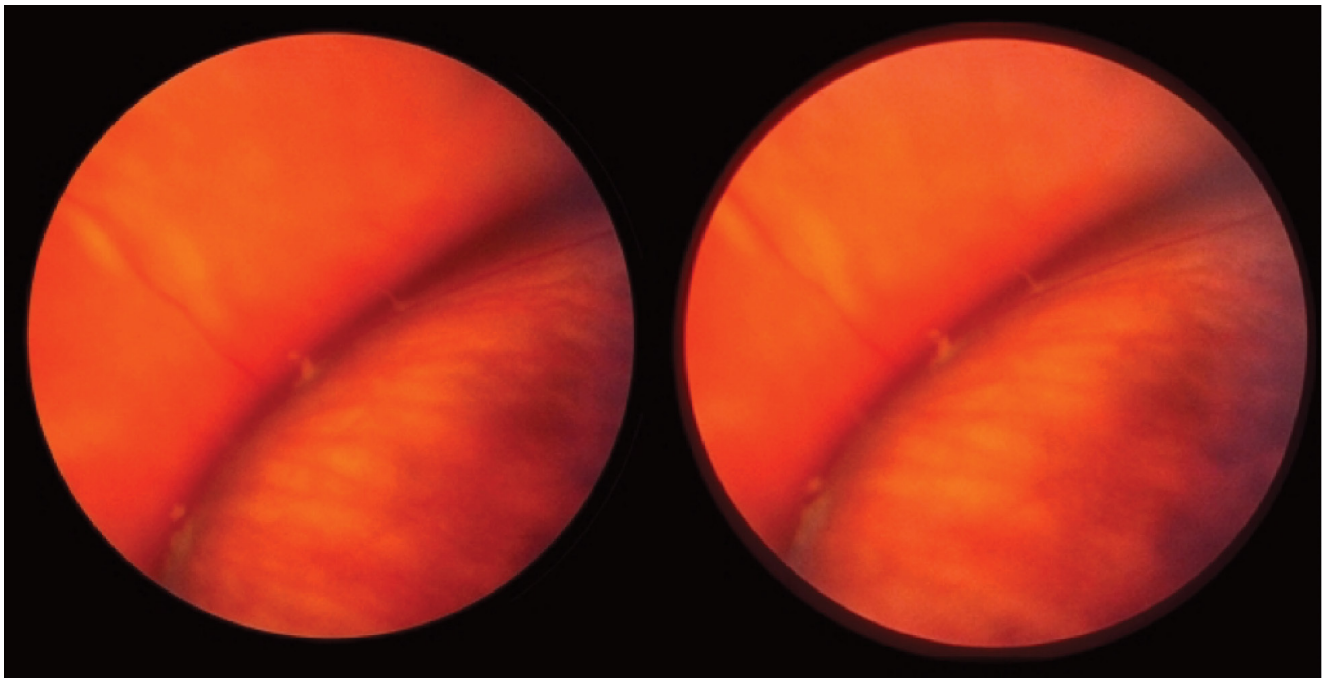

Figure 10. Retinal tufts identified by scleral depression; *photo courtesy of Ravi Dookeran, MD and Charbel Wahab, MD.*

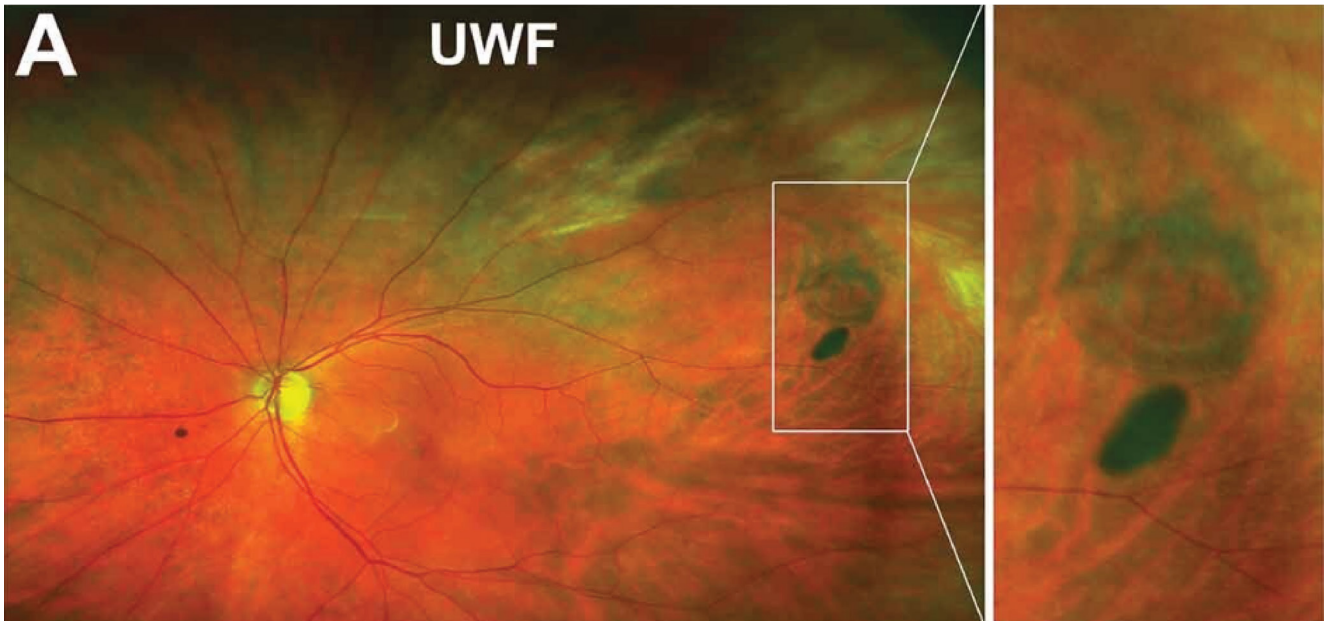

Figure 11. Ultra-wide field photo of the left eye showing an operculated hole; *courtesy of Cheung R, Ly A, Katalinic P, Minas Theodore Coroneo, Chang A, Kalloniatis M, et al. Visualisation of peripheral retinal degenerations and anomalies with ocular imaging. Seminars in Ophthalmology. 2022 Mar 7;37(5):554–82.*

detachment, thus prophylactic laser retinopexy is not recommended.

Retinal Tufts

Retinal tufts are regions of degeneration within the retina resulting from its adherence to and traction by the vitreous (**Figure 10**). They manifest in various forms such as cystic, non-cystic and zonular traction tufts. The prevalence varies, with non-cystic tufts found in as many as 72% of adults, cystic tufts in up to 5% and zonular traction tufts in up to 15%. These tufts may be associated with retinal breaks and tractional forces on the surrounding retina, predisposing patients to retinal detachment.[8] Prophylactic laser treatment is not recommended; routine monitoring is advised.

Retinal Holes and Tears

Peripheral retinal holes and tears are focal defects in the retinal tissue that can predispose to retinal detachment, particularly if located in areas of lattice degeneration. Prophylactic laser photocoagulation is often recommended for symptomatic horseshoe tears and in select symptomatic operculated holes where signs of subretinal fluid or anterior traction are evident. Generally operculated holes warrant observation only.[2] Close observation with serial examinations is justified for asymptomatic small holes or tears with surrounding pigmentation, with prompt treatment initiated if there are signs of progression or new symptoms (**Figure 11**).

Atrophic Holes

Atrophic holes are full-thickness defects in the neurosensory retina, typically found in the peripheral retina (**Figure 12**). These holes may result from a variety of etiologies, including lattice degeneration, trauma or myopia. Atrophic holes pose a risk for rhegmatogenous retinal detachment if they are located near areas of vitreoretinal adhesion. Clinical examination may reveal a circular or ovoid area of retinal thinning with surrounding pigment clumping.

There is consensus for observation over treatment of atrophic holes, especially asymptomatic atrophic holes.[2]

C) Chorioretinal Degeneration

Pavingstone Degeneration

Multiple rounded areas of choroidal and retinal atrophy, characterized by yellow-white lesions with discrete margins, may reveal underlying choroidal vessels as the sclera

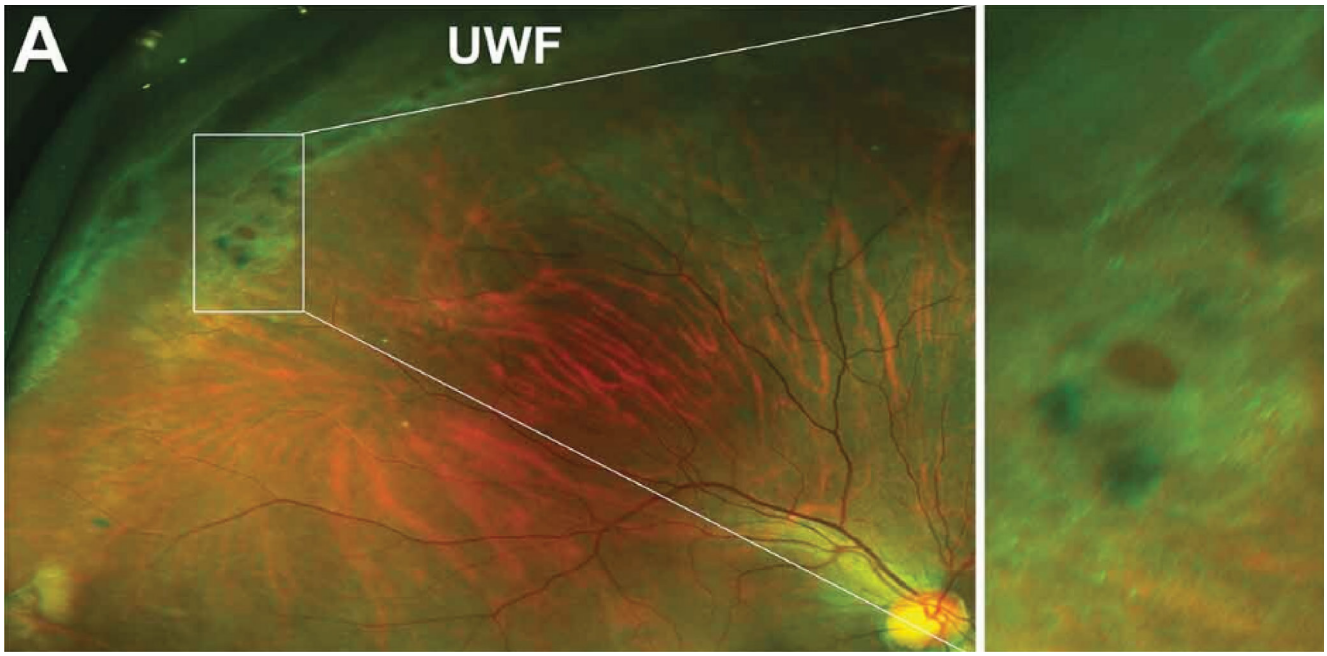

Figure 12. Ultra-wide field photo of the right eye showing atrophic hole within an area of lattice degeneration; *courtesy of Cheung R, Ly A, Katalinic P, Minas Theodore Coroneo, Chang A, Kalloniatis M, et al. Visualisation of peripheral retinal degenerations and anomalies with ocular imaging. Seminars in Ophthalmology. 2022 Mar 7;37(5):554–82.*

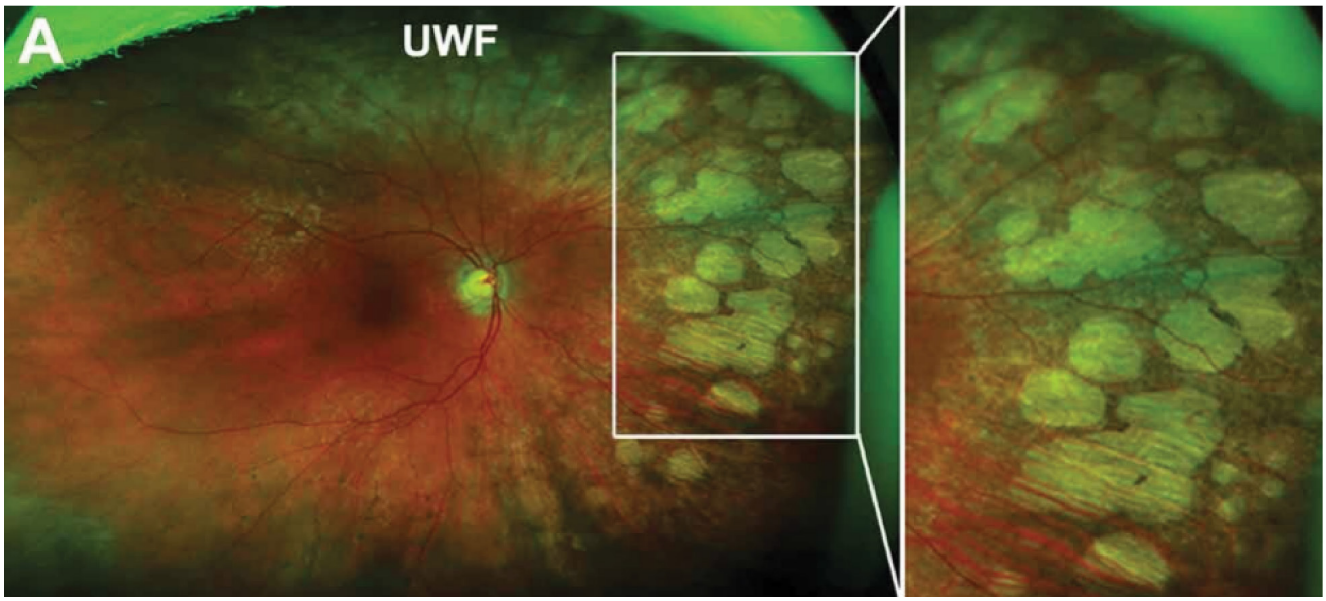

Figure 13. Ultra-wide field of the right eye showing pavingstone degeneration nasal to the optic nerve; *courtesy of Cheung R, Ly A, Katalinic P, Minas Theodore Coroneo, Chang A, Kalloniatis M, et al. Visualisation of peripheral retinal degenerations and anomalies with ocular imaging. Seminars in Ophthalmology. 2022 Mar 7;37(5):554–82.*

becomes partly visible through the atrophic choroid. These lesions, which may merge, are typically found between the ora and equator, ranging from one to several disc diameters in size, with a predilection for the infero-nasal and temporal quadrants. Large choroidal vessels are often visible within the lesions. Prevalent in 4–28% of patients, occurring bilaterally with no gender predilection, these lesions increase in frequency with age but are benign and not associated with complications (**Figure 13**).[18]

Peripheral Retinal Drusen

Extracellular protein and fat deposits commonly form between the retinal pigment epithelium (RPE) and Bruch's membrane, stemming from the degeneration of RPE cells. These deposits, characterized by a crystalline appearance, are typically small, round and distinctly outlined. They are frequently encountered in individuals age 40 years or older and are associated with benign degenerative changes. Prophylactic laser treatment is generally not considered necessary for managing these deposits.

Conclusion

The decision to perform prophylactic laser treatment in peripheral retinal diseases is guided by several factors, including the underlying pathology, risk of progression to sight-threatening complications, patient-specific characteristics, and available clinical evidence.

The AAO preferred practice patterns (**Table 1**) serve as a good guideline when determining whether to treat or observe peripheral retinal conditions.

As the adoption of wide field imaging modalities such as SS-OCT grows the ultra-structural imaging will expand our understanding of peripheral retinal pathologies and how they interact with the overlying vitreous and underlying RPE to more objectively and effectively guide our management in the future.

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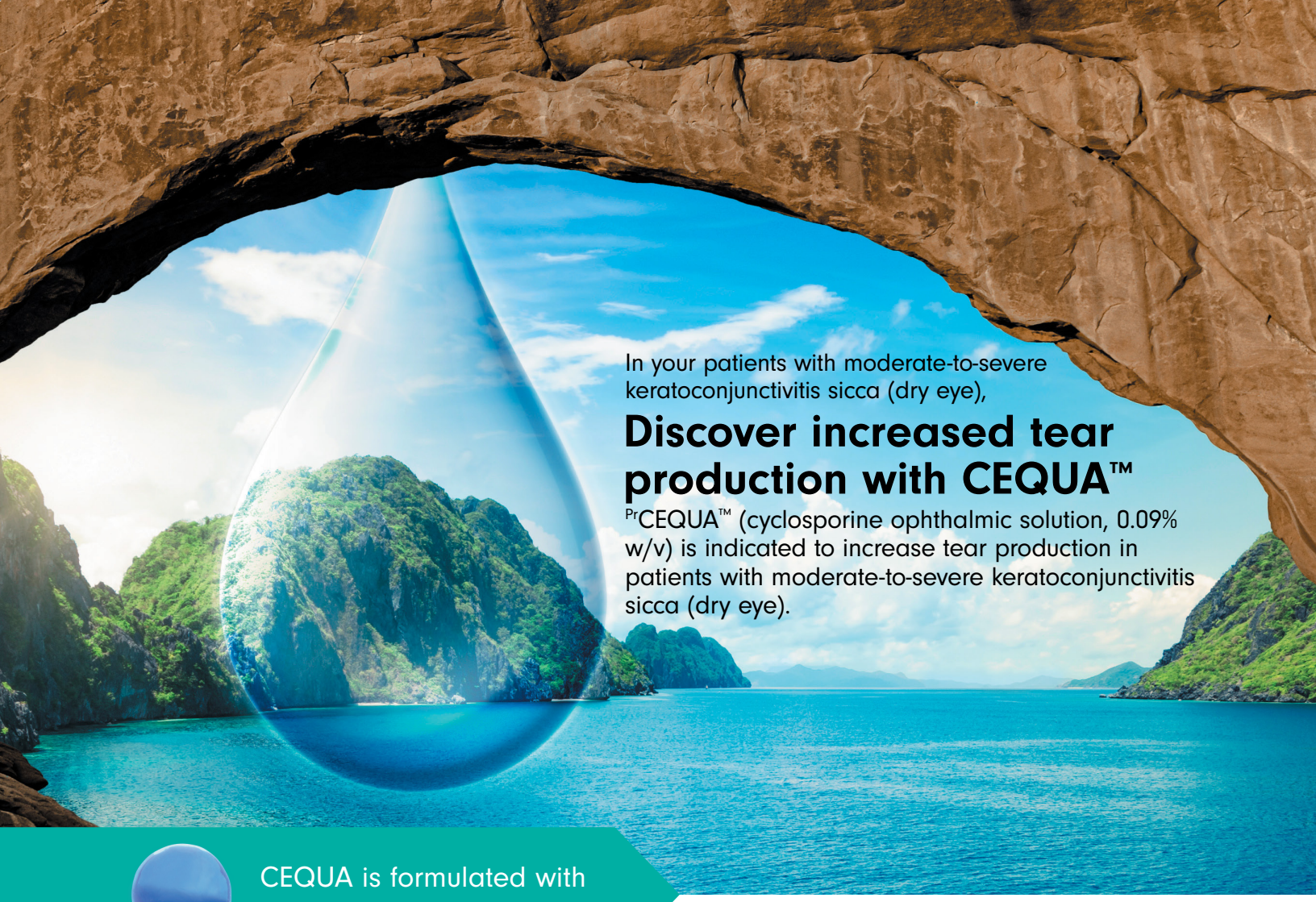

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Dr. Bitton completed her Optometry degree at the University of Waterloo (1988) in Canada, followed by a Master's in Physiological Optics (1994) from the *Université de Montréal* in the area of tear film clinical physiology and its relevance in patients exhibiting dry eye. Dr. Bitton presently holds the rank of full professor, and is the Director of the Externship Program at the School of Optometry at the *Université de Montréal*. She is a member of several national and international professional organizations. Her areas of interest are in the evaluation of the tear film, dry eye and contact lens wear. In 2012 she inaugurated and became the Director of the Dry Eye Clinic at the school, a first in an optometry school in North America. Dr. Bitton was invited by the Tear Film Ocular Society (TFOS) to participate in the TFOS DEWSII and the Lifestyle Epidemic: Ocular Surface Disease reports, a global initiate to redefine dry eye and its etiologies. She represents this organization as one of the ambassadors for Canada. In 2019 Dr. Bitton received a certificate on the Management of Dry Eye from the British Contact Lens Association.

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Challenges in the Diagnosis and Management of Anterior Blepharitis

Etty Bitton, OD, MSc, FAAO, FBCLA

Introduction

Blepharitis is defined as inflammation of the eyelids, classified according to anatomical location: anterior (eyelid skin, base of the lashes including the eyelash follicle) or posterior (meibomian glands) blepharitis.[1] Although blepharitis is one of the most common ocular disorders, epidemiological data on the condition is lacking, making prevalence difficult to assess. A 2009 survey of eyecare practitioners reported observing blepharitis in 37%–47% of patients in their clinical practice.[2] This observation may vary depending on the age, sex, and types of patients (i.e., dry eye) in the practice. Younger females are found to have more acute short-term presentation of blepharitis, whereas older, more fair-skinned females present with chronic blepharitis often concurrent with rosacea.[3] Large population-based studies, using a standardized definition and diagnostic technique, are needed to properly assess the prevalence and incidence of blepharitis and to allow for study comparisons among various age groups.

The ocular surface, including the lid margin, has a natural flora or microbiome, which is imperative in maintaining the health and defence mechanism of the ocular surface.[4,5] This can be affected by age, gender, inflammation, disease,

medication, cosmetics, and treatment (systemic or topical).[5] An overgrowth of microbes or an imbalance of the natural flora may result in an inflammatory response, leading to blepharitis, conjunctivitis, keratitis, or a combination of these.

Challenges in the diagnosis of anterior blepharitis

Various causative factors of blepharitis include bacterial (often staphylococcal), viral (herpes simplex, molluscum contagiosum), fungal (seborrheic), and parasitic (pediculosis palpebrarum, Demodex). Numerous other conditions may be associated with eyelid inflammation, such as immunological (Steven-Johnson's syndrome, graft versus host disease), dermatoses (i.e., psoriasis), eyelid tumours, trauma (including chemical, thermal, radiation), and toxic (medicamentosa).[1] Symptoms are similar across all types of blepharitis and may include: ocular irritation; conjunctival hyperemia; tearing; burning; itching; blurred or fluctuating vision; loss of lashes; photophobia; contact lens intolerance; and recurrent styes, typically worse in the morning.[1] It is clinically valuable to explore the timing of symptoms as this can differentiate from other causalities such as tear film evaporation, which typically worsens throughout the day. Blepharitis can progress to ocular surface inflammation and tear film disturbances, and can exacerbate ocular allergy and dry eye. The myriad of symptoms and the chronic nature of blepharitis, coupled with the ambiguity of its etiology, renders its diagnosis and management challenging for the clinician.

In addition to a comprehensive case history to assess severity, laterality, timing, and duration of symptoms, an external examination of the eyelids, with particular attention given to the lid margin, eyelashes, tear film, and ocular surface, is essential.[1] The lid margin should be assessed for uniformity, hyperemia, and telangiectasia. The eyelashes should be observed for misdirection (trichiasis), loss (milphosis/ciliary madarosis), and type and location of debris, if present. Diagnostic ophthalmic dyes are used to assess for tear film stability and the integrity of the ocular surface.

A careful examination of eyelash debris can be valuable in directing the clinician toward an etiology of anterior blepharitis. Staphylococcal blepharitis typically presents as matted, yellowish, hard scales or collarettes found anywhere along the eyelash. The collarettes move from the base to the tip of the eyelashes with eyelash growth. Milphosis and trichiasis are common in bacterial blepharitis.[1] Conversely, seborrheic blepharitis presents as oily, greasy debris on the lashes; however, it originates in the eyelid skin and is rarely associated with lash loss or misdirection.[1] This condition is typically co-managed with dermatology due to its dermatological etiology.

Demodex blepharitis[6,7] is caused by a microscopic parasite, which is light sensitive and resides in the human eyelash follicle (*Demodex folliculorum*) during the day. The debris on the eyelashes appears as a gelatinous clear sleeve surrounding the lash at its base, termed cylindrical dandruff (CD). CD is pathognomonic for Demodex and remain at the base of the eyelash despite eyelash growth, which is clinically relevant to assist in the differentiation with other types of anterior blepharitis.[8] Having the patient look down at the slit lamp will reveal the base of the eyelashes more clearly. CD along the upper lid margin may be overlooked if the observation is restricted to primary gaze. In cases of dermatochalasis of the eyelid, pulling the folded eyelid upwards while in downward gaze will also assist the visualization of the base of the eyelashes. The Demodex mite has a life cycle of 14–18 days, therefore frequent mating is crucial for effective propagation. Transmission is by direct contact from one individual to another; consequently, family members sharing a dwelling should be examined.

Patients with Demodex blepharitis may or may not be symptomatic. Of those who are symptomatic, itching, specifically along the lash line, is often reported.[9] This can be an additional element to assist in the differential diagnosis of anterior blepharitis. Comorbidities of Demodex infestation (termed demodicosis) include meibomian gland dysfunction (MGD); blepharitis; keratitis; chalazion; dry eye; acne rosacea; and contact lens intolerance and discontinuation, further rendering the etiology of blepharitis challenging.[10-15] There is a 2.5-fold increased risk of Demodex in blepharitis patients and a 3-fold increase in patients with acne rosacea.[10] Demodex blepharitis is confirmed with eyelash epilation and subsequent microscopic observation for confirmation of mites. In a clinical setting, microscopes are not readily available, hence alternative methods are suggested to observe the presence of mites *in situ*. Slit lamp observation can be achieved by selecting eyelashes with CD and, using a tweezer, can be rotated[16] or pulled

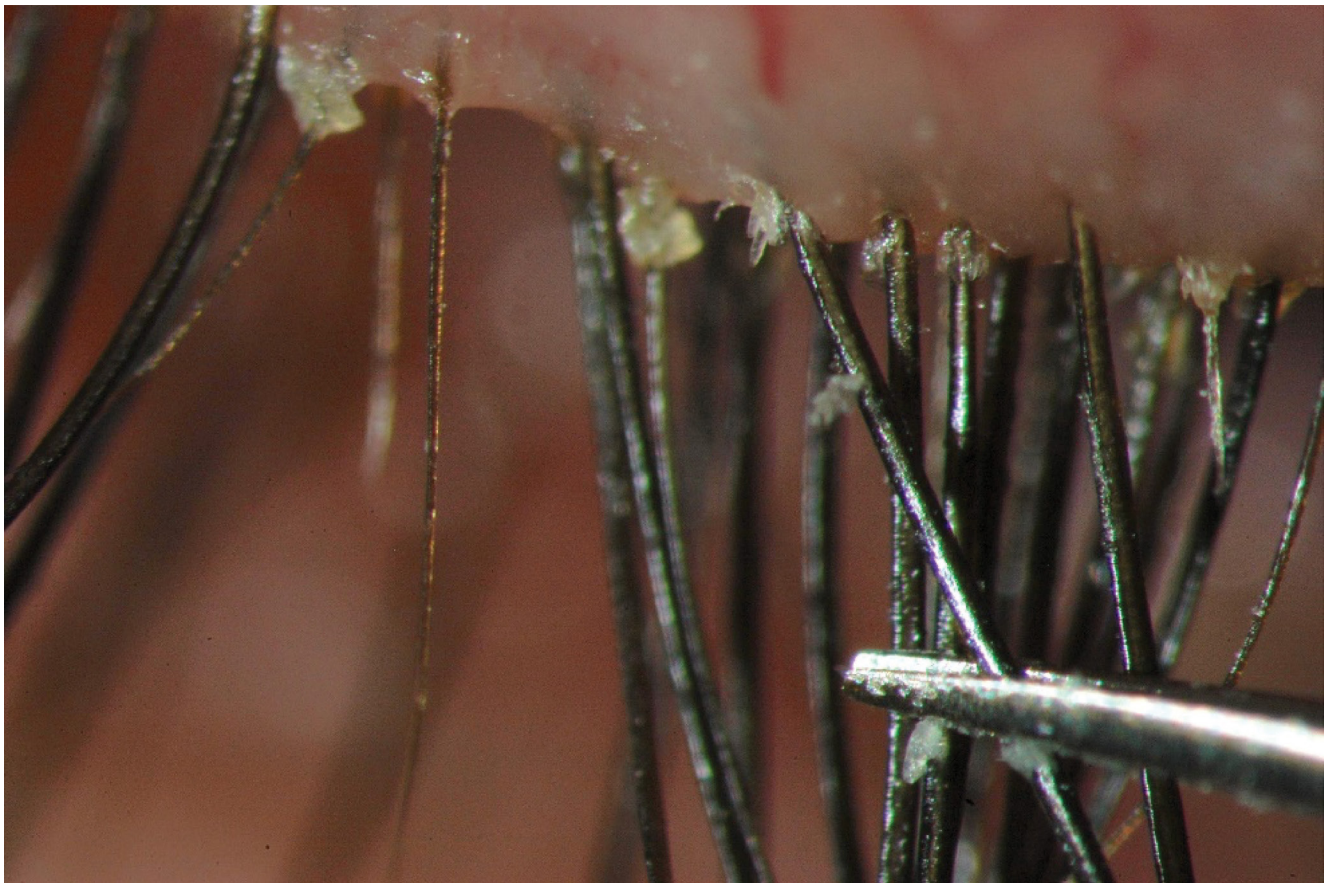

Figure 1. Lateral tension of an eyelash with cylindrical dandruff (CD) revealing the clear tail of a Demodex mite at the base of the lash; *photo courtesy of Etty Bitton.*

laterally[17] (**Figure 1**) to stimulate the mite tail to exit partially from the follicle. Since the mite is clear in colour, it may be necessary to remove the CD or pull it down along the lash shaft, prior to manipulation to facilitate the observation of the mite.[17]

Challenges in the Management of Anterior Blepharitis

Management of anterior blepharitis can be complex due to its multifaceted etiology and comorbidities. Consequently, the therapeutic management of anterior blepharitis should focus on decreasing the overgrowth of microbes (bacteria, virus, fungus, or parasite), to reduce inflammation and improve symptoms, in an attempt to restore the natural ocular flora. Management of anterior blepharitis can include at-home therapies (i.e., lid hygiene, therapeutics) or in-office procedures (i.e., microblephaoexfoliation, intense pulse light). Lid hygiene is a cornerstone treatment for all types of blepharitis.[18] Any mechanical cleaning of the lid margin and lashes will initially remove some of the debris and may even improve symptoms short term; however, unless antimicrobials are used, mechanical cleaning will not address the etiology of the blepharitis. The challenge for clinicians is to better understand the ingredients in lid hygiene formulations in order to identify which of these have antimicrobial properties. This will enable improved targeting of the specific type of anterior blepharitis.

Tea tree oil (TTO)[19] based lid cleansers possess antibacterial, antifungal, and antiparasitic properties and should be considered when a mixed presentation of anterior blepharitis is suspected or when the etiology is unknown. The most abundant ingredient in TTO is terpinen-4-ol (T4O),[20] which possesses a strong demodectic affinity; therefore, it is best suited for the management of Demodex blepharitis. Lid hygiene products with TTO and T4O are often in diluted concentrations as, in higher concentrations, they can cause significant

irritation to the skin and eyes.[21,22] A trial with TTO/T4O lid cleanser can be performed in-office, to educate patients, set patient expectations, and enhance compliance.[21,22] A recent *in vitro* study found T4O to be toxic to meibomian gland epithelial cells, even at very low concentrations.[23] Although further investigation in a clinical setting is warranted, clinicians should consider this finding when recommending T4O-containing lid hygiene products due to the proximity of the meibomian gland orifice along the lid margin.

Lid cleansers with caprylol glycine, hypochlorous acid (HOCl) and okra-based polysaccharide (Abelmoschus esculentus) can be useful in managing blepharitis as they, too, possess antimicrobial properties.[24-27] The added advantage of HOCl is its selective bactericidal activity, affecting the bacterial load while preserving the normal biofilm structure.[26] HOCl is available in spray form and can be used directly on closed lids or applied to a cotton pad for mechanical use along the lid margin. Using a full-spectrum antibiotic ointment on the lids will alleviate bacterial overgrowth unselectively, which may affect the homeostasis of the natural ocular microbiota.

Therapeutics for anterior blepharitis can include antibiotics, antivirals, and antifungals, depending on the clinical presentation and to assist in restoring the ocular flora. For Demodex blepharitis, therapeutics can include topical and systemic ivermectin and metronidazole.[28] Clinical trials with a recently developed antiparasitic agent, lotilaner ophthalmic solution, used twice a day for 28 days, has shown promise in reducing mite counts even after cessation, although this agent is not currently approved for use in Canada.[29]

In addition to at-home therapies, in-office procedures can be performed for anterior blepharitis. Microblepharoexfoliation (MBE) can be used for any type of anterior blepharitis to physically remove debris and biofilm along the lashes and lid margin. This involves use of a manual sponge with an antimicrobial lid cleanser, or mechanically, using a hand-held instrument with a rotating, disposable micro-sponge.[28] The procedure to clean all four lids can take between 5 and 10 minutes and a topical anaesthetic can be used to render the patient more comfortable. Treatment can be repeated in 4 to 6 months. Taking pre- and post-treatment photos (**Figure 2**) is useful in demonstrating to patients the benefits of the deep cleaning provided by MBE.

Intense pulse light (IPL) is well known in dermatology in the management of inflammatory diseases such as acne rosacea.[30] IPL has also been shown to improve meibomian gland expression and enhance the tear film in evaporative dry eye.[31] In addition, IPL has been shown to be effective against demodicosis, even for younger patients (5–16 years old).[32,33]

Conclusion

The diagnosis and management of anterior blepharitis can be challenging for the clinician and a source of frustration for the patient. A comprehensive history coupled with a detailed observation of the lid margin and eyelashes can assist the clinician in gaining an improved understanding of the source of the blepharitis, and guide the patient toward more appropriate management options. There are a multitude of lid hygiene products, pharmaceutical treatments, and in-office procedures available for the management of anterior blepharitis, to alleviate symptoms, improve ocular esthetics, and maintain the integrity of the ocular surface. Keeping abreast of these product innovations and technologies will be rewarding for your practice and your patients will be most appreciative.

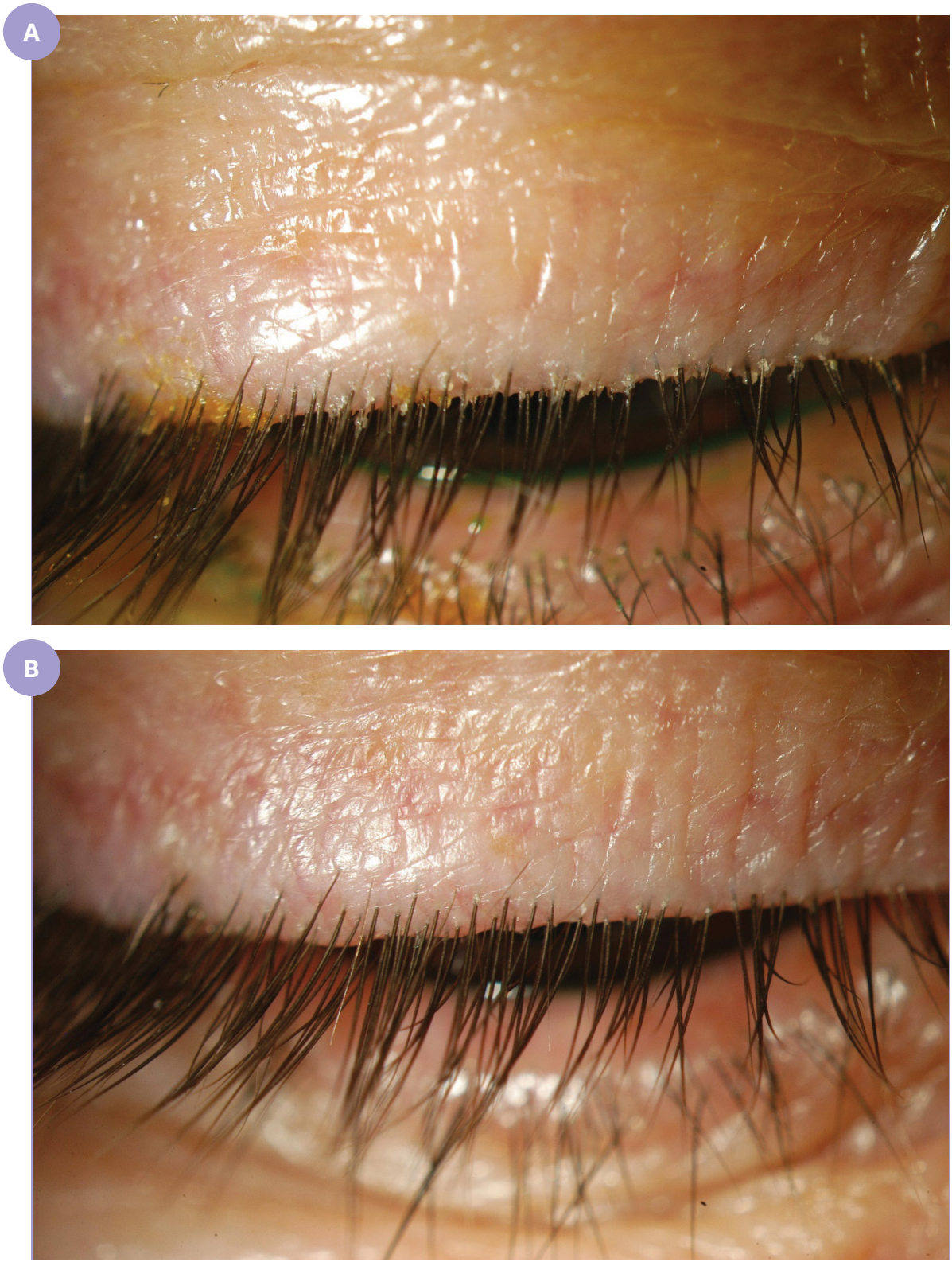

Figure 2. A) Pre-microblepharoexfoliation (MBE) appearance revealing cylindrical dandruff (CD) debris along the base of the upper lid; **B)** Post-microblepharoexfoliation immediately following treatment of the upper lid; *photo courtesy of Etty Bitton.*

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Pediatric Blepharokeratoconjunctivitis: An Update

Asim Ali, MD, FRCSC

Introduction

Pediatric blepharokeratoconjunctivitis (BKC) is a form of ocular surface inflammation which is a unique clinical entity in children. It is also known as phlyctenular conjunctivitis and rosacea keratitis. A recent definition obtained with a modified Delphi method by a group of experts defined BKC as "a frequently underdiagnosed, sight-threatening, chronic, and recurrent inflammatory eyelid margin disease associated with ocular surface involvement affecting children and adolescents. Its clinical spectrum includes chronic blepharitis, meibomitis, conjunctivitis, and corneal involvement, ranging from superficial punctate keratitis to corneal infiltrates with vascularization and scarring."[1] The pathophysiology of BKC is poorly understood but is believed to be related to staphylococcal hypersensitivity, with *Staphylococcus aureus* being the most common flora cultured from the lids in BKC. The robustness of the inflammatory response is thought to be age-related.

The age of onset of BKC is often as early as age 3–5 but can present in adolescence. Gender predilection varies between studies but is roughly equal in incidence for males and females. There is little good natural history data reported on the time course of the disease, but it can become chronic with multiple exacerbations over a period of years. In one study from the United Kingdom, there is the observation of increased incidence of severe disease in younger boys with South Asian or Middle Eastern background.[2] In our experience, however, severe disease can present in all ages and ethnic groups.

There is often a significant delay (up to 2 years) until definitive diagnosis because of lack of familiarity by clinicians with the diagnosis and frequent misidentification with other disorders.[2]

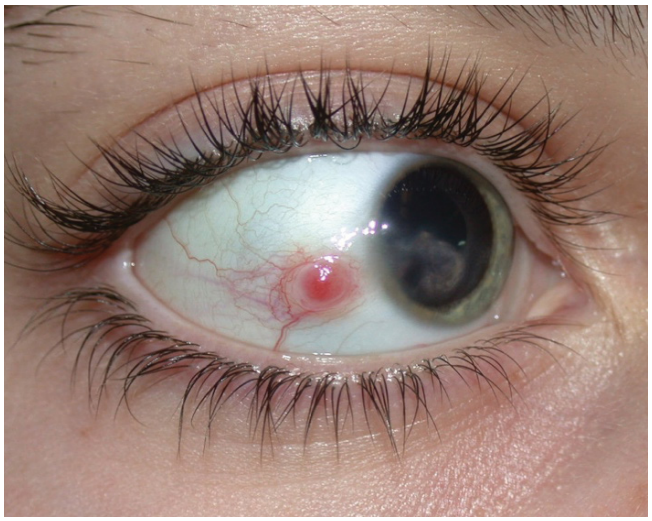

Figure 1. Conjunctival phlyctenule; *photo courtesy of Asim Ali, MD, FRCSC.*

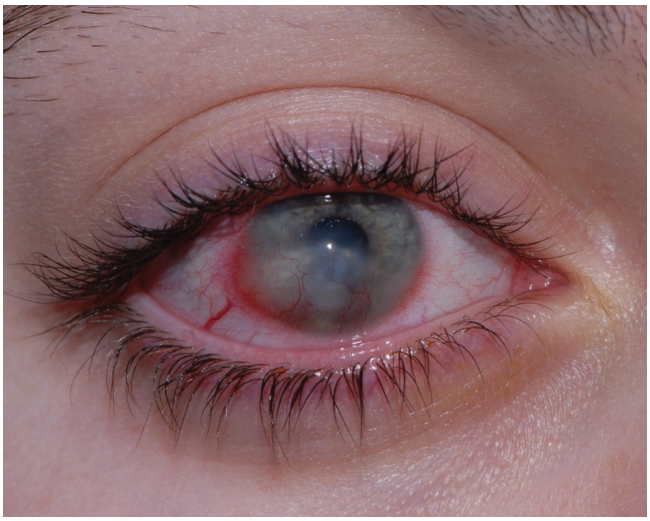

Figure 2. Corneal infiltrates and scarring from BKC; *photo courtesy of Asim Ali, MD, FRCSC.*

The differential diagnosis of BKC includes other chronic and relapsing causes of red eye in childhood including herpes simplex keratitis and vernal keratoconjunctivitis. The corneal infiltrates frequently mimic bacterial keratitis and many children are treated unsuccessfully with topical antibiotics. Historically, the phlyctenules seen in BKC have also been associated with tuberculosis and liver parasites, but even in countries where these disorders are endemic these causes are rare. Without a strongly suggestive history it would not be recommended to test for these pathogens on a routine basis.

Clinical Features

Symptoms of BKC include pain, redness and significant photophobia. Due to this photophobia, young children with active BKC may be very difficult to examine and a complete eye examination is often impossible. In select cases, especially with visible keratitis or recurrent symptoms, a sedated examination may be necessary in order to make the diagnosis.

Characteristic signs of BKC include meibomian gland stenosis, congestion, and inspissation. The extent of changes in the meibomian glands is often less impressive than that seen in adults. Changes to the lid margin including rounding of the lid margin, lash loss, and telangiectasia are less common in children than in adults. Anterior blepharitis can also be seen with crusting around the base of the lashes and inflammation of the lid margin. Chalazia may be seen at the same time as other signs but often these findings are asynchronous. Indeed, a history of chalazia in early childhood is often helpful in making the diagnosis of BKC in the absence of eyelid findings. While widely implicated in the etiology of adult blepharitis, the patterns seen in presumed Demodex infestations such as cylindrical dandruff are not typically seen in children. Malar telangiectasia and pustules on the skin can also develop in BKC in an analogous fashion to ocular rosacea in adults, but this is comparatively rare.

Conjunctival changes include the development of phlyctenules, which can often originate on the bulbar conjunctiva (**Figure 1**) and migrate toward the limbus and cornea, taking a serpentine route and causing scarring. On examination these lesions are elevated, injected and typically stain with fluorescein. The cornea can develop sterile infiltrates which may or may not stain with fluorescein. These are often not just at the periphery but can occur in the central cornea, which is distinct from the marginal infiltrates seen in adults (**Figure 2**). These infiltrates can mimic bacterial keratitis. Inferior punctate keratitis is frequently seen. The development of neovascularisation is also common and is typically superficial but can also be deep. Rarely these new vessels are associated with lipid keratopathy or crystals. Thinning of the cornea can develop and rarely this can progress to descemetocele and perforation. Perforation has been reported to be more likely in older adolescents of European descent.[3]

Treatment

Once a definitive diagnosis has been made a treatment plan should be developed to address both the acute ocular surface inflammation and the underlying blepharitis. Topical anti-inflammatory therapy is the mainstay of acute treatment. Corticosteroids are often used in the acute phase to relieve symptoms and are especially helpful when there is corneal involvement such as phlyctenules or infiltrates. Potent corticosteroids such as prednisolone or dexamethasone can be used in a tapering schedule over 4–6 weeks and this can rapidly improve the clinical situation. Symptoms such as photophobia respond very quickly. A treatment follow-up visit should be arranged within 1 month and in younger children the second examination is much easier to tolerate. Often, fundus examination and refraction can be deferred to this visit. Special care needs to be taken with the use of potent corticosteroids in children as their effect on IOP is greater in children than in adults with both a greater increase in pressure and early onset of this effect. There is no role for long-term potent corticosteroid use in the treatment of this disorder and families need to be educated about the associated risks.

Select oral antibiotics are very effective in achieving long-term remission of BKC due to their anti-inflammatory effect on meibomian glands through multiple mechanisms. The tetracyclines (including doxycycline and minocycline) are contraindicated in children with primary dentition due to staining of the permanent teeth, and thus can only be used in older children. Macrolides such as erythromycin, clarithromycin, and azithromycin do not have these age limitations and all can be used to control BKC in the long term. Oral azithromycin can be administered less frequently which helps with compliance in children.[4] In our practice, it is prescribed weekly, and is highly effective and well-tolerated by most children. The most common side effect is gastric upset but this rarely results in discontinuation of therapy. Topical azithromycin has also been described in the literature for the treatment of BKC, but it is not available in Canada.

In select children who are intolerant of oral therapies or who have mild disease, lower potency corticosteroids such as loteprednol and fluorometholone can be helpful. These agents have a lower risk of ocular hypertension, but regular monitoring is still important. Topical cyclosporine in various reported concentrations has also been used in similar scenarios and avoids the side effects of corticosteroid use. Stinging with instillation can make it difficult to use in the long term in many children.

Other concomitant management includes the use of topical antibiotics such as erythromycin and fucidic acid drops which are very helpful in children with anterior blepharitis. Both are active against *S. aureus* and help to decrease the overall bacterial load. Lid scrubs and warm compresses should be taught and recommended to families as an adjuvant therapy but are rarely effective as a primary therapy. The role for these measures is for maintenance after the acute inflammation has subsided with other treatment. The use of omega-3 supplements has been advocated in the literature but there is no good evidence for their use in children. Published dosing guidelines are not available and their toxicity profile is unknown.

Refractive Sequelae

Recurrent episodes of untreated corneal inflammation typically occur over a period of months to years which can lead to astigmatism and stromal scarring. These sequelae can result in amblyopia in younger children. In different series, the rate of amblyopia due to anisometropia or deprivation from scarring has been reported to be as high as 30%, but most children will develop excellent vision with appropriate treatment.[5,6] It is important to perform a cycloplegic refraction once the acute inflammation has been controlled, usually 1–2 months after presentation.

The resultant astigmatism may be either regular or irregular. Increasing amounts of astigmatism are associated with multiple recurrences of disease.[6] If the cornea is otherwise mostly clear, glasses should be tried first and the patient followed for any improvement in vision. If the vision plateaus, part-time patching therapy should be prescribed. Some patients may need either rigid gas-permeable contact lenses or scleral lenses for irregular astigmatism, although tolerance of these modalities in this patient group is poor. In a minority of individuals, deep anterior lamellar keratoplasty can be considered in cases with severe central scarring. Recovery of vision is often limited by underlying amblyopia, but graft survival is excellent in our institutional experience.

Summary

Pediatric BKC is an important cause of recurrent red eye in children and is frequently misdiagnosed. Pulse corticosteroid therapy combined with oral macrolide use can control symptoms and reduce scarring and vision loss. It is important to monitor for recurrence and address refractive error with glasses and amblyopia with patching. Using these approaches, the visual outcomes can be excellent.

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