As researchers and clinicians, our understanding and treatment of retinal disease has changed dramatically over the past 40 years. Historically, retinal surgeons wanted to talk about their technical success rather than restoring vision, because in reality, post-surgical patients used to say, “I don’t see any differently.”

Today, there are a host of retinal diseases that are treatable, and with the advent of new technology, we have gone from just “fixing things” to actually giving patients functional vision. It has truly been a remarkable ride.

As our understanding of retinal disease continues to evolve, we are excited to show results from some of our recent research into age-related macular degeneration, highlight our expanding and nationally renowned Uveitis Division, and share some of our expert retina team’s clinical and surgical tips with you in this special “retina” issue of Clinical Focus.

In other news, I’m proud to say that Moran’s Ophthalmology Residency Program at the University of Utah School of Medicine is now ranked 10th in the nation by U.S. News and World Report. Our retina fellowship garnered over 70 applicants to fill just one spot, and we’ve recently added a uveitis fellowship—one of only 15 in the country.

Randall J Olson, MD
Professor and Chair, Department of Ophthalmology and Visual Sciences; CEO, John A. Moran Eye Center, University of Utah
Personalizing Treatment for Uveitis Patients

The Moran Eye Center is nationally recognized as a regional referral center for difficult and complicated retina cases and is one of the few academic medical institutions to have a uveitis division. Uveitis specialists Albert T. Vitale, MD, and Akbar Shakoor, MD, collaborate closely with the University of Utah’s Divisions of Rheumatology (adult and pediatric), Infectious Diseases, and the Huntsman Cancer Institute to provide personalized and complete care.

Uveitis Affects Two Million Worldwide

Uveitis comprises between 10 to 15 percent of the total blindness in the United States and is the fifth leading cause of visual loss after diabetes and age-related diseases. The impact of that blindness is significant, as it frequently affects people in their productive prime.

One-Size-Fits-All Treatment—Not an Option

Uveitis is more than 30 separate disease entities with different clinical features, course and prognoses, and disease-specific indications for treatment. Inflammation can be confined to the eye or be systemic—non-infectious or infectious—or masquerade as malignancy; it even occurs in different anatomic locations in the eye. The approach to treatment needs to be individualized to the patient, to their disease, and to what they can or cannot tolerate.

Preferred Practices

In 2016, Dr. Albert T. Vitale and other members of the Ocular Immunology and Uveitis Foundation published their preferred practice guidelines for patients with ocular inflammatory disease in the Survey of Ophthalmology.* This approach is also articulated in the definitive textbook, Diagnosis and Treatment of Uveitis.*

Citation: *Survey of Ophthalmology, Volume 61, Issue 1, January–February 2016, Pages 1-17.
Citation: *Foster C. Stephen, Vitale, Albert T., Diagnosis and Treatment of Uveitis, Second Edition, 2013.
Establish a Diagnosis

Our mission is to control intraocular inflammation and to induce remission. To do this, we must first establish a diagnosis and rule out infection or malignancy. Appropriate antimicrobial therapy is essential in cases of infectious uveitis and may cure the disease. For patients with non-infectious uveitis, we employ corticosteroids to treat acute inflammation. The threshold in implementing steroid-sparing immunomodulatory therapy is low in an effort to minimize the total exposure to corticosteroids and to reduce the systemic and ocular complications associated with both chronic intraocular inflammation and corticosteroids. And, we hope to induce remission of the inflammatory disease processes while preserving visual function. While corticosteroids remain a major part of uveitis therapy, they are used to manage active uveitis, not for long-term therapy.

Step-Ladder Approach

In this treatment algorithm, the goal is to employ a staged, long-term treatment approach appropriate to the diagnosis, the anatomic location, and the severity of the intraocular inflammation. We use corticosteroids first and advance up the therapy ladder as needed when the patient no longer tolerates the treatment, or the treatment fails.

Treatment Goals for the Stepladder Algorithm

- Eliminate inflammation: control acute activity promptly; suppress chronic or recurrent disease; induce remission
- Treat, reduce, or prevent ocular structural complications
- Improve visual function; prevent visual loss
- Avoid or minimize potential systemic complications

Know Your Patient

Treating uveitis requires knowing your patient very well, medically, ocularly, and personally: If a patient tells me, I’m going to become a homicidal maniac if you give me systemic steroids, I will find an alternative. It also builds the foundation for a long-term relationship, which is essential for patients with chronic diseases—not only in terms of them understanding their disease and adhering to their treatment regimen and outcome—but also in terms of caring for the whole person. This strategy helps us achieve the ultimate goal of our mission—corticosteroid-free remission or being cured of the disease. —Albert T. Vitale, MD
A patient with no AMD or vision problems was referred to the retinal clinic for crystal deposits in the macular region of the retina in both eyes. With physician follow-up, we learned that for the past eight years, the patient took a daily lutein supplement (20 mg) in addition to a diet rich in lutein, which included a broccoli, kale, spinach, and avocado smoothie every morning; she was therefore consuming much more than twice the recommended dose of lutein for an AMD patient (10 mg per day).

Lutein is part of the AMD prevention supplement regimen that was created based on results from the AREDS2 (Age-Related Eye Disease Study 2) clinical trial. In that trial, we found that patients at high risk for visual loss from AMD who took lutein (10 mg) and zeaxanthin (2 mg) supplements reduced their risk of progressing to late stage AMD. Lutein and zeaxanthin are carotenoids—antioxidants made by plants—that are believed to neutralize light-induced damage in the eye. Humans don’t make carotenoids, so they can only be added to the body by eating plants or taking supplements.

When we looked at the patient’s carotenoid levels in serum, skin, and the retina, all measurements were at least two times greater than carotenoid levels in patients not taking nutritional supplements. The patient quit taking the lutein supplement, but maintained her diet rich in lutein, and, after seven months, the crystals in the right eye disappeared.

While AREDS2 supplements are recommended to patients at higher risk for AMD, there has also been increased use in the general population. My advice for my patients is that everyone should eat an ‘eye-healthy’ diet rich in colorful fruits and vegetables, and individuals should take an AREDS2 supplement if their ophthalmologist detects signs of AMD. This case report must be followed up by a larger clinical trial before the results can be considered conclusive, but it serves as an indicator that there may be negative effects from consuming lutein considerably higher than the recommended AREDS2 dose.

**Citation:** Rene Y. Choi, Susan C. Chortkoff, Aruna Gorusupudi, and Paul S. Bernstein. Crystalline Maculopathy Associated with High-Dose Lutein Supplementation. JAMA Ophthalmology, published October 27, 2016.
Why is this promising research important? Age-related macular degeneration is a leading cause of blindness in the elderly. In neovascular (wet) AMD, new blood vessels grow under the retina. These blood vessels then leak, making the RPE barrier weak, allowing abnormal cells to migrate across the RPE into the retina, compromising vision.

Since blood vessels grow in response to vascular endothelial growth factor (VEGF), one current treatment for vascular AMD is to block VEGF with anti-VEGF injections. This therapy is successful in about 40 percent of patients, but is far from perfect. Some problems with anti-VEGF injections are that VEGF can also be beneficial to specialized retinal cells. And, if you get to the point where you don’t need anti-VEGF anymore, continuing to remove VEGF, theoretically, could harm the eye and increase the likelihood of advanced dry forms of AMD.

In a cell, RAP1A turns on and off as needed to control the RPE cell’s ability to have strong barriers. What we discovered in this study is that RAP1A, when activated, prevented invading blood vessels as well as the anti-VEGF treatment did in RAP1A-deficient mice.

So as an alternative to anti-VEGF injection, being able to inject an activated RAP1A may also benefit not only AMD, but other conditions associated with a weak RPE barrier. This is new experimental research that may have a role in precision medicine, in which patients with deficiencies in the ability to activate RAP1A may benefit. As we learn more about people with certain genetic makeups that cause them to resist current therapies, novel therapies such as active RAP1A may provide an alternative.
Moran Retina Specialists Share Insights

Retina specialists often treat patients with some of the most sight-threatening conditions—so cultivating authentic patient rapport is as critical as surgical expertise. Here, Moran specialists share advice.

Because Moran is a regional referral center, I have seen every possible bad thing that can happen in treatment and surgery in the past 30 years—often fixing mistakes that happened elsewhere. This experience has given me a unique perspective that I try to pass on to our fellows—who are already very good surgeons—but my job is to teach them the finer details of clinical care and retinal surgery.
Clinical and Surgical Tips

Know When to Say “Enough is Enough”  

Michael Teske, MD

○ Have you established realistic expectations?
When you’re meeting a patient for the first time, find out what the patient’s expectations are, what’s realistic, and what we can do. Being able to drive or read again may be completely unrealistic. Take some time to explain what’s going on, why they don’t see, and what you can offer.

○ Are you honest with patients?
In retina, we deal with the worst blinding problems and patients who are really scared because their vision is half gone, or it’s going fast. We also get patients who have already had a couple surgeries, such as retinal detachments, and may have some scarring. A lot of times, we can help them, but a lot of times, we just can’t. So being able to develop an open honest relationship with a patient gives them confidence in our treatment plan.

○ Are you overtreating? Listen to your patient!
Some treatments call for injections—but don’t over-treat. Tests may show that the fluid hasn’t gone away, or there’s a little bit coming back, but it is important to first look at what the patient’s vision is and listen to what the patient is saying: If the vision is good, and the patient is happy, then stop.

○ Do you know where you are in the eye?
In surgery, when you look at the retina through a microscope, it looks flat—but it is actually curved. Know where your hands are. Hold your instrument in such a way that it will not hit the retina. It’s second nature to me, but it’s something we work to finesse.

○ What is your primary surgical goal?
Say your surgical goal is to get the traction off the macula, so you peel the epiretinal membrane off the macula. But maybe there’s a little bit more, so you keep going after it—STOP for a second. Ask yourself what was the goal? Peeling more may not be necessary to achieve your goals.

Don’t Treat Children as Adults

Akbar Shakoor, MD

We see a lot of children in our uveitis practice. Kids are super sensitive to anyone who is less than friendly or is cold and clinical, so it’s important to be a little more casual with children, to go the extra mile to provide a friendly environment and to generate feelings of trust towards you as a physician, as it doesn’t always come naturally. I’ve seen physicians who speak only to the parent and not to the child, but it’s important, within reason, to involve the child in a decision making process. Also, I tend to limit how many people are in the room at the same time with children—I never put more than two doctors in the room because it’s claustrophobic for any of us, but more so for kids.
Moran’s Global Outreach Division & Training in Retinal Specialties

For more than a decade, Dr. Albert T. Vitale has been an integral part of delivering comprehensive and sustainable retinal care in the developing world. He’s currently focusing his efforts on Myanmar, where he is teaching non-ophthalmic HIV physicians how to perform a variety of exams and treatments and to diagnose a variety of retinal infections.

In Southeast Asia, only 39 percent of people infected with HIV are receiving antiretroviral therapy (ART). Opportunistic infections, such as CMV retinitis or ocular tuberculosis, are still a problem for HIV patients there. Vitale, with his colleague Dr. David Heiden, has been working with non-governmental organizations to address the lack of ophthalmic care for AIDS patients in a resource-poor setting. “You can imagine that in a country like Myanmar there are very few ophthalmologists, and those ophthalmologists who are there are not really that interested in taking care of patients with HIV/AIDS,” says Vitale. “So, the idea has been to train doctors who take care of patients with HIV/AIDS to diagnose and treat the ocular complications of infections that patients with AIDS get,” Vitale conducts workshops to train internists to use indirect ophthalmoscopy and instructs them on how to diagnose infections and to perform intravitreal injections in their treatment. He is also conducting a pilot study on using barrier laser photocoagulation to prevent retinal detachment in patients who have healed CMV retinitis. In 2016, Vitale received the Utah Ophthalmology Society’s 2015 Lewis A. Petersen, MD, Humanitarian Award.

Dr. Paul Bernstein trains aspiring retina specialists from Nepal, Ghana, Ethiopia, and Bhutan who come to Moran to observe a variety of retina patients and learn vitreoretinal surgical techniques. After the trainees return home, Bernstein travels to their local hospitals where he helps them set up their equipment and provides further hands-on training.

Bernstein has helped train retina specialists at the Tilaganga Eye Hospital in Kathmandu, which is now the leading center for retina surgery in the Himalayas. In December 2012, He traveled to the Kingdom of Bhutan to help Dr. Bhim Rai inaugurate the first vitreoretinal operating room in the country. Together, they performed the first anti-VEGF injection ever done in Bhutan on a high-ranking lama.

Bernstein holds the Mary H. Boesche Endowed Professorship in Ophthalmology and was recently honored with the 2016 American Academy of Ophthalmology Outstanding Humanitarian Service Award.