Room to Wiggle

By Holden Caplan, BS | Faculty Reviewer: James P. Dunn, MD

Dr. James P. Dunn, courtesy of Roger Barone, Wills Eye.

What is black, white, and red all over?

Uveitis – inflammation of the inside of the eye and the fifth leading cause of vision loss in the USA. Uveitis (of which there are 30-40 types) may be infectious or non-infectious, unilateral or bilateral, of sudden onset or progressing over months to years, and present in any age group. Different etiologies cause different presentations, including both onset and location (front, middle, or back; **Table 1**) in the eye. To the average physician, identifying the cause of this inflammation is like asking a third-year med student to manage high-flow ventilator settings for a patient in the ICU. With good training it is possible, but the entire process is rather taxing and anxiety-inducing for everyone involved. Patients may suffer from chronic eye pain, blurred vision, floaters, and flashing lights and are often frustrated by a lack of information about their condition. That is why ophthalmologists such as Dr. James P. Dunn, Director of the Uveitis Unit at Wills Eye Hospital, have dedicated their career to helping these patients find answers. Acting as an internist of the eye,

Table 1. *Types of uveitis*

Type	Description
Anterior uveitis	Inflammation affecting the iris and ciliary body (iritis or iridocyclitis). *Seronegative spondyloarthropathies* associated with the HLA-B27 allele often present with acute unilateral anterior uveitis. *Pauciarticular juvenile rheumatoid arthritis* is commonly associated with a chronic bilateral anterior uveitis. *Herpesviral anterior uveitis* should always be considered when associated with elevated intraocular pressure. *Sarcoidosis* and syphilis can cause unilateral or bilateral anterior uveitis.
Intermediate uveitis	Inflammation affecting vitreous humor, often *autoimmune (pars planitis),* secondary to systemic conditions such as *sarcoidosis*, or due to infectious diseases such as *syphilis* (Dr. Dunn's favorite disease as every patient with it presents with an interesting story). *Multiple sclerosis* and *inflammatory bowel disease* can also cause intermediate uveitis, and in older patients with intermediate uveitis, *primary vitreoretinal lymphoma* may be a consideration.
Posterior uveitis	Inflammation affecting the retina and/or choroid, a classic cause of vision loss due to retinal hemorrhage and detachments. Autoimmune ocular diseases including the so-called *"white dot syndromes,"* infections (including *CMV retinitis* in immunocompromised patients*, syphilis, toxoplasmosis,* and *tuberculosis)*, and *retinal vasculitis* (purely ocular or part of a systemic vasculitis) are in the differential. *Sarcoidosis* can cause isolated posterior uveitis.
Panuveitis	Inflammation affecting the entire eye, is often the most devastating form of uveitis as it is often the sequelae of untreated inflammation. Autoimmune diseases (*sympathetic ophthalmia* following penetrating trauma, systemic diseases such as *Vogt-Koyanagi-Harada disease* or *Behcet's disease, syphilis, tuberculosis,* and herpesviral infections such as *acute retinal necrosis,* and sarcoidosis are the most common causes. Rarely, malignancies such as *retinoblastoma, lymphoma, or metastatic tumors of the eye* can cause panuveitis.

Dr. Dunn works in close conjunction with many internal medicine specialists to determine the cause of the uveitis and ensure the patient is treated for the systemic cause of the inflammation. Though ophthalmology is considered a visual field (pun intended), Dr. Dunn's practice emphasizes the equal importance of history taking when deducing the cause of ocular inflammation.

To say that Dr. Dunn's career was non-linear would be an understatement. "Mine

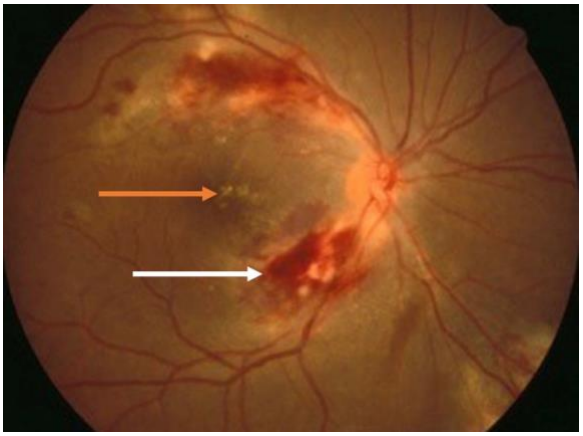

Figure 1. *CMV retinitis,[1] characterized on fundoscopy by cotton wool spots (early sign, orange arrow) and retinal hemorrhages (white arrow).*

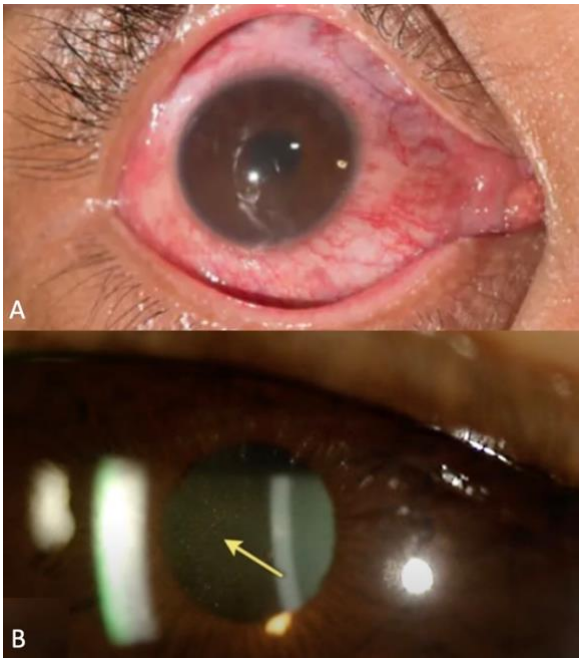

Figure 2. *Common active anterior uveitis exam findings:* (A) *Conjunctival injection[2] on external exam and* (B) *aqueous flare[3] on slit-lamp examination.*

was a very circuitous landing. If you told me in medical school that this is what I would be doing at 65, I never would have even known this career existed!" In school at New Jersey Medical College, Dr. Dunn always had an interest in internal medicine. However, he had done some work with the ophthalmology department and enjoyed the mix of interesting pathologies with a surgical practice. In 1985, Dr. Dunn moved to New York to complete an ophthalmology residency at New York University. There, he became extremely interested in corneal diseases as well as an AIDS-related eye diseases such as CMV retinitis (**Figure 1**). Much of his research as a resident was understanding the effects of Ganciclovir, a new drug at the time, on treating this disease. After graduating, he decided to pursue a cornea fellowship at UCLA where he continued to have an interest in AIDS research but had little time to pursue it during the surgery-intensive fellowship.

When it came time for the end of the fellowship, Dr. Dunn was at a crossroads: He knew he wanted an academic career but was unsure whether or not to find an assistant professor position or pursue further fellowship training. Eventually, he decided on pursuing another cornea fellowship, accepting an offer at Washington University in St. Louis, but upon returning to L.A. after the fellowship interview, a pleasant surprise awaited him. While he was away, his wife had received a call from the Proctor Foundation at UC San Francisco, a fellowship program that combined cornea and uveitis training that allowed him to pursue his interest in AIDS-based ophthalmic complications. They had heard about Dr. Dunn through one of his mentors at UCLA, so they had attempted

to call him at home. As his wife was the only one home to answer, she heard out their proposal and without missing a beat replied, "He'll take it." So, no, he was not going to St. Louis, but rather San Francisco ("My wife told me she would never have moved to St. Louis anyways, so it worked out for the best"). In San Francisco, Dr. Dunn found a way to combine his passion for infectious disease research with his surgical cornea practice, and for the first time was exposed to intensive training in uveitis.

In 1990, after completing the fellowship, he applied for a faculty position with Dr. Douglas Jabs in the Division of Ocular Immunology at the Wilmer Eye Institute at The Johns Hopkins School of Medicine. Dr. Jabs had created a new multicenter program centered at Johns Hopkins called the Studies of Ocular Complications of AIDS (SOCA), and he needed someone to take over some of the clinical responsibilities in the division so he could get SOCA up and running. Dr. Dunn had an unusual skill set in AIDS clinical care and research as well as being a highly trained cornea, uveitis, and cataract surgery specialist. For the next 23 years, Dr. Dunn would continue his research in CMV retinitis, and for 15 years was the director of the ophthalmology residency program at Hopkins. He thrived under the mentorship of Dr. Jabs, under whose leadership the Division of Ocular Immunology became one of the busiest and most respected uveitis centers in the world (and AIDS fortunately became a treatable disease with far fewer ocular complications). For the first time in his long career, he had finally found some footing and coincidentally was able to follow in person the team he had rooted for since he as a child – the Baltimore Orioles! In 2013, he decided he needed a change of scenery. As HIV became more treatable, ocular research in the field had become less prioritized. Dr. Dunn decided to follow his passion for uveitis and moved to Wills Eye Hospital to create its first uveitis specialty clinic in which he focused on all forms of uveitis as well as a maintaining an important role in resident education. The move wasn't all peaches and roses ("I made sure they wrote into my contract that I didn't have to adopt any Philly sports teams") but he loved the challenge of the new position.

"Do not think of your career linearly because you never know what is going to happen. You can always make a horizontal wiggle."

Dr. Dunn's passion for uveitis comes from the breadth of the field (interacting with every other subspecialty in ophthalmology) and the wonderful mentors he has had in his career. As a systematic understanding of the body is imperative to determining a diagnosis and treatment plan, Dr. Dunn works closely with doctors in other fields such as Rheumatology, Oncology, and Infectious Diseases, ensuring he is always learning something new. When it comes to patients, Dunn appreciates how a patient's background determines the nature of what you look for and see. He utilizes the *Who When Where What and Why* approach (**see right**) to ensure he orders the most specific test for these patients, with the goal of reducing the false positives common in the traditional "shotgun" approach that can lead to inadequate or inappropriate treatment.

Treatment for uveitis is focused on reducing inflammation and resolving the complications of that inflammation (cataract, glaucoma, retinal edema, corneal edema, synechiae around the pupil, etc.). This means using topical, oral, or intraocular steroids for most ocular inflammatory diseases but also immunosuppressive drugs, such as anti-metabolites like methotrexate, calcineurin inhibitors like tacrolimus, TNF-a inhibitors like infliximab, or other biologic drugs to reduce further damage to the eye. If there is an infectious cause, targeting the infection with antibacterial, antivirals, and

Who When Where What Why approach

***Who*:** Demographics, including age, race, ethnicity, job description, and social history.

***When*:** The onset of the inflammation. Was it sudden or insidious? Was it a single episode or recurrent? If previously treated, how long did it last?

***Where*:** Was it unilateral or bilateral? If bilateral, was the onset in the two eyes simultaneous or sequential? Visual confirmation of the location of the uveitis (anterior, intermediate, posterior, or panuveitis) is very helpful in narrowing the differential diagnosis.

***What*:** Careful clinical examination of the entire eye, looking for specific findings that might suggest a particular cause of uveitis. The clinical findings might support a diagnosis suggested by the history or might expand the differentia diagnosis. Ocular imaging such as OCT and fluorescein angiography is often part of the "what" category.

***Why*:** Only after a careful history and physical exam is complete (which typically narrows down the differential diagnosis from 30-40 disorders to perhaps 3-5) is diagnostic testing performed. Examples include blood work (looking for autoimmune/infectious/infectious/ genetic causes), MRI, chest CT (sarcoidosis can cause uveitis too!), and biopsy of ocular tissue.

antifungals will often resolve the uveitis. Surgery may be necessary to remove inflammatory products in the eye (pars plana vitrectomy) as well as cataracts that may form in the inflammatory setting. No matter what the form of treatment, uveitis specialists must consider what quality of life the patient has, and what medications are best tolerated by a given patient. In many cases, there will be permanent visual impairment. Dr. Dunn makes sure to ask his patients who may be struggling with the gravity of their situation, "**What is going well here?**" For example, can the patient still walk around their neighborhood on their own? Can they drive safely? Can they live by themselves? Would a Low Vision consultation (the ocular equivalent of occupational therapy or rehabilitation medicine) be helpful? Because the treatment for uveitis may have significant adverse effects, it is essential to discuss quality of life issues with affected patients. In some cases, treating the symptoms may be more feasible than curing the disease.

As with so many faculty at Wills, Dr. Dunn finds that the mentorship of medical students, residents, fellows, and even junior faculty is one of the best parts of the job. He urges students to find role models early, consider doing electives with them, and get plugged into the system. Throughout his own journey, he can name countless people who went out of their way to teach him. He feels like he owes it to the new generation to do the same.

"There is nothing like watching a student and the smile on their face as they figure out how to use the indirect lens for the first time or to see a former student became an academic ophthalmologist."

Although Dr. Dunn has been in ophthalmology for nearly 40 years, he is nowhere near retirement. He is eager to see the advancements made in uveitis diagnosis (such as genetic testing) and treatment (such as the use of biologics or new surgical approaches). He still has many more students to teach and still performs surgeries once a week. His career has been a whirlwind of hopping from one thing to another, ending up where he is happiest and able to do what he wants to help his patients. A mid-career job change opened up a whole new group of colleagues he loves working with. As students and residents consider their career options, worrying they may make the wrong choice early on and never recover, Dr. Dunn has this to say: "Do not think of your career linearly because you

never know what is going to happen. You can always make a horizontal wiggle and do something different."

So don't worry if you still are thinking about your career in medicine, there is always room to wiggle your way into a new, exciting field.

References:

1. Standardization of Uveitis Nomenclature (SUN) working group. Classification criteria for Cytomegalovirus retinitis. *Am J Ophthalmol*. 2021;228:245-54.
2. Boyd K. What is uveitis? American Academy of Ophthalmology.https://www.aao.org/eye-health/diseases/what-is-uveitis. Published December 8, 2022.
3. Timothy Root MD. "cell and Flare" in the eye (video). TimRoot.com. https://timroot.com/cell-and-flare-in-the-eye-video/. Published January 29, 2017.