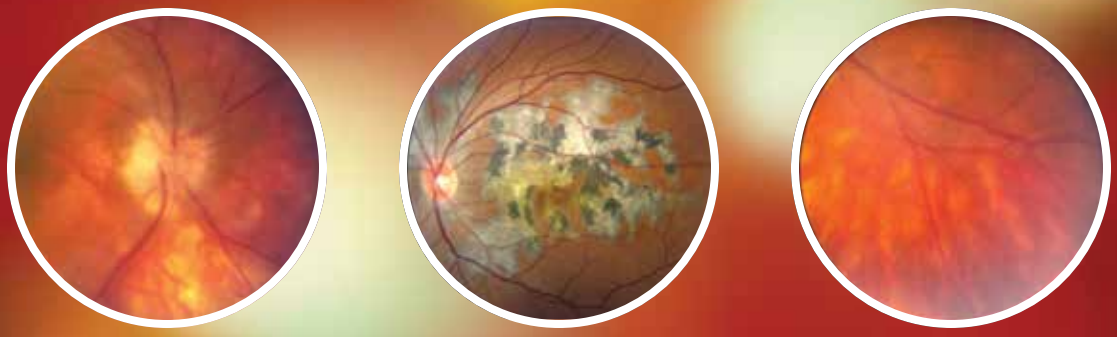
A supplement to
Ophthalmology Times

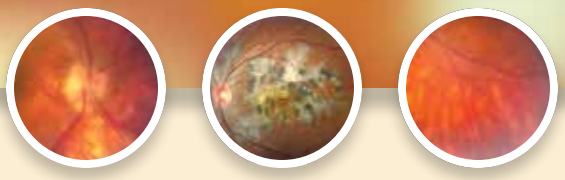
SEPTEMBER 2016

Managing Chronic Noninfectious Uveitis of the Posterior Segment



Proceedings from an Expert Roundtable Discussion
Held during the 16th Annual Meeting of the
Association for Research in Vision and Ophthalmology
April 30, 2016 • Seattle, Washington

THIS SUPPLEMENT IS SPONSORED BY Santen
A Clear Vision For Life®



FACULTY & DISCLOSURES

Sunil Srivastava, MD, *Program Chair and Moderator*

Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio

- Consultant/Advisory Board: Bausch and Lomb, Allergan, Alimera, Clearside, Regeneron, Eleven, Santen, Sanofi, Zeiss, Optos
- Research grants: Bausch and Lomb, Allergan, Novartis, Clearside, Zeiss, Sanofi
- Licensing royalty: Bioptigen, Synergetics
- Grant funding: NIH/NEI R01-EY023039-0, Ohio Department of Development TECH-13-059

Eric Suhler, MD, MPH

Casey Eye Institute, Oregon Health and Science University, Portland, Oregon

- Consultant: AbbVie, Mallinckrodt, Santen, and XOMA
- Research support: AbbVie, Bristol Meyers Squibb, Clearside, EyeGate, Genentech, and pSivida
- Institutional support: Research to Prevent Blindness and the Department of Veterans Affairs

Stephan Thurau, FEBO

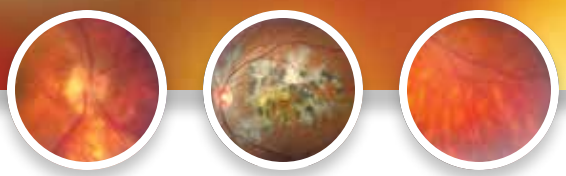
Medical Center, University of Munich, Eye Hospital, Munich, Germany

- Consultant/Advisor: Santen, AbbVie, Panoptes
- Travel support: Santen
- Financial support: Santen, AbbVie, Panoptes, Regeneron
- Grant recipient: EnzoBio

Steven Yeh, MD

Emory Eye Center, Emory University, Atlanta, Georgia

- Consultant/Advisor: Clearside Biomedical, Santen



PART 1
Managing Noninfectious Uveitis of the Posterior Segment (NIU-PS) as a Chronic Disease

Dr. Srivastava: How can you tell if a patient who walks into your clinic will need chronic therapy, rather than just a short course of treatment?

Dr. Yeh: It all starts with understanding the patient's treatment history. Patients with long-standing disease (at least 3–6 months) who have tried a number of therapies such as topical or systemic corticosteroids or corticosteroid injections—these are the patients whose disease is severe enough to need long-term therapy.

Dr. Suhler: I think that the anatomic location of the uveitis plays a big role in deciding whether or not chronic therapy is warranted if the patient's disease is chronic. Compared with anterior uveitis, which is often limited in duration and can typically be treated with topical corticosteroids, intermediate, posterior, or panuveitis have a greater tendency to be indolent or relapsing, and have a greater likelihood of causing visual harm if not treated effectively.[1] In these patients, we have a greater tendency to move on from corticosteroids to corticosteroid-sparing therapies.

Dr. Srivastava: What do you define as chronic uveitis?

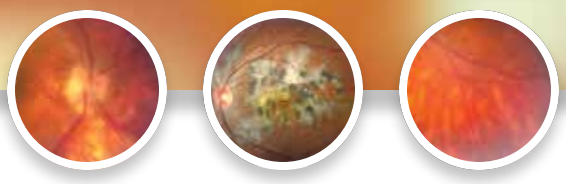
Dr. Suhler: The Working Group defined chronic uveitis as 3 months or longer, and I generally adhere to that definition.[2]

Dr. Thurau: I also define chronic uveitis in terms of the patient's corticosteroid needs, as most ophthalmologists would use corticosteroids as the first treatment option. Corticosteroids are broadly effective and target many different immune mechanisms, but sooner or later, you run into side effects, and this is where you have to make a decision to try a different treatment.[3] It is not just at 3 months.

Dr. Yeh: It also depends on the corticosteroids that they have been exposed to as well as comorbidities. For instance, some patients have diabetes, which is a relative contraindication to corticosteroids. In addition, there are certain diseases, such as Behçet disease or serpiginous chorioretinopathy, where there is a high likelihood of a chronic course.[1,4] There is a potential benefit to initiating long-term treatments sooner in these patients.

Dr. Srivastava: I know that I am finding more and more as we use imaging that diseases like retinal vasculitis or those that have a lot of retinal vascular leakage are the ones I am treating for a long period of time. These patients are going to need corticosteroids initially, but will need some other therapeutic option over the longer term.

Dr. Thurau: In addition to the forms that Dr. Yeh mentioned, there is uveitis associated with juvenile idiopathic arthritis, birdshot, and most types of chorioretinitis. These types of uveitis are very destructive in their nature, so you want to prevent



> Cystoid macular edema (CME) is the single biggest cause of loss of visual acuity in chronic uveitis patients, even more so than glaucoma.
>
> —*Dr. Stephan Thurau*

further damage. You cannot do this in the long term with corticosteroids, because the doses you need will just be too high.[5]

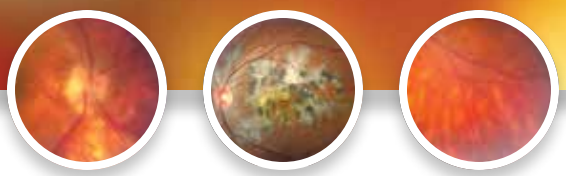
Dr. Srivastava: In my experience, US retina specialists, while they may give systemic corticosteroids, often will use corticosteroid injections first. How can we help these specialists to use corticosteroids appropriately and help them understand when corticosteroid injections may not be the correct treatments?

Dr. Suhler: When I trained at the National Institutes of Health, we were taught that periocular or intravitreal injections of corticosteroids were not definitive treatments in and of themselves. Rather, they are a bridge to appropriate therapy. The reality is that oral corticosteroids are very effective. They work quickly, they work well, and they are inexpensive. However, we all know that the side effects associated with chronic corticosteroid use (>3 months) may reduce both the quality and quantity of patients' lives. So, if you cannot taper patients to below a dose of 5 or 10 mg/d within 3 months, you have to move on to something else. The same is true of periocular or intraocular corticosteroids. If you give someone enough injections, it is not a matter of if but when you are going to develop cataracts, increased intraocular pressure, or other problems, often including saw-tooth decline from intermittent control of chronic inflammatory disease.

Dr. Srivastava: In many of my patients, I see a saw-tooth pattern with corticosteroid injections, where their vision improves after the injections but progressively worsens so that when they come back for their shots, their vision might have gone from 20/20 to 20/25 to 20/40. What clinical or imaging signs do you look for in these patients that indicate they are going to need a longer-term therapy that will help them avoid complications?

Dr. Yeh: The clinical signs of damage that I look for in chronic uveitis are not only progressive decline in visual acuity and visual field loss (from optic nerve damage and glaucoma) but also structural changes, such as posterior synechiae, cataract, or cystoid macular edema (CME), where their optical coherence tomography (OCT) scans are showing evidence of structural damage to or loss of the outer retinal architecture.

Dr. Thurau: CME is the single biggest cause of loss of visual acuity in chronic uveitis patients, even more so than glaucoma.[3] However, glaucoma



is one of the most severe side effects of intraocular corticosteroids.

Dr. Srivastava: So, with chronic immune suppression, we are trying to prevent chronic CME. Are there any other changes that you are concerned about in patients who have been treated for a while that would make you increase therapy? For example, pigmentary changes or chronic vascular leakage?

Dr. Suhler: I think that advances in multimodal imaging have really improved our ability to identify changes to the retina, such as inner or outer retinal atrophy, or peripheral leakage. We are becoming much better at understanding the anatomic underpinnings of these changes.

Dr. Srivastava: What percentage of patients who walk into your office do you believe will require chronic therapy for their NIU-PS?

Dr. Yeh: I would say 50% to 60% are going to require chronic therapy, not necessarily continuously, but perhaps also periodically over the long term.

Dr. Srivastava: How do you decide when you should taper somebody off of treatment?

Dr. Thurau: That's a very difficult question, because every patient is different and it is often a trial-and-error approach. Generally, after 2 to 3 years of quiescence, I try to taper patients off treatment slowly so that if the inflammation comes back, I can get a quick response when I increase treatment again.

Dr. Suhler: The first thing I do when I have a patient who needs chronic immunosuppressive therapy is put him or her on oral corticosteroids. Then, I add immunosuppressive drugs and try to taper the corticosteroids. The first time point that is relevant to me in deciding when to taper is when the patient is able to taper down the corticosteroid dose to 0, or at the very least, less than 5 mg/d. This is when I "start the clock." If the patient is quiet for 2 years after that, I will begin to have a conversation about coming off immunosuppressive therapy over the following year.

Dr. Srivastava: How successful are you at tapering patients completely off of immunosuppression?

> Advances in multimodal imaging have really improved our ability to identify changes to the retina…We are becoming much better at understanding the anatomic underpinnings of these changes.
>
> *—Dr. Eric Suhler*

Dr. Yeh: I think what we have learned from a number of retrospective studies, including the SITE studies, is that we are not as good as we think at tapering patients off.[6-8] In my practice, I am able to taper about 60% to 70% of patients completely off corticosteroids. So, about 1 in 3 will still be on corticosteroids and require additional therapy.

Dr. Srivastava: At what point do you add another agent if the patient has flared after attempting to taper off of corticosteroids?

Dr. Suhler: If at the 3-month time point I cannot effectively taper patients off corticosteroids, I become less convinced of the likelihood that they will be able to taper with their current regimen. Keeping in mind that immunosuppressants may take at least 6 months to work fully, at 3 months I am expecting to see at least some signal of effectiveness. At this time, if patients flare on attempted steroid taper, I am thinking that it may be time to either add an agent or switch, especially if the patient is having treatment-limiting side effects. Sometimes, if I get the patient down to 10 mg/d and I see a mild flare-up, I may try to increase the dose and wait a little bit longer with a slower taper.

Dr. Yeh: I fully agree with this approach.

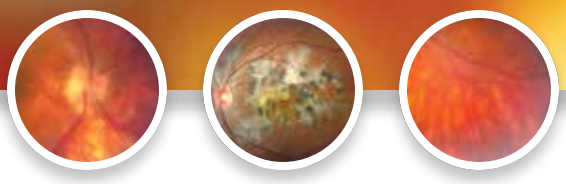
Dr. Srivastava: What is your first-line agent for immunosuppression after corticosteroids?

Dr. Thurau: In Germany, we are often restricted to using cyclosporine because it is the only immunosuppressant specifically approved for uveitis. If it weren't for this restriction, my first choices for NIU-PS would be mycophenolate or azathioprine. The recent approval of adalimumab in Europe has expanded the therapeutic options, however this agent is not intended for first line use.

Dr. Suhler: I start almost everybody on either methotrexate or mycophenolate to begin. I also use azathioprine mainly for women of child-bearing age, because our obstetricians believe that it is safer than the other 2 options. For patients who drink, mycophenolate would be my first choice.

Dr. Yeh: I probably start 70% of my patients on mycophenolate versus 30% on methotrexate, but I don't have very strong data to support the superiority of mycophenolate.

> We need to remember that uveitis is not a monolithic entity…I tell all my patients that, in essence, each of them is a clinical trial with an n of 1.
>
> *—Dr. Eric Suhler*



> We have to understand that, even if patients have similar types of uveitis and similar clinical presentations, their underlying immune systems may work very differently.
>
> *—Dr. Stephan Thurau*

Dr. Suhler: We need to remember that uveitis is not a monolithic entity. Sarcoidosis, pars planitis, sympathetic ophthalmia, birdshot—they are all different. I tell all my patients that, in essence, each of them is a clinical trial with an n of 1.

Dr. Srivastava: Do you think there are any drugs that might have a higher success rate than 50% to 60%? In my experience, anti-tumor necrosis factor (TNF) therapies have a slightly higher success rate, but this might be a bias of the type of patients I am treating.

Dr. Yeh: I have found a success rate of 60% to 70% with these drugs, but of course we are treating people who have already failed another therapy in most cases. We do not have a magic bullet. Nothing works all of the time.

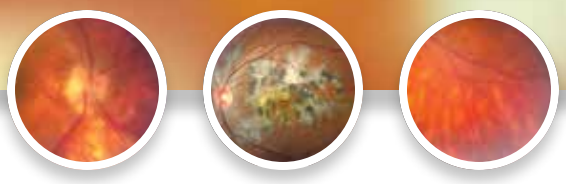
Dr. Thurau: That's true. We have to understand that, even if patients have similar types of uveitis and similar clinical presentations, their underlying immune systems may work very differently. So, when we have a treatment option that only works in 60% to 70% of patients, what immunologic factors are at play in the other 30% to 40%? Nobody is able to answer this question yet.

Dr. Srivastava: I think what we are all asking is: Is there room for something better? There are limitations associated with the medications that we currently have available.

Dr. Yeh: What is your second-line choice after methotrexate or mycophenolate? Do you use a TNF blocker?

Dr. Yeh: Yes, for patients in whom we believe a TNF blocker will be efficacious, such as those with Behçet disease, HLA-B27 uveitis, ankylosing spondylitis, and perhaps our rheumatoid arthritis patients with scleritis. I don't know that it is always a good choice. Recently, I had a patient who developed some demyelinating lesions while on one of these agents. Thus, you need to be cautious in some patients, for example, those with intermediate uveitis, where you are concerned about the possibility of multiple sclerosis.

Dr. Srivastava: Dr. Thurau, what second-line agents do you use in Germany?



> My happiest patients are the ones who have been on immunosuppressants for years, and when we switch to a corticosteroid implant, they say this is the best they have felt in years.
>
> —*Dr. Stephan Thurau*

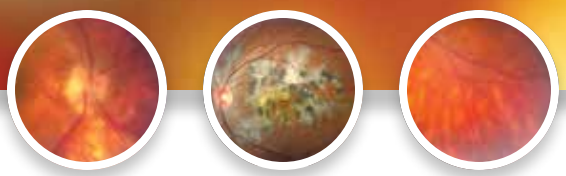
Dr. Thurau: We use cyclosporine, mycophenolate, and some azathioprine. After that, we go to TNF blockers. In Europe, however, we tend to use interferons a bit more in Behçet disease. They definitely have some severe side effects, especially flu-like symptoms.[9] Some patients do not tolerate them at all, but in those who do, they are great drugs. You can induce real remissions for many years.[10]

Dr. Yeh: There are a number of systemic second-line agents with proven efficacy in rheumatologic trials. But the reality is that we need to consider potential risks such as reactivation of latent tuberculosis, demyelinating disease with inflammation, and latent infections with anti-TNF agents.[11,12] There are also systemic side effects that patients may not even perceive because they happen gradually, such as fatigue with the antimetabolites.[11] This doesn't mean, however, that we should shy away from using these drugs.

Dr. Srivastava: I agree. My happiest patients are the ones who have been on immunosuppressants for years, and when we switch to a corticosteroid implant, they say this is the best they have felt in years. They had been tolerating immunosuppression for so long that they forgot what it was like not being on it.

Dr. Yeh: I think it is reasonable to say that we are still looking for a therapy that works most of the time and has minimal side effects.

> I think it is reasonable to say that we are still looking for a therapy that works most of the time and has minimal side effects.
>
> —*Dr. Steven Yeh*



PART 2
Case Studies

Case 1

Dr. Srivastava: This is a 45-year-old man who was referred to the uveitis clinic for having chronic blurred vision and floaters for several years. He had been treated with periocular corticosteroids in the past for mild inflammation and had a workup that was negative in the past. He now has had progressive symptoms for 6 months. Visual acuity in his eyes is 20/50 and 20/40. How would you describe his lesions (Figure 1)?

Dr. Yeh: The optic nerve has some pallor associated with it, and there are some peripapillary areas of deep pigmentation. Nasally, I see some cream-colored, likely choroidal, lesions.

Dr. Srivastava: What do you see on the angiogram (Figure 2)?

Dr. Suhler: When I look at the angiogram I see blood-ocular barrier breakdown in the outer retinal vasculature. To me, this is an imaging sign of disease chronicity. It is worrisome to see this much leakage in patients with good vision, because by that time there is severe retinal damage.

Dr. Srivastava: The patient was HLA-A29 positive and was ultimately diagnosed with birdshot chorio-retinopathy. What type of workup would you have done for him, assuming a negative review of systems?

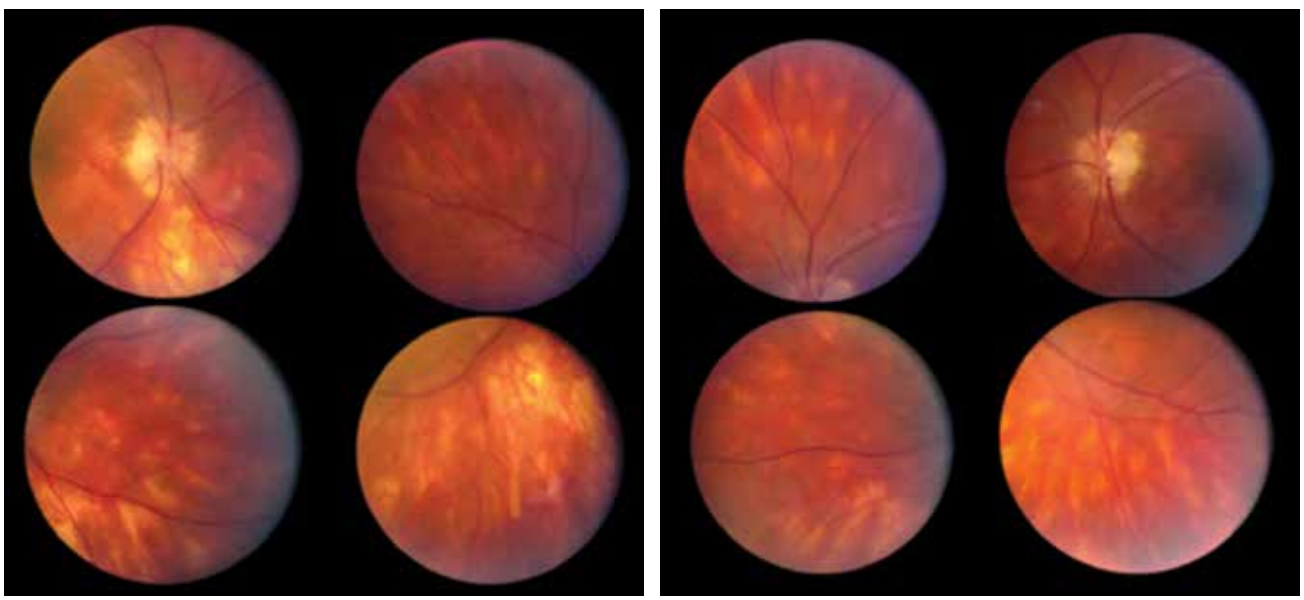
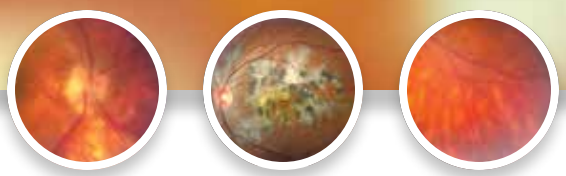


FIGURE 1. Fundoscopic exam of the right (left images) and left (right images) eye from a 45-year-old patient with chronic blurred vision and floaters (*Images courtesy of Dr. Srivastava*).



Dr. Suhler: The workup would essentially be for multifocal choroiditis, ruling out entities such as sarcoidosis, tuberculosis, and syphilis. In the presence of classic physical examination findings and a positive HLA-A29, I would pretty much stop there.

Dr. Yeh: I would include visual field testing and an electroretinogram (ERG) in the evaluation. These objective measures are good for showing the patient exactly what we are treating and that it can be potentially reversible with treatment.

Dr. Srivastava: The OCT in this patient showed mild macular edema. How would you treat this patient who clearly has active disease?

Dr. Thurau: I would start with systemic corticosteroids because he has bilateral disease. I would also start with immune suppression, given that birdshot is a chronic disease and without treatment would be active for many years.[1,13] The corticosteroids would not be able to suppress the disease over the long term. I would probably use mycophenolate, with a TNF blocker as the next step.

Dr. Suhler: I would almost always start this type of patient on oral corticosteroids and offer them either mycophenolate or cyclosporine. We use a lot less cyclosporine than we used to, but this is one disease where it can be effective.

Dr. Srivastava: The patient was actually started on 80 mg/d of corticosteroids and was offered a fluocinolone implant, which has shown some efficacy in birdshot. However, the insurance denied the implant but approved infliximab.

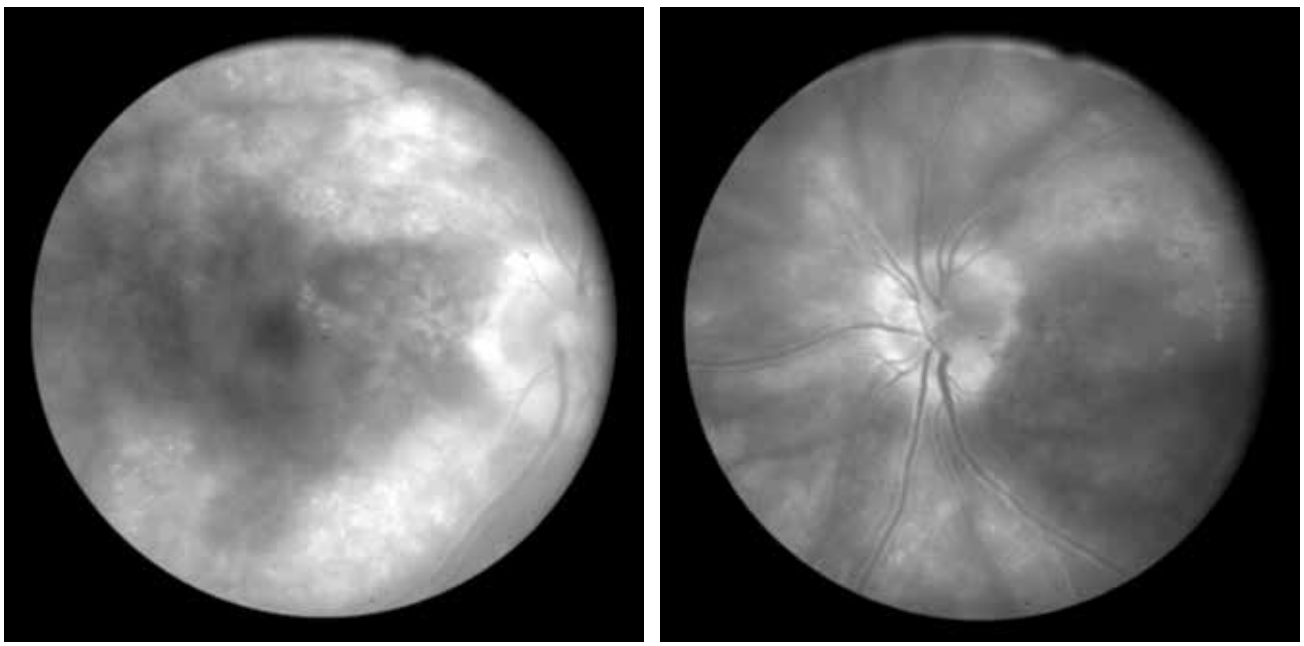
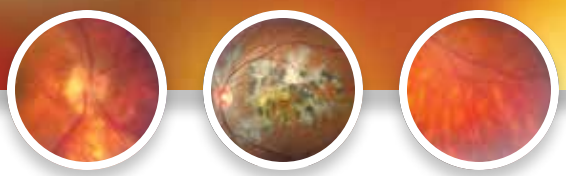


FIGURE 2. Angiogram images from a 45-year-old patient with chronic blurred vision and floaters (*Images courtesy of Dr. Srivastava*).



Unfortunately, after 7 months of treatment, the patient was still symptomatic.

Dr. Suhler: The use of infliximab at this stage and in this disease is surprising. I favor an antimetabolite and cyclosporine for birdshot first before going to a TNF blocker. I haven't found TNF blockers to be universally effective in birdshot patients, and it is reasonable to offer implant therapy as well.

Dr. Yeh: I agree. I think when the disease is this chronic, you may get a little more improvement with a local therapy.

Dr. Srivastava: In this case, the patient was switched to mycophenolate and cyclosporine, and you can see that he responded well over time based on the degree of leakage and the OCT characteristics. However, he developed hypertension on the cyclosporine, which required medication. How would you follow this patient to determine whether the uveitis is active or inactive?

Dr. Thurau: Once I am sure that most of the exudation is gone and the eye is fairly quiet, I like to use autofluorescence and indocyanine green (ICG) staining. Autofluorescence, especially, is very quick to do and extremely helpful for seeing minute changes when you compare images.

Dr. Yeh: Sometimes.

Dr. Suhler: With birdshot patients, I have always felt that the patient's report is as good an indicator as any that the uveitis is active. With the multiple forms of imaging available, we are getting new and better ways to corroborate this.

Case 2

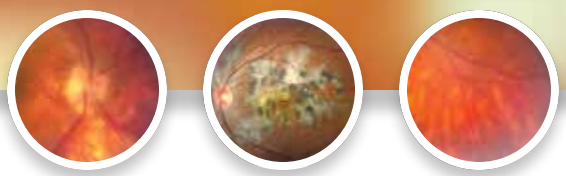
Dr. Yeh: This patient is a 46-year-old male diagnosed with serpiginous choroidopathy with a visual acuity of 20/20 on both eyes. His past medical history includes latent tuberculosis (TB) for which he received treatment. The infectious disease specialist was comfortable with prescribing immunosuppressive therapy to this patient. His treatment history includes 6 months of mycophenolate, to which he did not respond, and cyclosporine and azathioprine, both of which were discontinued due to side effects. He was maintained on prednisone. He recently developed symptoms suggestive of a scotoma in his right eye, which prompted him to increase his prednisone to 80 mg/d (Figure 3). What would be your treatment approach in this patient?

Dr. Thurau: It is my impression that for atypical serpiginous disease such as this patients require continued corticosteroid treatment, usually 20 to 30 mg/d, along with immunosuppression. This patient may also require TB therapy.

Dr. Yeh: There are published cases using azathioprine, cyclosporine, and prednisone. Use of high-dose, short-term chlorambucil has also been reported.[14,15] The patient's history of TB makes this challenging.

Dr. Srivastava: I am not sure any immunosuppressive medication outside of prednisone works well in TB-mediated disease. Is this patient symptomatic?

Dr. Yeh: He is exquisitely symptomatic. He describes having a jigsaw puzzle piece of his vision missing.



Dr. Suhler: We were taught that alkylating agents are appropriate for patients whose disease poses an imminent threat where you have to shut it down fast. So, there is an argument for using an alkylating agent or the fluocinolone intravitreal implant here.

Dr. Srivastava: How can you tell whether this patient is experiencing more active disease?

Dr. Yeh: I think that in the past, we would have spent a lot of time looking at photographs, OCTs, and also fluorescein angiographs, but in patients such as this, fundus autofluorescence can really help highlight disease activity (Figures 4, 5).

Dr. Srivastava: Yes, imaging can help detect subtle lesions that may not be readily seen on clinical exam. There really is a need for multimodal imaging in more complex cases, especially when changes in the retina have occurred.

Dr. Yeh: After a long discussion about treatment, the patient opted for the fluocinolone intravitreal implant. He was tired of systemic medications and wanted to stay on corticosteroids. The infectious disease specialist did not believe TB therapy was needed at that point. He did well for about 6 months before experiencing intermittent flare ups. He subsequently developed cataracts and needed bilateral tube shunts.

Dr. Srivastava: In a patient who is on prednisone, how many flares do you tolerate before you switch?

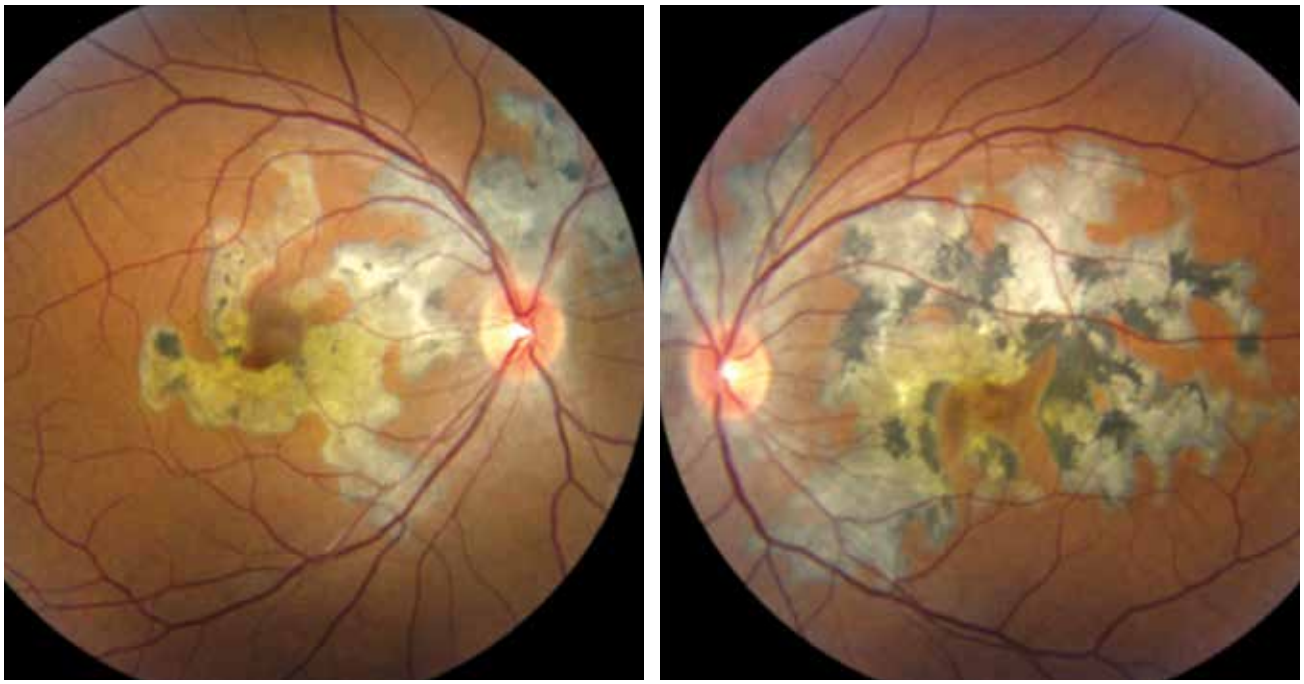


FIGURE 3. Fundoscopic exam from a 46-year-old patient diagnosed with serpiginous choroidopathy with a new scotoma in his right eye (*Images courtesy of Dr. Yeh*).

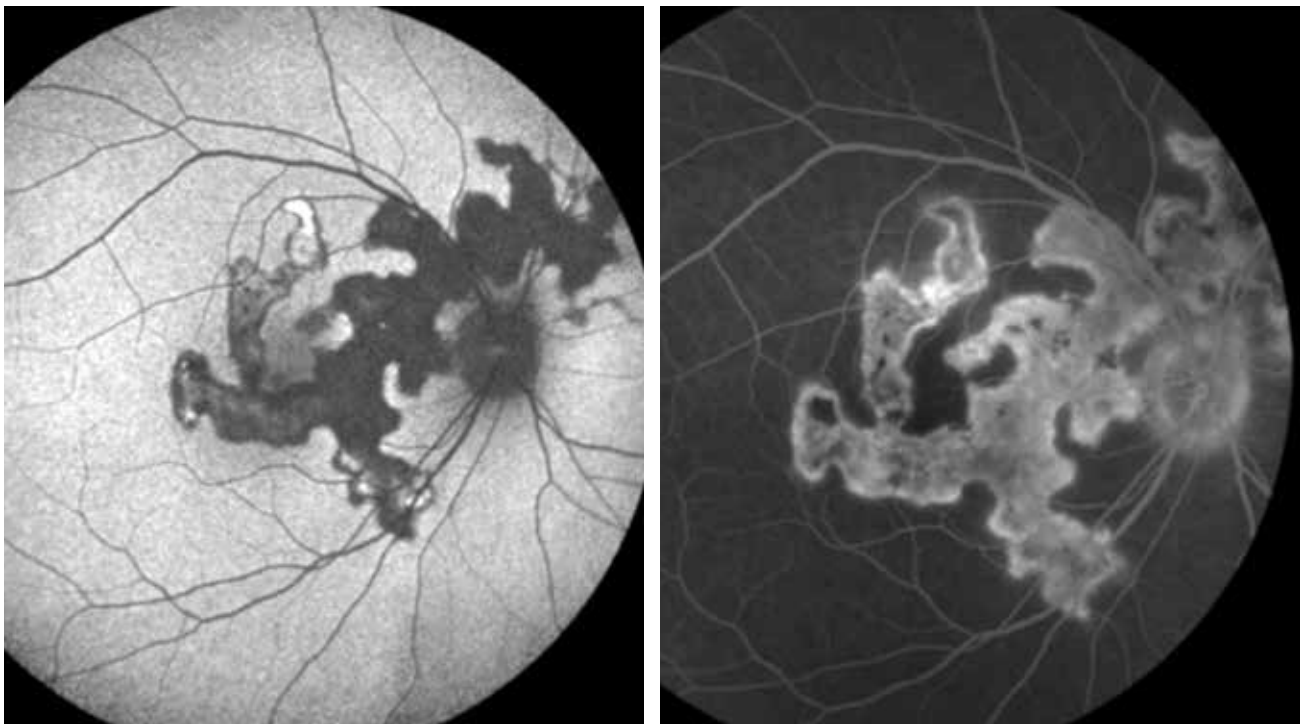


FIGURE 4. Fundus autofluorescence highlights active disease (*Images courtesy of Dr. Yeh*).

Dr. Suhler: I think in this situation you want to be more aggressive and move on to the next treatment perhaps sooner than you otherwise would. I would attempt to taper in 3 months, and if the patient is not responding, I would add an additional treatment.

Dr. Yeh: Is there something that can effectively dampen inflammation that is associated with a postinfection insult?

Dr. Suhler: I would consider something like high-dose, short-term chlorambucil or cyclophosphamide that might help reset the immune system.

Dr. Srivastava: An alkylating agent makes sense in this case.

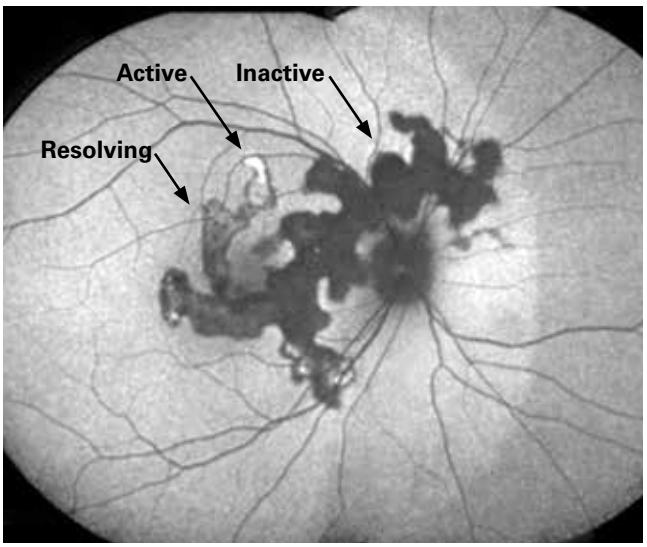
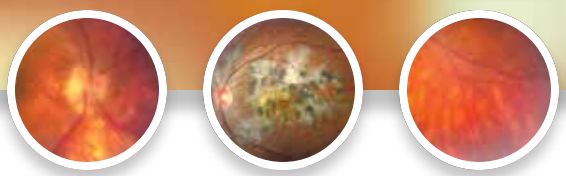


FIGURE 5. Differential autofluorescence characteristics are suggestive of stages of activity (*Images courtesy of Dr. Yeh*).



Case 3

Dr. Srivastava: This is a 50-year-old woman with a 4-year history of NIU-PS, primarily in the left eye. She has been treated with periocular and then intravitreal corticosteroid injections. The last injection was 1 month ago. She now presents to the clinic seeking a second opinion. She reports no systemic symptoms, and 3 years ago, she had a workup that showed a negative x-ray and negative HLA-B27, HLA-A29, syphilis, and TB tests. Her vision is 20/20 in the right eye and 20/50 in the left eye. At this point, because she is flaring, do you do another workup?

Dr. Suhler: Obviously, some things from the prior workup, like the genotyping, would not change. However, there are things that can change as the uveitis progresses. For example, if I suspect sarcoidosis, I would order another chest x-ray. There are a few other tests you might repeat if it has been 3 years since the last test, such as the angiotensin-converting enzyme (ACE) test, although this test has limitations with regard to sensitivity and specificity.

Dr. Srivastava: The clinical exam showed cataracts, along with some "punched out" spots on the periphery of the retina (Figure 6). The OCT revealed cystic structures in the outer retina that may be granulomas (Figure 7). During the workup, the technician observed the patient audibly wheezing, despite denying a history of asthma. What other tests would you order to make a diagnosis?

Dr. Thurau: At this point, I would suspect sarcoidosis and order a soluble interleukin-2 receptor measurement, as I believe it is a bit more sensitive and specific than an ACE test. It is also less expensive.

Dr. Srivastava: At this point, I tend to order a computed tomography (CT) scan rather than a chest x-ray. Primary chest CT has shown good sensitivity in the diagnosis of sarcoidosis.

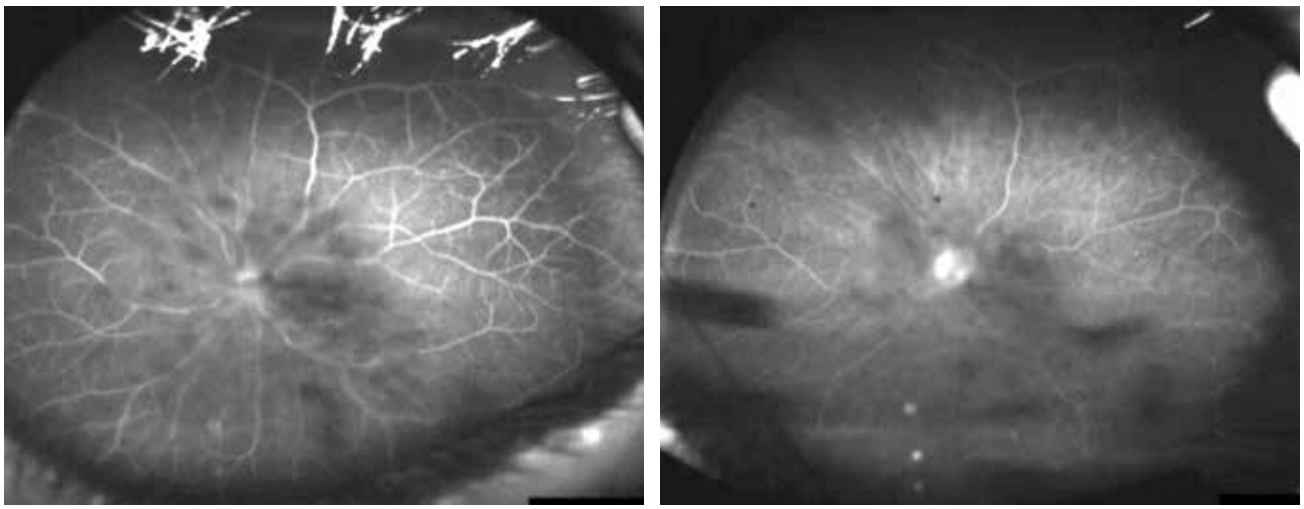


FIGURE 6. Fluorescein angiography of the left eye (*Images courtesy of Dr. Srivastava*).

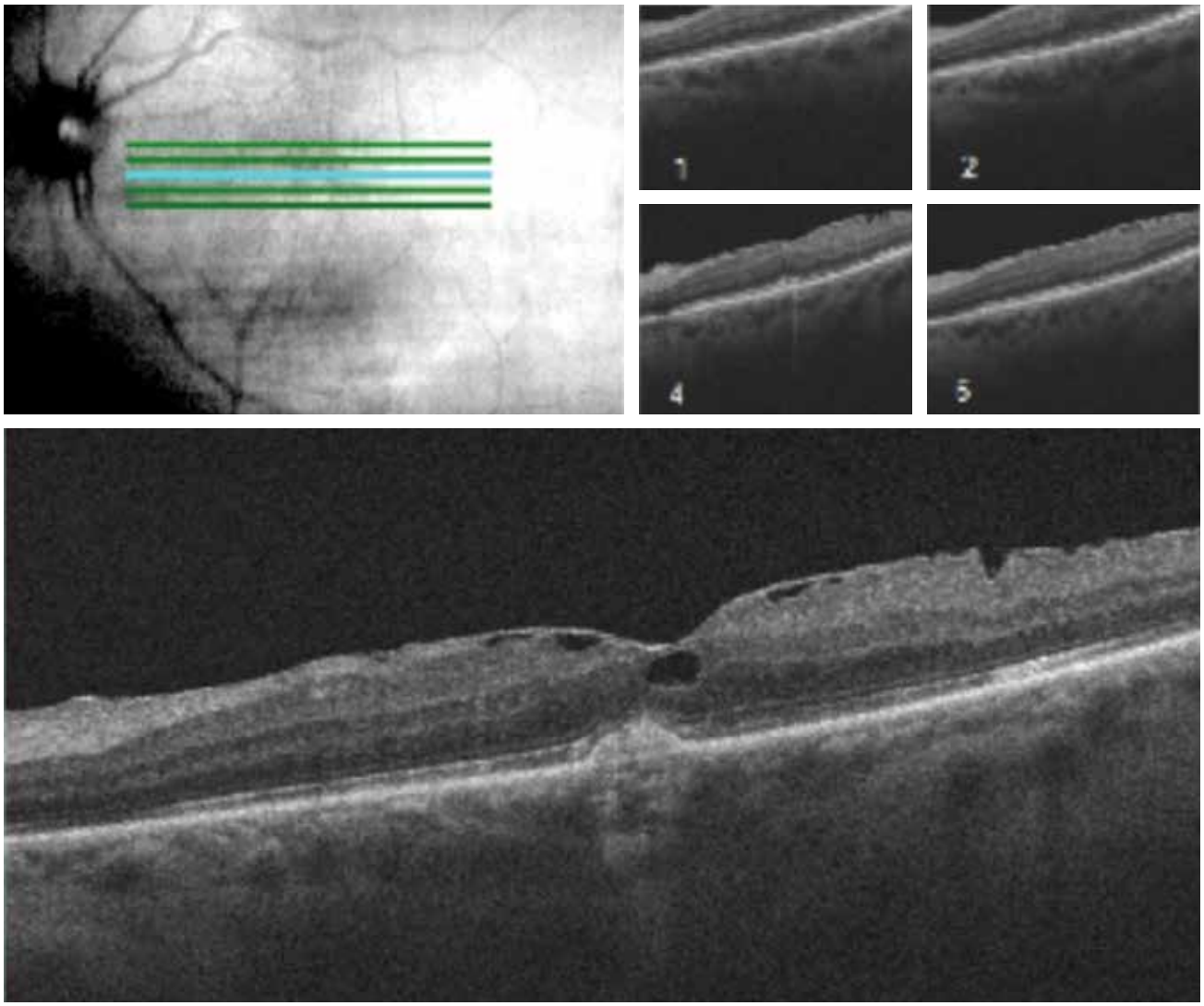
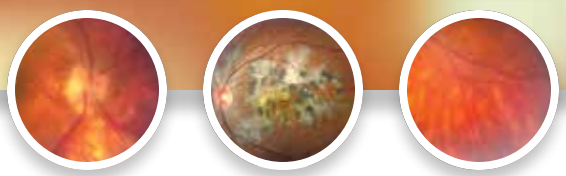


FIGURE 7. Optical coherence tomography of the left eye (*Images courtesy of Dr. Srivastava*).

In this case, a biopsy was ordered, which came back positive for sarcoidosis. Does the fact that a diagnosis of pulmonary sarcoidosis has been established influence your choice of treatment for her ocular sarcoidosis?

Dr. Suhler: Choosing between a local and systemic treatment is more difficult if the patient is asymptomatic from a pulmonary perspective. But because this individual has signs of lung disease in addition to her uveitis, I would treat her systemically.

Dr. Srivastava: What if, in this case, the pulmonologist feels that the patient's pulmonary sarcoidosis is mild enough to not require treatment?



Would you choose a local therapy or stick with a systemic treatment like methotrexate?

Dr. Suhler: I use quite a bit of systemic therapy. Therefore, if someone does not have systemic symptoms but has bilaterally active uveitis with macular edema and deteriorating vision, I would still lean toward systemic treatment. For patients who have unilateral or grossly asymmetric bilateral disease, I might try 1 or 2 injections to see if local therapy might be effective.

Dr. Srivastava: One of the things I hear from my retina colleagues is that they believe they can control the inflammation with an injection every 6 months.

Dr. Thurau: It doesn't work that way. You would have to give a shot every 3 months or even every 10 weeks or so. If you are really controlling the inflammation with injections every 6 months, then she has probably been misdiagnosed.

Dr. Srivastava: So your point is that there are other things going on that the physician is probably not looking for.

Dr. Yeh: There is currently some controversy around the use of as-needed (PRN) or treat-and-extend schedules.

Dr. Suhler: While PRN treatment may be appropriate for some people with mild or episodic disease, in others who have chronically smoldering disease, if you only treat when their uveitis is active, you are losing ground. So, if you are treating with a local therapy, you want to make sure that the patient has a good level of local immunosuppression for the duration of the injection.

Dr. Yeh: I agree, but would point out that one reason they are not treating patients in between is because they are concerned with corticosteroid-related side effects.

REFERENCES

1. Jabs DA, Rosenbaum JT, Foster CS, et al. Guidelines for the use of immunosuppressive drugs in patients with ocular inflammatory disorders: recommendations of an expert panel. *Am J Ophthalmol*. 2000;130(4):492–513.

2. Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol*. 2005;140(3):509–516.

3. Joshi L, Talat L, Yaganti S, et al. Outcomes of changing immunosuppressive therapy after treatment failure in patients with noninfectious uveitis. *Ophthalmology*. 2014;121(5):1119–1124.

4. Lim WK, Buggage RR, Nussenblatt RB. Serpiginous choroiditis. *Surv Ophthalmol*. 2005; 50(3):231–244.

5. Schiappapietra B, Varnier G, Rosina S, et al. Glucocorticoids in juvenile idiopathic arthritis. *Neuroimmunomodulation*. 2015;22(1–2):112–118.

6. Nguyen QD, Hatef E, Kayen B, et al. A cross-sectional study of the current treatment patterns in noninfectious uveitis among specialists in the United States. *Ophthalmology*. 2011;118(1):184–190.

7. Cunningham ET Jr, Goldstein DA, Zierhut M. Uveitis treatment trials—a cross-study perspective. *Ocul Immunol Inflamm*. 2012;20(2): 63–67.

8. Rathinam SR, Babu M, Thundikandy R, et al. A randomized clinical trial comparing methotrexate and mycophenolate mofetil for noninfectious uveitis. *Ophthalmology*. 2014;121(10): 1863–1870.

9. Benucci M, Li Gobbi F, Meacci F, et al. Anti-drug antibodies against TNF-blocking agents: correlations between disease activity, hypersensitivity reactions, and different classes of immunoglobulins. *Biologics*. 2015;9:7–12.

10. Zierhut M, Abu El-Asrar AM, Bodaghi B, Tugal-Tutkun I. Therapy of ocular Behçet disease. *Ocul Immunol Inflamm*. 2014;22(1):64–76.

11. Pasadhika S, Rosenbaum JT. Update on the use of systemic biologic agents in the treatment of noninfectious uveitis. *Biologics*. 2014;8:67–81.

12. Nanau RM, Neuman MG. Safety of anti-tumor necrosis factor therapies in arthritis patients. *J Pharm Pharm Sci*. 2014;17(3):324–361.

13. Menezo V, Taylor SR. Birdshot uveitis: current and emerging treatment options. *Clin Ophthalmol*. 2014;8:73–81.

14. Akpek EK, Baltatsis S, Yang J, Foster CS. Long-term immunosuppressive treatment of serpiginous choroiditis. *Ocul Immunol Inflamm*. 2001;9(3):153–167.

15. Akpek EK, Jabs DA, Tessler HH, et al. Successful treatment of serpiginous choroiditis with alkylating agents. *Ophthalmology*. 2002; 109(8):1506–1513.