

# Topics in OCULAR ANTIINFLAMMATORIES

A CONTINUING  
MEDICAL EDUCATION  
PUBLICATION



ISSUE 24

## Antiinflammatory Therapies for Uveitic Glaucoma

**VALERIE TRUBNIK, MD, FACS** Effective treatment of uveitic glaucoma requires adequate control of both inflammation and intraocular pressure (IOP). A rational approach to this challenging therapeutic entity begins with proper antiinflammatory therapy, as alleviation of intraocular inflammation can often control both the uveitis and secondary IOP increase.

Secondary glaucoma is a serious complication of uveitis, occurring in about 20% of cases.<sup>1</sup> In general, glaucoma is relatively more prevalent in anterior segment inflammation. More specifically, the forms of uveitis most commonly associated with glaucoma include Fuch's heterochromic iridocyclitis (FHIC); glaucomatocyclitic crisis (Possner-Schlossman syndrome); herpetic keratouveitis; and uveitis associated with juvenile rheumatoid arthritis (JRA), sarcoidosis, or ankylosing spondylitis. Tuberculosis and syphilis also commonly raise intraocular pressure (IOP) but are extremely rare in the US.

Patients with uveitic glaucoma (ie, inflammatory glaucoma) present a formidable challenge to clinicians, as the coexistence of uveitis and glaucoma results in a more complicated clinical presentation and calls for complex management decisions. This article discusses certain special considerations in the management of patients with uveitis and elevated IOP, highlighting the importance of careful clinical evaluation, the various mechanisms giving rise to IOP increases in uveitic eyes, and the central role of antiinflammatory therapy.

### GENERAL AND SPECIFIC SIGNS

Intraocular inflammation can produce a constellation of

clinical signs. Those indicative of anterior uveitis include keratic precipitates (KPs), cells and flare in the anterior chamber, iris nodules, peripheral anterior synechiae, posterior synechiae leading to pupillary block and iris bombé, pigment on the lens, and neovascularization of the angle. In the intermediate and posterior segment of the eye, signs of uveitis include vitreal inflammatory cells, snowball opacities, exudates over the pars plana (ie, "snowbanks"), retinal or choroidal inflammatory infiltrates, cystoid macular edema (CME), and vascular sheathing. Some clinical signs are more specific: epithelial dendrites are typical with herpes simplex infection and pseudo dendrites with herpes zoster; iris atrophy and neovascularization in the angle are often found in FHIC; and band keratopathy or corneal stromal scarring is usually seen with chronic uveitis.

In addition to a complete ocular examination, a comprehensive history and review of systems is important in patient assessment, as it helps elucidate the cause of uveitis. In any patient, recurrent, bilateral, or granulomatous uveitis should raise the suspicion of an underlying systemic etiology. As already mentioned, systemic conditions commonly associated with uveitic glaucoma include sarcoidosis, ankylosing spondylitis, JRA, syphilis, and tuberculosis. For patients suspected of having any of these conditions, a systemic workup including blood-based diagnostic tests and chest X-rays is warranted.

### MECHANISMS OF IOP ELEVATION

Although many uveitic patients have a lower IOP—because of decreased aqueous humor production and even ciliary body

**See INSIDE for:**  
**Contact Lens Wear, Inflammation, and Disease**  
by Bennie H. Jeng, MD

**TARGET AUDIENCE** This educational activity is intended for ophthalmologists and ophthalmologists in residency or fellowship training.

**LEARNING OBJECTIVES** Upon completion of this activity, participants will be able to:

1. Describe the mechanisms of ocular hypertension in uveitic glaucoma.
2. Formulate appropriate treatment plans directed at inflammation and raised IOP, respectively, for patients presenting with uveitic glaucoma.
3. Identify and better manage contact lens discomfort.
4. Differentiate inflammatory from infectious keratitis.

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shutdown caused by intraocular inflammation—ocular hypertension can develop through varying mechanisms. It is not uncommon for different mechanisms to coexist in the same patient.

Most commonly, uveitic ocular hypertension occurs with an open anterior chamber angle yet diminished aqueous outflow. Acute intraocular inflammation frequently disrupts the blood-aqueous barrier, allowing inflammatory cells and large molecules such as proteins to enter the aqueous humor. Such inflammatory products may raise the intraocular pressure via increased aqueous viscosity or physical blockade of the trabecular meshwork. In addition, inflammation may cause swelling of trabecular lamellae and endothelial cells, leading to a physical narrowing of trabecular pores and dysfunction of the trabecular meshwork. Over time, permanent reduction in conventional outflow may occur with irreversible trabecular damage or scarring from inflammation.

Elevated IOP in uveitic eyes can also develop through angle-closure mechanisms. Accumulation of inflammatory cells and debris such as proteins and fibrin during the uveitic process may cause closure of the drainage angle (peripheral anterior synechiae [PAS]) or adhesion of the iris to the anterior lens surface (posterior synechiae). Synechial closure is usually chronic, though extensive adhesion can cause pupillary block and consequently an acute attack of elevated IOP.

Corticosteroids, the mainstay of treatment for uveitis, may also raise IOP. The IOP-raising effect of corticosteroids has been documented for decades.<sup>2,3</sup> Elevated IOP can occur with any mode of corticosteroid administration and is thought to be primarily due to decreased outflow. Corticosteroids are thought to increase outflow resistance in the trabecular meshwork by altering trabeculocytes' cytoskeleton, modifying the trabecular extracellular matrix, and suppressing phagocytosis within the meshwork.<sup>4</sup> Corticosteroid responders constitute about 18% to 36% of the general population.<sup>5</sup> For patients with uveitic glaucoma, whose trabecular

## TOPICS IN OCULAR ANTIINFLAMMATORIES, ISSUE 24

### STATEMENT OF NEED

The control of ocular inflammation is a critical aspect of medical and surgical ophthalmic practice. Despite their side effects, antiinflammatory drugs are used to treat a very wide range of conditions throughout the eye, from ocular surface disease and allergic conjunctivitis to posterior segment conditions. Use of antiinflammatory agents is also critical in ocular surgery, contributing greatly to patient comfort and positive outcomes.

The ocular antiinflammatory landscape is changing as research reveals more about the role of inflammation in a range of ocular conditions and as new antiinflammatory agents enter the market.<sup>1,2</sup> Twenty years ago, for example, the idea of using a topical corticosteroid to treat dry eye and/or allergic conjunctivitis was viewed with alarm; today, it is accepted practice.

Although corticosteroids and nonsteroidal antiinflammatory drugs (NSAIDs) have been the mainstays of the ocular anti-inflammatory armamentarium, a number of new agents with novel mechanisms of action (and new ocular drug delivery systems) have come to market or are being made ready for market.<sup>3,4</sup>

As indications expand and change, and as new drugs, formulations, and delivery systems become available, clinicians require up-to-date protocols for drug selection and use. Such protocols are also needed for routine (but nevertheless off-label) uses of corticosteroids and NSAIDs because important differences in efficacy, safety, and tolerability exist between these classes and among formulations within each of these classes.<sup>5,6</sup>

By putting the latest published evidence into the context of current clinical practice, *Topics in Ocular Antiinflammatories* equips ophthalmologists to maintain competencies and narrow gaps between their actual and optimal inflammation management practices, across the range of clinical situations in which current and novel ocular antiinflammatories may be used.

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meshwork may already have been clogged by inflammatory cells or fibrin, the potent antiinflammatory effect of corticosteroids comes with the risk of even further pressure elevation.

#### TREATING INFLAMMATION COMPLICATED BY RAISED IOP

The aim of medical therapy for patients presenting with uveitis and secondary glaucoma is to control both the inflammation and the elevated IOP.<sup>6</sup> In addition, any underlying systemic condition should be treated—by either a uveitis specialist or a rheumatologist—to help control the ocular inflammation and possibly the IOP as a result.

Corticosteroids are highly effective against ocular inflammation, and the treatment of inflammation itself should help the management of IOP in uveitis patients by preventing damage and blockage of outflow channels. Still, corticosteroid therapy carries an inherent risk of IOP elevation. To minimize the risk, one of the things clinicians can do when prescribing is to consider the relative IOP-raising potential of a corticosteroid. Topical corticosteroid preparations differ in their ability to produce an ocular hypertensive response; my own clinical experience suggests that difluprednate and dexamethasone have a relatively high propensity for IOP elevation.

My first-choice corticosteroid drop is usually prednisolone acetate 1%, dosed every hour when the eye is actively inflamed and tapered gradually as the inflammation subsides. I usually add a cycloplegic, either a short-acting drop such as cyclopentolate hydrochloride or a long-acting one such as atropine, to help break or prevent the formation of posterior synechiae. If the patient is already on corticosteroid therapy, I make sure there is no need to adjust the medication. If it happens to be difluprednate or dexamethasone, what I typically do is switch over to prednisolone acetate and, if the pressure elevation persists, loteprednol or fluorometholone.

The addition of oral nonsteroidal antiinflammatory drugs (NSAIDs) may greatly benefit patients whose uveitis is difficult to control on topical corticosteroids. Certain oral NSAIDs, such as meloxicam, may help wean patients from topical corticosteroid therapy. If the corticosteroid cannot be successfully tapered with oral NSAIDs, I would then consider short-term use of oral corticosteroids. Immunosuppressive therapy can be particularly useful in the treatment of chronic uveitis. Some of my patients have been able to avoid glaucoma surgery by going on immunosuppressive agents. Because patients receiving immunosuppressive therapy need close monitoring with bloodwork and other tests, I usually refer them to a uveitis specialist or a rheumatologist.

The bottom line is that active inflammation in the anterior segment with an IOP rise is often a sign of trabeculitis. The most important first step in managing affected patients is to reduce the severity of inflammation: prescribe a corticosteroid drop and wait 2 to 4 weeks to see if the eye is still inflamed. Often, inflammation control is all that is needed to lower IOP and no additional IOP-lowering interventions are required. If the pressure remains elevated when the inflammation has abated, consider switching to a less potent corticosteroid. When corticosteroid switch still fails to bring IOP under

## CORE CONCEPTS

- ◆ Secondary glaucoma is especially common in certain uveitis entities. These include FHIC, glaucomatocyclitic crisis, herpes virus-associated uveitis, and uveitis associated with JRA, sarcoidosis or ankylosing spondylitis.
- ◆ The mechanisms responsible for IOP elevation in uveitis are complex and diverse. Many of the various mechanisms, such as trabecular meshwork obstruction, damage from intraocular inflammation, and/or corticosteroid-induced glaucoma, can be present simultaneously in the same patient.
- ◆ The foremost priority in the management of patients with uveitis and uveitic glaucoma is the control of intraocular inflammation. Antiinflammatory therapy with a topical corticosteroid is appropriate as a first step to manage most cases of uveitis, even if the IOP is elevated.
- ◆ Control of intraocular inflammation is usually sufficient to normalize the IOP. If not, it is recommended that the clinician should try switching to a less potent corticosteroid before initiating any glaucoma treatment.
- ◆ Glaucoma therapy is indicated in patients with uveitic glaucoma when IOP does not spontaneously decrease after the inflammation is under control or when the level of IOP is dangerously high. If IOP-lowering medications fail, surgical intervention is warranted. Treatments that may exacerbate inflammation—such as PGAs and laser trabeculoplasty—should be avoided.

control, it is then time to consider glaucoma treatment.

#### MANAGING IOP IN AN INFLAMED EYE

That said, the most important consideration in determining when to treat uveitic glaucoma is the severity of pressure elevations and, if any, the extent of optic nerve damage. If the patient is fairly healthy, with normal pachymetry, a healthy nerve, and a pressure in the 20s or even low 30s, my approach is to treat the inflammation, adjust the corticosteroids, and, after that, add IOP-lowering medications. But if the patient has a thin cornea or prior damage to the optic nerve, with a pressure in the high 30s, 40s, or even 50s, I would treat glaucoma right away—with medications or, to quickly lower the pressure, an anterior chamber paracentesis. When patients present with such unsafe or damaging IOP levels, the risk of vision loss is too high to switch around the corticosteroids to see if the inflammation can be better controlled.

My typical first-line therapy for uveitic glaucoma is a topical beta blocker, alpha agonist, or carbonic anhydrase inhibitor (CAI). If topical medications do not suffice, the next step is to add an oral CAI (eg, Diamox or Neptazane) for short-term use. In my practice, surgical intervention is indicated when maximum medical therapy (glaucoma drops plus oral carbonic anhydrase inhibitor) fails to adequately control IOP or when a patient requires repeated paracentesis to reduce IOP.

Prostaglandin analogs (PGAs) are relatively contraindicat-

ed in patients with uveitic glaucoma. As inflammatory mediators, PGAs carry the theoretical risk of exacerbating inflammation, and they have been reported to reactivate herpes simplex keratitis.<sup>7</sup> Prostaglandin analogs are my first-choice agents for patients with primary open-angle glaucoma, but in the treatment of uveitic glaucoma I usually stay away from this drug class unless all other medical options have been exhausted. Another drug class I try to avoid in uveitic patients is miotics, which can disrupt the blood-aqueous barrier and worsen inflammation.

In terms of surgical management, I prefer to implant a glaucoma drainage device. Trabeculectomies may be effective as well, but in my clinical experience have a higher chance of bleb fibrosis as compared to a valve in a uveitic patient. To reduce the risk of hypotony after implantation, I usually stick with the Ahmed glaucoma valve. When extensive posterior synechiae leads to pupillary block that medications fail to break, laser peripheral iridotomy is indicated. It is the only laser procedure I would consider performing in the acute setting of uveitic glaucoma; selective laser trabeculoplasty (SLT) and argon laser trabeculoplasty (ALT) are contraindicated because they can create more inflammation and promote formation of peripheral anterior synechiae at the trabecular meshwork. I do not perform any of the minimally invasive glaucoma surgeries (MIGS) for fear that the devices may be clogged by inflammatory debris and lose their effectiveness.

#### INFLAMMATION CONTROL IN SURGICAL MANAGEMENT

Prior to performing a surgical procedure on a uveitic eye, achieving as much inflammation control as possible is considered necessary to achieve desired outcomes. Many uveitis patients develop cataracts as a result of chronic intraocular inflammation and corticosteroid use. It is recommended that intraocular inflammation be completely controlled in uveitis patients for about three months prior to cataract surgery.<sup>8,9</sup>

As for glaucoma surgery, it is not always possible to wait until the eye is clinically quiescent for the procedure. When

patients have uncontrolled high IOP and are therefore at risk of vision loss by central retinal vein or artery occlusion, they should be taken to the operating room as soon as possible. Even then, inflammation control is beneficial because excessive inflammation can lead to bleb fibrosis and failure. To improve success with glaucoma drainage implantation or trabeculectomy, the best approach is to administer antiinflammatory therapy using high doses of a potent corticosteroid (eg, prednisolone acetate 1% dosed every hour or difluprednate 0.05%, dosed four times a day) to achieve a quiet eye prior to the procedure.

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## Contact Lens Wear, Inflammation, and Disease

**BENNIE H. JENG, MD** Contact lens wear can upset the delicate balance of ocular surface biodynamics, aggravating underlying inflammatory conditions or introducing new ones. Contact lens-related discomfort alone might be an inflammatory or preinflammatory state. Having a clear idea of contributing factors and management options for contact lens-wearing patients with discomfort is essential to daily practice for eye care providers.

#### CONTACT LENS DISCOMFORT DEFINED

While eye care providers (ECPs) have long accepted that contact lens wear can cause discomfort, the defining of contact lens discomfort (CLD) as a distinct entity or syndrome is relatively new. According to the 2013 Tear Film and Ocular Surface Society (TFOS) International Workshop on Contact Lens Discomfort, CLD is best defined as “a condition characterized by episodic or persistent adverse ocular sensations related to lens wear, either with or without visual disturbance, resulting from reduced compatibility between the contact lens and the ocular environment, which can lead to decreased wearing time and discontinuation of contact lens wear.”<sup>1</sup>

Adverse ocular sensations—including dryness, irritation,

grittiness, and fatigue, with or without accompanying physical signs such as redness—characteristically progress throughout the day, are worst at night, and are mitigated by removal of the lens.<sup>1</sup> Note that CLD, by this definition, refers to symptoms among adapted contact lens wearers rather than neophytes; further, CLD is distinct from “contact lens-related dry eye,” a term which consortium members suggest should be reserved for patients with dry eye disease (DED) originating prior to and exacerbated by contact lens wear.<sup>1</sup> Similarly, CLD should be considered distinct from other inflammatory or infectious complications of contact lens wear, such as allergic conjunctivitis or microbial keratitis.

Contact lenses are known to disrupt innate ocular surface homeostasis by dividing and destabilizing the tear film; they also induce mechanical, chemical, and hypoxic stress (although the newest materials induce significantly less hypoxia than older designs) and serve as a vehicle for toxins and microbes to access the ocular surface.<sup>1</sup> These and other factors may contribute to ocular surface inflammation, which is thought to be a principal culprit—perhaps *the* principal culprit—in CLD.<sup>1-3</sup> Consequences of CLD are significant. Corneal inflammatory and infiltrative complications have been reported to affect 7% to 44% of CL wearers each year and are associated with significant morbidity and economic cost.<sup>2</sup> Along with dryness, CLD is a leading cause of patient dissatisfaction with lenses and lens discontinuation.<sup>1</sup>

Research has shown that uncomplicated contact lens wear induces molecular, cellular, and physical changes consistent with subclinical inflammation. Tear analyses reveal upregulation of proinflammatory mediators interleukin (IL)-6, IL-8, TNF- $\alpha$ , matrix metalloproteinase (MMP)-9 and others with contact lens wear;<sup>2</sup> in vivo confocal microscopy and conjunctival impression cytology reveal ocular surface alterations and damage, including reduced goblet cell density and mucin expression, increased conjunctival cell metaplasia, and increased cellular apoptosis.<sup>2</sup> Otherwise healthy contact lens wearers may experience conjunctival redness, corneal edema, and elevated ocular surface temperature, lending further support to a link between everyday contact lens wear and an uptick in surface inflammation.<sup>4</sup>

Efforts to correlate specific contact lens-induced inflammatory changes with symptoms of discomfort have been less than conclusive to date, with one exception: a prospective, controlled study by Masoudi and coworkers showed that, among multiple inflammatory mediators assayed, tear concentrations of leukotriene B4 (LTB4) significantly increased throughout the day among contact lens wearers compared with nonwearers.<sup>3</sup> It is conceivable then that LTB4, a lipid derived from arachidonic acid metabolism and a potent activator of polymorphonuclear cells, may play a role in CLD, although more research is needed.

### INFLAMMATION OR PARAINFLAMMATION

In one sense, inflammation is a natural, healthy response to a foreign body—including advanced technology contact lenses—that is placed on the eye. Which begs the question, is

## CORE CONCEPTS

- ◆ Contact lens wear produces subclinical inflammatory changes, including
  - ◆ Upregulation of leukotrienes and cytokines in tears
  - ◆ Conjunctival epithelial metaplasia
- ◆ CLD is discomfort that is not caused by a more serious disorder
  - ◆ CLD may be due to inflammation
- ◆ Treatment of inflammation in contact lens wearers involves
  - ◆ Stopping contact lens wear
  - ◆ Treating the underlying disorder, if present
  - ◆ Changing contact lens wear schedule, material, or solution
- ◆ Scleral lenses and BSCL are effective at treating slow healing or injured corneas

inflammation really a problem? As outlined in his 2015 presentation, award-winning researcher Nathan Efron, PhD, made the case that “contact lens wear is intrinsically inflammatory” and suggested that low-grade inflammation associated with contact lens wear might be an adaptive or protective response.<sup>5</sup> Yale researcher Medzhitov, in his 2008 publication in *Nature* entitled “Origin and Physiologic Roles of Inflammation,” defines parainflammation as a state of subclinical inflammation in which a tissue is stressed and somewhat malfunctioning but not irreversibly damaged.<sup>6</sup> It is a state in between homeostasis and inflammation that may benefit patients since it represents a state of readiness to ward off an acute infectious or noxious challenge.<sup>6</sup>

But even if CLD is a kind of pre- or parainflammatory state without major disruption to the ocular surface, the fact remains that patients in this state are often uncomfortable, and there remains a possibility of progression to a more damaging, fully inflammatory state.<sup>5</sup>

### CLD RISK FACTORS

Some risk factors have been uncovered which help to partially explain why some patients struggle with CLD while others do not. Ocular surface inflammation has been associated with patient comorbidities, such as diabetes, genetic variables, and the ocular resident flora or microbiota.<sup>2</sup> Shin and coworkers showed that contact lens wear alters the ocular surface microbiota so that it more resembles that of skin than the eye.<sup>7</sup> Hygienic factors—such as improper cleaning and storing; exposure to tap water; sleeping, showering, or swimming in lenses—may also play a role in ocular surface inflammation. Reminding patients about proper cleaning and storage of their contact lenses may reduce their risk for complications.<sup>1,2</sup>

### CLD MANAGEMENT

The first step to managing complaints of discomfort associated with contact lens wear is to rule out other conditions that

might be responsible; these include DED, meibomian gland dysfunction, allergic conjunctivitis, episcleritis, and infection. If a full work-up leaves CLD as the leading diagnosis, a 2-week contact lens “holiday” and lubrication with preservative-free artificial tears is recommended. A topical antiinflammatory agent, such as a short course of loteprednol, may be indicated if symptoms or inflammation are moderate to severe. Improvement on the holiday, followed by worsening upon re-exposure to contact lens wear, is consistent with a diagnosis of CLD.

The next step is to recommend a change in the patient’s contact lens material, care solution, or routine in order to minimize their risk for a return of bothersome symptoms. Suggestions include changing material or design, changing care solution, or adjusting frequency.<sup>8</sup> My favorite tactic is to eliminate care solutions and lens storage altogether by switching the patient to daily disposable lenses. In my experience, the daily disposable class is the least antigenic and best tolerated, and their packaging solutions tend to be the least inflammatory.

### CL WEAR AND DED

Patients with bona fide DED that is revealed or exacerbated by wearing contact lenses requires discontinuation of contact lens wear followed by evaluation and treatment of DED, just as one would for a non-contact lens wearer.

Effective DED treatment starts with identifying DED subtype—aqueous deficiency, lipid deficiency (evaporative), or mechanical (blink-related) DED subtypes—and directing treatment toward the root cause of the problem. First line therapy for aqueous deficiency DED is supplementation with preservative-free artificial tears; for evaporative DED, treatment of meibomian gland dysfunction and blepharitis. Patients with incomplete or reduced blink related to Parkinson’s disease, nocturnal lagophthalmos, or lower lid ptosis require specialized treatment aimed at correcting lid mechanics.

Disease severity and effectiveness of prior treatment are also important considerations in the treatment of DED. Patients with evidence of low-level inflammation or who have failed to respond to initial, more conservative therapies require topical antiinflammatory treatment with cyclosporine 0.05% or lifitegrast ophthalmic solution 5%. Patients with moderate to severe inflammation might need a short course of a topical ocular corticosteroid. Those with severe DED—such as patients with graft vs host disease or Stevens-Johnson syndrome—might benefit from treatment with a scleral lens (see below).

Much has been written about DED in recent years; for more in-depth diagnostic and treatment algorithms, please see the American Association of Ophthalmology (AAO) preferred practice pattern,<sup>9</sup> the Tear Film and Ocular Surface Society Dry Eye Workshop II<sup>10</sup>, or the Cornea External Disease and Refractive Society guidelines.<sup>11</sup>

### CONTACT LENSES AND ALLERGY

Similar to contact lens-wearing patients with DED, those with allergic disorders of the eye should discontinue contact

lens wear until the underlying inflammatory process is adequately treated. For patients with seasonal or perennial allergic conjunctivitis, treatment with olopatadine or a combined antihistamine/mast cell stabilizer agent may be indicated. Sometimes a patient will be very resistant to discontinuing contact lens wear; if they are otherwise very compliant and reliable, I will occasionally bend my own rule and allow use of a drop, such as olopatadine, before and after contact lens placement. I *do not*, however, permit topical corticosteroid use in conjunction with contact lens wear under any circumstances due to the increased risk for infection.

Comprehensive guidelines for the management of allergic conjunctivitis are available from the AAO.<sup>12</sup>

Patients with giant papillary conjunctivitis (GPC) require discontinuation of contact lens wear—which is the cause of GPC—and treatment with a short course of a topical ocular corticosteroid. When cleared for contact lens wear, I will typically have them switch the contact lens type: those who had been wearing a rigid gas permeable are switched to a soft daily wear lens; those on a daily wear to a daily disposable.

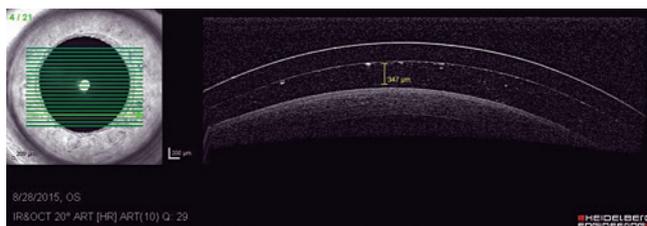
### CONTACT LENSES AND MICROBIAL KERATITIS

The ability to differentiate an inflammatory from an infectious condition is critical to evaluating contact lens-related discomfort. The natural history and management of microbial keratitis—which may occur with or without contact lens wear—is distinct, and haphazard use of antiinflammatory treatments can lead to worsening and poor outcomes, including blindness.<sup>13</sup>

Contact lens-induced peripheral ulcer (CLPU) and immune-mediated infiltrate are inflammatory conditions with characteristic—albeit not foolproof—appearances on examination. Inflammatory conditions such as infiltrative keratitis are commonly peripherally located (often about a millimeter from the limbus) and appear as small white infiltrates. They are sometimes associated with minor epithelial breakdown that appears as positive punctate staining.<sup>13</sup> An area of epithelial breakdown that is smaller than the underlying infiltrate is a clue that the direction of the tissue involvement is from the inside out and suggests a primary inflammatory process.

By contrast, infectious ulcers tend to be larger, irregular-edged lesions located more centrally; they may be surrounded by smaller satellite lesions. An ugly or “soupy” appearance should raise concern for an infectious cause, such as *Pseudomonas* species. Infectious lesions start on the external surface and move inward; thus, the size of the epithelial involvement and the underlying infiltrate is typically the same initially. Associated symptoms may be significant and may include pain, edema, redness, tearing, discharge, photophobia, and visual disturbance.<sup>13</sup>

Patients with CLD and evidence of an infiltrate should be advised to discontinue contact lens wear. Those with only inflammatory findings could also receive a topical corticosteroid; evidence of improvement typically appears within 24 hours of the start of therapy. On the other hand, if the ulcer appearance suggests an infectious cause, my practice is to



**FIGURE 1** A properly positioned scleral lens protects the ocular surface without directly contacting the cornea. (Image courtesy of Dr. Jeng and Luis Toledo, OD.)

have the patients stop wearing their contact lenses; I scrape and culture the ulcer, treat with fortified antibiotics to cover the possibility of infection, and then have them return to the clinic in 24 hours for reevaluation. At this point, I do not necessarily expect drastic improvement, but I would like to make sure they are not worse.

Distinguishing an inflammatory versus an early infectious ulcer in a contact lens wearer is challenging when the ocular surface has mild, mixed, or unusual characteristics. In such instances, it is wise to err on the side of caution, following up within 24 hours of stopping contact lens wear and again 24 hours later if antiinflammatory and/or antibiotic treatment is started.

### THERAPEUTIC CONTACT LENSES

While conventional contact lenses may induce inflammation, other types are specifically designed to alleviate inflammation. Scleral contact lenses are rigid gas permeable lenses large enough to rest on the conjunctiva, vaulting over the whole cornea and bathing the ocular surface with its fluid-filled reservoir. Scleral lenses provide symptomatic relief to patients, protect against sheering forces of the lid, and promote healing of the ocular surface (Figure 1).

Scleral lenses may be used to treat a variety of conditions associated with moderate to severe corneal or conjunctival inflammation, including keratoconjunctivitis sicca, cicatrizing conjunctivitis, recurrent erosions, neurotrophic keratopathy, exposure keratopathy, non-healing epithelial defects, and limbal stem cell deficiency.<sup>14,15</sup> Scleral lenses are also effective and well tolerated for the treatment of severe or recalcitrant DED, i.e., in patients for whom topical antiinflammatory treatment options have been exhausted.<sup>16</sup>

A downside to scleral lens use is its somewhat more complex fitting process compared to regular contact lenses, which may involve multiple office visits.<sup>15</sup> As the research base expands and more designs come to market, scleral lenses may become more widely used for both disease treatment and refractive purposes.<sup>15</sup> The bandage soft contact lens (BSCL) is

another therapeutic extended-wear contact lens type that assists in healing various types of corneal disruption, typically that associated with surgery or trauma.

### CONCLUSION

CLD is a diagnosis of exclusion. Discomfort associated with contact lens wear warrants a workup for dry eye, allergy, and other underlying disorders. Treatment should always be directed at the root cause and supported by symptomatic care and antiinflammatory measures. Contact lenses that promote ocular surface healing are available.

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1. Which of the following therapies is recommended by Dr. Trubnik as the first step in managing patients who present with uveitis and moderately raised IOP?
  - A. A topical corticosteroid
  - B. A topical NSAID
  - C. An IOP-lowering drop
  - D. An immunosuppressive agent
2. Mechanisms by which contact lenses may stress the ocular surface include:
  - A. Disrupting the tear film
  - B. Inducing hypoxic stress
  - C. Serving as a vehicle for microbes and their toxins
  - D. All of the above
3. According to Dr. Trubnik, which class of IOP-lowering medications should be avoided in patients with uveitic glaucoma?
  - A. Prostaglandin analogs
  - B. Beta blockers
  - C. Alpha agonists
  - D. Carbonic anhydrase inhibitors
4. According to research by Shin and coworkers, ocular surface microbiota in contact lens wearers is similar to:
  - A. Skin microbiota
  - B. Oral microbiota
  - C. Ocular surface microbiota of non-contact lens wearers
  - D. None of the above
5. Which of the following uveitis types are commonly associated with secondary glaucoma?
  - A. Herpes virus-associated uveitis
  - B. Fuch's heterochromic iridocyclitis
  - C. Sarcoidosis-associated uveitis
  - D. All of the above
6. Which of the following statements is FALSE about uveitic glaucoma?
  - A. Its overall prevalence in uveitic patients is about 20%
  - B. It occurs more commonly with anterior segment inflammation
  - C. It occurs in the form of both open-angle and angle-closure glaucoma
  - D. Most cases require surgical intervention to lower IOP
7. Corticosteroids are thought to raise IOP by causing:
  - A. Synechial closure
  - B. Increased aqueous viscosity
  - C. Alterations in trabecular cells and the extracellular matrix
  - D. Trabecular neovascularization
8. Which of the following is NOT a typical characteristic of an inflammatory ulcer from contact lens wear?
  - A. Central location
  - B. Large soupy infiltrate
  - C. Epithelial breakdown smaller than infiltrate
  - D. Both A and B
9. Which of the following is a soft, extended-wear contact lens that may be used in post-operative recovery?
  - A. Scleral lens
  - B. Bandage contact lens
  - C. Both
  - D. Neither
10. According to the TFOS definition, CLD results from:
  - A. Elevated levels of IL-6, IL-8, and TNF- $\alpha$
  - B. Reduced compatibility between the contact lens and the ocular environment
  - C. Smoking and poor hygiene
  - D. A shift in the ocular surface microbiota