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TOPICS IN Ocular Antiinfectives

Herpetic Anterior Uveitis

C. Stephen Foster, MD, FACS

Herpetic infection is an under-recognized cause of anterior uveitis. Being mindful of the distinguishing characteristics of herpetic infection is critical in establishing an accurate diagnosis for timely treatment.

Anterior uveitis is the most common form of intraocular inflammation in the US, representing approximately 90% of uveitis cases seen at community-based practices and more than 50% at tertiary referral centers.[1,2] In most cases, anterior uveitis is either idiopathic or associated with immune processes. A small portion of cases, however, can have an underlying infectious etiology, and identifying these cases is of critical importance, as the treatment and prognosis of infection-mediated inflammation differ from those of noninfectious entities.

Herpesviruses are the most common infectious causes of anterior uveitis.[3] Each episode of herpetic anterior uveitis can last from 1 week to several months,[4,5] and it is common for patients to have recurrences. With every episode of recurring disease, there is the possibility of damage to ocular structures. To prevent serious visual complications such as neurotrophic cornea, cystoid macular edema, glaucomatous optic neuropathy, and necrotizing retinitis, timely diagnosis and accurate treatment are essential.

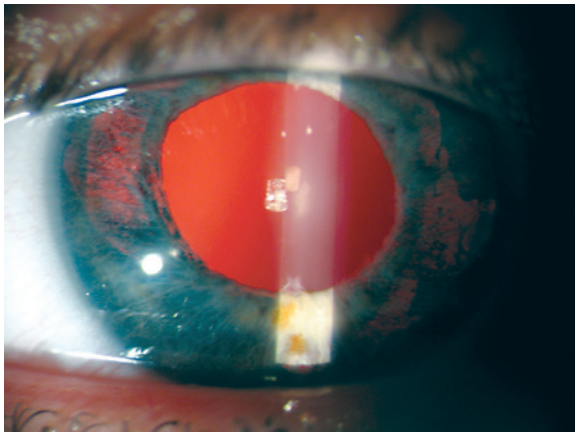

FIGURE 1 Herpes simplex uveitis, multiple attacks over 8 years. Note the iris transillumination defects temporally and nasally with retroillumination technique.

Herpesviruses

Herpesviruses are a large family of DNA viruses known as Herpesviridae. Among them, eight types can infect humans: herpes simplex viruses (HSV) 1 and 2 (human herpesvirus 1 and 2), varicella-zoster virus (VZV) (human herpesvirus 3), Epstein-Barr virus (EBV) (human herpesvirus 4), human cytomegalovirus (CMV) (human herpesvirus 5), and human herpesvirus (HHV) 6, 7, and 8 (human herpesvirus 8 is also known as Kaposi's sarcoma-associated herpesvirus). HSV and VZV are two main viruses responsible for anterior uveitis.[6] VZV may be identified more often in the elderly, but the vast majority of cases are HSV-related.

Recent studies suggest that many uveitis cases deemed idiopathic actu-

See INSIDE for:

Pragmatic Microbiology for Eye Care Providers

by Deepinder K. Dhaliwal, 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. Recognize a herpetic etiology in patients with anterior uveitis based on distinctive clinical findings.
2. Formulate the appropriate treatment strategy for presumed or proved herpetic anterior uveitis to reduce tissue damage and serious complications.
3. Obtain an adequate ocular tissue sample to identify pathogens present in superficial ocular infections.
4. Determine which cases are most in need of microbiology laboratory assessment.

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ally have a viral etiology.[7,8] Little is known about the role of HHV 6, 7, or 8 in ocular inflammation—they have not been studied extensively and are rarely associated with uveitis. But even EBV, a virus that colonizes the human population almost universally, is greatly underappreciated as an infectious cause of anterior uveitis. Research has suggested there is some likelihood that recurrent anterior uveitis of unknown origin is caused by EBV. Such patients are found to have high levels of antibody against early antigen D—a sign of a productive EBV infection—and shown to harbor human herpesvirus 4 in the aqueous humor.

Clinical Diagnosis

The diagnosis of herpetic anterior uveitis is based mainly on its clinical features. If a patient with anterior uveitis has shingles dermatitis that involves the ophthalmic division of the trigeminal nerve, chances are high that VZV is responsible for the anterior segment inflammation. Similarly, when a patient with a history of recurrent herpes simplex keratitis develops anterior uveitis, there is a great likelihood the inflammation is secondary to HSV reactivation.

In cases where neither cutaneous nor corneal involvement is present, there are a number of diagnostic hallmarks that can help one suspect the diagnosis. Sectoral iris atrophy, which results from ischemic necrosis of the iris stroma due to vasculitis, is a characteristic sign of recurrent herpetic anterior uveitis associated with either HSV or VZV.[9,10] The atrophic iris change is best demonstrated by retroillumination at the slit lamp as

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STATEMENT OF NEED

Ophthalmologists face numerous challenges in optimizing their competencies and clinical practices in the realm of preventing, diagnosing, and treating ocular infections and their sequelae; these challenges include:

- The widespread "off-label" use of topical ophthalmic antibiotics to prevent and treat serious and sight-threatening infections—given the reality that the most widely used topical antibiotics in ophthalmology have FDA approvals restricted to bacterial conjunctivitis.
- The escalating levels of multi-drug resistance in common ocular pathogens.[1]
- The emergence and increasing prevalence of once-atypical infections that may require diagnostic and treatment techniques relatively unfamiliar to comprehensive ophthalmologists.[2]
- The introduction of new and potentially more efficacious and/or safe ophthalmic antiinfectives.[3]
- The introduction of new and potentially more accurate diagnostic techniques for ophthalmic infections.[4]
- Widespread discussion over the efficacy and safety of novel or alternative delivery techniques and vehicles for prophylactic ophthalmic antibiotics (including but not limited to intracameral injection and topical mucoadhesives).[5,6]
- Increased understanding of the inflammatory damage caused by ocular infections and the best ways to prevent/alleviate inflammation without fueling the growth of pathogenic organisms.

Given the continually evolving challenges described above, *Topics in Ocular Antiinfectives* aims to help ophthalmologists update outdated competencies and narrow gaps between actual and optimal clinical practices. As an ongoing resource, this series will support evidence-based and rational antiinfective choices across a range of ophthalmic clinical situations.

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FACULTY AND DISCLOSURE STATEMENTS

Nisha Acharya, MD (Faculty Advisor), is an associate professor of ophthalmology and epidemiology at the University of California, San Francisco and director of the Uveitis Service at the F.I. Proctor Foundation. She states that in the past 12 months, she has not had a financial relationship with any commercial organization that produces, markets, re-sells, or distributes healthcare goods or services consumed by or used on patients.

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focal or patchy transillumination defects (Figure 1).

Another finding supportive of the diagnosis of herpetic anterior uveitis is localized or diffuse decreased corneal sensation. HSV 1 and 2 and VZV are neurotrophic viruses. They have the ability to remain latent within ganglion tissue that can evade the immune system. Periodically the virus will reactivate from latency, produce new virus particles, and march along the axons of the nerve. Reactivation of the latent virus may or may not produce clinically significant recurring disease—individuals colonized by HSV are known to shed the virus with some regularity in saliva and tears without developing herpes keratitis or a cold sore. Still, periodic episodes of such productive infection of the nerve can be damaging. Patients colonized with HSV in the trigeminal ganglion may suffer damage to their ophthalmic nerve, which supplies sensory innervations to the cornea. These patients can demonstrate decreased corneal sensation even if they have never had a single episode of clinical keratitis.

The Cochet-Bonnet esthesiometer is a useful diagnostic tool that allows careful mapping of corneal sensibility. Diminished sensation—localized or diffuse—in the eye with sectoral iris atrophy should be considered as a strong indication of the presence of HSV or VZV infection. (In the absence of a Cochet-Bonnet esthesiometer, the physician can use a piece of dental floss and touch it to the four quandrants of the cornea and conjunctiva and compare the eyes.)

Elevated intraocular pressure (IOP), a common finding in uveitis caused by microbial infection, is yet another supporting clinical feature in the diagnosis of herpetic anterior uveitis.[9,11] The acute increase in IOP has been attributed to inflammation of the trabecular meshwork,[12] and HSV- and VZV-associated anterior uveitis has been reported to have similar prevalence of IOP more than 30 mm Hg (25% to 50%) and development of glaucoma (18% to 30%).[13]

Diagnostic Testing

Since a majority of the general population is seropositive for herpesviruses even without a clear history of herpetic disease,[14] serologic testing for virus antibodies has little value in the diagnosis of herpetic anterior uveitis. That said, on the rare chance that the blood test turns out negative, it is strong evidence that herpesviruses are unlikely the causative factor unless it is a case of primary infection. Then again, patients with first-time infections will not have such a characteristic sign as sectoral iris atrophy.

Confirmation of a viral etiology in anterior uveitis is possible by means of aqueous humor studies. Viral cultures of aqueous humor samples are difficult, time-consuming, and no longer in clinical use. A more sensitive molecular technique—polymerase chain reaction (PCR)—has been commonly used to identify a specific etiology of infectious uveitis.[15] Negative PCR results do not exclude the possibility of herpetic infection, but detection of DNA from a herpesvirus in the aqueous is good evidence that the inflammation is being caused by that particular virus.

Despite being a valuable diagnostic tool, PCR-based aqueous humor analysis has its own limits. The results of PCR can be influenced by the quality of primers or contaminants. The test must be performed under stringent conditions to ensure high sensitivity and specificity. Additionally, the cost of a PCR test is not trivial. It is simply not cost-effective to perform an anterior chamber tap for PCR studies in every patient.

When an anterior uveitis patient presents with a constellation of clinical findings characteristic of an HSV or VZV etiology (eg, iris transillumination defects coupled with diminished corneal sensibility and sometimes elevated IOP), I no longer run an anterior chamber tap and PCR to confirm the diagnosis. CMV usually does not produce the same characteristic signs as HSV or VZV do. In cases of recurrent uveitis where I have high suspicion for CMV—often based on corneal findings such as posterior keratitis with unique fine stellate keratic precipitates—I usually order a PCR test for CMV to help establish the diagnosis.

CORE CONCEPTS

- Differentiation between an infectious and noninfectious etiology is important in managing anterior uveitis. While HSV and VZV are the most common viruses in the etiology of infectious anterior uveitis, other members of the human herpesvirus family, such as EBV, can be an underestimated causative factor in idiopathic cases.
- The diagnosis of herpetic anterior uveitis usually is based on clinical grounds. Findings that point to a herpetic etiology include a history of recurrent herpetic disease, presence of herpetic skin and corneal lesions, sectoral atrophy of the iris, decreased corneal sensibility, and an acute rise in IOP.
- Serologic studies are rarely useful in establishing the specific diagnosis of herpetic anterior uveitis. PCR-based aqueous humor analysis, on the other hand, can provide valuable information to confirm or exclude a suspected herpetic etiology in patients with anterior uveitis.
- Herpetic anterior uveitis is associated with recurrent disease. Multiple episodes of recurring infection due to virus reactivation can cause serious complications leading to poor visual outcome in the long term. Systemic antiviral therapy in most cases is beneficial for controlling the infection and sending the virus back to a quiescent state.

Medical Therapy

Treatment for herpetic anterior uveitis is primarily targeted at the infectious agent, the mainstay being oral antivirals. Patients with recurrent disease usually require long-term suppressive therapy with low doses of systemic antivirals. Oral acyclovir 800 milligrams twice

daily in most cases can effectively put a stop to recurrent episodes of HSV-related anterior segment inflammation. For cases likely associated with EBV (seropositive for early antigen D with an absence of other known causes of uveitis), oral valganciclovir twice daily for one to several months has shown notable efficacy in chasing the virus back to latency.[16,17] Topical antiviral agents are just about ineffective when it comes to herpetic uveitis but are sometimes used with topical corticosteroids to prevent keratitis.

In addition to antiviral therapy, chronic topical or systemic corticosteroids are traditionally used for herpetic anterior uveitis to help control the host immune reaction elicited by the virus.[18] Logically, steroid-sparing immunomodulatory therapy can accomplish the same goal while sparing the patient the side effects of chronic steroid use such as cataract and glaucoma. Our animal model work further supports the usefulness of steroid-sparing immunomodulatory therapy in ocular inflammation of infectious etiology.[19-23] In patients who have had a long history of recurrent uveitis and have developed extensive iris damage, in particular, an autoimmune response may be triggered to attack the damaged tissue depending on individual genetics. For such complicated cases, steroid-sparing immunomodulatory therapy (methotrexate, azathioprine, or mycophenolate mofetil) in addition to long-term suppressive doses of antivirals is often beneficial.

One aspect of management that is often neglected is ocular hypertension and prevention of glaucoma. An acute rise in IOP can be dangerous, and in corticosteroid responders the risk can be aggravated by use of topical corticosteroids. To prevent permanent damage from high IOP and glaucoma, the patient should be monitored weekly and treated with antihypertensive agents whenever the IOP shows a clear tendency to increase.

C. Stephen Foster, MD, is clinical professor of ophthalmology at Harvard Medical School in Boston, MA. He is founder and president of the Massachusetts Eye Research and Surgery Institution and CEO of the Ocular Immunology and Uveitis Foundation in Waltham, MA. Dr. Foster has received grant/research support from Alcon, Aldeyra Therapeutics, Bausch + Lomb, Clearside Biomedical, Eyegate Pharmaceuticals, Mallinckrodt Pharmaceuticals, Novartis, pSivida, and Santen Pharmaceutical Co., Ltd. He has also been a consultant to Aldeyra Therapeutics, Bausch + Lomb Surgical, Eyegate Pharmaceuticals, Novartis, pSivida, and XOMA, served on the speakers' bureau for Alcon and Allergan, and is a stock shareholder of Eyegate Pharmaceuticals. Medical writer Ying Guo, MBBS, assisted in the preparation of this article.

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Pragmatic Microbiology for Eye Care Providers

Deepinder K. Dhaliwal, MD

Knowing the cause of an infection greatly improves the chance of treating it properly. As the first point of contact, clinicians have a variety of tools available to identify ocular pathogens, including tapping the expertise of their microbiology laboratory colleagues.

CORE CONCEPTS

- Using the microbiology lab can take some of the guesswork out of treating ocular infection.
- Communicate with the lab: learn what they need to help you—and do this in advance of need.
- Consider taking baseline smear and culture specimens in severe or unusual conjunctivitis and blepharitis.
- In keratitis, corneal tissue scraping may be preferred to using swabs to obtain smear and culture specimens.
- Keep *Acanthamoeba* keratitis in mind, particularly among contact lens wearers.
- Ask patients about their contact lens cleaning regimen; make sure they avoid tap water (even if the lens solution packaging says otherwise).

At the University of Pittsburgh Medical Center, we are fortunate to have an ophthalmology-specific microbiology laboratory, the Charles T. Campbell Ophthalmic Microbiology Laboratory, which is well equipped to identify the organisms behind the ocular infections we face. But all eye care practitioners—regardless of their office setup or university affiliation—can and should avail themselves of the latest in microbiologic technology by using the many resources available at local, regional, and national microbiology laboratories.

Why Test?

Obtaining a culture prior to initiating antimicrobial therapy for a suspected ocular infection is the best way to identify the pathogen and select the most appropriate antimicrobial therapy. That said, it is impractical to culture every patient, especially outside academic settings; fortunately, the patient history can guide initial evaluation and management.

The availability of broad-spectrum topical ocular antibiotics obviates the need to obtain a culture in most routine cases of blepharitis, conjunctivitis, or small (1 mm or less) peripheral corneal infiltrates. Larger, more central, atypical-appearing corneal infiltrates, infections unresponsive to initial empirical therapy, or those associated with risk factors such as trauma, contact lens wear, immunocompromised status, or institutional exposure are more likely to require culturing.

Quality Smears 101

Every ophthalmologist should be able to obtain a quality smear, which can be critical to early and appropriate treatment of keratitis and conjunctivitis, including helping to distinguish infection from inflammation. There are a variety of acceptable ways to do this. Always communicate with the laboratory to make sure that whatever in-office technique is being used for obtaining smears and cultures aligns with the lab's expectations and capabilities.

Items to consider may include choice of swab material, transport medium, labeling, and the timing and temperature of transport. With regard to individual patients, it can be important to discuss the differential diagnosis with the lab in order to align priorities should the specimen size be smaller than desired.

Our website, ***http://eyemicrobiology.upmc.com***, offers a wealth of information and practical suggestions for ophthalmic microbiologic testing, including recommended techniques and materials for obtaining good specimens from patients with conjunctivitis, blepharitis, keratitis, and other ocular infections. In addition, clinicians and lab personnel are invited to contact our lab directly with questions.

For bacteriologic testing in cases of conjunctivitis or blepharitis, which may be useful when infection is severe or the diagnosis is in doubt, collect the specimen using a soft-tipped applicator that has been pre-moistened with a nonpreserved sterile medium. Cotton or Dacron swabs are best since calcium alginate is partially antimicrobial.

A device that contains both swab and media is also acceptable for these indications. For conjunctivitis, apply the applicator to the lower bulbar conjunctiva without contacting the lid. For blepharitis, apply a moistened swab to the eyelash area and lid margins. It is good practice to culture both eyes, even if only one eye is affected.[1]

Corneal Ulcer Specimens

Obtaining a corneal ulcer specimen for testing requires training and experience to perform safely, as the tissue is more delicate and topical anesthesia is indicated. For the best quality and quantity of tissue, use a spatula, blade, or jeweler's forceps; soft-tipped swabs may be useful adjunctively after obtaining the initial sample with the spatula.[2] There is evidence that swabs may be an acceptable alternative to scraping (Figure 1). It is important to focus on the ulcer periphery, since the periphery harbors a greater concentration of multiplying organisms than the center of the ulcer. Be gentle, but obtain as much tissue as

possible to increase yield.[1]

Samples collected on soft-tipped swabs may also be submitted for *Chlamydia*, *Acanthamoeba*, or fungal testing. A transport medium such as Bartels® ChlamTransTM Transport Medium (Trinity Biotech, Wicklow, Ireland) can be used for culture and polymerase chain reaction (PCR) testing of ocular viruses (eg, adenovirus and herpes family viruses), *Chlamydia*, and *Acanthamoeba*.[1] Fungal PCR is not yet available for clinical use. Again, it is critically important to communicate with your lab before requesting a test to find out the lab's preferred methodology.

Acanthamoeba

Failure to suspect the presence of an atypical organism when a patient is not responding to therapy can be a costly mistake, as a delayed diagnosis can negatively affect the outcome. This is especially true if an unusual or particularly pernicious organism is present. *Acanthamoeba* keratitis (AK), for example, is a sight-threatening infection that must be on the differential diagnosis of any contact lens-wearing patient who presents with a dendritic or pseudodendritic lesion.

Acanthamoeba should also be suspected when an ocular surface infection is unresponsive or poorly responsive to anti-herpetic or antibacterial treatment. AK typically occurs in contact lens wearers and may present with pain disproportionate to the physical findings. *However*, AK doesn't always present as expected; it has occurred among non-contact lens wearers and is not always associated with great pain.[3]

Corticosteroids

Prescribing a topical corticosteroid or corticosteroid-containing combination agent for symptomatic relief when the diagnosis is in question should be avoided, as corticosteroids may prolong or worsen an underlying infection. If a patient is dependent on corticosteroids for symptom relief, AK should be considered.

Some clinicians look to the results of the Steroids for Corneal Ulcers Trial (SCUT) to support the use of corticosteroids as adjunctive treatment for infectious keratitis. SCUT showed that at 3 months there was no difference when corneal ulcers were treated with adjunctive corticosteroids vs those that were not. The SCUT did show improved outcomes in the corticosteroid group in a severely affected subpopulation.[4]

FIGURE 1 Swab and spatula for specimen collection. *(Photo courtesy the Charles T. Campbell Ophthalmic Microbiology Laboratory.)*

However, the findings from SCUT must be interpreted carefully. Patients included in the trial had culture-proven bacterial keratitis and were not contact lens wearers; furthermore, they received 48 hours of topical moxifloxacin—significantly reducing the infectious burden—prior to the addition of corticosteroids. In addition, the study was conducted in the US and India, with most patients enrolled in India; it is not clear whether similar results would be found in other populations.

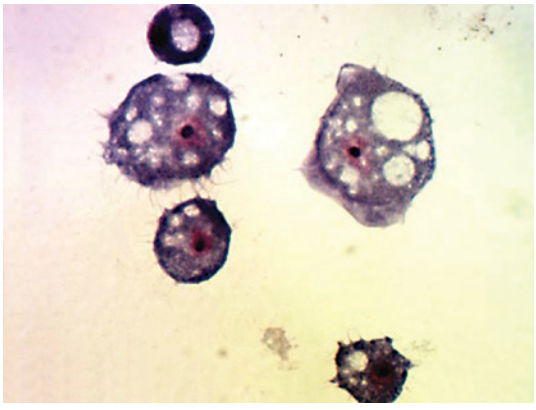

FIGURE 2 Giemsa-stained *Acanthamoeba* trophozoites. *(Photo courtesy the Charles T. Campbell Ophthalmic Microbiology Laboratory.)*

To illustrate the importance of appropriate treatment, we were recently referred a patient with undiagnosed advanced *Acanthamoeba* keratitis who had received 3 months of antiviral and corticosteroid treatment prior to referral—the presumed diagnosis was herpetic keratitis. She ultimately required multiple corneal transplants and had permanent loss of vision in the affected eye (not an uncommon outcome in this rare but potentially devastating infection). This case underscores the importance of maintaining a high index of suspicion for *Acanthamoeba* among contact lens wearers and refraining from administering corticosteroids when a keratitis diagnosis is unclear (Figure 2).

Physicians can help prevent amoebic ocular infection by warning patients not to use tap water in contact lens care. Tap water should never touch contact lenses (regardless of lens material) or lens cases at any point in a patient's regimen—even though this advice contradicts the instructions on the labels of many gas permeable lens solutions. Ask patients about their contact lens cleaning practices in detail and make sure they avoid using tap water, even if their lens solution bottle says otherwise. This advice is especially important now, as disinfectant levels are decreasing in some municipal water systems, opening the door for rising amoebic exposure.[5]

Choosing a Therapy

Susceptibility testing and laboratory antibiograms are useful guides to antimicrobial therapy choice when a pathogen has been identified. One must bear in mind that antibiotic susceptibilities are based on systemic standards; and topical therapies may be quite effective against organisms labeled "resistant," because topical dosing can produce far higher concentrations of drug at the infection site than can typically be achieved with

systemic administration. Antifungal susceptibility testing is not routinely performed but can be requested when necessary.

Correct diagnosis of an ocular infection starts with a careful history and ocular examination, and, in selected cases, may proceed quickly to laboratory assessment of possible pathogens. Obtaining specimens for smear and culture is a fundamental tool for ophthalmologists; good communication with colleagues and with the laboratory is also essential. Following up carefully and remaining vigilant for poor therapeutic response can help clinicians detect slow-growing or unusual pathogens in time to make a measurable difference in outcome.

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EXAMINATION QUESTIONS TOPICS IN OCULAR ANTIINFECTIVES, ISSUE 59

This CME program is sponsored by the University of Florida College of Medicine and supported by an unrestricted educational grant from Bausch + Lomb, Inc. **DIRECTIONS:** Select the one best answer to each question in the Exam (Questions 1–10) and in the Evaluation (Questions 11–16) below by circling one letter for each answer. Participants must score at least 80% on the questions and complete the entire Evaluation section on the form below. The University of Florida College of Medicine designates this enduring material for a maximum of 1.0 *AMA PRA Category 1 Credit*™. There is no fee to participate in this activity. *You can take the test online at* **http://cme.ufl.edu/ocular**.

1. Which of the following should prompt consideration of *Acanthamoeba* keratitis?
   A. Acute red eye with fever and rhinorrhea
   B. Corneal dendrite unresponsive to anti-herpetic treatment
   C. Red eye in a contact lens wearer who rinses her case in tap water
   D. Both B and C

2. Which of the following is responsible for the majority of herpetic anterior uveitis?
   A. HSV
   B. VZV
   C. CMV
   D. Rubella virus

3. Which of the following characterizes the study population in the Steroids for Corneal Ulcers Trial (SCUT)?
   A. Culture-proven bacterial keratitis
   B. Cases drawn from European, American, and Asian populations
   C. Contact lens wearers
   D. Received either antibiotic or corticosteroid

4. Which of the following diagnostic tools is most useful in identifying a herpetic cause of anterior uveitis?
   A. Serologic testing for virus antibodies
   B. PCR analysis of the aqueous humor
   C. Viral culture of the aqueous humor
   D. The Cochet-Bonnet esthesiometer

5. Collecting specimens for smear and culture may be useful for pathogen identification in:
   A. Cases of severe conjunctivitis
   B. Peripheral corneal ulcer >2 mm
   C. Severe cases of blepharitis
   D. All of the above

6. Which of the following clinical findings in patients with anterior uveitis should trigger suspicion of a herpetic etiology?
   A. Decreased corneal sensation
   B. Low IOP
   C. Sectoral atrophy of the iris
   D. Both A and C

7. According to Dr. Foster, which of the following should be the primary therapy for herpetic anterior uveitis?
   A. Systemic corticosteroids
   B. Topical corticosteroids
   C. Systemic antivirals
   D. Topical antivirals

8. Which of the following is LEAST important when collecting a sample from a corneal ulcer?
   A. Topical anesthesia
   B. Being skilled in the technique
   C. Swabbing the very center of the ulcer
   D. Obtaining a sample of adequate size

9. Which of the following is/are appropriate topic(s) of discussion with one's microbiologist?
   A. Availability of polymerase chain (PCR) test to detect suspected pathogens
   B. *Acanthamoeba* detection
   C. Turnaround time for microbial detection
   D. All of the above

10. Which of the following statements is NOT true of EBV?
    A. It is ubiquitous in the population
    B. It produces early antigen D
    C. It causes latent infection of the trigeminal ganglion
    D. It has been identified as causative factor in idiopathic uveitis

EXAMINATION ANSWER SHEET TOPICS IN OCULAR ANTIINFECTIVES, ISSUE 59

This CME activity is jointly sponsored by the University of Florida and Candeo Clinical/Science Communications, LLC, and supported by an unrestricted educational grant from Bausch + Lomb, Inc. Mail to: University of Florida CME Office, PO Box 100233, Gainesville, FL 32610-0233. **DIRECTIONS:** Select the one best answer for each question in the exam above (Questions 1–10). Participants must score at least 80% on the questions and complete the entire Evaluation (Questions 11–16) to receive CME credit. CME exam expires February 28, 2017.

ANSWERS:

1.	A	B	C	D	**6.**	A	B	C	D
2.	A	B	C	D	**7.**	A	B	C	D
3.	A	B	C	D	**8.**	A	B	C	D
4.	A	B	C	D	**9.**	A	B	C	D
5.	A	B	C	D	**10.**	A	B	C	D

EVALUATION:

1=Poor 2=Fair 3=Satisfactory 4=Good 5=Outstanding

11. Extent to which the activity met the identified:
    Objective 1: 1 2 3 4 5
    Objective 2: 1 2 3 4 5
    Objective 3: 1 2 3 4 5
    Objective 4: 1 2 3 4 5

12. Rate the overall effectiveness of how the activity:
    Related to my practice: 1 2 3 4 5
    Will influence how I practice: 1 2 3 4 5
    Will help me improve patient care: 1 2 3 4 5
    Stimulated my intellectual curiosity: 1 2 3 4 5
    Overall quality of material: 1 2 3 4 5
    Overall met my expectations: 1 2 3 4 5
    Avoided commercial bias/influence: 1 2 3 4 5

13. Will the information presented cause you to make any changes in your practice? Yes No

14. If yes, please describe: _____

15. How committed are you to making these changes? 1 2 3 4 5

16. Are future activities on this topic important to you? Yes No

If you wish to receive credit for this activity, please fill in the following information. Retain a copy for your records.

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