Chapter 5
Infection

The Eyes Have It by Tim Root

Why are you naked?
I'm not naked... this is just a dream!

I often dream of showing up to clinic completely naked.
Oh

Is your phone on vibrate?
Eye Infections
by Tim Root, M.D.

The eye is well protected from infection by the conjunctiva and the corneal epithelium. In addition, the tear film contains antimicrobials while the tear flow itself tends to wash away pathogens. The eye also harbors a host of non-pathogenic bacteria that competitively prohibit new bacteria growth. However, these eye-defenses can be breached by trauma, improper tearing, or contact lens wear and lead to an infection. An eye infection not only threatens vision, but the orbit can act as an entry portal to the rest of the body and infections can progress to systemic involvement, meningitis, and even death.

You will see a lot of conjunctivitis, blepharitis, and corneal ulcers in an ophthalmology walk-in clinic. Here’s a review of the common, less common, and potentially devastating infections you should know about.

Pink Eye: the three types of conjunctivitis

The conjunctiva is the semi-transparent skin covering the white part of the eye. This layer protects the eye from foreign bodies, infections, and irritants. However, the conjunctiva itself is susceptible to irritation and infection from virus and bacteria. Conjunctivitis, or “pink eye,” is the term used to describe inflammation of the conjunctiva and commonly occurs from three different sources: viral, bacterial, or allergic.

1. Viral conjunctivitis is the most common type, making up half of all cases of conjunctivitis in the adult. It is usually caused by an adenovirus, often following an upper respiratory infection or cold. Viral conjunctivitis is quite contagious and other family members may also complain of having “red eye.” Infected patients typically present with eye redness and watery tearing, but little mucous discharge. Often, only one eye is infected, but the infection may spread to the other eye. Two specific signs on exam are enlarged follicular bumps on the inside of the eyelids (these look like tiny blisters under the microscope) and swelling of the preauricular node located in front of the ear. Most of these infections clear up on their own within a few days. Like the common cold, treatment is geared toward relieving symptoms. Viral conjunctivitis is so contagious that I also recommend good hygiene and no towel/makeup sharing in the home.
2. **Bacterial conjunctivitis** presents with a *mucupurulent* (pus) discharge. This creamy discharge may cause your patient to complain of sticky eyelashes, with patients finding their eyes matted shut upon waking in the morning. Bacterial conjunctivitis often develops a papillary conjunctival reaction (red bumps on the inside of the lids) and, unlike viral infections, typically does NOT have preauricular node enlargement. The most common culprits are staph and strep, although with children you should also consider Hemophilus influenza bacteria. In addition, sexually active adults may harbor chlamydial and gonococcal infections (especially with severe or sudden discharge). I treat most conjunctivitis with erythromycin ointment.

3. **Allergic Conjunctivitis:** Finally, patients with allergic conjunctivitis present with red, watery eyes. The hallmark symptoms of allergy are itching and swelling. On exam you may see swelling around the eyes that we call “allergic shiners.” Patients often have a history of seasonal allergies and will usually present with other allergic symptoms such as a stuffy nose and cough. Treatment for allergic conjunctivitis involves avoidance of the offending allergens. These patients may need antihistamines, mast-cell stabilizers, and possibly steroids.

**Why is that eye red?**

The cause of conjunctivitis is not always apparent and it’s sometimes impossible to determine the cause. Typically, you treat with cool compresses, Tylenol, and vigorous hand-washing. If you suspect bacteria, you treat with an antibiotic like erythromycin. Pathognomonic symptoms include:

1. **Viral:** watering, follicles, swollen lymph nodes
2. **Bacterial:** creamy discharge, unilateral
3. **Allergy:** bilateral itching and swelling
Blepharitis:
Blepharitis means inflammation (itis) of the eyelids (bleph), specifically the eyelid margin. This condition is a common diagnosis in an eye clinic, with patients complaining of stinging, tearing, and a “gritty” sensation in their eyes. Blepharitis has been classified many ways (seborrheic blepharitis, staphylococcal blepharitis, etc.) but I prefer to distinguish it as either:

A. Anterior blepharitis:
With these patients you'll find a buildup of debris, or “scurf,” that form as collarettes at the base of the eyelashes. Bacteria and irritants live in this debris and constantly shed irritants into the tear film. If severe, you can see small ulcerations and eyelash loss in affected areas.

B. Posterior blepharitis:
This is when the meibomian gland orifices clog up. When examining the eyelids, I always push on the lid edges with a Q-Tip. If pus-like material oozes out of the pores, then I know that the gland isn't draining properly. I usually note this in the chart as MGD (meibomian gland dysfunction)
The primary treatment for blepharitis involves good lid hygiene. Most cases can be relieved in a few weeks by having your patient wash their eyelashes daily with baby shampoo and a washcloth. Warm compresses will also help as they open up the orifices of the meibomian glands. Tougher cases of anterior blepharitis may require topical antibiotics. You can also use oral doxycycline – which works not by its antibiotic effect, but by changing the fatty acid oil composition of the meibomian glands, allowing the fluid to flow better.

Blepharitis is common and a large percentage of patients seem to suffer from it. This is a chronic irritation such that compresses and lid scrub regimens may need to be continued indefinitely.

Fun Fact
In addition to long lashes, camels have an extra eyelid to protect their cornea from blowing desert sands. This extra eyelid is so thin that the camel can close the lid and still see through it - this is helpful when traveling through sandstorms.
Chalazion:
Chalazions are granulomatous inflammations of the meibomian gland. These glands produce the lipid component of the tear film and are deeply located within the supporting tarsal plate of the lid. Chalazions occur when meibomian gland pores become clogged (such as in blepharitis) -- lipid backs up into the gland, and a noninfectious inflammatory granuloma reaction occurs.

On exam, the patient will have a firm and mobile nodular bump on their eyelid. When you evert the lid, you'll often see this bump more clearly. They are non-tender and are not painful.

Early treatment involves warm compresses, massage, and lid scrubs in an attempt to reopen the meibomian pore and allow the material to flow out. If this doesn't work, we flip the lid and incise/drain the chalazion from the inner eyelid surface. Some people are more prone to developing chalazions and they tend to reoccur.

Chlamydial Conjunctivitis:
Chlamydia causes two different kinds of conjunctivitis: inclusion conjunctivitis and trachoma. Both of these infections are caused by different serotypes of chlamydia bacteria. We don't see either of these infections often, but they are a major cause of blindness in developing countries.

Inclusion Conjunctivitis:
Inclusion conjunctivitis is the typical “sexual” chlamydial infection of the eye that you’re most likely to see here in the US. Patients present with a chronic conjunctivitis that has persisted for more than three weeks. As with other bacterial infections, the patient will have injection of the conjunctiva and purulent discharge. They may also show follicular “cobbledstoning” that develops on the inner eyelids.

This infection occurs mainly in newborns or sexually active teens with a concurrent genital infection. Migration of the bacteria to the eye occurs from hand-eye transmission and can also spread person to person from shared cosmetics or from improperly chlorinated hot tubs. Newborns can also be infected while passing through the birth tract. The bacteria can be detected with a chlamydial immunofluorescence test or by culture of the conjunctiva. A Giemsa stain will show the classic basophilic inclusion bodies within epithelial cells.
Therapy involves topical antibiotics. Because the bacteria is usually contracted sexually, eyedrops alone won’t address the entire problem so oral azithromycin is also given. Sexual partners also need to be treated. Newborns are also treated with systemic erythromycin to avoid chlamydial pneumonitis (chlamydia has a propensity for infecting mucous membranes).

**Trachoma:**
Trachoma is the “non-sexual” chlamydial infection of the eye that occurs in countries with poor sanitation. In less developed countries, trachoma is the leading cause of blindness. The chlamydia bacteria spreads through contact with family members, and can also spread within communities by flies and gnats.

The disease creates a long-lasting, chronic follicular conjunctivitis that eventually progresses to scarring of the eyelids. This scarring can close off the lacrimal gland pores and lead to chronic dry eyes. Scarring can cause the eyelids to rotate inward (entropion), and change the direction of eyelash growth - a condition called trichiasis. Constant rubbing of the lashes against the cornea leads to corneal scarring and eventually blindness.

**Gonococcal Infection:**
While gonococcal infection is much rarer than chlamydial infection, it is very serious as gonorrhea can progress rapidly. These patients will present with redness of the conjunctiva and profuse mucopurulent discharge. This is a serious infection, as the organism can penetrate through a healthy cornea and perforate within 24-48 hours, leading to endophthalmitis and loss of the eye. The eye can also act as an entry portal for meningitis and septicemia.

With any severe and profuse exudate you should obtain scrapings and run a culture. A Gram’s stain will reveal the hallmark gram-negative diplococci inside infected cells.

*Drawing: Intra-cellular gram-negative diplococci, usually inside WBCs*

Because the infection advances so rapidly, treatment requires systemic coverage with a drug like ceftriaxone. Topical antibiotics can act as an adjunct but don’t work well alone as the diffuse tearing washes the antibiotic away. If there is severe corneal involvement, or you are worried about your patient’s compliance, you may need to admit them so they can be followed more closely.

Babies can contract gonococcal infection during birth -- this is why most states require they receive prophylactic silver nitrate or erythromycin ointment after birth. We use erythromycin here because silver is irritating and creates a temporary “chemical conjunctivitis.”
Corneal Abrasions and Ulcers:
Corneal abrasions are very common and the most common consult that I get from the ER. Superficial epithelial defects can occur after trauma, infection, or from exposure. The cornea contains more nerve endings per area than anywhere else in the body, so scratches here are painful, and patients will often have photophobia (pain with bright lights) with the sensation that “something is in the eye.” Fortunately, with aggressive lubrication, the superficial epithelial layer heals quickly, literally within a day or two, and the patient feels better. We’ll often treat the eye with empiric erythromycin until the epithelium reforms.

If an epithelial defect has an associated bacterial infiltrate, this is called a corneal ulcer. Ulcers are treated aggressively with antibiotics and should be followed closely until the epithelial defect has closed. For straightforward, small ulcers, I typically use a fluoroquinolone like ciprofloxacin or moxifloxacin. If the ulcer is large, centrally located, or not healing, then we culture and tailor antibiotics accordingly.

Dirty Contacts
Contact lens wearers are more likely to have a dangerous infection with *pseudomonas*. In these patients, we cover with ciprofloxacin. If the ulcer looks bad, they might need hourly fortified antibiotics (ex: vancomycin and amikacin). Also, we treat any “dirty” ulcer (i.e., caused by tree branch, fingernail, soil) with more aggressive antibiotics.

With sterile epithelial defects you can patch the eye to promote lubrication and speed healing. However, you don’t want to patch an eye with a potential infection and you should follow patched eyes closely to make sure a perforating ulcer isn’t brewing under that patch.
Pre- and Post-septal Cellulitis:
Patients may present with a swollen eyelid that appears to be infected (swelling, erythema, warmth, systemic fever). When approaching a patient with a taut, infected eyelid the important distinction you must determine is whether the infection is located pre- or post-septal.

The “septum” is a layer of connective tissue that runs from the tarsal plate of the eyelid to the surrounding orbital rim. Infections superficial to this septum can look bad, but generally resolve without problems. However, if an infection tracks back behind the septum, you’re in trouble and will need to admit the patient for IV antibiotics and possible surgical abscess drainage. Orbital cellulitis occurs most commonly from sinus disease, especially in children, with bacteria eroding through the thin ethmoid bone into the orbit. They can also arise from tooth abscess and even from fungal infections in patients who are immuno-compromised with glycemic problems.

Symptoms of post-septal orbital involvement are pretty obvious: soft-tissue swelling will cause proptosis and chemosis (swelling of the conjunctiva). Intraocular muscle inflammation causes decreased motility and painful eye movement. If the optic nerve is affected they’ll have decreased vision and possibly an APD.

Whenever you see a big swollen eyelid you should always check for these signs of post-septal involvement and if suspected, order a CT scan.

Herpes Simplex Virus:
Herpes infection around the eye is quite common - when herpes attacks the cornea, we call this “herpetic keratitis.”

Herpetic keratitis is caused by HSV Type-1. This is a common virus, and the vast majority of people contract it during childhood with almost 100% of people over 65 years with latent infection. The virus lies dormant in the trigeminal ganglion and can reactivate, causing cold sores in some people. This reactivation can be triggered by fever, trauma, psychological stress, and UV sunlight. The factors leading to occurrence of the disease in the eye is unclear, though it may have something to do with the virus strain or the patient's immune system.

Patients will present with a red, injected eye and complain of pain. Patients may
also exhibit the classical vesicular rash near the orbit. The infection almost always occurs in only one eye, though you can see bilateral cases, especially in atopic children. When examining these patients under the slit-lamp, you will see the classic “dendritic ulcer” that stains brightly with fluorescein. The initial infection typically involves only the superficial cornea and doesn’t lead to any long-term sequela. Unfortunately, the infection tends to reactivate. With repeat infections, the virus attacks deeper and deeper areas of the cornea and can lead to scarring if the corneal stroma is involved. Deep infection also kills the sensory nerves of the cornea. This decreases corneal sensitivity (you can check with a cotton-swab prior to anesthetic) and can give patients the false illusion that they are getting better.

Treatment is aggressive in order to avoid deeper penetration of the cornea. Debridement of the area with a cotton-tipped swab may help, and topical antiviral drops like Viroptic are always given. Acyclovir is often given orally, and continued prophylactic oral acyclovir may decrease the rate of recurrent outbreaks. I also treat nearby skin lesions with topical acyclovir - this topical drug doesn’t penetrate well into the skin, but may decrease viral shedding into the eye. Topical steroids must be avoided in the presence of epithelial defects, as steroids increase viral replication and can lead to a terrible geographic ulcer on the cornea. With significant corneal scarring, these patients may need a corneal transplant to regain sight.

AIDS and the Eye:
Nearly all AIDS patients develop a condition called AIDS retinopathy, a relatively benign state that is common with CD4+ counts below 200. On fundus exam, you’ll see cotton-wool spots (infarctions of the surface ganglion nerve layer), microaneurysms, and hemorrhaging. The cotton-wool spots are so prevalent that when finding these spots in a healthy patient without underlying diabetes or hypertension you should consider HIV testing. The mechanism behind AIDS retinopathy is unclear, but may result from immune complex deposition in the retinal vessel walls. While AIDS retinopathy doesn’t cause vision problems itself, its continued presence may indicate poor HIV control.

The cytomegalovirus (CMV) is the most common opportunistic infection of the eye and is the leading cause of blindness in AIDS patients. Most people contract CMV during childhood, developing a mono-like illness, and then go on to maintain lifelong immunity with viral suppression. However, the virus can reactivate in AIDS patients because of their decreased immune response. CMV reactivation typically occurs with CD4+ counts below 50; and the overall prevalence of CMV retinitis is rising as better prophylactic treatment for other deadly infections have allowed more AIDS patients to survive with very low CD4+ counts.

CMV typically attacks the retina and creates a necrotizing retinitis. Fundus exam shows peripheral areas of white retinal necrosis and associated
hemorrhaging. The infection is treated with antivirals like gancyclovir or foscarnet. These drugs are only virostatic, though -- they will suppress the infection, but won’t eradicate the virus from the eye. Thus, antiviral treatment needs to be maintained to avoid reactivation. The antivirals can be given by IV (you will likely need to admit the patient for gancyclovir induction) with long-term oral maintenance. Also, after induction a gancyclovir implant can be placed inside the eye itself to allow a slow depot release of the drug.

AIDS patients are susceptible to many other eye infections, including herpes simplex of the retina, toxoplasma, zoster, and syphilis. Discussion of these infections is beyond the scope of this book, though, so let’s move on.

**Endophthalmitis**

Endophthalmitis describes a serious infection inside the eye and is the dreaded complication we most fear after eye surgery. The eye contains delicate structures and is essentially a large cavity that can quickly turn into an abscess (an eyeball filled with pus). Endophthalmitis can occur for many reasons: after inoculation from trauma or even years after an uncomplicated eye surgery. It can also occur from endogenous infections elsewhere in the body.

While the cause of infection is not always obvious, the infection itself is easy to spot as the eye fills with hazy inflammatory cells and you often can’t view the retina. The anterior chamber inflammation may be so bad that a layer of pus (called a hypopion) forms along the bottom.

Treatment of these patients depends upon their vision … typically, if they see hand motion or better, we perform a “tap and inject.” This is where you put a needle into the eye to draw out a sample for culture and inject broad-spectrum antibiotics back into the eye. If the vision is “light perception” or worse you take the patients to surgery for a vitrectomy to manually clean the eye out. This is only a rule of thumb: the urgency of treatment is also dictated by the cause of infection, such that cataract-induced endophthalmitis is treated differently than glaucoma-surgery induced infection. No matter the cause, however, visual prognosis is universally poor.
**Conclusion:**

We could discuss many more eye infections, but these are the important entities to know for the wards and your boards. Some of these infections, like blepharitis and corneal ulcers, are very common and you will see these almost daily in an ophthalmology clinic. Others, like gonococcal keratitis and post-surgical endophthalmitis, are rarer, but important to recognize because of their devastating effects if not treated early.

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### Pimp Questions

1. **A patient comes into your office in great distress because their eye looks incredibly red. On exam, you see they have a spot of hemorrhage under the conjunctiva. Is this a problem and should they be worried?**

   A few drops of blood spread under the conjunctiva looks impressive and can be alarming. Subconjunctival hemorrhage occurs when a conjunctival blood vessel “pops,” usually after a valsalva or when bending over. This is generally benign as the blood will go away in a few weeks. If the hemorrhage is recurrent, though, start thinking about bleeding disorders.

2. **What antibiotic would you use for a small corneal ulcer in a contact lens wearer?**

   While most small ulcers can be treated with erythromycin, you must worry about pseudomonas in contact lens wearers. Treat all CL wearers with ciprofloxacin or moxifloxacin. If the ulcer is large, jump right to fortified antibiotics like vancomycin and tobramycin.

3. **Can you patch an eye to promote healing and comfort? Are there situations where you’d avoid patching?**

   You can patch an eye with an epithelial defect as patching makes the eye feel better and may speed up surface healing by decreasing exposure. However, you definitely don’t want to patch the eye if there is any chance of infection. Thus, you shouldn’t patch anyone with bacterial infiltrate, contact lens, or trauma by “dirty material” such as from vegetable matter, animals, or dirt.
4. What are the three kinds of conjunctivitis? How do you differentiate them on history and physical exam?
The cause of a conjunctivitis is not always obvious. Generally you’ll see the following classic findings:

- **Viral** watery discharge, follicles, enlarged nodes
- **Bacterial** mucous discharge, often unilateral
- **Allergic** bilateral itching and swelling

5. What’s the most common cause of conjunctivitis? How do you treat it?
Viral conjunctivitis, usually caused by adenovirus, is the most common cause of pink eye in the adult. Adenovirus also causes cold symptoms (rhinovirus actually causes the majority of colds) and these patients will often describe concurrent respiratory illness. You treat these patients supportively with cool compresses, Tylenol, and chicken soup. Warn the patient that they are contagious and encourage them to wash their hands, don’t share towels, and throw out their makeup.

6. What’s our favorite diagnosis in the eye-clinic (good for explaining chronically irritated, grainy-feeling eyes with stinging and occasional watering). How do you treat it?
This sounds like blepharitis, which, along with dry eye is probably the most common diagnosis in an eye clinic. You treat blepharitis with artificial tears, warm compresses, and lid scrubs. If this doesn’t seem to be working, you can try topical erythromycin or oral doxycycline (don’t use in kids or pregnant women).

7. What’s a chalazion, stye, and hordeolum? How do you treat them?
A chalazion is a non-infectious granulomatous inflammation of a meibomian gland sitting in the tarsal plate (see the anatomy chapter). A stye is like a pimple at the lid margin, usually at the base of an eyelash. A “hordeolum” is a general term that describes an “inflamed gland.” It is debatable what this means, so I don’t like to use the term “hordeolum” myself but you may run across it.

8. What are the signs/symptoms of herpetic keratitis? How do you treat it?
The hallmark of herpetic infection is the classic dendritic ulcer. You treat with oral acyclovir and topical antiviral drops such as Viroptic.
9. You suspect a patient of having a herpetic corneal infection, based on the shape of her epithelial defect, and you are concerned about corneal scarring. Can you use a steroid to decrease inflammation and the resulting scarring?
You should NEVER use a steroid drop in herpetic disease if there is still an epithelial defect, as this will cause the virus infection to worsen and develop into a terrible “geographic ulcer.” You use topical antivirals like Viroptic and oral acyclovir and wait until the epithelium has healed before considering steroids to decrease scarring.

10. Are eyes with herpetic keratitis more or less sensitive to touch?
These eyes are less sensitive to touch as the virus kills the corneal nerves. When HSV is suspected, we check corneal sensitivity with a cotton swab or a monofilament prior to anesthetic. Eye sensitivity is an important component of the protective blink reflex.

11. What’s the difference between a corneal abrasion and a corneal ulcer?
A corneal ulcer is an abrasion PLUS an infectious infiltrate. Ulcers require antibiotic coverage and possible culturing depending upon the severity, size, and location of the lesion.

12. A 21 y.o. man presents with a grossly swollen eyelid – a few days before he had a pimple that his girlfriend popped with nail clippers. Since then his eyelid has swollen, with redness, mild warmth and tenderness to touch. What specific findings would make you concerned for deeper involvement.
This patient sounds like he has an infection of the eyelid. The question is whether he has any post-septal involvement (i.e., orbital cellulitis). You need to check for decreased vision, proptosis, chemosis, decreased eye motion, and pain with eye movement. These findings would suggest a dangerous orbital infection with the need for admission, imaging, abscess drainage, etc..

13. You are considering doxycycline therapy for a patient with blepharitis. What should you warn your patient about this medication?
Doxycycline is not the easiest medication to take! It is inactivated by milk and your patient may be more susceptible to sunlight and be more prone to sunburn. This medication shouldn’t be used in children or breast-feeding women. Finally, tell your patient to avoid using it at bed-time – the tablet can get caught in the esophagus or stomach and ulcer through overnight.