

Feline Red Eye: At the Surface

Jessica Meekins, DVM, DACVO reviews surface causes of “red eye” in cats including feline herpesvirus-1, bacterial infections, and neoplastic conditions.

Speaker Bio:

Jessica Meekins, DVM, DACVO is an Associate Professor of Ophthalmology at Kansas State University. She received her undergraduate degree in biology before attending veterinary school at the Ohio State University. She then completed a one-year rotating internship at a private specialty hospital in Albuquerque, New Mexico before being accepted into the ophthalmology residency program at Purdue University. She became a board certified diplomate of the American College of Veterinary Ophthalmologists in 2012, and she has been on faculty at K-State for 9 years. Dr. Meekins' clinical and research interests include management of viral surface ocular diseases in cats and comparative exotic animal ophthalmology. She is also interested in clinical teaching and the integration of competency-based veterinary education into instruction and assessment of students participating in clinical rotations.

Learning Objectives:

1. Distinguish between FHV-1, as the most common cause of surface ocular inflammation in cats, and other differential diagnoses on the basis of clinical exam findings
2. Recognize the indications for specific basic ocular diagnostic tests during the initial workup of a red eye
3. Recall, for each disease condition, when to recommend treating in-house vs. referring to a specialist
4. Manage client expectations regarding cost, prognosis, and outcome

Feline Red Eye: At the Surface



Jessica Meekins, DVM, MS, Diplomate ACVO

Hello, my name is Jessica Meekins and I'm an associate professor of ophthalmology at Kansas State University. It's my pleasure to provide a continuing education presentation, on the topic of feline red eye. With a specific focus on diseases that affect the ocular surface. In a separate presentation, I'll also address the topic of intraocular causes a feline red eye.

- Clinically relevant A&P review
- Basic ocular diagnostic tests for a red eye
- Viral (feline herpesvirus-1 [FHV-1]) surface ocular disease
 - Conjunctivitis
 - Corneal disease
- Other types of conjunctivitis
- Summary/My approach

I'll start our discussion, by providing you with a brief overview of the clinically relevant anatomy of the ocular surface. We'll then discuss the basic ocular diagnostic tests, that are important to perform in any cat presenting with a red eye. I'll also provide some insight into client communication tips that I use, and that may be helpful to you as you explain these tests to your clients, and attempt to prioritize them for your patients.

In terms of specific diseases that affect the feline ocular surface, and result in red eye, we'll cover two main areas. First, we'll have an in-depth discussion of feline herpes virus, and its corneal and conjunctival manifestations. Then, will cover conjunctivitis, specifically focusing on the clinical appearance that will differentiate the various ideologies of non-viral conjunctivitis in cats.

Throughout our discussion, I'll provide additional tips on client education that I use for each disease, and discuss what you can tackle out in practice, versus what you should consider referring to an ophthalmologist if that's an option. I'll end with a summary of the most important concepts covered during the presentation and include some key concepts of my approach to working at the cat presenting with a red eye, localized to the ocular surface.

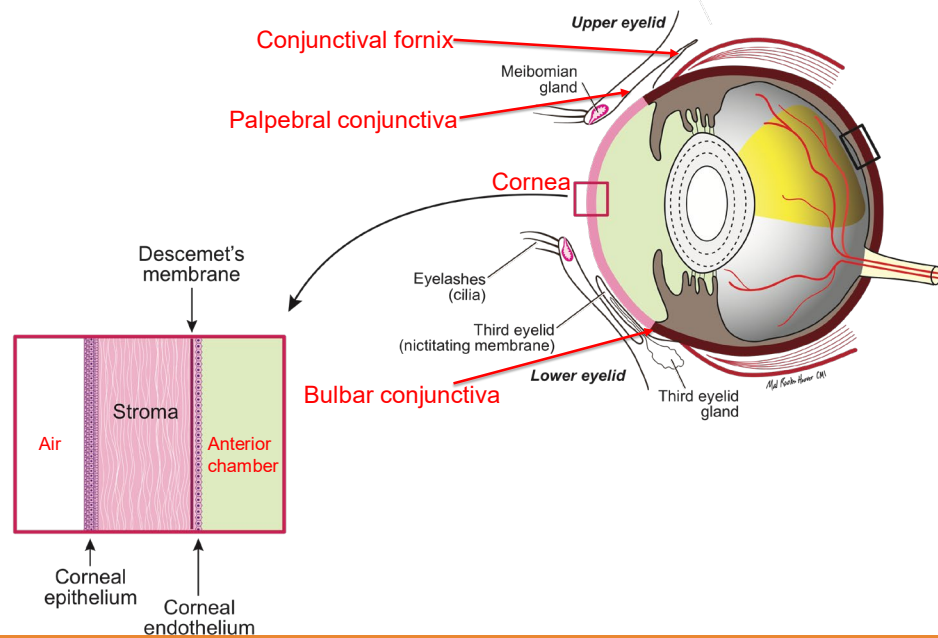


Figure 1

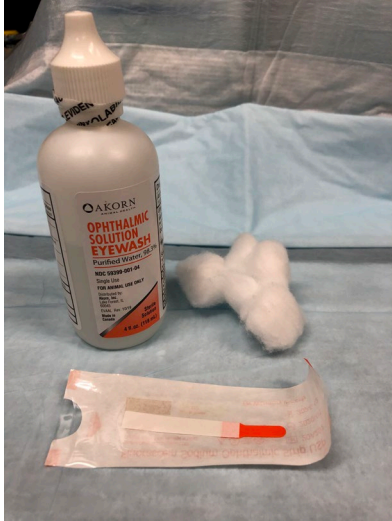
The surface ocular tissue's targeted by certain disease processes resulting in a red eye, include the conjunctiva and the cornea. The conjunctiva, is technically a mucous membrane that lines the anterior sclera, the inside of the eyelids, and the third eyelid. It's a continuous mucosal layer composed of non-keratinized epithelium, and goblet cells, which are the cells that produce the missing and component of the tear film.

The bulbar conjunctiva lines the anterior sclera, then reflects on itself at the conjunctival fornix, to then line the inside of the eyelids. The third eyelid, or nictating membrane, is also lined by conjunctiva. The conjunctival it is essentially an exposed mucous membrane, and serves as its role in ocular surface immune defense with the presence of lymphoid follicles, and lymphatics.

The cornea, along with the sclera make up the outermost or the fibrous tunic of the eye. The cornea is composed of four layers in our veterinary species, including the epithelium, the stroma, descemet's membrane and the endothelium. The majority of diseases that affect the feline ocular surface and result in a red eye, target that conjunctiva.

However, there are also certain ocular surface diseases. Most notably viral surface ocular disease, that also affect the cornea. The conjunctiva and the cornea will be our two areas of focus as we work through surface ocular diseases causing feline red eye.

Diagnostic Tests: Fluorescein Staining*



Feline Red Eye: At the Surface

Fluorescein staining and intraocular pressure measurements are the two basic ocular diagnostic tests that are most important to perform in any case presenting with a red eye. Of these big three, basic ocular diagnostic tests that we perform which include a schirmer tear test to measure tear production, fluorescing staining to check for corneal ulcers, and intraocular pressure measurement to screen for glaucoma or uveitis. I do not routinely perform only tear measurement and cats, but I do very routinely perform the other two tests.

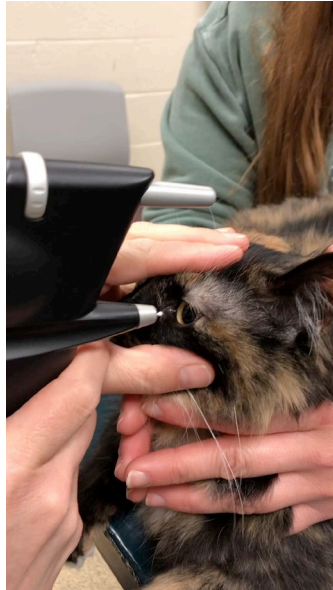
Tear production is not typically measured in cats that I manage, because they are really rarely affected by quantitative tear film abnormalities, which we also refer to as curative conjunctivitis sicca, or dry eye disease. Fluorescein staining should be prioritized in cats with evidence of a surface ocular cause of red eye. When discussing the necessary diagnostic tests of the client, I tend to emphasize the need to screen a cat for evidence of corneal ulceration, as this would impact the recommended treatment plan, and also lend support to the diagnosis of a viral surface ocular disease.

I'm sure most or all of you have performed fluorescein staining many times, and have likely developed your own technique for this diagnostic test. I prefer to apply eyewash directly to the Fluorescein strip in order to create a drop that can be placed in the eye, as if from a dropper bottle. As the video shows, if the drop doesn't roll from the strip effectively to create a drop, the tip of the strip can be gently touched to the bulbar conjunctiva that covers the sclera.

I avoid touching the tip directly to the cornea, as this can leave a denser footprint of stain, that can be misinterpreted as uptake. In some cases, instead of using the eyewash bottle as you see in the first video, I'll soak cotton balls, and use them to squeeze a smaller volume with less intense spray effect, than what comes from the nozzle of the bottle. In general I discourage the use of a syringe of eyewash with the strip

inside the syringe, to apply the stain, as it's easy to sort of inadvertently dilute overly dilute the stain, and cause a false negative result. If you prefer the syringe method, I suggest using a fixed volume of no more than 0.2 to 0.3 mLs of fluid, as this would be closer to the volume of a few drops.

Diagnostic Tests: Intraocular Pressure



I'll discuss tonometry more, when we cover intraocular causes a feline red eye. While this is an important basic ocular diagnostic test, there are specific signs of intraocular disease that would trigger the recommendation to prioritize this basic ocular diagnostic test for your patients. A cloudy cornea, infiltrate in the anterior chamber, and a fixed and dilated pupil are three specific signs that would prompt me to recommend tonometry to a client. When I make this recommendation, I find it important to explain that tonometry is a screening tool for glaucoma and uveitis-- both causes of red eye in a cat.

At K. State we use the rebound tonometer. And as seen in the video, a small probe is deployed from the instrument, to gently make contact with the cornea. The instrument then measures the velocity of the probe as it returns to the instrument home base. And this extrapolates the IOP for a display on a digital readout screen as you can see on the right-hand side of the slide.

Cats are measured under the dog setting, which is denoted by the letter D on the left-hand part of the digital readout. Remember that intraocular pressure range in cats shifted a little bit higher than dogs, with normal often ranging from between 10 and 15 to around 30 millimeters mercury. Tonometry's an essential diagnostic for screening of intraocular causes of feline red eye. But this test may be skipped, if the physical exam points more to a surface ocular cause. Particularly if the client has budgetary constraints.

Feline Herpesvirus-1 (FHV-1) Surface Ocular Disease

● General clinical signs

- Conjunctival hyperemia
- Chemosis
- Swelling/mass effect
- Ocular discharge
- Blepharospasm



Conjunctival hyperemia, chemosis,
serous ocular discharge

We'll devote a fairly significant portion of the presentation to a discussion of feline herpes virus surface ocular disease. Herpes virus is arguably the most common cause of surface ocular disease and the presenting complaint of a red eye in cats. Feline herpes virus is a species specific, alpha herpes virus, that has a hallmark feature of neuronal latency. This means that every kitten or cat that experiences a primary infection, will go on to become a lifelong carrier and may suffer from periodic reactivation of the virus with resultant clinical signs.

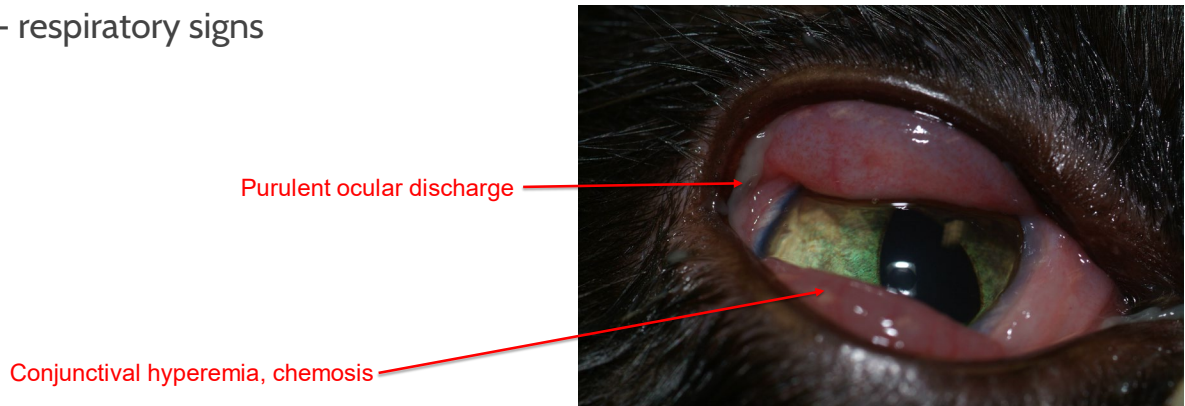
The virus is spread in the ocular, respiratory, and oral secretions of infected cats. And it's highly contagious. Though it's easily killed in the environment with common disinfectants, it can readily spread from cat to cat in densely populated environments such as shelters and catteries. Primary infection typically occurs in young kittens after maternal antibodies wane and at a naive young adult cats.

Typical ocular clinical signs include-- conjunctival hyperemia which is often referred to as conjunctivitis, chemosis or conjunctivitis edema that can sometimes cause a swelling or mass effect, ocular discharge from serous or clear to purulent or yellow green, and varying degrees of blepharospasm as well. This clinical photograph provides a good illustration of the conjunctival of hyperemia, chemosynthesis, and clear or serious ocular discharge that is typical for a cat affected by ocular feeling herpes virus.

FHV-1: Conjunctivitis

- **Most common ocular clinical sign!**

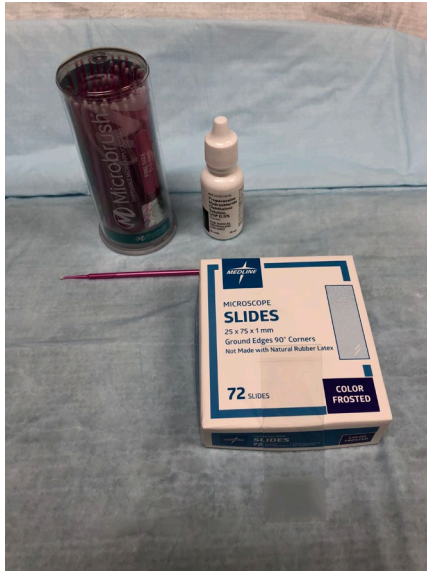
- One or both eyes
- +/- respiratory signs



Conjunctivitis is by far the most common ocular clinical sign of feline herpes virus. Primary infection usually results in signs of upper respiratory tract disease in addition to ocular clinical signs, while recrudescence later in life often causes only ocular clinical signs that can affect one or both eyes. In this clinical photograph, you can see a great example of chemosis, and how that can differ from conjunctivitis.

In addition to being hyperemic, the conjunctiva is swollen or edematous, and this results in a pillow-like appearance to the conjunctival tissue. If you look closely, you can also detect purulent ocular discharge accumulating in the conjunctival fornix, and at the medial canthus as denoted by the red arrows.

Diagnostic Tests: Conjunctival Sampling (Cytology)*



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The diagnostic test I use regularly during workup of a feline red eye that's specifically localized to the ocular surface is conjunctival cytology. While not specifically diagnostic for viral surface ocular disease, this test can lend support to your preliminary or tentative diagnosis. If you are dealing with a cat that has a red eye localized to the ocular surface, you should automatically think feline herpes virus as the number one differential diagnosis.

Viral inclusions are intranuclear though and too small to see with standard light microscopy. So instead, conjunctival cytology can be used to look for the expected types of inflammatory cells, that would accompany a viral conjunctivitis. Acutely neutrophils predominate, and more chronically lymphocytic plasmocytic inflammation would be expected.

The necessary supplies to perform conjunctival cytology, are shown in the picture on the left of the slide, and include-- a topical anesthetic such as proparacaine, a tool to collect cells, and a glass slide, in addition to the supplies you would need to stain the slide. In the first video, I'm demonstrating the correct technique for applying a drop of proparacaine to the ocular surface.

You should allow about 1 minute to elapse after the drop, before attempting to collect a sample, to ensure that adequate local anesthesia has been achieved. The anesthetic effects of proparacaine on the conjunctiva are less predictable and less profound than for the cornea. So be prepared for some cats to exhibit a reaction to the sensation of sample collection, despite having a numbing agent on board.

To collect a sample, I prefer to use small fine tipped brushes called micro brushes. These brushes were developed for use in human dentistry because their precision allows application of sealant on the teeth and other uses that require very precise movements. I like these brushes because they're affordable,

readily available with purchase options even on Amazon.com, believe it or not. And really great at capturing cells and then releasing them onto a glass slide.

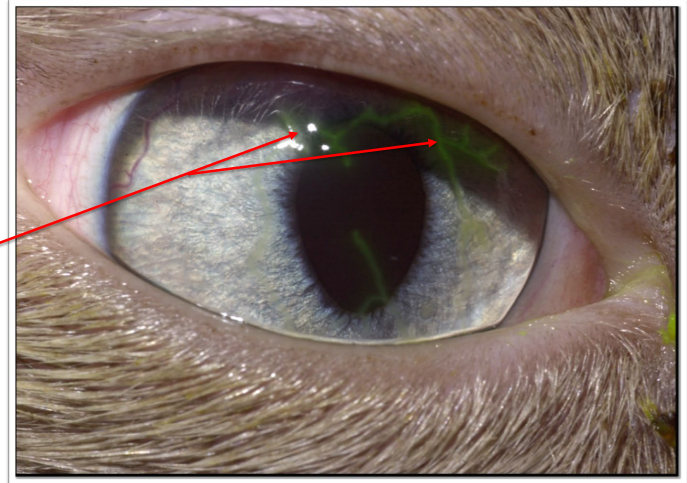
In this next video, you can see I insert the tip of the brush in the conjunctival fornix and roll it in a sweeping directional motion, before removing it and then smearing it on the glass slide for fixation and staining. In addition to looking for the characteristic but again non-specific signs of inflammation that would accompany viral surface ocular disease, conjunctival cytology allows you to screen for other causes a feline conjunctivitis that we'll discuss subsequently during the presentation.

FHV-1 Corneal Disease: Ulcers

- #2 ocular clinical sign

- Dendritic pattern early in disease
- Any ulcer is viral until proven otherwise!

Linear branching (dendritic) fluorescein positive areas of superficial corneal ulceration

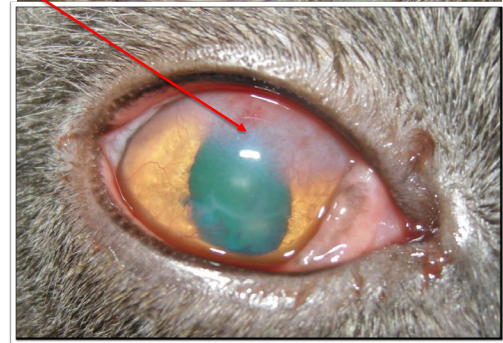
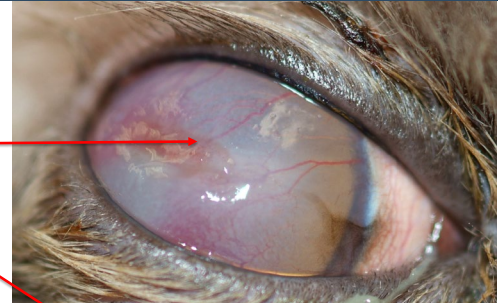
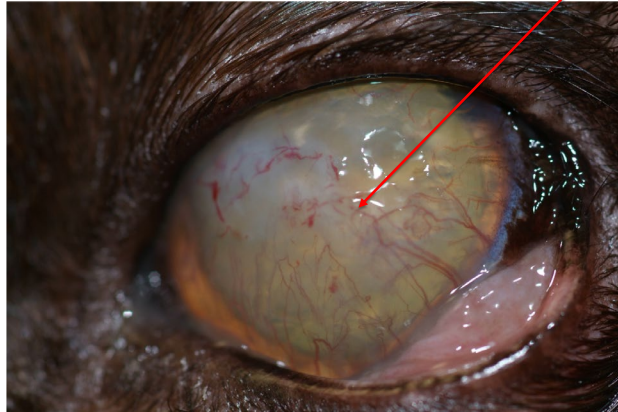


In addition to causing conjunctivitis, corneal ulceration is the second most common ocular manifestation of feline herpes virus. As seen in the clinical photo, linear branching or dendritic superficial corneal ulceration, is considered pathognomonic for a viral corneal ulcer. However, this pattern to the corneal ulcer tends to develop quite early in the course of disease. These linear branching areas often coalesce into broader areas of geographic superficial ulceration by the time a cat's presented for evaluation. And for that reason, in my experience, any feline corneal ulcer is viral until proven otherwise. There are so few so few things besides feline herpes virus that cause ulcers in cats, making the diagnosis straightforward when a superficial ulcer is detected.

FHV-1 Corneal Disease: Keratitis (non-ulcerative inflammation)

- Immune-mediated

Superficial to mid stromal corneal vessels, cellular haze, edema



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Conjunctivitis and corneal ulceration are by far the most typical manifestations of viral surface ocular disease that you'll encounter in practice.

I thought it'd be interesting though to briefly highlight some of the less common types of viral surface ocular disease that may be seen. We'll focus later in the presentation on treatment of the traditional form of viral surface ocular disease that occurs due to active virus replication. And here just mentioned what to look for that may indicate you're dealing with an odd, atypical manifestation of feline herpes virus in select cats.

Immune mediated keratitis should be considered in a cat presenting with signs of corneal inflammation in the absence of a corneal ulcer or significant conjunctivitis. When feline herpes virus is actively replicating, it's invading the host's epithelium to take over the host cell machinery and make new virus, resulting in clinical signs of conjunctivitis and corneal ulceration. If you examine a cat with corneal vascularization, a haze of cellular infiltrate, and variable amounts of edema as illustrated in these clinical photos, the next step is to perform fluorescein staining. If stain negative, you should consider immune mediated, also called stromal keratitis. This particular manifestation of feline herpes virus, occurs when the surface ocular immune system reacts to the presence of sequestered virus within the corneal tissue. The inflammatory reaction is often intense as depicted in the photos, but there is an absence of corneal ulceration, and this indicates that there is not actively replicating virus at the ocular surface.

FHV-1 Corneal Disease: Keratitis (non-ulcerative inflammation)

- **Neurotrophic: Trigeminal (CN V) neuropathy**
 - Corneal inflammation in a *comfortable* eye

Superficial corneal ulcer

Corneal vascularization and cellular haze; NO blepharospasm



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Stromal keratitis is accompanied by varying degrees of blepharospasm. If you examine a cat with evidence of corneal inflammation in a comfortable eye, especially for corneal ulcers concurrently present, you should think about a neuropathy impacting the trigeminal nerve. The trigeminal nerve, remember, is a cranial nerve that supplies sensation to the cornea. Its ganglia are also a well described site of neuronal latency a feline herpes virus.

Trigeminal neuropathy, due to nerve damage induced by the virus, is a well described complication of herpes simplex keratitis in people. Though uncommon, I've occasionally diagnosed a neurotrophic keratitis in cats with a history of herpetic surface ocular disease, presumably due to a similar mechanism as what occurs in people with herpes simplex trigeminal neuropathy. Again the key to making this diagnosis is to look for signs of ulceration, and inflammation, in a comfortable eye.

Such findings in the absence of ocular pain, should automatically prompt you to pause, and reflect on this conflicting information. Ulcers should be painful. So why isn't the cat squinting? The most likely explanation would be a viral trigeminal neuropathy, causing corneal inflammation and ulceration secondary to hypoesthesia or desensitization of the cornea. Note the complete absence of any outward signs of ocular pain and the cat in this photo, with evidence of a large superficial corneal ulcer and intense corneal inflammation.

FHV-1: When and How to Treat?



- Is it a primary infection or recrudescent flare-up?
- How severe are the clinical signs?
- Is there a corneal ulcer?

- Topical vs. Systemic?
- Duration?

After reviewing the various clinical manifestations of viral surface ocular disease, we'll now move on to discuss treatment. Prior to initiating therapy, there are several questions I ask myself in every cat that I manage with presumed herpes virus surface ocular disease. First, am I dealing with primary infection or a viral flare up resulting in recrudescent disease? And the answer to this question, specifically informs my recommendations on supportive therapy.

Primarily infected kittens and cats generally exhibit signs of systemic disease and benefit from prophylactic systemic antibiotics, to prevent secondary bacterial respiratory tract infections, as well as more intensive supportive care with fluids and different tactics to stimulate the appetite. Since this presentation is focused more on the ocular manifestations of feline herpes virus, supportive care and other considerations for systemic support are beyond the scope of our discussion today.

Many cats I manage are experiencing an episode of virus reactivation, and this is often manifest exclusively within the ocular surface, sometimes only in one eye. Other questions I ask myself, are how severe are the clinical signs? And is there a corneal ulcer present? These questions complement each other as a corneal ulcer is generally considered more significant manifestation of viral surface ocular disease. If there is moderate to severe conjunctivitis, signs of ocular pain in the form of blepharospasm that is moderate to severe in intensity, or if an ulcer is present, these criteria help guide my decision on whether to prescribe antiviral therapy. Remember, most cats with a competent immune system, will be able to mount a defense against reactivated herpes virus, with a competent immune system. And if clinical signs are mild intervention with specific targeted antiviral treatment, may not be necessary.

However, if any of the aforementioned criteria are met, I then ask myself whether to select a topical, or systemic route for antiviral therapy. And also how long to treat. We'll cover the answers to these last two clinical questions as we discuss treatment options in the next few slides.

FHV-1 Antiviral Therapy: Topicals



● Cidofovir 0.5%

- BID
- Must be compounded
- Fairly expensive (~\$80 per 5 ml)
 - ~\$16 per ml

● Idoxuridine 0.1%

- \geq QID
- Must be compounded
- Relatively inexpensive (~\$42 per 15 ml)
 - ~\$2.80 per ml

I choose topical antiviral therapy if clinical signs are exclusively ocular. The two main options I use are cidofovir and idoxuridine. There are no commercially available approved antiviral therapies for cats in the United States. So these medications must be compounded. When deciding which of these to prescribe a major benefit of cidofovir is that it can be used twice a day, as compared to idoxuridine, which must be used at least four times a day. A drawback of cidofovir is cost, it's roughly five to six times more than idoxuridine. So if a client is working with a more limited budget I will prescribe idoxuridine. Again the major trade off is frequency of administration. We know that the biggest risk factor for reactivation of feline herpes virus is stress. So if a cat hates receiving topical ophthalmic medications, treatment may be counterproductive. This is especially true if the treatment frequency is more than a few times a day. When considering duration of treatment, it's important to remember that all the antiviral drugs that we work with are viristatic, not viricidal. This means that the drug slows down actively replicating virus, but it doesn't kill the virus. Knowing this, it makes sense to treat at least one to two weeks after clinical resolution. Doing so, you decrease the risk of a relapse in the form of a flare up in virus replication, if treatment is stopped too abruptly. For any given case, you would continue drop therapy for a week after corneal ulcer resolution, or after the conjunctivitis has fully resolved.

FHV-1 Antiviral Therapy: Oral

● Famciclovir

- Pro-drug of penciclovir
- Must be metabolized to active form in the body
 - Hepatic metabolism
 - Renal excretion
 - Reduced *frequency* with CKD
- Current recommendation: 90 mg/kg PO BID (~500mg per cat BID)

Blepharospasm,
serous ocular discharge



Conjunctival hyperemia, chemosis,
serous ocular discharge



There is only one choice for oral antiviral therapy, so that makes this part of the discussion quite easy. I use this round of treatment if there are concurrent respiratory signs, or if the cat is unable to experience a stress-free topical drug administration. Famciclovir is the oral prodrug of Penciclovir that must be metabolized to its active form in the cat's body. It undergoes hepatic metabolism and renal excretion. It's generally a well-tolerated drug though due to renal excretion, it's recommended that the dosing frequency be reduced in cats with chronic kidney disease. And this recommendation is extrapolated from what's been recommended in people with kidney disease receiving famciclovir. A lot of really excellent research has been conducted at University of California at Davis, to determine an effective dosing recommendation that will achieve therapeutic drug levels in cats.

And the current recommendation is 90 milligrams per kilogram by mouth every 12 hours. This works out to be approximately 500 milligrams per cat, every 12 hours in an average sized 5 kilogram cat. The clinical photos depict a distance view on the top, and a close up on the bottom of the left eye of a cat affected by viral conjunctivitis. This cat is exhibiting blepharospasm, conjunctival hyperemia, chemosis, and serous ocular discharge. So all of the major clinical signs of viral surface ocular disease.

In this case, in the absence of respiratory signs, I would prescribe a topical antiviral. If the cat was intolerant of topical therapy, I would then prescribe oral famciclovir. Based on recent research, it's important to use FDA approved famciclovir tablets, rather than compounded tablets or suspensions. A recent study demonstrated that compounded famciclovir formulations, did not contain an accurate amount of drug, when compared to the labeled content, had variability on drug content in batches from different pharmacies, and that the drug content changed over time in all compounded formulations.

FHV-1 Treatment: Other

- **Ulcer-specific**
 - Prophylactic topical antibiotics
 - Debridement (cotton swab)
- **Lysine**
 - 500 mg PO BID

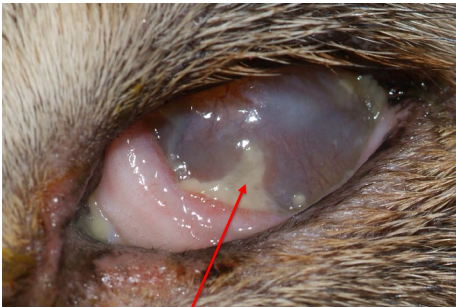


Other treatments are sometimes indicated for viral surface ocular disease. Prophylactic topical antibiotics should be prescribed for corneal ulcer is present, in order to prevent secondary bacterial infection of that ulcer. Cotton swab debridement can be performed after application of topical anesthetic, if redundant loose epithelium is appreciable at the borders of the ulcer. This serves the dual purpose of physically debulking the viral load from the ocular surface, and removing dead non-appearance epithelium. L-Lysine-- an immune booster that competitively inhibits arginine, an essential amino acid for viral replication, can be used at a dose of 500 milligrams by mouth every 12 hours. There are plenty of very palatable formulations of lysine available on the veterinary market today.

FHV-1 Surface Ocular Disease: When to Refer?

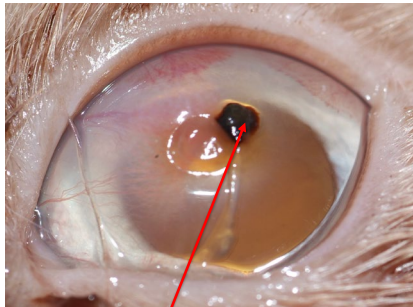
- **Complicated viral ulcers**

Bacterial infection



Corneal cellular infiltrate, stromal loss

Sequestrum



Necrotic corneal plaque

Symblepharon



Adhesions between conjunctiva and cornea

With the exception of unusual immune mediated neurotrophic manifestations of viral surface ocular disease, I consider everything we've discussed so far to be reasonable for you to manage in practice. There are a few exceptions, and things to look for that may indicate referral would be the best option if feasible. There are three specific instances when a case of herpetic surface ocular disease should be referred, in case a surgical treatment option may be indicated. If a viral ulcer becomes complicated by bacterial infection and stromal loss, referral may be indicated for surgical stabilization, depending on the degree of depth or stromal loss.

In the image on the left of the slide, you can see a dense area of cellular infiltrate in the cornea. And though it's difficult to appreciate, there's also area of shallow stromal loss. This case example would be best served with intensive medical therapy to control the bacterial infection. Ulcers with significant depth, maybe surgically stabilize though with procedures such as conjunctival pedicle grafts, or a corneal conjunctival transpositions.

The best tip is to look for evidence of a divot or visible indentation on the surface of the cornea, that retains fluorescein stain during your exam. Some cats with chronic non healing ulcers which is often the case with herpetic ulcers, are at risk for development of a corneal sequestrum as shown in the center image. While spontaneous sloughing can occur leading to self-resolution, it's often difficult to judge the depth of involvement of the corneal tissue with the sequestrum.

Deeper sequestrae, can leave a significant defect, if left to spontaneously slough. And therefore the best option when a sequestrum is diagnosed to offer referral, as surgical removal and possible grafting to reinforce the weakened area of the cornea, may be indicated. Corneal sequestrae are a very unique feline

corneal disease, with a characteristic appearance of amber brown to black plaque like lesions on the corneal surface.

Finally, symblepharon, is a complication of often severe herpetic conjunctivitis, and corneal ulceration. This complication occurs more frequently in young primarily infected kittens, and then follows them into adulthood. Symblepharon develops when the ulcerated conjunctival tissue contacts the ulcerated cornea leading to a permanent adhesion forming between the two surfaces of the ocular tissues.

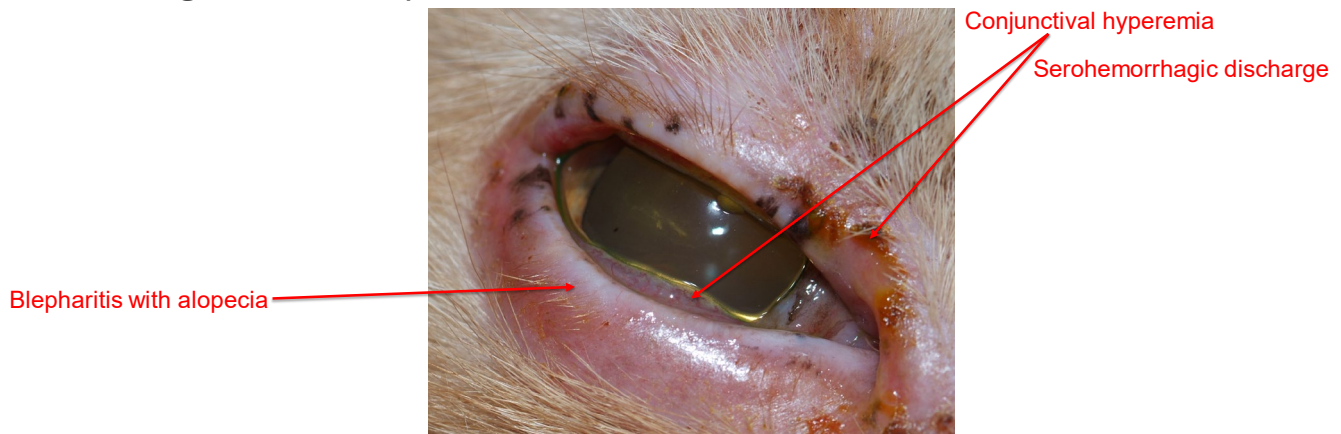
As seen in the photo on the right of the slide, significant corneoconjunctival symblepharon while non painful, can be blinding as it obscures the ability of the cat to see through the opaque cornea. If caught early, there are sometimes procedural or surgical treatment options to break apart the adhesions and prevent them from reforming. Though to be quite honest, symblepharon can be quite challenging to manage, particularly if this severe.

Putting aside these few complications that may require a referral, the typical uncomplicated viral surface ocular disease, may seem fairly straightforward to manage based on the information I summarized in this presentation. However, the interaction between the host cat's immune system and the virus is quite complex and sometimes very unpredictable, which can pose a significant challenge in case management. While it's unlikely that I'll be able to offer anything more than you can do in general practice, with most uncomplicated viral surface ocular disease cases, you may want to consider recommending referral if you aren't making much headway with your initial treatment.

FHV-1 Client Communication

- **Client education tips:**

- Primary infection, then *lifelong carrier state*
- Reactivation of latent virus during periods of stress
- Drugs slow virus replication but don't kill virus



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I find it extremely important to take the time to provide a few basic client education tips when dealing with a cat with feline herpes virus. First, clients must understand that cats are lifelong carriers after they recover from primary infection. It's estimated that more than 80% of domestic cats are carriers of feline herpes virus. Primary infection doesn't mean that a cat will have chronic problems as a carrier for the rest of its life, but this can be very difficult to predict, and clients should be prepared for that possibility. Also, stress is the most significant risk factor for reactivation of latent herpes.

This includes-- environmental stress, such as moving or introducing a new cat into the household, or physiologic stress, such as an illness. Finally, when treating active herpetic disease, drugs slow virus replication, but don't kill the virus. Therefore treatment is required for a period of time beyond clinical remission. It's also important to emphasize that treatment should not be stressful. If a cat is intolerant to drops or won't eat pills, the owner should communicate that issue with you promptly, so you can work as a team to develop another approach.

Having to wrap a cat in the infamous kitty burrito towel to give drops, or drag the cat out from a hiding spot under the bed to shove a pill down its throat, are completely counterproductive to the process of treating active feline herpes related disease.

This final clinical photograph of a cat with a viral surface ocular disease, is a great summary of the most common clinical signs of conjunctivitis and ocular discharge. And additionally, you can appreciate a mild marginal blepharitis or inflammation of the eyelids with hair loss. These eyelid signs are not something we covered yet in the presentation, we sometimes see dermatologic manifestations of herpes virus in the ocular skin area, or on the face. Or another possibility for this particular example is a drug reaction. If you see the signs develop in a cat already undergoing treatment for herpetic surface ocular disease. I've

occasionally seen cats have a sensitivity reaction to cidofovir specifically, which manifests as blepharitis and alopecia of the eyelids.

Other Causes of Feline Conjunctivitis: What if It Isn't FHV-1?

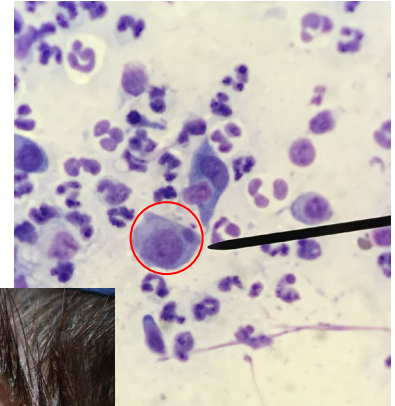


- **How do we prove it's herpetic? Or rule FHV-1 out?**
 - Clinical appearance
 - When you hear hoofbeats... look for horses, not zebras!
 - Response to treatment
 - Are the antivirals working?
 - +/- diagnostic testing
 - Limited clinical benefit
- **Maybe it's something else...**
 - Other infectious
 - Immune mediated
 - Inflammatory (sterile)
 - Neoplastic

Well as promised, about half of this presentation has been devoted to covering the topic of viral surface ocular disease, resulting in a feline red eye. It bears mentioning at this point, I'm not a big believer in specific diagnostics such as PCR, in an attempt to diagnose feline herpes virus. Rather, I rely on history, clinical signs, response to treatment and sometimes conjunctival cytology as a supportive diagnostic. The old saying to look for horses when you hear hoofbeats, rather than zebras, is definitely applicable in the management of feline red eye localized to the ocular surface. The majority of cats with conjunctivitis, and essentially all cats with corneal ulcers, are experiencing herpetic surface ocular disease. Response to therapy, though somewhat variable, and difficult to predict from cat to cat, is a fairly reliable way to confirm that you're on the right track with your presumptive diagnosis. And beyond using conjunctival or cytology as a supportive diagnostic tool, I find specific diagnostic testing for feline herpes virus to be of limited clinical benefit. It doesn't really change what I'm going to do, at least initially. And I know that most cats are carriers for herpes virus and experience episodes of viral reactivation during life. So I use that knowledge, combined with history, clinical signs, and response to therapy, to make the diagnosis. But there are certainly times when I'm wrong, and herpes can't always take all the blame. So what else could it be? That will be the focus of the remainder of the presentation, and we'll specifically cover other infectious causes of feline conjunctivitis, as well as immune mediated, inflammatory, and neoplastic causes.

Conjunctivitis: Other Infectious

- **Bacterial: *Chlamydia felis***
- **Obligate intracellular organism**
- **Clinical signs**
 - Conjunctivitis but *no ulcers*
 - Often unilateral, young (<5 years old)
 - Lymphoid follicles possible
- **Diagnostics**
 - Cytology, PCR
- **Treatment**
 - Topical and/or *systemic* tetracyclines
 - T-QID Oxytetracycline (Terramycin®) ointment
 - 10 mg/kg/day, divided into BID dosing
- **Referral?**



There are two other infectious etiologies, both bacterial, that have been implicated in causing feline conjunctivitis. The most significant organism is *Chlamydia felis*, an obligate intracellular organism, that causes conjunctivitis but notably not corneal ulcers. This can be a distinguishing clinical feature between chlamydial conjunctivitis and viral conjunctivitis. Chlamydial conjunctivitis often occurs unilaterally in younger cats, and the organism sometimes triggers an immune response with prominent lymphoid follicle development within the conjunctiva, as depicted in the clinical photograph on the bottom of the slide. The organism can persistently infect the respiratory, gastrointestinal, and genitourinary tracts, which explains why relapse may occur following topical therapy alone. Intracytoplasmic inclusions are sometimes detectable on conjunctival cytology, as shown in the photo micrograph on the top corner of the slide. Identification of basophilic, perinuclear and intracytoplasmic inclusions, allows you to make the diagnosis.

As we discussed previously conjunctival cytology can be helpful as a diagnostic tool in the work up a feline conjunctivitis. And this is particularly true when deciding on viral versus chlamydial causes of conjunctivitis. However, intracytoplasmic inclusions, can be easily missed depending on the quality of the sample, and molecular diagnostics such as PCR, are the preferred diagnostic tests to confirm chlamydial conjunctivitis if necessary.

Vigorous swabbing is necessary to ensure that enough epithelial cells are collected to obtain a diagnostic quality sample, and for treatment tetracyclines of the drug of choice. Similar to the approach with management of viral surface ocular disease, the decision regarding route of therapy may initially be based on whether non-ocular clinical signs are present. Topical oxytetracycline, or Terramycin ointment, three to four times a day, can be prescribed if the clinical signs are exclusively ocular.

If respiratory signs are present, or if you're dealing with a case refractory to topical therapy, oral tetracycline can be prescribed at a dose of 10 mgs per kg per day, divided into twice daily dosing. Referral for management of chlamydial conjunctivitis cases, is generally unnecessary. Unless you manage a particularly challenging case, in which advanced diagnostics such as conjunctival biopsy to confirm the diagnosis, may be helpful.

Chlamydial Conjunctivitis: Client Communication



- Risk of esophageal stricture
 - Wrap capsules, provide water bolus with each dose
 - Pradofloxacin alternative therapy
 - 5-7.5 mg/kg PO q 24 h x 6 weeks
- Prolonged course of treatment
 - 3-4 week minimum with doxycycline
 - Recommended to treat beyond clinical resolution
- Zoonotic?
 - *C. psittaci*

From a client education, or communication standpoint, the discussion is somewhat simpler for chlamydial conjunctivitis than for viral surface ocular disease. Though cats may be chronic carriers of chlamydia in the respiratory gastrointestinal and genitourinary tract, generally systemic therapy helps to clear them when they are affected in these areas. Since the main systemic treatment is doxycycline, clients should be instructed to wrap capsules in pill packets or another ingestible barrier material, and to provide a water bolus with each dose. This is to ensure that the cat will mix it into the stomach promptly, so as to prevent contact with the esophageal lining, and the risk of stricture. Alternatively, pradofloxacin can be used at a dose of 5 to 7 and 1/2 milligrams per kilogram by mouth every 24 hours, for a total of six weeks. I generally advise against the use of any other fluoroquinolone, especially enrofloxacin or Baytril, due to reports of retinal toxicity and blindness in some treated cats.

A prolonged course of treatment usually a minimum of three to four weeks, is necessary with tetracyclines. And finally though there is zoonotic potential with some chlamydial species, specifically chlamydia psittaci. Cases of chlamydia felis conjunctivitis in people are rare. So it's worth mentioning to owners that of cats that are diagnosed with chlamydial conjunctivitis, that they should practice good hygiene when interacting with the affected cat, including thorough handwashing, before and after administering treatments.

Conjunctivitis: Other Infectious

- **Bacterial: *Mycoplasma felis* and *gateae***

- Role as pathogen?
- Conjunctival and URT commensals
 - Co-infection?

- **Clinical signs**

- Unilateral conjunctivitis

- **Diagnostics**

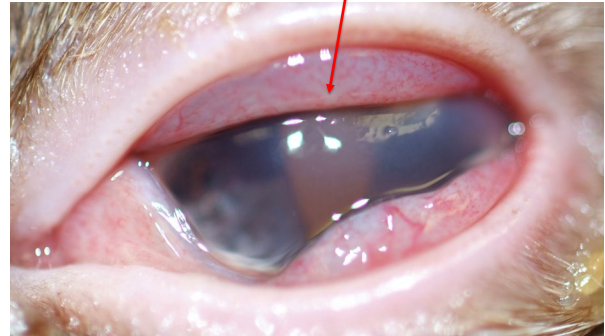
- Cytology, PCR
 - Cell associated - requires vigorous swabbing

- **Treatment**

- Tetracyclines or fluoroquinolone (same as for chlamydial conjunctivitis)

- **Referral?**

Conjunctival hyperemia and chemosis



The other potential bacterial etiology of feline conjunctivitis is mycoplasma. Specifically *mycoplasma felis* and *mycoplasma gateae*, though the role of mycoplasma organisms as primary conjunctival pathogens is somewhat questionable. Mycoplasma species are also found as part of the normal feline ocular surface in upper respiratory tract of bacterial flora, so the direct role as a cause of conjunctivitis might be difficult to prove. When present, it's speculated that mycoplasma overgrowth occurs as part of a co-infection, with another more pathogenic organism. The clinical signs of mycoplasma conjunctivitis share much overlap with chlamydial conjunctivitis, with unilateral involvement in a younger cat, no corneal ulceration present concurrently. Unlike chlamydial conjunctivitis however, mycoplasmal conjunctivitis has not been associated with the development of prominent lymphoid follicles. So this gives you another clue into trying to initially distinguish during examination, between the potential etiologies of infectious conjunctivitis in a cat. Diagnosis and treatment of mycoplasma conjunctivitis are also the same as for chlamydia conjunctivitis, making the definitive diagnosis of mycoplasma as the primary pathogen really less important. Because of the cell associated nature of the organism, just like with chlamydial sampling, vigorous swabbing is necessary to obtain a diagnostic quality sample for PCR.

Culture can be performed to try and confirm mycoplasmal conjunctivitis but requires special media and handling, that may take days to weeks to complete. Also, conjunctival swabs are considered a poor source of sample for culture, when compared to blood, synovial fluid, or other bodily fluids. Mycoplasma is generally considered fairly wimpy and responsive to the treatment that we would already be employing in terms of antibiotics for a bacterial conjunctivitis in a cat.

As with chlamydia conjunctivitis, referral is generally not indicated, unless you're dealing with a particularly refractory case.

Mycoplasmal Conjunctivitis: Client Communication



- Risk of esophageal stricture
 - Wrap capsules, provide water bolus with each dose
 - Pradofloxacin alternative therapy
 - 5-7.5 mg/kg PO q 24 h x 6 weeks
- Prolonged course of treatment
 - 3-4 week minimum with doxycycline
- Zoonotic?
 - Unlikely

Just briefly, as with chlamydia or conjunctivitis, client communication discussion is focusing on mitigation of the possible side effects of treatment with mycoplasmal conjunctivitis, as well as preparing the client for a prolonged course of therapy. Doxycycline therapy is the first choice. Care again should be taken to advise clients on how to avoid the risk of esophageal stricture, and pradofloxacin would be an alternative antibiotic as with chlamydia or conjunctivitis. The zoonotic potential of *Mycoplasma felis* and *Mycoplasma gateae* is even less than for *Chlamydia felis*, though I again always encourage hygiene and clients administering treatments to my patients.

Conjunctivitis: Other Infectious

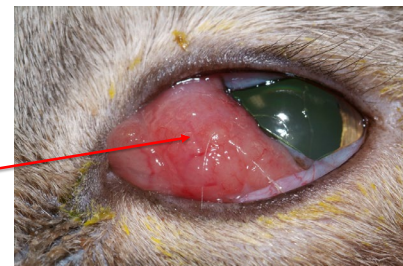
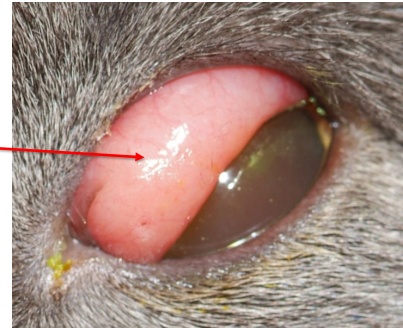
- **Fungal: Adnexal histoplasmosis**

- *Histoplasma capsulatum*

Palpebral conjunctival swelling/mass effect

- **Clinical signs**

- Mass effect/proliferative tissue
- Most common on TEL and palpebral conjunctiva/lid margin
- Concurrent uveitis or systemic disease?
 - Vision loss (chorioretinitis)
 - Weight loss



Thickening and proliferation of TEL conjunctiva

One other infectious agent that may target the feline ocular surface, is *Histoplasma capsulatum*. It's a dimorphic fungus found in bat and bird feces. The root of infection is inhalation of spores, and disseminated histoplasmosis, often results in nonspecific general clinical signs of chronic weight loss, decreased or absent appetite, and anemia. Fungal agents in general are highly regionally specific, and the Midwestern United States where I practice is an endemic area for histo.

Ocular lesions may develop along the adnexa, which refers to the ocular structures excluding the eye itself, such as-- the eyelids, the conjunctiva, and the third eyelid. The most common sites of adnexal involvement include third eyelid and palpebral conjunctiva, near the lid margin, as depicted in these two clinical photographs. Adnexal histo typically results in a focal mass like lesion, rather than a diffuse non-specific conjunctivitis as we've discussed with the other infectious causes of conjunctivitis. And this might provide a clue on prioritizing the differential diagnosis list and targeting diagnostic testing, during your initial exam. It's generally expected that at adnexal histo, may be an ocular manifestation of systemic disease, as is the case in cats presenting with disseminated histo and uveitis, or concurrent non-ocular clinical signs such as chronic weight loss. Though ocular adnexal lesions are considered uncommon, histo should be ruled out for an inflammatory ocular adnexal lesion, in a cat living in an endemic area.

Adnexal Histoplasmosis

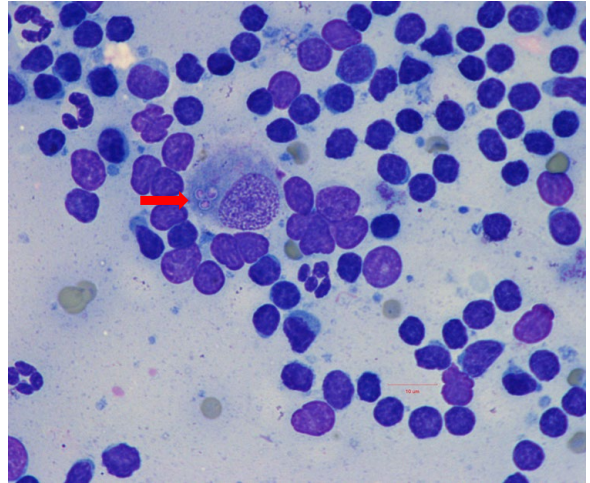
● Diagnostics

- Cytology: 2-4 μm with clear thin rim
- Biopsy with histopathology
- Systemic screening?
 - Antigen testing
 - Imaging

● Treatment

- Fluconazole 50 mg/cat PO q 12 hours
- +/- oral prednisolone
- +/- topical anti-inflammatory

● Referral?



The photo micrograph from an adnexal lesion cytology sample, shows fungal organisms within a macrophage. Lesions may also be identified on biopsy with histopathology. The organisms are really tiny, at 2 to 4 micrometers in size, with a clear thin rim that surrounds them. Histo can also be identified in monocytes circulating in the body via blood smear, or by sampling the other affected organs such as the liver, under ultrasound guidance.

A thorough physical exam should be performed in any cat with any suspected or confirmed ocular adnexal histo lesion, so that the cat can be staged for disseminated involvement. In addition to thoracic and abdominal imaging with sampling of lesions, antigen testing through Miravista laboratories, can be performed on serum or urine, and the test is considered highly sensitive and specific. Treatment of disseminated histo consists of systemic antifungal therapy. My preference for good ocular penetration is oral fluconazole, at 10 milligrams per kilogram, or 50 total milligrams per cat every 12 hours. With a predilection for the lungs, histo may also cause respiratory distress when treatment is initiated and fungal die off leads to airway inflammation, and for this reason thoracic radiograph should ideally be performed to evaluate the lungs before starting antifungal therapy. And some clinicians advocate starting an anti-inflammatory dose of oral steroids at the time of initiating antifungal therapy, in order to mitigate the risk of respiratory distress.

Generally the adnexal lesions respond well, to systemic antifungal therapy, as there is a good blood flow to the adnexa, and effective delivery of oral fluconazole, is achieved to those lesions. However, topical nonsteroidal or steroid inflammatory, can be prescribed as needed for symptomatic control of inflammation associated with the lesions. Referral is indicated in cases of ocular adnexal histo if you are

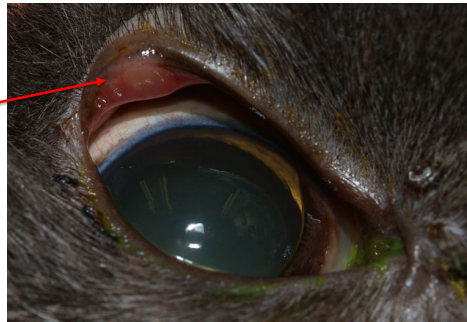
uncomfortable obtaining a sample of the lesion, due to its location, or if there are not obvious non ocular physical exam abnormalities to help guide the diagnostic workup. As ocular adnexal lesions are likely a manifestation of disseminated histoplasmosis, referral to a facility with ophthalmology and internal medicine specialists would be beneficial for an affected cat in most cases.

Adnexal Histoplasmosis: Client Communication

- **Prolonged course of therapy for disseminated disease**

- Minimum 4-6 months
 - When can treatment safely be stopped?
- Periodic monitoring to ensure tolerance of therapy
 - Voriconazole as an alternative to fluconazole

Focal thickening of palpebral conjunctiva, ulceration at lid margin



Feline Red Eye: At the Surface

More than for any other form of feline conjunctivitis, prognosis is an important part of the conversation with the client, when discussing the diagnosis of adnexal histo. This form of conjunctivitis should truly be considered an ocular manifestation of systemic disease in most cases, and prognosis depends on the degree of involvement of non-ocular areas of the body associated with the disseminated fungal disease. Screening or staging a cat with adnexal histo is key to determine prognosis for response to treatment, and ultimately for survival. The duration of treatment is quite lengthy, usually a minimum of four to six months, and an antigen test is handy not just from the initial diagnosis standpoint, but also as a guide for cessation of treatment, as a negative test can be confirmed prior to discontinuing therapy, and this ensures it's safe to stop therapy.

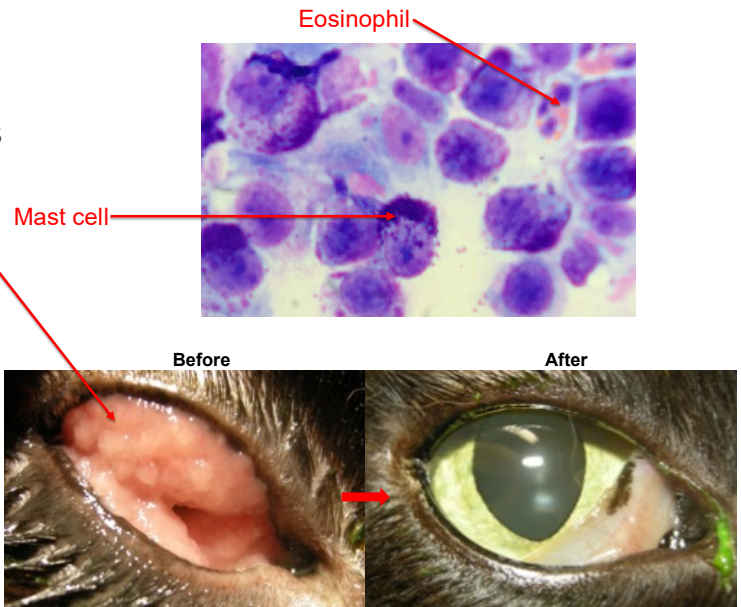
Then the patient can be retested once more-- one to two months after discontinuing therapy, to ensure that the antigen detection status remains negative. Due to the potential for fluconazole to cause hepatotoxicity, liver enzymes should be serially evaluated during the course of treatment, and my general approach is to check a baseline before treatment, at two weeks after treatment, at one month after starting treatment, and then every one to two months for the duration of treatment.

For cats intolerant of fluconazole due to GI hepatic side effects, you can start by reducing the dose and sometimes consider other antifungal options, but this should really be determined based on consultation with an internal medicine specialist.

The clinical photograph on the slide, fix another manifestation of ocular adnexal histo, those diagnosed on conjunctival cytology, of the focal thickening of the palpebral conjunctiva, and ulcerated lid margin.

Conjunctivitis: Other → Immune-mediated

- Eosinophilic conjunctivitis
- Clinical signs
 - Irregular, proliferative conjunctival lesions
- Diagnostics
 - Cytology!
- Treatment
 - Topical steroids
 - Topical compounded megestrol acetate 0.5%
 - In cats at risk for herpetic reactivation
 - Other
- Referral?



Switching gears from the discussion of infectious causes of feline conjunctivitis, we'll now review immune-mediated sterile inflammatory and neoplastic causes to wrap up the presentation. Eosinophilic conjunctivitis, is a unique form of immune-mediated conjunctivitis in cats. It more commonly affects the cornea and is called eosinophilic keratitis in those cases. But the conjunctiva can be involved exclusively or as a component of eosinophilic surface ocular disease that also involves the cornea. Eosinophilic lesions, consist of proliferative irregular areas of the conjunctiva that are most often diffuse. And the exact cause of this condition, is not well understood, but considering that mast cells and eosinophilic or recovered with cytology, and diagnostic for the disease, an allergic etiology has been speculated.

Interestingly, cats with the eosinophilic conjunctivitis, don't appear to be at risk for the development of eosinophilic granuloma complex, and vice versa is also true. Eosinophilic conjunctivitis is generally very responsive to topical steroid therapy. Due to the risk of reactivating latent herpes virus, this is truly the only feline surface ocular condition, for which topical steroids initially indicated. Prednisolone acetate, or dexamethasone, which is present within a neopolydex suspension are commonly used, and hydrocortisone is avoided because it's not as potent, and it poorly penetrates the corneal tissue and the conjunctival tissue.

Remember that topical steroid liquids are suspensions. So they must be shaken for about 15 seconds before administration, to suspend the drug in the vehicle and effectively treat the eye. And this is a seemingly minor, but important client education tip, when discussing how to give treatments. The frequency of treatment is usually dictated by the severity of the lesion but in general a guideline is three to four times per day at the time of diagnosis, and then gradual tapering as the lesion responds to treatment.

Topical compounded megestrol acetate, was recently investigated as another option to treat eosinophilic surface ocular disease with good success. Megestrol acetate has weak glucocorticoid activity, and thus may be less likely to trigger herpetic reactivation when compared to topical steroids. Other treatments such as high concentration cyclosporine, and topical NSAIDs have also been tried with mixed results, and so might go to is to stick with either steroids, or megestrol acetate compounded topically.

Eosinophilic conjunctivitis is feline surface ocular disease that can be easily managed, in general practice and referral is generally unnecessary. As long as you're able to recognize a suspicious lesion, and sample it with cytology to confirm the diagnosis, you'll be on the right track toward managing the condition.

- Risk of reactivating latent FHV-1 with topical steroids
 - Consider alternatives
 - In cats with a history of herpetic disease
 - In cats with concurrent corneal ulceration
- Duration of treatment
 - Most cats require long term maintenance

The main client communication tip regarding management of eosinophilic conjunctivitis is the risk of reactivating latent herpes virus during the course of treatment, specifically with topical steroids. This risk must be considered in any cat receiving topical steroid therapy. And so I carefully question clients to determine if there may be a history of previous, recurrent viral surface ocular disease, and if so, I'll prescribe antivirals to be administered simultaneously during topical steroid treatment. My go to steroid sparing alternative therapy, in cats that are considered at quite high risk, has become topical compounded megestrol acetate. Unlike infectious causes of feline conjunctivitis which require a prolonged course of therapy that can ultimately be discontinued, cats with eosinophilic conjunctivitis often require some form of long-term therapy. When the lesion is controlled, my strategy is to slowly taper the frequency until the lowest dose that holds the disease in remission is achieved. And it's important to explain this to clients up front at the initial diagnosis. In my experience, some cats can be managed on very low frequency of maintenance medication, even at about once every other day.

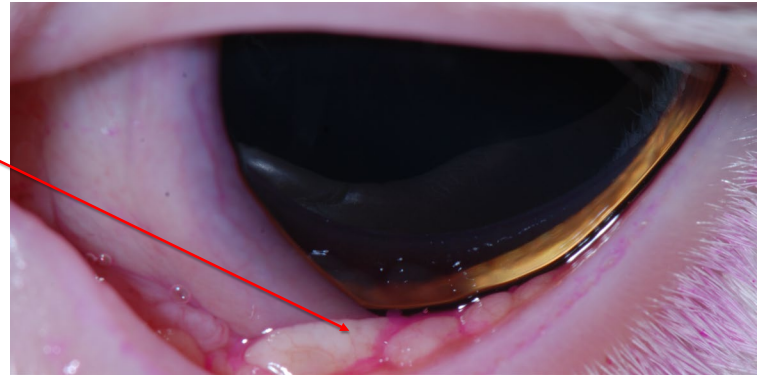
Conjunctivitis: Other → Inflammatory

● Lipogranulomatous

- Association with Meibomian glands

● Clinical signs

- Nodules along palpebral conjunctiva
- Near lid margin, more common dorsally
- More common in white-faced cats
 - Persians overrepresented



● Diagnostics

- Clinical appearance
- Histopathology

● Treatment- anti-inflammatory therapy

- Doxycycline 10 mg/kg/day, divided into BID dosing
- Prednisolone 0.5-1 mg/kg/day

● Referral?

There's an uncommon form of feline conjunctivitis associated with a sterile inflammatory process. Lipogranulomatous conjunctivitis causes a unique palpebral conjunctival reaction, in the area around the meibomian glands near the eyelid margin. Smooth tan non-ulcerated nodules that are roughly 2 to 3 millimeters in size, develop adjacent to the lid margin. The upper eyelid tends to be more commonly affected than the lower eyelid, though you can see in the clinical photo that this cat experienced lesions along the ventral eyelid. This tends to be a problem that develops in older cats, and cats with predominantly white faces, or with scant pigment are really overrepresented for this condition. Though it is rare.

The Persian breed has also occasionally been reported as overrepresented. Diagnosis is made, based on clinical appearance and sometimes biopsy with histopathology, which identifies lipid laden lakes, surrounded by macrophages, lymphocytes and plasma cells, all within the submucosal connective tissue. The pathogenesis of the condition is thought to differ from the classic meibomian gland inflammation that we sometimes see in dogs and people, but medical therapy regimen has been extrapolated from the treatment of meibomian gland inflammation in those species.

Doxycycline at the same dosing frequency as for the other conditions we discussed, as well as an anti-inflammatory dose of prednisolone have been recommended. Referral may be suggested if a general practitioner diagnoses a case of suspected lipogranulomatous conjunctivitis, given that it is rare. And if medical therapy is unsuccessful, surgical debulking of the affected tissue can be considered. And this would certainly be a referral procedure.

Lipogranulomatous Conjunctivitis: Client Communication

- Surgery in poorly responsive or severe cases
- Potential impact on tear film quality

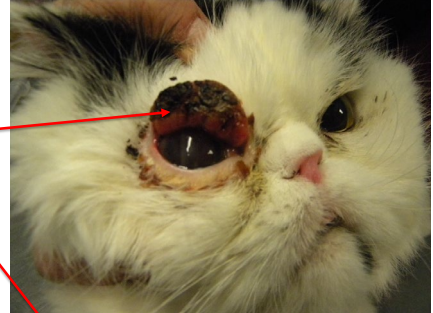


Feline Red Eye: At the Surface

Clients should be educated that surgery to debulk the lesions, may be indicated in poorly responsive or severe cases. Ideally surgery would be a referral procedure as I said before. And if it becomes necessary, prior to surgery a discussion should be had on the potential impact of the procedure on the tear film quality. Due to the close proximity of the lesions to meibomian glands, those structures would likely be damaged in surgery. And since the meibomian glands produce the lipid component of the tears, this could lead to a problem with the quality of the film.

Conjunctivitis: Other → Neoplastic

- **Lymphoma**
 - Presumed solitary (PSOL) vs. metastatic
- **Clinical signs**
 - Conjunctival mass
- **Diagnostics**
 - Biopsy with histopathology- immunophenotyping
 - Regional LN aspirates/Staging
- **Treatment**
 - Surgical excision... enucleation
 - Radiation?
 - Chemotherapy?
- **Referral?**



Feline Red Eye: At the Surface

Neoplastic causes a feline red eye, are the last topic to cover. The three types of neoplasia affecting the feline ocular surface that we will review are lymphoma, squamous cell carcinoma, and mast cell tumor. First, ocular surface lymphoma may be a primary ocular tumor, which is often referred to as presumed solitary ocular lymphoma, or it may be a manifestation of metastatic disease. Cats present with variable size, usually discrete masses affecting the conjunctiva, as seen in the clinical photographs on the slide. When compared to the alimentary hepatic splenic and renal forms of lymphoma that account for approximately 80% of lymphoma and cats, presumed solitary ocular lymphoma is considered rare. Diagnosis is straightforward with biopsy and histopathology, and phenotype is often recommended in an effort to formulate a treatment plan and to provide the client with an idea of prognosis. Staging with regional lymphoma aspirates, abdominal ultrasound to screen for metastasis from a distant site to the eye, are both important steps. For presumed solitary ocular lymphoma, surgical excision can be performed. In a case such as the cat pictured here it'd be impossible to remove the mass with clear margins, without also sacrificing the eye. Enucleation is often necessary in an effort to achieve clear surgical margins in these cases. Radiation and chemotherapy, may be options to consider if surgical margins are incomplete, or if there's evidence of distant site lymphoma with ocular involvement. Due to the rare nature of conjunctival lymphoma, and the need for advanced diagnostics and treatment, I would recommend referral to a multi-specialty institution, after making even a preliminary diagnosis, if the owner seems interested in pursuing treatment.

Conjunctival Lymphoma: Client Communication

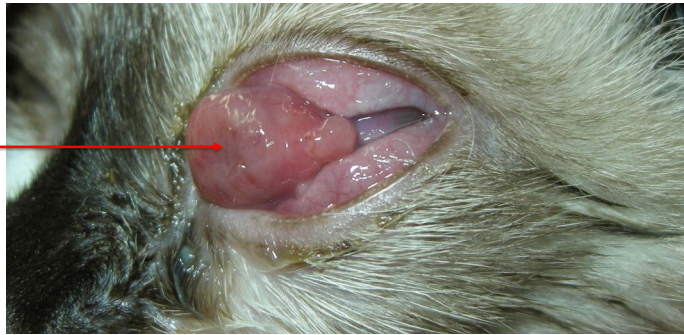
- **PSOL vs. metastatic disease**

- PSOL is rare

- **Prognosis**

- Guarded, depending on immunophenotyping, regional metastasis, etc.

Mass affecting the
TEL conjunctiva



Feline Red Eye: At the Surface

Again presumed solitary ocular lymphoma is considered rare. This clinical photo shows a conjunctival mass affecting the third eyelid ultimately diagnosed as lymphoma. If you diagnose a case of lymphoma arising from the conjunctiva on cytology or histopathology, it's important to emphasize to the client that this is more likely an ocular manifestation of systemic disease due to metastasis of lymphoma from another site. This will prepare the client understand the importance of staging the cat to screen for evidence of disease elsewhere. Immunophenotyping to determine if you're dealing with a B cell or T cell lymphoma, screening for evidence of regional metastasis, or distant site metastasis, from a distant site to the eye, will provide valuable information as a treatment plan is being developed. This information can also help you to better explain a prognosis to the client, which may inform the decision-making process with regard to what type of treatment to pursue.

Conjunctivitis: Other → Neoplastic

- Squamous cell carcinoma (SCC)

- White/poorly pigmented cats
- Outdoor exposure

- Clinical signs

- Erosive, ulcerative lesion *affecting the eyelid margin*

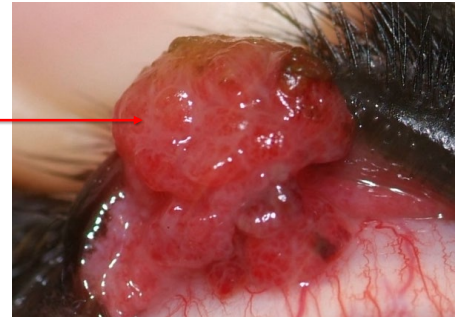
- Diagnostics

- Biopsy with histopathology

- Treatment

- Excision with ancillary therapy
- Enucleation

- Referral?



Squamous cell carcinoma is another uncommon feline conjunctival tumor that may result in the presentation of a red eye, and it most commonly affects cats with poorly pigmented periocular tissues. It can also affect cats with normal amounts of periocular pigment though as depicted in this clinical photograph.

Due to the association between UV light exposure, and squamous cell carcinoma development, cats that spend a lot of time outdoors are considered at an increased risk. Squamous cell carcinoma often causes erosive ulcerative lesions of the palpebral conjunctiva, that notably also involve the eyelid margin.

Diagnosis of conjunctival or squamous cell carcinoma, can be made on biopsy with histopathology. If the lesion is classic at the time of initial evaluation, treatment involving excision with ancillary therapy such as cryotherapy, carbon dioxide laser therapy, or strontium radiotherapy, can be performed for diagnostic and therapeutic purposes simultaneously.

In advanced cases of conjunctival and eyelid squamous cell carcinoma, enucleation may be necessary in order to achieve a cure. Fortunately squamous cell carcinoma does not tend to metastasize distantly, though there is a relatively high risk of local recurrence, if adequate surgical margins are not achieved.

Referral would be a good option in a cat diagnosed with ocular surface squamous cell carcinoma, particularly if the client was interested in pursuing globe sparing treatment that would require excision, with an ancillary treatment modality not commonly available in general practice.

Conjunctival SCC: Client Communication

- High risk of local recurrence without aggressive surgery
 - 4-5 mm clear surgical margins
 - May require sacrificing a normal eye
- Metastasis late in disease

Ulcerative, erosive
lesion diffusely
affecting the lid margin



Feline Red Eye: At the Surface

Client communication is key when discussing the treatment approach after making a diagnosis of ocular surface squamous cell carcinoma. There is a high risk of local recurrence without aggressive surgery in many cases. And in cases of extensive disease, curing the cat may require sacrificing a normal eye. Although, also though unlikely, early on regional metastasis occurs later in the course of disease. This clinical photo provides a good example of why a normal I would need to be sacrificed due to periocular, or ocular surface squamous cell carcinoma. You can see this expansile ulcerative in erosive lesion diffusely affecting the eyelid margin. Resection of a mass involving the majority of the eyelid would require advanced reconstructive surgery to re-establish a functioning eyelid to protect the eye and keep it healthy. So unfortunately this is often not a feasible option in our feline patients, and the difficult recommendation to sacrifice the eye must be made.

Conjunctivitis: Other → Neoplastic

- Mast cell tumor (MCT)

- Clinical signs

- Conjunctival mass
- Eyelid/periocular involvement

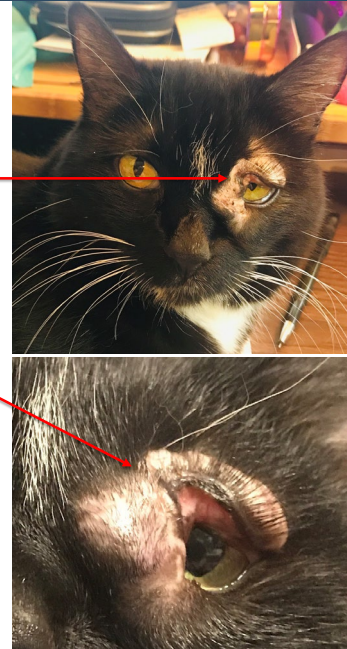
- Diagnostics

- *Cytology (FNA), biopsy with histopathology
- Staging

- Treatment

- Excision (surgical margins not as important in cats)
- Medical therapy
 - *Diphenhydramine 2-4 mg/kg PO q 12 h
 - Famotidine 1 mg/kg PO q 12 h
 - Prednisolone 1-2 mg/kg/day PO

- Referral?



Ocular surface and periocular mast cell tumors, are the final tumors to review. Mast cell tumors may be confined to the conjunctiva, or involve the eyelid and ocular area as shown in the clinical photos. When occurring on the eyelid, mast cell tumors are considered a form of cutaneous mast cell tumor, and do not tend to affect the eyelid margin itself. Lack of eyelid margin involvement combined with a smooth, hairless normal serrated appearance distinguish periocular mast cell tumors from squamous cell carcinomas.

Diagnosis is based on cytology or biopsy with histopathology, but cytology is generally sufficient due to the highly exfoliative nature of this tumor. Though typically more benign in biologic behavior, it's important to consider screening a cat diagnosed with periocular mast cell tumor for metastasis. The cat pictured in these photos had a conjunctival mast cell tumor excised with no recurrence for approximately one year, before clinical signs of ocular involvement developed.

At the time of these photos staging identified metastases to the regional lymph nodes and spleen. With some exceptions, such as the case discussed here, periocular mast cell tumors tend to be amenable to surgical excision. Achieving margins for cutaneous cell tumors is not considered as important in cats as in dogs. Medical therapy consisting of diphenhydramine, famotidine, and prednisolone can be prescribed palliatively, as in the case in these photos, if the tumor is deemed nonresectable, or if there is evidence of metastatic disease.

As with the sampling suspected mast cell tumors elsewhere on the body, I recommend pre-treating a cat with injectable diphenhydramine, prior to sample collection. Referral for evaluation and treatment of periocular mast cell tumor, in a cat, may be indicated for more advanced cases such as this, in which

radical excision and reconstruction would be necessary. Or for those cats owned by clients who are interested in exploring oncologic treatment options.

Conjunctival MCT: Client Communication



- **Cutaneous (eyelid origin) MCTs carry a favorable prognosis**
 - Even without complete surgical excision
- **Conjunctival origin MCTs may be more aggressive**
 - Splenic metastasis in my experience
 - Mastocytemia is more common in cats with MCTs; evaluate blood smear prior to surgery

As demonstrated by the case I briefly described, while cutaneous mast cell tumors tend to carry a favorable prognosis, even without complete surgical excision, conjunctival origin mast cell tumors may be more aggressive. Staging to evaluate for regional lymph node or splenic metastasis is important in any case of ocular surface, or periocular mast cell disease. Especially if your exam indicates the origin is conjunctival, rather than cutaneous.

These concepts serve to inform the discussion of the client, after obtaining the diagnosis of mast cell tumor. You should be prepared to emphasize that the site of origin is important for prognosis, and that stagings should be done prior to considering a radical surgical procedure. If there's already evidence of tumor spread, the battle to prevent metastasis by performing an aggressive surgery has unfortunately already been lost.

In addition to staging, evaluation of a blood smear, can also be performed prior to surgery as circulating mast cells are more common in cats. As with ocular surface lymphoma, client education and the conversation that's had with clients surrounding ocular mast cell disease, should focus on explaining that this disease could impact the overall health of a cat. As such additional information gleaned from screening diagnostic tests will be helpful in formulating a treatment plan.

Summary: My Approach

- Cytology for diffuse non-specific conjunctivitis
- Biopsy and histopathology for focal, nodular conjunctival masses
- FHV-1 is the most common cause of Feline Red Eye with a surface localization
 - Treat empirically based on history, clinical signs
 - Diagnose based on response to therapy

I know that we covered a fairly broad array of diseases that may cause the red eye presentation in a cat. To summarize, I approach each case in a systematic way, starting with a complete ophthalmic exam. After localizing the problem to the ocular surface, I perform fluorescein staining at minimum, to determine if a corneal ulcer is present. If a cat presents with an ulcer, or a diffuse non-specific conjunctivitis, 99% of the time you'll be dealing with feline herpes virus surface ocular disease.

Cytology can be used to support that diagnosis, and to rule out other infectious or potentially immune mediated causes of conjunctivitis. Diagnosis of focal, nodular mass like conjunctival lesions on the other hand, is best achieved with biopsy and histopathology, or fine needle aspirate and cytology. I may seem biased, but I really can't overemphasize that feline herpes virus, should be number one, number two, and number three on your list of differential diagnoses for a feline red eye that's localized to the ocular surface.

You treat empirically based on history and clinical signs and ultimately confirm the diagnosis with response to therapy. Well that's all I have for you on the topic of feline red eye at the surface. Thank you so much for joining me for this presentation. I look forward to discussing intraocular causes a feline red eye in a separate presentation.

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