OCULAR MANIFESTATIONS OF SEXUALLY TRANSMITTED DISEASES

Speaker: Ronald Plotnik, MD, MBA

2/8/2017
Ocular Manifestations of Sexually Transmitted Diseases

[video transcript]

[00:00:05]

Good afternoon. This is Margie Urban here in Rochester, New York. For those of you who don't know me, I'm the medical director of the New York State STD Center of Excellence and I'm happy to welcome you to our sexually transmitted infection Lunch and Learn series. Before we start, I'd like to acknowledge the support of the New York State AIDS Institute Clinical Education Initiative, which does sponsor the STD Center of Excellence and our presentation today. Today's topic will be the Ocular Manifestations of STDs presented by my colleague Dr. Ronald Plotnik. Dr. Plotnik has been here at the University of Rochester for 26 years. He's Associate Professor in the Department of Ophthalmology at the Flaum Institute here in Rochester. Actually, Dr. Plotnik was our very first presenter for our CEI STD ECHO series which was in September a year ago. And if you're familiar with that series, it's quite a short presentation, about 15 minutes, and he promised to come back and give us a more detailed and extensive presentation and he is here today to do that. Before we start, just a few logistics. Everyone will be muted today on this Zoom presentation. And if you have questions, there is a chat box at the bottom of your screen. Please type your questions in and we'll take all questions at the end of the presentation so I'll be able to read them out and we can have our presenter address the questions. Also, if you have any sort of technical difficulties in seeing or hearing the presentation, you could also type in your questions in the chat box related to that. And with that, I'll give you Dr. Plotnik and we'll begin our presentation Ocular Manifestations of Sexually Transmitted Diseases.

[00:02:09]

Thank you very much. It's my privilege to be here. We're going to be talking mostly about syphilis.

[00:02:15]

And our goals will be to gain awareness of sexually transmitted ocular diseases, primarily syphilis, recognize key points in the history and physical and non-ophthalmic ocular exam which would suggest syphilitic ocular disease, and to understand the relationship between neuro-syphilis and ocular disease.

[00:02:38]

I have no commercial interests.

[00:02:46]

Let's define syphilis first. It's a sexually acquired infection, as you know, by direct contact. The etiologic agent is treponema pallidum, which is a spiral-shaped, gram negative bacterium. Humans are the only natural host. In syphilis, the numbers I think are important because we have all sorts of different stages of syphilis and some go on to others, some don't. Some involve ocular disease. And so, I think, for us anyway, more than any other sexually transmitted disease and really compared to most diseases in general to the eye, the background is very important. It enters the body via compromised skin or intact mucous membranes and goes to the circulatory system including the lymphatics. The transmission is
primarily sexual but can be vertical and as you know, remains a significant public health problem in the United States and worldwide.

Just as a quick overview and then we’ll go into it a little bit more in-depth, one gets an infection with Treponema pallidum. It can lead to primary syphilis, which can lead to secondary syphilis, latent syphilis we’ll talk about, and tertiary syphilis along with neuro-syphilis.

Starting at the beginning, primary syphilis. The primary disease entity here is a chancre. Typically it clears two to six weeks after infection. It’s a single, firm, painless, non-itchy skin ulceration with a clean base and sharp borders. That’s the typical. But they can be multiple, painful, and non-genital as well. It can be a macule to a papule, which is raised, or it can be ulcerated. It can affect the cervix, penis, the anal region. And typically lasts three to six weeks without treatment. Now, the second large manifestation of primary syphilis is a regional lymphadenopathy where there are large lymph nodes adjacent to the area of infection.

Secondary syphilis is something that follows primary in a certain percentage. It occurs 4 to 10 weeks following that infection. And it’s characterized by constitutional symptoms such as fever and malaise and the regional lymphadenopathy can turn into a generalized lymphadenopathy. The skin rash can become disseminated. It can involve mucous membranes. But it can also involve the hands and the feet and other parts of the body. The lesions are typically a condyloma latum, which is a flat, broad, whitish, wart-like lesion that can appear very differently on different people and in different parts of the body. Tends to be on the genitals and mucous membranes but can be palms and soles and extremities. It tends to be symmetrical, reddish-pink, can be flat or elevated or pustular and these lesions are infectious.

Tertiary syphilis is characterized by neurologic involvement and cardiovascular involvement. This can occur months to years, typically 13 to 15, following infection and without treatment, approximately one third of infected people, somewhere between a quarter and a third, develop tertiary disease. These lesions tend not to be infectious but they produce significant morbidity. There are three main forms. The first is the gummatous syphilis, which also can be referred to as late benign. It’s a soft tumor-like mass which varies considerably in size and can affect the skin, bone, livers, and other body sites. The second form is late neuro-syphilis, which we’ll get to in a little bit. And the third is cardiovascular syphilis, which can cause an aortitis, which can, in some occasions, lead to an aneurism.

Latent syphilis gets sort put in after secondary but it’s really when there’s disease that’s clinically undetectable but with serologic proof of infection. And this can be either primary, secondary, or tertiary having had those prior and can persist for many years. And typically this is not sexually transmitted.
There are two types: early and late. The early is less than one year after seroconversion. The late is greater than a year. When the patient has early latent, there may be a relapse of symptoms, it's more contagious. After a year after seroconversion, it's less symptomatic and less contagious.

Now, neuro-syphilis is important for what I do because all of the ocular disease falls into the category of neuro-syphilis. So, the T. pallidum invades the central nervous system. It can occur at any stage early or late. And this is really key because it can occur early during any of the other stages but it can also occur years later, even long past anyone remembering that there was any ever syphilis. Typically occurs 4 to 25 years, three months to greater than 25 years as a range. And symptoms can be altered mental status, stroke symptoms, hearing abnormalities, loss of vibration sense, motor deficits, sensory deficits, and all the symptoms of ocular inflammation that we'll go into and just a little bit. The timing is divided into early and late. The early neuro-syphilis may be without symptoms and one may have just diagnosed this with a CSF exam, cerebral spinal fluid, which we'll get to in a moment. Or they may present just a mild meningitis, which may or may not bring the patient to the physician. In late neuro-syphilis, you can have meningovascular syphilis, general paresis, tabes dorsalis, which is also referred to as syphilitic myelopathy, where there is demyelination of part of the dorsal columns, and then ocular involvement.

This is an example of neuro-syphilis where we see the brain itself being involved here. And then here is a lesion as well on the left of your screen.

As providers, the cerebral spinal fluid exam is very important to know in terms of indications and when to refer. We see patients in the office not infrequently who have been treated for the ocular manifestations who have not had a cerebral spinal fluid evaluation only because it wasn't known that this needed to be done. So, any patient with primary or secondary syphilis who demonstrate any neurologic signs or symptoms or any eye signs or symptoms needs evaluation. If there's evidence of active tertiary syphilis, even without any neurologic symptoms or eye symptoms, those patients also need a CSF exam. If there's treatment failure with primary or secondary syphilis or if there is HIV infection with a CD4 count of less than 350 or non-treponemal serologic test, which we'll talk about in a moment, greater than 1:32. Now, a lot of these fall more into the infectious disease category than the ophthalmic category but we see these patients and it's important to make appropriate referrals, not just to ophthalmology but to those individuals who would perform a CSF exam.

The findings one would define on a cerebral spinal fluid exam would be a leukocytosis, although you can see this in HIV alone, of white blood cells in the spinal fluid. Elevated protein, and this also you can see with HIV alone. Positive VDRL, which we'll get into the VDRL in just a little bit. It has high specificity from the spinal fluid but poor sensitivity so its absence doesn't mean that the patient doesn't have syphilis. The spinal fluid is typically clear and the glucose is normal though there sometimes is increased pressure. The spinal fluid exam is also important if the CSF initially showed pleocytosis, which is
elevation of various white blood cells, and can be repeated every six months until the cell count is normal as an indicator of progress. Things like VDRL in the cerebral spinal fluid are not good indicators of progress and are not as accurate as looking at the white blood cells. So, the leukocyte count is a sensitive measure of the effectiveness of therapy, but as far as I know, no other part of the cerebral spinal fluid exam is as specific.

[00:12:37]

Now the fun stuff for me: the eye. So, I would like to go through just a little bit of eye anatomy before we get into more specifics. So, if we look at the diagram on your left, the front of the eye, the front window the eye is the cornea and it's clear and we look through that. It's kind of like the watch glass. The iris gets bigger and smaller with light and is a vascular tissue in the front because we're looking at a cross-section here. Behind the pupil, which is the hole in the middle of the iris that the light goes through, we have the lens. And so, when we do a slit lamp exam and evaluate patients looking at the front of the eye, we're looking at the cornea, we're looking at the iris, and we're looking at the lens and the relationship between all these structures. In order to see into the eye beyond this, we need to dilate the pupil and that's why if you go to the eye doctor they dilate your pupil to make the pupil larger so that we can look all the way through. When you look through the center, what you see is the retina lining the inside of the eye. But there are really three layers to the eye wall and the middle layer, in terms of syphilis, is the most important. Starting with the iris, and it's outlined in yellow here, we have the iris. This area here right behind it is called the ciliary body and it produces the fluid that keeps the eyeball firm. And then this vascular layer continues all the way around and is deep to the retina. And it's typically this vascular layer which is affected by syphilis and most of the other damage, not all of it, but most of the other damage has to do with inflammation of this layer which goes all the way around. Although other layers can be specifically affected. So here's another picture on your right. Again, just a little bit different representation where we have the cornea on the front. There's fluid behind the cornea where if there's inflammation in the iris, this is the iris here in cross-section, we would see cells floating around the front of the eye. This is the lens and when one gets a cataract that's what is opaque instead of being clear. The vitreous gel is the fluid which fills the middle of the eye and then the retina is lining the back of the eye with that vascular layer which starts up here at the iris and goes back to the ciliary body going all the way to the back and when it's back here, it's called the choroid. This whole tract from front to back of the vascular layer is called the uveal tract and so the inflammation of the uveal tract is called a uveitis or inflammation of the uvea.

[00:15:28]

Now, this inflammation of the uveal tract is the most common area of the eye that's affected. And this is just a different representation to try to help with the familiarity with the eye and what parts are affected by inflammation. So, the iris of the eye is in the front and when that's inflamed it's called an iritis and we know that there's an iritis because we see cells floating around in the front. The ciliary body, this part right here, when that's inflamed again, there's inflammation and white blood cells which accumulate in this space next to the ciliary body. And when the choroid, the most posterior part of the uveal tract is affected, again we have cells that are produced that we see accumulating and you can also have the entire tract being affected from front to back. When the front's affected, it can be very difficult
to see the back and we can look with ultrasound if we need to to try to get a better feel for what's happening in the back or what we call the posterior pole.

[00:16:40]

A case definition for ocular syphilis is a person with clinical symptoms or signs consistent with ocular disease with syphilis of any stage. And those symptoms can be light sensitivity, decreased visual acuity, complete blindness. There are certain signs of optic neuropathy such as pain on eye movement and decreased color vision. One can have interstitial keratitis, which we'll talk about, where there's inflammation of the cornea itself. The blood vessels themselves can be inflamed and that gives us a specific set of symptoms. And so, I think for a non-ophthalmologist or non-optometrist, really any sign in terms of redness, decreased vision, pain, pain on eye movement, or when you look at the eye, if the eye is red or looks different in some way, those would all be indications for an ophthalmic examination. So, syphilis plus ocular complaints means an immediate referral. Now often, we have the ocular complaints. We don't know that the patient's had syphilis and so we do a workup for those ocular complaints and sometimes we make the first diagnosis of syphilis but that's not the typical. So, these symptoms and the underlying cause being syphilis can lead to decreased visual acuity and permanent blindness. And so, this is something that's fairly easily treated if one knows what we're treating. It's curable in most cases but an accurate diagnosis and treatment regimen obviously is very important, not just for preventing the spread of further infection but also for treating the patient primarily. These eye signings can be but don't have to be associated with additional neurologic involvement and then we get back to the syphilis plus ocular complaints, even without any neurologic involvement, means unless proven otherwise, neuro-syphilis. And so, that's why I think it's so important to understand kind of the basis and the primary and the secondary and the latent and the neuro because you can get neuro-syphilis from any stage of disease and it can go out many many years post-treatment as well. So, just to be specific, a form of neuro-syphilis can occur in any stage of the disease.

[00:19:11]

Some more guidelines. The condition should be aware of ocular syphilis and screen for visual complaints in any patient at risk for syphilis. So, if you have an HIV-infected individual with low cell counts, if there's a person with other risk factors and they have visual complaints or respond positively or endorse visual complaints, that would be a person for referral. But sometimes you have to ask in order to get an answer. Patients may not volunteer that information because they don't put the eye together necessarily with their other symptoms of syphilis. All patients with syphilis should receive an HIV test if the status is unknown or if previously HIV negative. Patients with positive syphilis serology, and we'll talk about the serology in just a moment, in early syphilis without ocular symptoms should receive a careful neurologic exam including all the cranial nerves and be asked specifically about visual complaints. And patients with syphilis and ocular or visual complaints should receive immediate ophthalmologic evaluation. Immediate doesn't mean necessarily that day but you know as soon as possible they should get in, within a week. Probably before would be better but longer than that's probably too long.

[00:20:31]
Some of this is a little bit of a repeat but I think it bears repeating. A lumbar puncture with cerebral spinal fluid exam should be performed in patients with syphilis and ocular complaints and ocular syphilis should be managed according to the treatment recommendations for neuro-syphilis. All of these treatment guidelines are outlined by the CDC publications that go very specifically into each of the forms of syphilis and what the treatment regimen should be. For neuro-syphilis it's aqueous crystalline penicillin G, 18 to 24 million units per day administered as three to four million units IV every four hours or continuous infusion for 10 to 14 days. Now, there are other ways to do this but this is the CDC recommendation. If there's an issue with patient compliance, you can use procaine penicillin IM with probenecid but other types of penicillin should not be used as primary treatments. New cases of ocular syphilis need to be reported and molecular typing is helpful but not required. It's helpful for research but not-- I don't think it's helpful for the patient themselves as far as I know.

The testing is divided into non-treponemal and treponemal. This is very important because a lot of the previous screening tests for syphilis did this wrong. The current guidelines for screening tests make intuitive sense and will pick up almost all the patients who have syphilis. What we were initially doing was screening with non-treponemal tests. Non-treponemal tests have both a qualitative and a quantitative aspect to them. Those are VDRL and RPR, TRUST tests, and USR. They reflect both disease activity and response to therapy and can be used to test reinfection but, a very large but, low sensitivity and specificity. This measures the antibody against cardiolipin-lecithin-cholesterol host antigen, which is released following tissue damage. So, it's an indirect type of test and it's good for looking at activity. The problem is for the eye, the activity as measured by the VDRL and the RPR does not correlate with the ocular disease. It also doesn't pick up patients who have had syphilis in the past who don't have active disease at the present time. Those people are best picked up by a treponemal test and the use of one type of serologic test, either non-treponemal or treponemal, is insufficient for diagnosis of ocular disease. The treponemal tests have a lot of letters, the MHA-TP, FTA-ABS, ELISA, amino assay. These are very sensitive, usually reactive for life. Titers can't be used for assessment of treatment response though. There you're better off using the VDRL or the RPR. And this is a direct test measuring serum antibody directed specifically against T. pallidum antigen.

Now, these two confusing graphs are really the same graph. One is labelled with the test that one gets the other is with the antibody. So, if you look at the graph on your right, we see the time post infection on the horizontal axis and the percentage of patients who test positive on the vertical axis. And so, when a patient is infected, when we look at the FTA-ABS or the treponemal test, and this is an IGG test, you see that it goes up relatively quickly and it stays positive. Now, these are IGG tests. The treponemal IGM test goes up and down. So, you're really better off getting usually the screening is an IGG for these and then for the VDRL and the RPR, that depends on whether the patient's treated or not treated over a period of time and treated patients they end up with lower positivity than patients who are untreated. And if you go to your left, this is really it looks like the exact same graph but here we're calling it instead of the FTABS what we're looking at is treponemal IGG. And here for VDRL and RPR, we're looking at non-treponemal IGG and IGM antibody. And down here again, IGM and IGG non-treponemal looking at
antibody. So, for ocular disease because they don't have to have active disease we care most about getting these treponemal tests to know whether or not they've ever had syphilis in the past. And that's much more sensitive in terms of identifying syphilis as a cause of ocular disease than by only getting a non-treponemal test like the VDRL or the RPR.

This reverse sequence testing is what has been set up by the CDC and this test, in my opinion, really makes intuitive sense. And so, what you do is you send off for a syphilis panel and the first test that is performed is a treponemal test. This treponemal test starts with a highly sensitive but not that specific amino acid. So, we want to catch everybody with this and so we do a treponemal test. If the treponemal test is negative because it's so specific then they don't have syphilis. If it's positive then we say OK, they're likely to have syphilis but it could be something else like syphilis that's a false positive. So, we're going to do a non-treponemal test and see how active the disease is. If the disease is active, then we know when the RPR's positive that this initial treponemal test being positive was indeed syphilis. So, here we treat for syphilis. If the RPR is negative, they could still have syphilis. And so, now we're going to do a treponemal test which is more specific, not as sensitive, but more specific. And here if this test is positive, they have syphilis. If it's negative, syphilis is unlikely but not impossible. And so, this screening really sort of picks up everybody but allows some false positives and then does its best as you move down to weed out the false positives.

Now, ocular syphilis can be both acute and chronic and it can affect any part of the eye. This is an exhaustive list and we're not going to hit everything but just kind of going through. The lids can be affected with any of the skin lesions. The conjunctiva, which is the clear layer over the white of the eye, can be affected by a lot of the lesions that affect the skin. The orbit can be a place of gumma lesions. The cornea can have inflammation which can range from just a few extra blood vessels to ulceration and perforation. The sclera, which is often affected in things like rheumatoid arthritis and ulcerative colitis and is a bystander often for inflammation, damage which initiated in another part of the body, the sclera can be affected. The anterior chamber is the area behind the cornea where I had mentioned before that you can see some cells which indicate that the iris is involved. Hypopyon is when there are so many white blood cells that it layers out. The iris and ciliary body we talked about and we'll look at some pictures of that. The pupil itself. There are some neurologic issues that can occur with syphilis that I'll mention. The lens can be stationary but cataractus meaning that there's opacity or the lens itself can be weak and actually fall from its spot in the eye. And I'll show you some photos of that. The optic nerve can be involved. There's all sorts of specific syndromes which affect the optic nerve in the setting of syphilis. Ocular motility. There are six muscles that attach to each eye that move the eye and you can have problems either with the muscle itself or the nerve to the muscle. And the retina and vitreous. The retina, remember, lines the back of the eye. That's what gathers the light. The retina can be primarily affected. It can be affected by the vascular tissue beneath it and the vitreous which is the clear fluid which fills the middle of the eye and that can be affected as well.
We're going to get into some photographs of the eye. Most of these pictures are taken with a slit lamp which is really sort of a bio microscope to look at the structures of the eye at higher magnification. And what we see here on your left, this is the back of the upper lid. The lid's been everted. And each one of these little lesions here where you see the light reflects, like this is a reflection from a light where there's a bump underneath. And all these regions here are granulomas from a patient with syphilis. So, these are actually syphilitic lesions within the conjunctiva. And here we see the same thing but a little bit larger. I apologize. A little bit larger here and these rub on the cornea and can cause ulceration to the tissues beneath this because remember the lid is everted here, it's turned inside out.

Now, the front of the eye when we look over the white of the eye, we don't just have the white. There is a clear layer over the white and when we get pinkeye or an infection or something, it's usually not the white of the eye that becomes red. It's usually the clear layer which has blood vessels which are inactive. The blood vessels become active and cause a lot of redness. Now, here what we see is we see a syphilitic lesion in the sclera. And the reason that it's outlined like this is there's blood around it and this is sticking up a little bit through the area of bleeding. And this is a very localized involvement and this would be a scleritis where the sclera is, the white of the eye is edematous and inflamed. On your left is an eye where the syphilis is much more widespread. And so, we have involvement of the conjunctiva, the clear outer layer. We also here have involvement of the deeper layers. So, where it's a little bit whiter but you still see the blood vessels, that's an area where the conjunctiva is just involved but these deeper areas where the vessels are more confluent where I have my cursor and over here, in these regions the sclera is involved so it's a much deeper involvement. When we have patients who have inflammation of the conjunctiva, usually just some topical steroids help even in the setting of infections like syphilis. When there's deeper involvement then topical steroids don't help. And here, we just have some inflammation down below on the conjunctiva and this lines the inside of the lid.

This has some subtle findings as well as the more overt findings. Here we have, where my cursor is, inflammation of the sclera and we have inflammation of the sclera down here so much so that it's confluent. I mean, the whole thing is red as opposed to these areas here which are a little less red. But there's an additional finding here. If you follow my cursor here in this circle around the limbus, the limbus is the area where the white sclera meets the clear cornea. And when you have what we call limbal involvement, when the limbus, when this area here is red like this, that's usually an indicator that there's inflammation of the colored iris. Now the colored iris in this photo is inside the eye. The cornea would be the outer wall. But this limbal vasculitis here is a good indicator that there's deeper involvement within the eye itself. And this is something you can see with a pen light.

Here's two other cases of scleritis and on your left you can see this entire area is affected. And one of the characteristics of a scleritis that you can see is where the eye next to the area of the scleritis is totally unaffected and that there can be a very clean demarcation between the area affected and the area not affected. So, this whole region is affected here but you can see here there appears to be some
elevation and there's more local investment of the syphilis itself. In the eye on your right, this whole area is affected and if there was a picture here of the whole eye, you'd see that there really wasn't any area like here on the left that wasn't affected. The entire sclera in this eye is affected. Now, interestingly enough, we don't have that limbal vasculitis here in either one. So, this may be localized to the sclera and not involve the iris.

Here's a photo of what I had just mentioned where there's clearly inflammation at the limbus and when one looks in the eye with a pen light you can see this. Now, you're not going to see the cells floating around the front of the eye. That you really need a microscope to see. This is probably the most frequent ocular manifestation of syphilis. It can be one eye or both eyes. We divide this inflammation into granulomatous and non-granulomatous. The non-granulomatous, the inflammation is from things like arthritis and some other entities where the inflammation is very tiny. The cells are not grouped together, everything's very small. Granulomatous iritis we get large nodules and I'm going to show you some of them in just a moment. And again, the ciliary flush, which is the limbal vasculitis. Ciliary flush is another term that you may see that refers to this limbal vasculitis.

Now, what this is is these areas here are collections of white blood cells that are on the back of the cornea and this would be called a granulomatous inflammation because the collections of white blood cells are not single cells, they're big clumps of cells. And these cells can clump on the iris, on the back of the cornea, anything that's in the front of the eye. And we see this on the inside of the cornea with really only a couple conditions. Syphilis and sarcoid are really the only things that cause these really large, what we call keratic precipitates. Keratic refers to the cornea and they're white blood cell precipitates. On your right we have another patient where it's not quite as extensive as on your left but we can see these large clumps of cells. And these large clumps of cells can be also on the iris itself forming a nodule on the iris. With the pupil dilated like this, we're looking actually at the front of the lens, which is right behind the iris and this is just the light reflects. The bright light is not anything that one needs to worry about.

This is another eye where we see this ciliary flush or limbal vasculitis. We see a scleritis along with it, a lot of blood vessels. And one of the things that can happen, this actually was a much redder eye prior to this. This area of white here, a lot of this white, is not white because the eye is not affected. It's white because the blood vessels have closed and there's ischemia due to the vasculitis. And so, the area here is really the only area where there are still blood vessels. We can see the big blood vessels all the way around. It's the small capillaries that have been lost. And even though this eye appearing a little more white seems like it would be in better shape, this eye is really in worse shape.

What this is is this is the iris and this pupil should be round. And we're looking at the lens through there and what we're seeing is there have formed adhesions between the iris and the lens. And so, we put in a
dilating drop and so the dilating drop dilates the pupil by activating these muscles here that pull the iris open but the iris is stuck down with these what's called posterior synechiae or posterior scarring. And you can put dilating drops in and try to break these but this is a case and in many cases you really can't break them unless you go in surgically and lift this off the lens. But you're looking here in the middle though at the lens. It's a structure right behind the iris that these are adherent to.

[00:38:54]

This is a case where the iris, when the pupil was not dilated, was adherent to the lens and we put in dilating drops and were able to break these adhesions except for this one down below. And so, a lot of the pigment from the iris is now sitting on the front of the lens. And we see this remaining synechia, this remaining scar, but seeing something like this, even in a quiet eye is indicative of a previous inflammation. Not necessarily syphilis but certainly syphilis is the differential and that's what this case is.

[00:39:34]

This is another case which has many of the findings that we've talked about. We have the lens here with lots of precipitates even on the lens itself. We have precipitates on the back of the cornea. We have synechiae where the pupil has been dilated where it's scarred to the lens. And we're starting to get some opacity of the lens itself which is what a cataract is. All these down here on the bottom, those are all precipitates on the back of the cornea. And again, when you see large things like this it's really syphilis or sarcoid.

[00:40:16]

Now, this is not syphilis. This is just to contrast the granulomatous versus non-granulomatous inflammation. This is an example of non-granulomatous where the cell clumps are very tiny. You don't see those big what we call mashed potato keratic precipitates like somebody had mashed potatoes in a spoon and flung it at the back of the cornea. So, this is an example of what typically you wouldn't see in syphilis, just to give you some context.

[00:40:53]

When there are cells in the front of the eye and we see those precipitates on the back of the cornea, this is a difficult picture because it's a certain type of technique, but the cornea is actually on your right and the lens is on your left. In the area between them is the space where there's fluid between them and that space is supposed to be clear. And what you see here is it's full of clumps of cells. And so, we grade that on a scale 0-4 where 4 is the worst. And this is the main thing that we look at to indicate to us that there's inflammation of the iris when we do a slit lamp exam.

[00:41:35]

The cornea itself can be affected and it can be affected from congenital syphilis or acquired syphilis. And on your right, you should be able to see the colored iris through the clear cornea very easily. But instead what you see is a lot of scarring, a lot of white, a lot of blood vessels. And sometimes what will happen is these blood vessels will stay but there won't be any active blood in them and they'll form what we call ghost vessels where we can see the vessels as dark lines, and you can see some of them here, but we
don’t actually see blood in them. So, here we have the entire cornea being opaque except for this region here which has not been affected. If you shine a light into a dilated pupil and you get a cat eye reflex, so the light’s actually coming back from the retina, you can see sometimes how the cornea is affected. So, this is not the retina. This is just the light coming from the retina and these are the blood vessels in the cornea that should not be there. There shouldn't be any blood vessels in the cornea. It's an avascular structure.

[00:42:43]

And here's another patient where there is blood vessels in the cornea. And sometimes what you see is an opacity and you don't see blood vessels from an old case of syphilitic cornea disease. When syphilis affects the cornea, we call it an interstitial keratitis. Keratitis just means inflammation of the cornea but it's because the inflammation is not on the surface, it's in the main stroma. It's in the main bulk of the cornea.

[00:43:15]

I'd mentioned previously that sometimes syphilis can weaken the little strings that hold the lens in place. And on your left is a lens, which is supposed to be behind the iris held in with a bunch of little strings like a trampoline, has come forward through the pupil and is sitting in the front of the eye. When you see this, in the setting of trauma especially, it should suggest syphilis. This is another slide, both of these from the University of Iowa not mine, where the lens little strings are weak here and broke and the lens is in the right place in terms of being behind the iris but it has gone off to the side. And typically, what happens after a while is it just falls into the eye and you have to go in and get it.

[00:44:08]

You've seen some of these signs before. You've seen the pigment on the front of the lens, you've seen the synechiae from the iris to the lens. But this is a case where the lens instead of being clear has become cloudy. And so, this is a cataract. Denser than the cataracts we typically take out you know when we you know take out a cataract in an elderly individual, this is an inflammatory kind of cataract and it's very white and very dense and very difficult to get out.

[00:44:40]

These are two more examples of cataracts in the setting of syphilis. Very, very white. You can see the corneal findings that we've talked about before, the keratic precipitates. These are actually on the iris themselves. This is inflammation that's kind of settled out on the iris. Here is also these little dots are inflammation that's settled out in the iris. These down here are on the back of the cornea. We see our synechiae, our scarring, our irregular pupil, and a very dense cataract. Similar over here. Not quite as bad. We see our synechiae and we have a dense cataract.

[00:45:21]

The choroid and retina. The choroid, remember, is the vascular layer which lines the back of the eye and the retina which sits interior to it can be affected at any level. The vascular layer can be affected, that's the usual, but the retina can be affected on its own. And the lesions can be either active and infectious
or can be late inflammatory lesions. So, what we have here is the optic nerve that's normal. But you
have these white spots. None of these white spots should be there. They all indicate infection and then
we have a very active infection here which is very large and it has a fluffy border. And typically, in front
of it has cells sitting in the vitreous cavity.

[00:46:03]
Here's an example in the retina of old syphilis. And you can see that there's been a loss of retina, that's
what all this white is. But the margins are very well-defined. And so, it just has a different look to it than
what we saw before which was very fluffy and elevated.

[00:46:25]
Here's some more lesions. Very fluffy, very infectious, very elevated, very acute in both eyes.

[00:46:36] This is an old lesion where we have these punched out lesions in the vascular layer. And if you
put dye into the arm and watch the dye as it goes through the eye, the dye is white, you'll see it doesn't
fill a lot of these areas because those areas have been lost due to ischemia, due to the blood vessels
being lost in those areas. And that's all the dark in these scans.

[00:47:05]
And again, very intense inflammation in the choroid, the retina, and here the optic nerve is very swollen
as well, which can also be affected by the syphilis.

[00:47:20]
And these are just more examples. Anything white for the most part is bad.

[00:47:31]
This is an example here. You can see that there's involvement. I don't think there's a whole lot to take
away here other than seeing the inflammation in the retina that shouldn't be there.

[00:47:44]
And this is a patient here where there's a lot of hemorrhaging due to vasculitis and loss of blood vessels.
And what you see is the large blood vessels which are remaining show up with the dye because they're
all leaking. And that's what this kind of Christmas tree picture looks like.

[00:48:08]
Hemorrhages, scarring, subsequent scarring.

[00:48:17]
And this is a retinal detachment in both eyes where the bacteria made a hole in the retina, fluid leaked
in and dissected the retina off the eye into the eye itself.

[00:48:33]
I think I’m going to skip just a few of these things to make sure that I have enough time to answer questions. I did want to mention pupils real quick. The Argyll Robertson pupil is what’s seen with neurosyphilis, it can be seen. Normally the pupils constrict to light and also when you look at near and the pupil in someone with neuro-syphilis and with this condition, the pupils constrict when they look at near but they don’t constrict to light.

[00:49:04]

And I just wanted to say that the CDC has a very good guide that can be printed and it folds into threes and goes through a lot of this information which I find helpful for the residents.

[00:49:22]

Thank you.

[00:49:23]

Thanks very much.

[00:49:25]

And here on your screen, if you’re not familiar, is our CEI line. This is a clinical consultation line where you can call and direct, clinicians can call in with questions about HIV, Hep C, PrEP, PEP or STIs, including syphilis. I field a number of the STI questions and I would say overwhelmingly they are about syphilis. I think let me just escape here so that we can see questions.

[00:49:58]

I’m going to start with one question. You really emphasized how inflammatory a condition ocular syphilis is and I know that the treatment of choice is IV penicillin but do you ever use steroids, you know, because of sort of a time crunch that maybe there’s imminent sight loss or something like that?

[00:50:25]

There are really two ways that syphilis affects the eye. One is when the syphilis is active and infectious and inflammatory and the other is the eye can be affected even as a very late bystander of residual latent disease. And so, we do use steroids once the infectious component is under control because if you don’t, you end up losing ocular tissue. The one thing you don’t want to be doing is using steroids without having treated the syphilis. That's a recipe for disaster. But we use steroids all the time. And once they've been treated initially, steroids are really the mainstay of treatment.

[00:51:07]

And that's systemic steroids or just ocular?

[00:51:08]

Typically, systemic steroids when there's very, very deep involvement in the eye but typically either steroid drops or steroids injected next to the eye or in the eye actually.
And then I think we do have some questions in here. So, we have one question. What percentage of patients with ocular symptoms have negative RPRs? Similar question, what percentage of patients with neuro-syphilis would have a negative RPR, excluding a prozone? So, they're saying not a falsely negative RPR. Several questions in there. Let's just start with that. Often, I think clinically, what we recognize as ocular manifestations of syphilis are often happening in early syphilis when people typically have quite high RPRs and secondary syphilis for instance when you might see iritis or uveitis. And you made the point that you really want to do the specific antibody because the RPR might be negative. How often would you say that you see people that the RPR is negative?

Well, we send off treponemal antibody for all patients who have inflammation in the eye as part of our battery of tests. And when it's positive then we kind of go from there. We see a fair amount of RPR-negative syphilitic ocular disease. And in the olden days, they wouldn't get a treponemal test unless the RPR was positive and we'd have to specifically say no no no please get the treponemal and the non-treponemal test. Now the screen does both. And so for us it's very important to have both tests.

Another question says does the treponemal EIA measure both IGM and IGG? I think I could-- I think that really depends on what test your laboratory is using because there are marketed both IGM and IGG, which I think is the bulk of them, but there are some that are IGG only. And then there is another question. Should all patients with ocular syphilis who have a penicillin allergy be desensitized and treated with penicillin? So, Ron's pointing at me. That's a little tough.

There are CDC recommendations for pen-allergic individuals at each stage of syphilis. And the CDC document that goes through this is very specific about what to do and what not to do. I can't say that I-- I don't want to outspake my level of knowledge here to give you bad information but that document is very clear.

Right. So, the recommendation is to give IV penicillin or parenteral penicillin at least for ocular syphilis and neuro-syphilis. And then there is a little caveat that there are some data about ceftriaxone and those patients should be followed very closely. So, I don't know if that's what this person is getting at that you know have you actually treated anybody with ocular syphilis with ceftriaxone? I personally have not.

I haven't either.
I don't know that we can give a firm answer to that. And then it was mentioned that all patients diagnosed with syphilis need a neurologic exam by a neurologist. Did you say that was what the CDC recommended? Are you saying a neurologist provided neurologic--

[00:55:09]

No, no, just a physical exam. Just a basic physical exam and make sure that there's nothing that wasn't obvious to the patient that may be you know elicited in the exam. No, they don't need, not that I-- we don't do that. I don't think they need a neurologic referral.

[00:55:24]

And then I had one more question of I had a patient that we specifically asked who had secondary syphilis with a lot of manifestations of secondary syphilis that you mentioned; adenopathy, rash, some oral lesions, pretty high titer secondary syphilis, and specifically did not have ocular symptoms on that day. Received their penicillin, IM penicillin, and came back a few days later reporting symptoms of Jarisch-Herxheimer, which is a reaction you can get after treatment with sort of a febrile illness, achey. And now had ocular symptoms. And actually, I believe you saw this patient as well. We referred him and in fact he was admitted for ocular syphilis. And I always wondered was it just that he was just developing symptoms or you know didn't answer the question exactly correctly or maybe we weren't clear enough of what we were looking at or was this sort of like a Jarisch-Herxheimer kind of response or was it really ocular syphilis as we normally think of it?

[00:56:32]

I don't know the answer to that for sure. I do know that a lot of what we see is immune and not necessarily active infectious. And so, how to quantify that I'm not sure. Were they on the border and then we just pushed them over or was the reaction so severe that there was enough antibody and antigen around to cause a problem? I don't know. But the treatment for the patient was pretty clear. I mean, they needed treatment for secondary syphilis. And I don't remember-- did they end up having eye problems? I can't remember.

[00:57:11]

We admitted him for IV penicillin and his symptoms did improve then over time, yes. So, he ended up on you know parenteral penicillin. And he had a negative path, interestingly enough but clearly had a uveitis when he was seen.

[00:57:31]

Maybe it was due to something else.

[00:57:35] I think that's all of our time. Thank you, Dr. Plotnik for coming in and giving the presentation. And for those of you who take part in our ECHO sessions or if you're interested in ECHO, which is a virtual case conference where we present two cases and then have a short didactic, 15-minute didactic, the next ECHO session is November 22nd. That's next Wednesday and it's from 12 to 1 November 22nd. The didactic topic that day will be congenital syphilis. If you've not participated in the ECHO before, you can look on ceitraining.org and just type in "ECHO" and it will pull up the information so that you can
register for the session. Thank you very much for your attention and our next lunch and learn will be the second Monday in January, which is January 8th. Thanks again and have a good day.

[Video End]