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ECHO: OCULAR MANIFESTATIONS OF SYSTEMIC SEXUALLY TRANSMITTED DISEASE

Ronald Plotnik, MD, MBA

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[video transcript]

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I'm going to speak today on the opthalmic manifestations of syphilis. Here we go. I don't have any financial relationships or commercial interests. Syphilis the etiologic agent is Treponema pallidum which is a spiral shaped gram negative mobile bacterium, where humans are the only natural host. It's typically sexually acquired but can also be vertically transmitted. 30 to 60% of those exposed to primary or secondary syphilis will acquire the disease enters the body through compromised skin and intact mucous membranes and travels via the the circulatory system is divided into stages, as you know, based on clinical findings, which I'll just review fairly quickly. Primary Syphilis is characterized by the formation of a chancre typically appears three weeks after infection at the site of inoculation. It can be single, typically, but can be multiple firm painless, typically, but can have some pain. With a clean base and sharp borders, it can be maculopapular. To a frank ulcer, it can be associated with large enlarged lymph nodes. It's usually general or can be non general, and lasts three to six weeks without treatment. In terms of secondary syphilis, four to 10 weeks following the primary infection, nonspecific symptoms and certain specific lesions so the nonspecific symptoms, constitutional symptoms like fever and malaise, skin, mucous membrane, and lymph nodes can be involved, and the symptoms usually resolve after three to six weeks, the lesions are flat or broad whitish, wart like lesions, known as condyloma. acuminata are infectious also involve palms and soles, as you can see in the photographs down below, symmetrical kind of reddish pink, not usually itchy, and forms of maculopapular all the way to a particular rash. So that's secondary syphilis. Tertiary Syphilis is characterized by neurologic and cardiovascular manifestations, it occurs months to years, typically three to 15 following infection, without treatment about a third go on to develop this non infectious at this stage, but may produce significant morbidity can be classified into early or late and needs HIV testing, and CSF examination. based on certain criteria, there are four forms of tertiary syphilis three, but up to four. So three is is late benign, where you get gummas soft tumor like masses of inflammation, which can vary in size and can also have involvement of skin, bone and liver, late neurosyphilis, cardiovascular syphilis, and then included in this list more recently has been psychiatric manifestations. Memory loss, personality changes, other psychiatric issues. So latent Syphilis is separate from the primary, secondary and tertiary classification, because it can form from either of these. It's not transmitted sexually and can persist for years. They are sero positive there's sero reactive without other evidence of primary, secondary or tertiary disease. We treat these people to prevent medical complications of syphilis, and can be transmitted vertically. There are two types early latent and late latent. The early latent is less than a year, the late latent is more than a year. The late latent, it's usually asymptomatic and less contagious. The early latent may be accompanied by a relapse of symptoms, it's more contagious, can't be reliably diagnosed solely on the basis of non Treponemal titers. And characteristically during the year preceding the diagnosis, they've had documented seroconversion or sustained four times increase in non Treponemal test tighter, unequivocal, unequivocal symptoms of primary secondary syphilis, syphilis, or a sex partner documented to have primary secondary or early late and syphilis or a person with reactive non

Treponemal and Treponemal tests was only possible source of exposure occurred during the preceding months.

05:15
Separate from these is neurosyphilis. So, neurosyphilis is we have invasion of Treponemal with Paladin into the central nervous system. This can occur at any stage of syphilis. So studies have shown now that even in primary and secondary syphilis, a certain percentage of those patients will have a positive spinal tap for syphilis. The significance of this, maybe our other physicians can comment but appears to be unknown for these primary and secondary patients. This typically occurs four to 25 years after initial infection, may be without symptoms, or they present with mild symptoms late is meningo vascular syphilis, these are general paresis Tabes dorsalis, these are all patients who are symptomatic Tabes dorsalis, slow degeneration of the neural tracks, primarily the dorsal root of the spinal cord, it's a it's a demyelination. And so symptoms of neurosyphilis are altered mental status, stroke symptoms, auditory abnormalities, loss of sounds, motor deficits, sensory deficits, more but primarily at this point, as opposed to just ocular involvement, which used to mean neurosyphilis we now have to have brainstem involvement with symptoms related to cranial nerves. So we'll we'll get back to this. We'll continue to explore this in a minute and get back to it. So this is just a slide with a couple of scans with syphilis lesions of the brain on the left, small one and much larger on the right.

07:06
All right, so the spinal fluid exam basic invasion by the T pallidum, accompanied by the typical lab abnormalities leukocytosis protein, positive vdrl, normal glucose and often increased pressure. No evidence exists to support variation for recommended diagnosis and treatment for syphilis at any stage without clinical neurologic findings except tertiary syphilis. So basically, what used to be the the ocular symptoms meant tertiary no longer do they mean that specifically means neurosyphilis. No longer does it mean that specifically clinical evidence of neurologic involvement as observed motor deficits cognitive dysfunction, sensory deficits, cranial nerve palsy, these are symptoms and signs of meningitis or stroke, that a CFS CSFs exam should be performed before treatment. If there's just ocular exams. What used to be yes is now a no in terms of needing CSF examination prior to treatment. So the changes for us are syphilitic uveitis or inflammation of the uveal track of the eye the uveal track is, is the colored iris and the tissue that extends back from the iris, which we'll go over in detail in a moment. But if you get the typical eye findings of an inflammation in this uveal track that can occur at any stage of syphilis and can be isolated as an abnormality or associated with neurosyphilis. Only if cranial nerve dysfunction is present is a CSF as present as a CSF evaluation needed. For isolated ocular symptoms. CSF exam is not necessary before treatment. And if ocular Syphilis is suspected, if there are any eye signs or symptoms at all, they need to be referred to ophthalmology for referral. And ocular syphilis should be treated similarly to neurosyphilis even if the CSF exam is normal. So these are all newer findings compared to when I presented this previously. In terms of neurosyphilis just want to go through quickly. The treatment regimen regimen which is also for ocular syphilis and otosyphilis which is aqueous crystal penicillin G 18 to 24 million units per day, administered as three to 4 million units IV every four hours are continuous infusion for 10 to 14 days. Alternatively they can be given procaine penicillin plus probenecid. The durations of the recommended a treatment for neurosyphilis are shorter than the duration for the regimen

use for latent syphilis. So if there's a question of latent syphilis, the treatment needs to be extended beyond that for neurosyphilis. There are specific recommendations for HIV positive and pregnant. And all of these recommendations are in the state handout guidelines for sexually transmitted diseases, which is what the slide is taken from. So, in terms of the antibody based serum tests, there are non treponemal and treponemal tasks. The non treponemal tasks are the vdrl and RPR. Typically, they are quantifiable reflecting disease activity and response to therapy. So, they can be followed with response to therapy can be used for test for reinfection, but they have a low sensitivity and specificity and are measured, measuring antibody directed against cardio life and loss of then cluster a host antigen. Whereas treponemal antigen MHA ATP, FTA ABS others enzyme immuno assay, Eliza highly sensitive usually reactive for life titers can't be used to access treat with response though, because they measure serum antibody directed specifically it goes T pallidum. And the use of only one type of test is insufficient for diagnosis.

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So what is recommended is the reverse sequence testing, where we start off at the top by doing an EIA or CIA, which is highly sensitive, but not that specific. If that's negative, though, then you're done and they don't have syphilis. If they did, then you do a non treponemal test such as the RPR, or vdrl. If that's positive then they have syphilis, if that's negative, then you still have to do the treponemal test the FTA TP. The MHA-TP the TP-PA FTA-ABS. And then if that's positive, then Syphilis is definite either past or present. And if TPA is negative, then unlikely. Alright, so this is my main specialty for the eye. So let's just go over a little bit of anatomy first. On the right, we can see a cross section of the eye, where we have the cornea, as the watch class on the surface, and then fluid behind it. The lens is behind that the retina lines the back of the eye, and the middle of the eye was filled with vitreous, the vascular layer is an intermediate layer. So on the left, it's in yellow with red specks. And so it involves the iris eye goes back to involve the ciliary body, which is what makes the fluid for the eye to keep the eyes by to nourish the retina. So the back of the eye has the white eyewall and then our vascular layer or of uveal track, and then our retina. So the uveal tract, the vascular layer consists of the iris, the ciliary body, and then the choroid as we go backwards. And that is the typical thing that is inflamed with syphilis. So inflammation, if any, you can get corneal inflammation sclera, the wider the eye inflammation nerve. But typically it's the uveal track. And so, the classification of uveitis, or inflammation or the uveal track gets divided into anterior intermediate and posterior. Anterior uveitis is the iris intermediate involves the ciliary body, and the posterior uveitis involves the choroid. Pan uveitis is when all are involved and that's actually fairly common to have some degree of inflammation at all of the three different layers of the uveal track. So our case definition for ocular syphilis, and I'll just read this is a person with clinical symptoms and signs consistent with ocular disease. This is visual acuity issues blindness, often neuropathy, Corneal interstitial keratitis, itis and retinal vasculitis with syphilis of any stage. Ensure an immediate ophthalmic exam for any patients with syphilis and ocular complaint. Can lead to permanent blindness. So this is something that needs to be taken care of. We consider it always in the differential diagnosis of ocular inflammation. So when we have a patient who comes in with inflammation of the uveal tract, we will send off that reverse test panel for syphilis. And again, when associated with neurological involvement consistent with neurosyphilis, but not necessarily on its own, especially in the form of uveitis the mission should be aware of ocular

syphilis and screen for official complaints and any patient with risk of syphilis. Up definitely syphilis serology obviously need a careful cranial nerve exam. All right, in terms of specifics related to ocular manifestations of syphilis, but with a lot of carryover to other treatments. During Pregnancy parenteral penicillin G is the only therapy and so those sensitized and treated if they have neurosyphilis, and patients with HIV infection, they should be treated similarly to those who don't have HIV. The Jarisch Herxheimer reaction is acute febrile reaction that can be seen with patients treated within the first 24 hours.

16:35
And first exposed to sexual contact a person with primary secondary or early latent syphilis should be evaluated clinically, and serologically. These are the things that we share with our residents, who often see these patients first, and after hours to make sure that these considerations are taken into account. So even if it's not neurosyphilis it matters to the treatments for which is aqueous crystalline penicillin, D IV, or procaine penicillin with probenecid or benzene. Okay, so I mentioned the uveal track, but this is a list of all the different parts of the eye and actually all the parts of the eye can be affected, you can get the lids, you can get the skin lesions, the conjunctiva, you can get the typical skin lesions as well plus specific ocular lesions. In the orbit, you can have lesions as well, the cornea can develop ulcers and infections as well as secondary, other secondary changes, the sclera can be affected primarily. The pupil can have a light near dissociation, which I'll miss mentioned in just a little bit, the lens can be affected the optic nerve can be affected, and this is one of the most devastating in terms of vision, the optic nerve is affected, the motility can be affected how the eye moves, dudes, typically issues with the muscle itself, or due to cranial nerves, three 4x, and then the retina can be affected and along with the optic nerve are the greatest risks of blindness. So what I'm going to do here is go through and show you photos of findings that we see with stuff. I will try to sort of integrate the anatomy as well. So Iritis is inflammation of the iris, which is remember as the anterior part of the uveal track. This is for us, one of the most frequent manifestations can be worn both and it causes something called ciliary flush. And if you look at this photograph, the redness is around the iris, it's adjacent to where the cornea meets the sclera. And when that part is red preferentially, that usually means inflammation inside the eye. And that it's not just the eye wall or the outside the eye that's been affected. And that's called ciliary flush. And that's that rarely sees typically circular and around the cornea, of which you're looking through to see the colored Iris. Alright, so on the upper left again, we have ciliary flush. So you can see that the further we get away from cornea the less inflammation there is so when there's inflammation next to where the cornea is that ciliary flush, but there's another characteristic to it as well as here you can see the blood vessels, but you can also see sort of a flush, like between the blood vessels is also red. And so that's very typical, as opposed to just the usual dilated blood vessels that you would see, for instance, further away from where the iris and cornea are. Now sometimes if you go to the upper right, it can be sectoral. And so the iris affected here would be counterclockwise from let's say, the 730 position around to the 12 o'clock position with relative sparing of a certain amount of the this area. And so that's not uncommon either. On the lower left, you can see a patient who is only affected on one eye. And on the lower right, again, we see sort of sectoral areas of ciliary flush, the white that you're seeing is just the light reflex. All of this is due to inflammation of the colored part of the iris. Now when there's inflammation of the iris, behind the cornea, there's a chamber it's called the anterior chamber, which is fluid in that

chamber. And fluid, the iris sheds inflammatory cells, white blood cells, and those white blood cells collect on the back of the clear cornea, the watch class of the eye. And when they're small and tiny, we call that non granulomatous. But when they're relatively large, we call it granulomas.

21:27
There's a term called mutton fat K p, or credit precipitates, or mashed potato k p where you took mashed potatoes on a spoon and flung it at the back of the cornea. That's how dance these granulomas in color, blood cell B. And so on the right we can see when we shine a slit in that all these little collections on the back of the cornea are white blood cells. And when they're that big, they're very characteristic of syphilis, the two collections prints or large collections are sarcoid, and syphilis. And so when you see this, you have a pretty good idea, it's going to be one of those two things. In the upper right, we have another patient with large credit precipitates or KP, coating the back of the cornea. And on the lower right, they're so large that they're coalescing with each other, forming sort of geographic patterns of precipitate on the back of the cornea, which again, is really only seen in syphilis and sarcoid. Here on the left, we have a little bit less dense but larger from syphilis, and a larger, sorry, a higher magnification view on the right. And if you look real close, those lesions seem granular, because they're actually formed from collections of white blood cells, with granuloma, hence, the granulomatous credit facilities. Now, this is a patient who down below has keratic precipitation. Back here we have in our arrow on the right, such a large one, that it actually forms a small mass, these things have Iris itself. And so you can get granulomas, instead of collecting on the back of the cornea, they're collecting on the iris. Now the inflammation comes from the iris, but typically it's it's shed in such a way that you don't see these on the iris itself on the case to see both. And then these two little white spots here are actually not on the back of the cornea, but inflammation within the cornea itself. And we'll see some more examples of that. Now, when there's a lot of inflammation in the iris, the iris can not only form precipitates on the iris and into the fluid in front of the iris and collect on the back of the cornea. There can actually be scarring from the iris to the lens which is behind it. So why is this sort of shaped like a flower? Well, when the pupil is small before we put drops in to dilate the pupil, that's when the scarring occurs. And so the small pupil is stuck to the lens, and then we put the dilating drops in and it pulls it apart. But in areas where it can't separate the iris from the lens, you get what's called a posterior synechiae or scar between the iris and the lens and you end up with a pupil like this that's permanent typically, unless you go in and break those adhesions between the colored iris and the lens which is behind it. When you start seeing these white areas here, that's usually means that the scarring is not going to break on its own with just putting in dilating drops. Now here's a patient who had scarring between the iris and the lens, we put dilating drops in, and we broke all those adhesions except this one little strand down below. So this pigment will stay on the front of the lens, but it's really of no consequence. It's only when you can't break those that there's a problem. And so this is a good example. So this might, this might break with more dilating drops, you know, maintaining them on drops for a couple of weeks. If not, you can always go in but these single adhesions like this usually don't cause a problem. Here's another cornea, which shows a variety of things that we've already seen. So we have the synechiae here on the about 10 o'clock, we have on the back of the cornea, we have our keratic precipitates, we have some so large, they're actually sitting down below, we have some Iris nodules as well. And we have an abnormal pupil, where

it's fairly round where we are able to break the synechiae. But in the areas where the synechiaein this case, with a broad base, and with a more linear type of adhesion, the irises irregular in that space. And this is, kinda looks when you just look at the picture kind of looks like those cornea findings. But actually, these are cells floating around in the front of the eye. In the in the within that chamber between the back of the cornea and Iris and input itself, we see cells floating around. And so if you ever see our notes that say one plus cell or or two plus cell and goes up to four plus cell, it's the amount of cells that are floating around in the front of the eye. And we see that with the Tyndall Effect, which is have you ever been like in an attic with a bright light coming in the window and you see the dust floating around, you see the actual reflections off the dust, that's called the Tyndall effect. And that's that's how we look at the front of the eye to see whether there are inflammatory cells floating around. By looking at the reflections off the individual cells or small clumps of cells. And when they're this large, again, it's typically syphilis or sarcoid.

27:14
And again, you can see the cells in between the light on the back of the cornea and the light on the iris, I'm sorry, the lens, and this area in the middle is that space, and you can see it's full of inflammation.

27:32
Now we're moving on here from the uveal tract to the conjunctiva. The conjunctiva lines the entire front of the eye in the back of the lids except for the cornea. And what we see here is inflammation. So instead of, you know, sort of being almost just a light white to pink, this is a fairly dark red, with elevations collections of white blood cells within it with thickening of the whole layer, and the inflammation of the uveal track responds best to topical steroid drops, this responds best to topical steroid drops as well, and actually quiets down quite quickly. Whereas the uveitis takes much longer to quiet down with topical steroids. But the treatment is topical steroids. This is a case where the not only the conjunctiva over the eyes and flames but the conjunctiva lines inside of the lids as well. And we see inflammation, the whole sort of inferior half of the eye, not as much sclera sorry, ciliary flush, like we saw before, except maybe here and here, but a lot of inflammation down below. Now on the right, this is actually what's called a nodular scleritis, and it forms a little nodule, but it's not the it's not the conjunctiva this superficial layer or the next layer down the epi sclera it's actually the white of the eye itself or the sclera. And this is much deeper and this is much harder to treat and can cause the sclera to thin and so even though for instance the case on the left has more inflammation topically I'd be more concerned about this area on the right where the deeper tissues are involved. And this is a case of both combination of Sclerosis which is the deeper red here and epi scleritis or conjunctivitis, which is the area which is not as deeply affected. And again this can run off back up in woods if you're wondering this little hole here is a tear duct takes the tears from the eye. Alright, here's another scleritis. It's forms a nodule or that all sclera is well. You can actually have loss of sclera to the point where there's no tissue and up Paloma of uveal tissue coming through on the right again sclera itis both of these cases very severe, Vision threatening and associated with other ocular findings as well. All right, now the cornea is the clear part. And on the right, we can see the cornea should be a vascular shouldn't have any blood vessels in it at all. But if there's inflammation in the cornea, it can pull in blood vessels. And so that's what these are these blood

vessels being pulled into the cornea with scarring. And when that happens, it's called an interstitial keratitis. the interstitium of cornea is just the main bulk of the cornea proper, and you get scarring. And this can involve the center. This can be seen with congenital syphilis as well. And we see that in adults, as often, they never knew that they had congenital syphilis, but we'll see this in the cornea, do our treponemal testing and end up with patients who are positive. If you look at the red reflex, like the cat eye reflex, if you look at the light coming back out, it's just a way to see those blood vessels in the cornea, as these are different patients, but when you see blood vessels like this, that's that's an interstitial keratitis. And the differential for that, primarily is TB, and syphilis. And it can leave you just with a central scar, without the active inflammation. And we'll see that not and infrequently. Sometimes you can get scarring around the blood vessels. And so the blood vessels in this case are called ghost vessels, they're actually the clear part with lipid from those vessels, the having leaked out and collected around the vessels. So they kind of look like vessels, but they're actually sort of negative vessels, or ghost vessels with lipid everywhere but in the vessel proper.

32:07
Okay, so this is an example of a dislocated lens, the lens in the eye supposed to be supported behind the iris. And typically in syphilis, combined with trauma, you can get a dislocation of the lens, the lens usually has little strings attaching it in place, but those strings are weak, especially with congenital syphilis. And on the right, this lens should be in the center, but it's less so dislocated to the right, and you can kind of just barely see the little strings that are supposed to be holding it in place that have broken. And so again, since long standing syphilis This is more likely to happen than then acutely. But this is a good example of both of these are examples of dislocated lens on the left and a partially dislocated lens on the right. The other thing that can happen with the lens other than we had talked about pigment being left from the synechiae or scarring from the iris to the lens here are synechiae that are still there, but you could also get a cataract. So you can see this is all white cataract can be kind of dark and yellow, that can also be sort of a whitish yellow and obviously decreasing the vision. So a cataract extraction would involve removing that lens and breaking the synechiae just by physically the iris off of the lens in the areas where it's adherent. This is combination of cataract and the adhesions between the lens and the iris. Here you can see adhesions here, we can see large keratic stone below. And in this case, we have credit precipitates or collections of white blood cells up here as well and involving most parts of the cornea. Here it's hard to see because the lens behind it is so white. Now that it's a little bit more limited. We have a cataract. And we do have some posterior synechiae, but it's not actively inflamed. The way the patient on the left is with those infiltrates. So collections of white blood cells. Now when you get back to the retina and the cord, the cord being that vascular layer, Retina. These are often vision threatening early once they appear. So you're left we have that white is all syphilis inflammation of the retina. You can also see the optic nerve on the right is very crisp. And that's how it should be with an isolated leaves out in the periphery. But on our left, we see that not only do we have the retina involved, but the optic nerve is swollen as well. And you can see that by the margins appearing feathery and swollen compared to what's a normal, well circumscribed nerve would be in both these cases, the nerve is coming into the eye, and we're seeing a cross section. That's why it's round like that. And so here we have a specific retinal lesion on the right, in a patient with syphilis, but all these little white spots are also syphilis. All settled in the retina. Typically, mucus, superior patch of

inflammation from the choride, there's still some retina there, you can see the blood vessels from the retina going over it. But for all intents and purposes, there's no functioning retina where that white is and so that part of the visual field that would be represented by that retina would be gone, and you would not be able to see in that region, and that's permanent. Okay, again, we have lesions that are not only in the retina and the courtyard, but actually extending up as a physical entity as a mass of inflammation, choride above the surface into the vitreous, which is the clear fluid that fills the middle of the eye. So these are actually elevated nodules within the retina choroid and extending pushing forward into the vitreous. On the right, we have more isolated and more isolated lesion.

36:40
Now it can involve the choroid diffusely. This is a case of late stage syphilis, that sort of burned out where we have scarring of the retina. And in every area where there's a yellow or dark and there's a scar is an area that's not going to see the retina is fairly fluid in terms of it overlaps with each other. And so, for instance, this patient might not have real bad vision, unless the center of vision or the macular was affected. And once the macula is affected, there's really not a whole lot of flexibility but in the periphery, where the rods are which account for your night vision and your peripheral vision, those can be maintained late, whereas if the macula is affected, you lose your clear vision and your color vision very early. And two cases with more extensive damage. The thing that's notable about these is how much optic nerve inflammation there is especially on the right. There's also hemorrhages seen within the retina along with the white syphilis. You can also get these small little dots in the retina. And choroid which correspond to the types of carotid precipitates are those those anterior precipitates that we saw on the back of the cornea and the iris. You can also see those on the retina itself, which are a little bit smaller and less likely to cause acute vision loss. Here again, we have extensive involvement of both eyes with involvement of the optic nerve. And based on time, I'm going to spend a little less time here just to show you this is an angiogram showing the blood vessels which are acutely inflamed all of the areas where they're very bright. The vessels themselves are inflamed. That's typical of syphilis or sarcoid. As is this sectoral bleeding and whitening of the retina, which can be seen with those conditions, but also cytomegalovirus. But you can see that there's extensive retina involvement possible. Here you can see a very swollen optic nerve and extensive retina and involvement. This is a retinal detachment where there's about a hole in the retina and fluid has leaked in underneath the retina to lift the retina off, and you can also get these bleeds within the retina. These are all syphilis. And here's extensive bilateral retinal detachment with a retinal hole on this on the left and a retinal hole on the right. All right, I have other things to go over, but I think I should stop because of time.

[End Transcript]