



OCULAR SYPHILIS



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All about the Eye

Dr. Krati Gupta

Dr. Saurabh Deshmukh

www.eyelearn.in



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Introduction- Syphilis is a multisystem, chronic bacterial infection caused by the spirochete *Treponema pallidum* that is associated with numerous ocular manifestations in both the acquired and congenital forms of the disease.

Transmission occurs most often through sexual contact; however, transplacental infection of the fetus may occur **after the tenth week of pregnancy**.

Congenital syphilis

- Primary or secondary syphilis in the mother is more likely to be transmitted to the baby than is latent syphilis; the longer the mother had syphilis, the less likely is the transmission.

Systemic findings

Early congenital syphilis (age 2 years or younger)	Late manifestations (age 3 years or older)
1. Hepatosplenomegaly,	1. Result from scarring during early systemic disease
2. Characteristic changes of the long bones on radiography	2. Hutchinson teeth,
3. Abdominal distention,	3. Mulberry molars,
4. Desquamative skin rash,	4. Abnormal facies,
5. Low birth weight,	5. Cranial nerve VIII deafness,
6. Pneumonia,	6. Bony changes such as saber shins and perforations of the hard palate,
7. Severe anemia.	7. Cutaneous lesions such as rhagades, and neurosyphilis.

- Cardiovascular complications are unusual in late congenital syphilis.

Ocular signs

1. Ocular inflammatory signs of congenital syphilis may present at birth or decades later and **include uveitis, interstitial keratitis, optic neuritis, glaucoma, and congenital cataract.**
2. **A multifocal chorioretinitis and, less commonly, retinal vasculitis** are the **most frequent uveitic manifestations of early congenital infection.**
 - i. They may result in a bilateral salt-and-pepper fundus, which affects the peripheral retina, posterior pole, or a single quadrant.
 - ii. These changes are not progressive, and the patient may have normal vision.
3. A less commonly described fundusoscopic variation is that of a **bilateral secondary degeneration of the RPE,**
 - i. **which may mimic retinitis pigmentosa**
 - ii. with narrowing of the retinal and choroidal vessels,
 - iii. optic disc pallor with sharp margins,
 - iv. and morphologically variable deposits of pigment.
4. **Non-ulcerative stromal interstitial keratitis**, often accompanied by **anterior uveitis**, is the most common inflammatory sign of **untreated late congenital syphilis,**
 - i. Occurring in up to 50% of cases, most commonly in girls.
 - ii. Keratouveitis is thought to be an allergic response to *T pallidum* in the cornea.
 - iii. Symptoms include intense pain and photophobia.
 - iv. Blood vessels invade the cornea, and late stages show deep “ghost” (nonperfused) stromal vessels and corneal opacities.
 - v. Left untreated, the corneal inflammation may regress but leave the cornea diffusely opaque, with reduced vision, even to the level of light perception only.
 - vi. Anterior uveitis accompanying interstitial keratitis may be difficult to observe because of corneal haze.
 - vii. Glaucoma may also occur.
 - viii. **The constellation of interstitial keratitis, cranial nerve VIII deafness, and Hutchinson teeth is called the Hutchinson triad.**



Acquired syphilis

1. Primary syphilis	Follows an incubation period of approximately 3 weeks and is characterized by a chancre, a painless, solitary lesion that originates at the site of inoculation, Resolving spontaneously within 12 weeks regardless of treatment. The central nervous system (CNS) may be seeded with treponemes during this period although there is an absence of neurologic findings. Uveitis can occur
2. Secondary syphilis	Occurs 6–8 weeks later and is heralded by the appearance of lymphadenopathy and a generalized maculopapular rash that may be prominent on the palms and soles. Uveitis occurs in approximately 10% of cases.
3. Latent syphilis	2 nd phase is followed by a latent period ranging from 1 year (early latency) to decades (late latency).
4. Tertiary syphilis	1/3 rd of untreated patients incur tertiary syphilis, Benign tertiary syphilis- the characteristic lesion being gumma, most frequently found on the skin and mucous membranes but also in the choroid and iris, Cardiovascular syphilis- aortitis Neurosyphilis. uveitis may occur in up to 5%

Ocular features

- Ocular syphilis is best regarded as a variant of neurosyphilis, a notion that has important diagnostic and therapeutic implications.
- The ocular manifestations of syphilis are protean and affect all structures, including the **conjunctiva, sclera, cornea, lens, uveal tract, retina, retinal vasculature, optic nerve, cranial nerves, and pupillomotor pathways.**

Symptoms-Patients present with pain, redness, photophobia, blurred vision, and floaters.

Signs

- Uveitis**- Intraocular inflammation may be
 - Granulomatous or nongranulomatous,
 - Unilateral or bilateral,
 - It may affect the anterior, intermediate, or posterior segments.

- Anterior segment findings** can include

1. Iris roseola,	5. Interstitial keratitis,
2. Vascularized papules (iris papulosa)	6. Posterior synechiae,
3. Larger red nodules (iris nodosa),	7. Lens dislocation,
4. Gummata.	8. Iris atrophy

- Posterior segment findings** of acquired syphilis include

1. Vitritis,	5. Retinal vasculitis,
2. Chorioretinitis,	6. Exudative retinal detachment,
3. Focal retinitis,	7. Isolated papillitis,
4. Necrotizing retinitis	8. Neuroretinitis.

- A focal or multifocal chorioretinitis**

- usually associated with a variable degree of vitritis, is the **most common manifestation**
- These lesions are typically small, grayish yellow, and located in the post-equatorial fundus, but they may become confluent.
- Retinal vasculitis and disc edema, with exudates appearing around the disc and the retinal arterioles,
- together with serous retinal detachment, may accompany the chorioretinitis.

- A syphilitic posterior placoid chorioretinitis**

- Solitary or multifocal, macular or papillary, placoid, yellowish gray lesions at the level of RPE with accompanying vitritis,
- display corresponding early hypofluorescence and late staining, along with retinal perivenous staining on FA.
- ICG shows hypofluorescent spots corresponding to lesions.
- Clinical appearance and angiographic characteristics of which are thought to be pathognomonic of secondary syphilis.

- Less common posterior segment involvement** includes

- Focal retinitis, periphlebitis, and, infrequently, exudative retinal detachment.
- Syphilis may present as a focal retinitis or as a peripheral necrotizing retinitis that may resemble ARN or PORN.
- Focal retinal vasculitis may masquerade as a branch retinal vein occlusion
- Punctate inner retinal infiltrates have also been described

- The foci of retinitis may become confluent and are frequently associated with retinal vasculitis,
 - Syphilitic retinitis is more slowly progressive and responds dramatically to therapy with intravenous penicillin, often with a good visual outcome.
 - Isolated retinal vasculitis that affects the retinal arterioles, capillaries, and larger arteries or veins (or both) is another feature of syphilitic intraocular inflammation that may best be appreciated on FA.
7. Syphilis is an important entity to consider in the differential diagnosis of patients with **neuroretinitis and papillitis** who present with macular star formation.
 8. Neuro-ophthalmic manifestations of syphilis include the Argyll Robertson pupil, ocular motor nerve palsies, optic neuropathy, and retrobulbar optic neuritis, all of which appear most often in patients with tertiary syphilis or in neurosyphilis.
 9. **HIV and syphilis**
 - Patients with syphilis who are immunocompromised or who have HIV/AIDS may have atypical or more fulminant ocular disease patterns.
 - Optic neuritis and neuroretinitis are more common in the initial presentation of these patients, and disease recurrences are noted even after appropriate antibacterial therapy.

Diagnosis

1. The diagnosis of syphilitic uveitis is usually made according to the **history and clinical presentation and is supported by serologic testing.**
2. **Primary syphilis** may be diagnosed by direct visualization of spirochetes with **dark-field microscopy and by direct fluorescent antibody tests** of lesion exudates or tissue.
3. **Serodiagnosis** is based on the results of both non-treponemal and treponemal antigen tests.

Non-treponemal tests	Treponemal tests
Venereal Disease Research Laboratory (VDRL) rapid plasma reagin (RPR) evaluations	fluorescent treponemal antibody absorption (FTA-ABS) assay microhemagglutination assay for T pallidum antibodies (MHA-TP)
Correlate with disease activity increasing during primary or secondary syphilis & decreasing when the spirochetes are not active during latent syphilis or after adequate antibiotic Rx. for monitoring therapy for both systemic and ocular disease	Results become positive during the secondary stage of syphilis and remain positive, with rare exceptions, throughout the patient's life; They are not useful in assessing therapeutic response.
False-positive test- High SLE, leprosy, advanced age, intravenous drug abuse, bacterial endocarditis, tuberculosis, vaccinations, infectious mononucleosis, HIV infection, atypical pneumonia, malaria, pregnancy, rickettsial infections, and other spirochetal infections (eg, Lyme disease)	False-positive test- Rare (1%–2%) other spirochetal infections (Lyme disease, leptospirosis), autoimmune disease (SLE, primary biliary cirrhosis, and rheumatoid arthritis), leprosy, malaria, and advanced age.
appropriate for screening large populations with a relatively lower risk for syphilis	FTA-ABS has a higher predictive value in patients with uveitis and should be used in conjunction with non-treponemal tests in diagnosing and treating ocular syphilis

4. **Testing in HIV**
 - Testing for HIV infection should be performed in all patients with syphilis, given the high frequency of coinfection.
 - Both the false-positive and false-negative rates of serologic testing may be greater in HIV-infected patients.
5. **Testing in Infants**
 - As a result of the passive transfer of immunoglobulin G (IgG) across the placenta, the VDRL and FTA-ABS IgG test results are positive among infants born to mothers with syphilis.
 - For this reason, serodiagnosis of congenital syphilis is made using the IgM FTA-ABS test, which indicates infection in the infant.
6. **LP**
 - A lumbar puncture with examination of CSF is warranted in every case of syphilitic uveitis.
 - A positive CSF VDRL result is diagnostic for neurosyphilis, but it may be nonreactive in some cases of active CNS involvement.
 - CSF FTA-ABS test is highly sensitive, less specific and may be useful in excluding neurosyphilis.
 - Follow-up for patients with chorioretinitis and abnormal CSF findings requires spinal fluid examination every 6 months until the cell count, protein, and VDRL results return to normal.

7. PCR

- Specific ELISA- and PCR-based DNA amplification techniques are being used with increasing frequency in the serodiagnosis of syphilis.
- Given their high sensitivity and specificity, these techniques, particularly PCR analysis of intraocular and/or cerebrospinal fluids, may be valuable in confirming the diagnosis in atypical cases.

Treatment

1. Acquired syphilis

Stage of Disease	Primary Treatment Regimen	Alternative Treatment Regimen
Primary, secondary, or early latent disease	Benzathine penicillin G 2.4 million U intramuscularly as a single dose	Doxycycline 100 mg orally 2 times per day for 2 weeks or tetracycline 500 mg orally 4 times per day for 2 weeks
Late latent or latent syphilis of uncertain duration, tertiary disease in the absence of neurosyphilis	Benzathine penicillin G 2.4 million U intramuscularly, weekly for 3 doses	Doxycycline 100 mg orally 2 times per day for 4 weeks or tetracycline 500 mg orally 4 times per day for 4 weeks
Neurosyphilis	Aqueous penicillin G 18–24 million U/day given intravenously as 3–4 million U every 4 hours or continuous infusion, for 10–14 days	Procaine penicillin 2.4 million U/day intramuscularly <i>plus</i> probenecid 500 mg orally 4 times per day, both for 10–14 days

2. Treatment regimen for **congenital syphilis** in infants during the first months of life is

Primary treatment regimen	Alternative
IV aqueous crystalline penicillin G, 100,000–150,000 units/kg/day, administered IV as 50,000 units/kg/dose every 12 hours during the first 7 days of life and every 8 hours thereafter, for 10 days.	procaine penicillin G, 50,000 units/kg/dose, may be administered intramuscularly in a single daily dose for 10 days

3. Penicillin allergy in

Neurosyphilis, congenital infection, or disease in pregnant women or patients coinfectd with HIV	No signs of neurosyphilis and who are HIV-seronegative
Require desensitization and then treatment with penicillin	Doxycycline or tetracycline, Ceftriaxone and chloramphenicol

4. Jarisch-Herxheimer reaction

- A hypersensitivity response of the host to treponemal antigens that are released in large numbers as spirochetes are killed during the first 24 hours of treatment.
 - Patients present with constitutional symptoms, such as fever, chills, hypotension, tachycardia, and malaise, but they may also experience a concomitant increase in the severity of ocular inflammation that may require local and/or systemic corticosteroids.
 - In the vast majority of cases, however, supportive care and observation are sufficient.
5. Topical, periocular, and/or systemic corticosteroids, under appropriate antibiotic cover, may be useful adjuncts for treating the **anterior and posterior segment inflammation associated with syphilitic uveitis.**