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Review Article

Ocular Changes in Sexually Transmitted Diseases: Review of literature

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Abstract

Sexually transmitted infections that are acquired through sexual route. They can affect various organs n the body .Eye is also commonly involved but this mode is rarely suspected in ocular diseases. Ocular involvement may be trivial or sight threatening even. We review ocular changes in sexually transmitted infections to highlight the importance of keeping a differential of sexually transmitted diseases.

Keywords: *Sexually transmitted infections, ocular changes, sight threatening.*

Introduction

Sexually transmitted infections (STI) are group of infections which can be caused by bacteria, virus or protozoa. They are transmitted among humans usually by unprotected sex. They may be transmitted transplacentally or during delivery from infected mother to her child.

Sexually transmitted diseases may not only affect the reproductive tract but they may involve other organs like lungs, liver, brain, skin, ear and eye. Eye involvement is seen in almost all common STI and may be the primary site involved. Eyes may get involved directly through oculogenital contact or through auto inoculation.[1] Neonatal infection can occur transplacentally or during passage through birth canal. Eyes may get involved by haematogenous spread in syphilis. The presentation may vary from a minor irritation to sight threatening condition.[1] In this review we shall be discussing common ocular manifestations of STI.

Syphilis

Syphilis is a chronic STI caused by *Treponema pallidum*. This disease may involve any organ of the body.[2] Ocular involvement is seen in all components of eye.[3] There are classically different stages of syphilis: primary, secondary, latent (earlylatent and late latent), and tertiary syphilis. Eye involvement may be seen in congenital[4] or acquired syphilis.Eye can be involved in any stage or type of syphilis. Visual symptoms may be first manifestation of syphilis.[3] Usually ocular manifestations in secondary syphilis often occur 6 months after the initial infection when most systemic manifestations such as the skin rash have already resolved.[5] Only half of the patients with ocular manifestations in the tertiary stage have concomitant non-ocular signs of disease.

Table 1: Brief review of sexually transmitted diseases.

STD	Causative organism	Incubation period	Genital symptoms	Diagnosis
Syphilis	*Treponema pallidum*	3-90 days	Genital ulcer	Blood tests include venerealdisease research laboratory(VDRL)and rapid plasma regain (RPR), confirmation is requiredwith a treponemal test such as Treponemal pallidum particle agglutination or fluorescent treponemal antibody adsorption test
Gonorrhoea	*Neisseria gonorrhoea*	2-30 days	Thick purulent disharge per urethra, dysuria in males and asymptomatic in females	Gram stain and culture, polymerase chain reaction
Chlamydia	*Chlamydia trachomatis*	2-6 weeks	Commonly asymptomatic urethritis, proctitis, epididymitis prostatitis cervicitis	Polymerase chain reaction, transcription mediated amplification, and the DNA strand displacement amplification
Herpes	*Herpes simplex virus type 1 and 2*	1-3 weeks	Polycyclic painful genital ulcers	culture of the virus, directfluorescent antibodystudies to detect virus, skin biopsy, and polymerase chain reaction to test forpresence of viral DNA.
Molluscumcontagiosum	*Molluscumcontagiosum virus*	2-3 months	Pearly white umbilicated papules	Microscopic examination shows molluscum bodies
Phthiriasis pubis	*Phthiriasis pubis*	5 days to several weeks		Examination of pubic hair,eye lashes for nits, nymphs, lice

Eye brow-Madarosis is a common manifestation of syphilis.

Eyelids – Chancre,gumma,tarsitis, ulcers, blepharitis. tertiary stage.[6]

Corneal involvement occurs due to immune mediated phenomena

Orbit- Periosteitis, gumma

Conjunctival chancres are seen in primary stage, papillary or granulomatous conjunctivitis in secondary and gummasin tertiary syphilis.[7] Gummas are necrotic granulomatous lesions produced by focal obliterative endarteritis.

Episcleritis usually presents in secondary syphilis and scleritis in tertiary stage[7]

Corneal involvement occurs due to immune mediated (e.g. Jarisch –Herxheimer phenomena) presenting as interstitial keratitis.[8]It is a common manifestation of congenital syphilis. It usually manifests between the age of 5-20 years. Corneal stromal edema is the initial manifestation. Salmon patch is formed due to stromal infiltration. Stromal scarring may lead to reabsorption of superficial vessels and deeper vessels may be constricted resulting in ghost vessels. Pannus formation may be seen.In congenital syphilis keratitis is usually bilateral. In acquired syphilis interstitial keratitis is rare and is often unilateral. Congenital interstitial keratitis can be prevented if treatment is given to mother before second trimester or infant below age of 3 months.[9] Corneal ulcer, deep punctate keratitis, keratitis profunda, and keratitis linearismigrans are the other corneal syphilitic involvement.

Uveal tract can be involved in any stage of syphilis. It is the commonest tissue involved in eye due to treponemal infection and is non specific.[10] Anterior uveitis is seen in 5% of untreated cases.[11] It is bilateral in 50 % cases.[12] It may present as ggranulomatous or non-granulomatousiridocyclitis, iris nodules, dilated iris vessels (roseolae of the iris)(Fig.1), iris atrophy, posterior synechiae, and lens dislocation. Transient iris roseola may precede uveitis.In tertiary syphilis the anterior uveitis may be

chronic and granulomatous (Koeppe and Busacca nodules)[13].gummatous lesions at pupillary border and near the root of the iris may lead to sectoral iris atrophy.[14]

Posterior uveitis may present as vitritis ,[15] focal retinitis, chorio retinitis,[16] periphlebitis,retinal and vitreal haemorrhages *(cotton wool or flame shaped*), papillitis, subretinalneovascular membrane formation, exudative retinal detachment,[17] neuroretinitis and vascular occlusions. Neuritis presents as disc edema , veins and macular star (Fig.2) Healing of fundal lesions may lead to salt and pepper fundal appearance (Fig.3) or tractional band between disc and macule. There may be paracentral scotomas and blind spot enlargement. In 1990 Gass coined the term acute syphilitic posterior placoidchorioretinitis (ASPPC).In which one or more macular or juxtapapillaryplacoid lesions are seen at level of retinal pigment epithelium.[18]Occasional pigmentary changes with perivascular bony spicules lead to changes similar to retinitis pigmentosa. In congenital syphilis chorioretinitis is more common than uveitis in infancy (Fig.4). Interstitial keratitis usually presents in childhood The placoid lesions in ASPPC are larger but solitary in contrast to acute posterior multifocal placoid pigment epitheliopathy (APMPPE). The small leopard-spot alterations of the pigment epithelium seen on fluoresce in angiography in the cicatricial phase of ASPPC is not seen in APMPPE and is sufficiently characteristic to suggest a diagnosis of syphilis according to Gass.

Table 2: Difference of necrotizing retinitis from herpetic retinal necrosis .

Syphilitic necrotizing retinitis	**Acute herpetic retinal necrosis**
Necrotic lesions on posterior pole	Necrotic lesions at periphery
Surface of lesion covered by exudate	Surface of lesion clear
Mottled necrosis	Homogenous necrosis

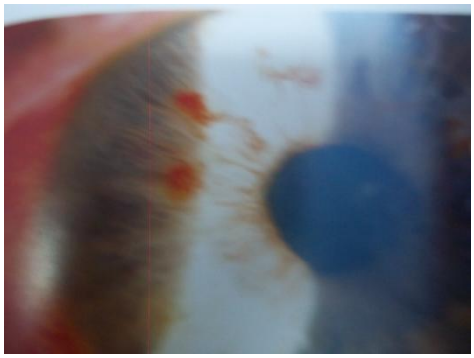

Fig. 1 Iris roseola

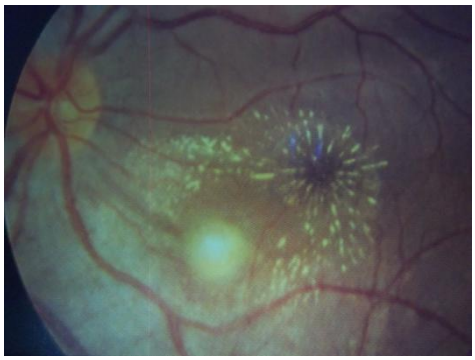

Fig. 2 Macular star

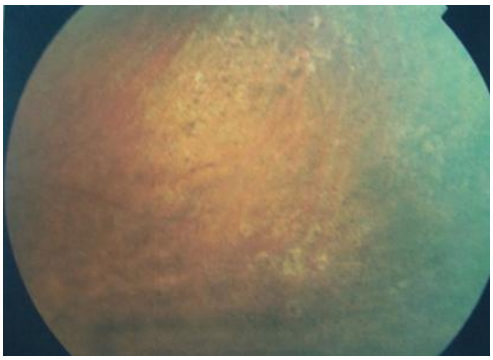

Fig. 3 Salt and pepper retina in syphilis

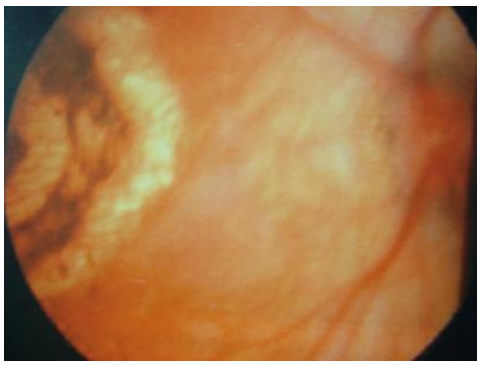

Fig. 4 Chorioretinal scar in congenital syphilis

Syphilitic eye disease may present as intermediate uveitis with retinal vasculitis, cystoid macular oedema and a pars plana exudate is not present in syphilitic vitreitis. Simultaneous involvement of

the anterior and the posterior segment or panuveitis is highly variable and ranges from 27% to 66%. Optic nerve involvement is seen in secondary and tertiary syphilis (Table 3).

Table 3: Involvement of optic nerve has various presentations

Optic perineuritis Inflammation of meningeal sheaths of nerve	Swelling of optic disc No affect on visual acuity or field of vision
Anterior optic neuritis	Visual loss and field defects seen
Neuroretinitis(anterior optic neuritis +deposition of lipids)	Visual loss and field defects seen Hard exudates in papillomatous region
Retrobulbar neuritis (secondary to syphilitic retinitis,meningitis or periosteitis)	
Pappiloedema(due to meningitis)	Enlargement of blind spot

Optic atrophy: It is seen secondary to endarteritis of small intramural arterioles with lymphocytic infiltration of pial sheaths of optic nerve. Endarteritis is seen in late syphilis in one third of untreated patients. it is seen as sharply defined pale optic disc with narrowing of retinal arterioles. About 5 % of neurosyphilis may present with optic atrophy.

Ocular motor nerve involvement may lead to palsies secondary to third, fourth and sixth cranial nerve involvement. These nerves can be involved secondary to syphilitic meningitis, gummas along the nerves, brain stem infarcts, periosteitis of superior orbital fissure or due to syphilitic aneurysm.

Pupils-Argyll Robertson pupil (ARP) can be seen in syphilis. Pupillary reaction to accommodation is present while it does not react to light. This dissociated response is due to interruption of internuncial neurons connecting the Edinger Westphal and other pretectal nuclei. ARP is also seen in diabetes, alcoholism, encephalitis and multiple sclerosis.

Table 4: Visual field defects

Visual field defect	Structure involved
Ring scotoma	choroidoretinitis
Central scotoma	Optic neuritis
Peripheral constriction, central or cecocentral scotoma,sectoral defect	Tabeitic optic atrophy
Irregular bitemporal,binasal hemianopia	Basilar meningitis
Complete /partial homonymous hemianopia Or quadrantiopia	Middle cerebral artery arteritis

Acute meningitis occurs in 1% to 2% of patients with secondary syphilis and this can cause increased intracranial pressure and papilledema. In pure papilledema there is an enlargement of the blind spot but no signs of inflammatory cells in the vitreous. Papilledema should be differentiated from inflammatory optic disk edema due to optic neuritis, papillitis, and neuroretinitis. These patients have marked loss of visual acuity and display central and cecocentral, or nerve fibre bundle defects, and often have signs of vitreous inflammation. In papillitis there is a swollen disk with intraretinal exudates and perivasculitis around it.

Serological testing is done in suspected cases. The nontreponemal tests, such as the venereal disease research laboratory (VDRL) test and the rapid plasma reagin (RPR) card test are used for diagnosing active disease. Treponemal tests, such as the fluorescent treponemal antibody absorption (FTA-ABS) test, the micro hemagglutination- T. pallidum (MHA-TA) test and the T. pallidum-particle agglutination test, are used for confirmation of previous or current infection.

Penicillin G in dosage of 3-4 million units every 4 hourly or Procaine penicillin 2.4 million units once daily for 10-14 days along with probenecid 500mg 4 times a day. Topical steroids are given for treatment of anterior ocular involvement while systemic steroids are required for posterior segment disease.

Gonorrhea

Gonorrhea is a STI caused by gram negative diplococcus *Neisseria gonorrhoea*. Incubation

period of ocular infection is usually 3-19 days.[19]Urethral symptoms usually precede eye complaints. *Neisseria gonorrhoea*is one of the few organisms which can penetrate intact corneal epithelium Severe purulent conjunctivitis is the hallmark of the disease (Fig.5). Intense conjunctivitis, hyperaemia, chemosis and pseudo membrane formation may be seen(Fig.6). Infection can spread leading to keratitis (which may vary from mild corneal melt to diffuseedema, Ulceration (marginal orring ulcers), descemeto-coele formation and ultimately perforation and endophthalmitis may occur[20]. Preseptal cellulitis may result in swelling of eyelids.

Opthalmianeonatorum is conjunctivitis occurring in neonates secondary to passage through infected birth canal. The common causative organisms are *Neisseria gonorrhoea, herpes simplex and Chlamydia trachomitis.* The risk of neonate getting gonococcal eye infection from mother is 30 %.

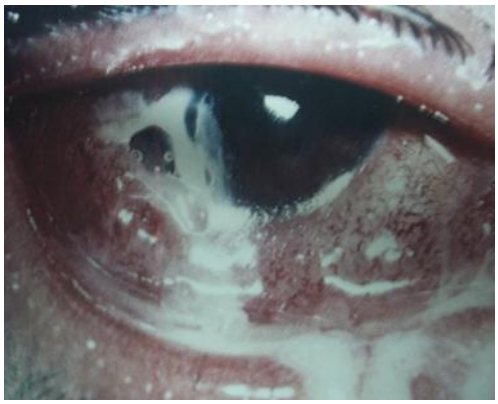

Fig. 5 Purulent discharge in gonococcal conjunctivitis

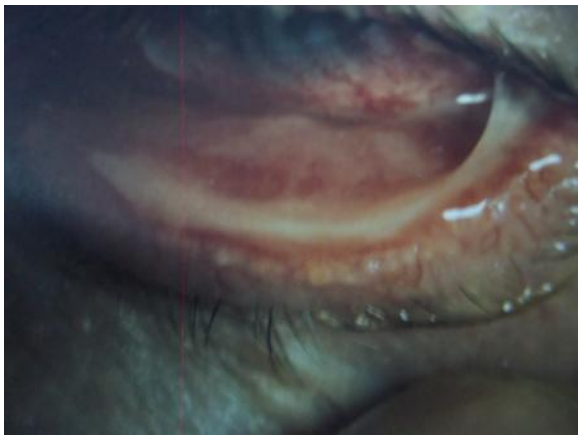

Fig 6 Pseudomembrane in gonococcal eye disease

Conjunctival scrapings will show gram negative diplococci. Theoutcome of gonococcal conjunctivitis depend upon severity of disease at start of therapy. CDC recommends treatment with parenterally administered antibiotics like ceftriaxone 1 gram as a single dose. Treatment with spectinomycin (2gram IM for 3 days) or norfloxacillin 1200 mg for 3 days are also effective.[21] Topical antibiotics and saline lavage can be given in neonatal infections. In areas of high prevalence disinfection of infant's conjunctiva with 1 % aqueous silver nitrate, or benzyl penicillin solution, tetracycline 1% or erythromycin 0.5 % can be done.

Chlamydial infection

Chamydialtrachomitis is the most common sexually transmitted infection worldwide. *C. trachomatis* is an obligateintra cellular pathogen. Urethritisis caused by serovars D, K. Serovars B and Ba have been isolated from eye and genital tract. Genital ulcers can be caused by lymphogranuloma venereum (LGV, serovars L1, 2 and 3). Conjunctival infection usually has a incubation period of 2 weeks. Inclusion conjunctivitis is usually of the follicular type most commonly involving the inferior tarsal conjunctiva (Fig.7).[22]

Preauricular lymphadenopathy is almost always present. Usually there is a persistence of conjunctivitis of more than 3 weeks duration. There is an associated stringy discharge. Signs include conjunctival injection, superficial peripheral punctuate keratitis, superior corneal pannus, peripheral subepithelial infiltrates (Fig 8), iritis and follicles. This resolves spontaneously in 6-18 months. Direct monoclonal fluoroscopy and vision microscopy, ELISA for chlamydia antigen, Mc Coy cell culture and polymerase chain reaction are various investigations which can help in diagnosis. Systemic therapy with 1g azithromycin as a single dose or doxycycline 100mg BID for 7 days is required to treat both urethritis and conjunctivitis. Sexual partners should also be treated. Co-infection with

gonorrhoea is common both the diseases should be treated simultaneously.

Inclusion conjunctivitis may be non sexually transmitted also.

In any conjunctivitis in a neonate inclusion conjunctivitis should be kept in the differential diagnosis. It usually develops within 5-19 days of birth. In contrast to follicular conjunctivitis in adults there is diffuse papillary type in children .This is because of the absence of lymphoid cells in neonates. This type of response is seen till 3 months of age. Child should be given topical and systemic erythromycin. oral erythroethyl succinate 25 mg/kg BD for 2 weeks.

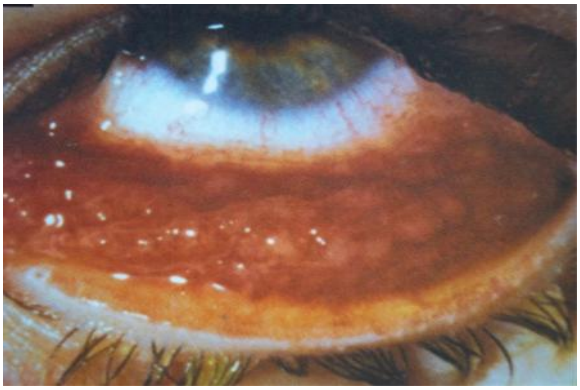

Fig 7 Inferior tarsal follicles in Chlamydia

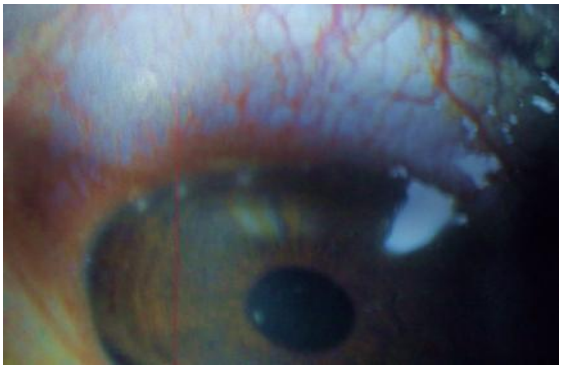

Fig. 8 Limbalin filterates in chlamydia

Reiter's syndrome

Reiter's syndrome is classically defined as triad of arthritis, urethritis and conjunctivitis. it can occur in 1-3 % of males following genital chlamydial infection. Systemic infection usually occurs one month after infection. conjunctivitis is seen in 60-90 % cases. It is mild, symmetric and bilateral with mucopurulent discharge. It usually resolves within 10 days. In 37 % cases uveitis may develop. Uveitis more commonly develops in patients with HLAB 27 positivity and sacroilitis. Hypopyon formation may be seen. Treatment is with topical steroids and mydriatics (to prevent synechiae formation). Ocular inflammation may subside spontaneously in 3 months but recurrences may be seen. Occasional reports of episcleritis, scleritis, posterior uveitis and keratitis have been seen.

Herpes simplex virus infection

Both HSV 1 and 2 can involve the eyes. Ocular HSV occurs usually 1-2 weeks after genital lesions. Photophobia, foreign body sensation blurred vision, follicular conjunctivitis, blepharitis, keratitis, erosive dermatitis (Fig.9) may develop. Virus can lie dormant in trigeminal, ciliary nerve or superior cervical ganglia. Ocular HSV recurrence seen in 50 % cases. Dendritic epithelial keratitis is the hallmark of the disease (Fig.10). Patient presents with photophobia, epiphora and variable loss of vision depending upon the area involved. Further recurrences may lead to hypoesthesia. Disciform stromal keratitis consists of central dense area of inflammation and oedema surrounded by immune cells and forms Wessely's ring. Recurrences may later lead to necrotizing interstitial keratitis, chronic uveitis and secondary glaucoma. Spontaneous resolution of conjunctival lesion occurs. Recurrent HSV may require topical trifluridine upto 2-3 hourly till dendritic lesions regress and later maintained thrice daily for another one week. Cycloplegics are required if uveitis is present. In disciform keratitis permanent visual loss may occur. Use of corticosteroids in this condition is controversial but recent reports suggest that steroids reduce persisters and progressers of stromal inflammation. Tapering of steroids should be done over 10-16 weeks. With concomitant instillation of trifluridine 1% solution.

For neonatal herpes IV acyclovir (20mg/kg) every 8 hours may be required along with topical povidone iodine to prevent superadded bacterial infection.

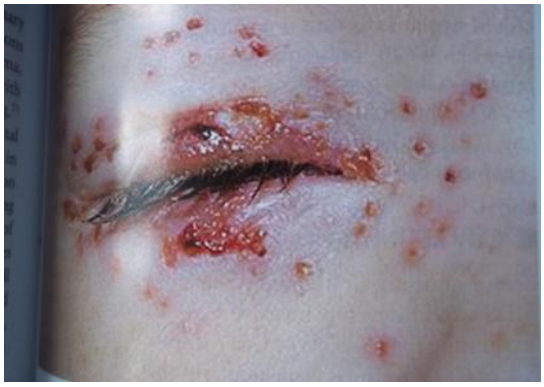

Fig 9 herpetic polycyclic lesions

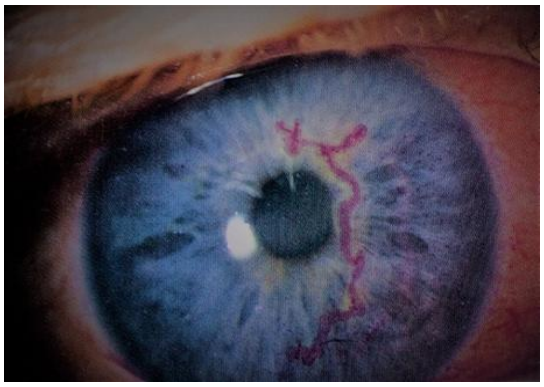

Fig. 10 Dendritic ulcer (Rose Bengal stain)

Pubic lice (Phthirus pubis)

Eye lashes may get infested by crab louse (Fig. 11). This infection normally occurs secondary to infestation of pubic hair. Lid margins are pruritic and associated with blepharo conjunctivitis. Slit lamp examination will show crusting and blood tinged deposits at lid margins. reddish brown faecal matter at base of eyelashes. The predilection of P. pubis for the eyelashes is curious and believed to be due to the distance between cilia, which corresponds to the grasping span of the lice.

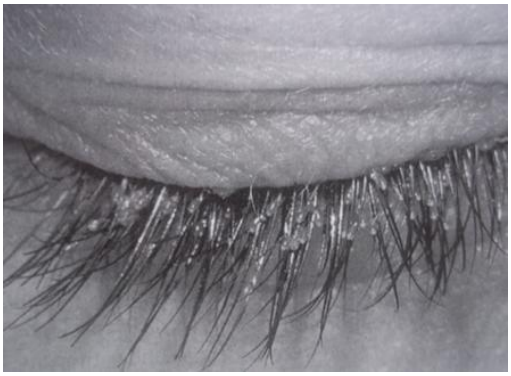

Fig.11 Phthirus pubis

Treatment involves physical removal. Supplementary therapy is also required. Smearing of bland petroleum jelly or bacitracin ointment is helpful. Treatment has to be continued for 2 weeks as nits are resistant to this therapy.

Physostigmine 0.25% ointment poisons the respiratory tract of adult mite. Yellow mercuric oxide 1% or ammoniated mercury 3%,sodium fluorescein can also work for eradication of mite. Pilocarpine (4%) scrubbed over eyelashes twice a day for 4 days can eradicate eggs and mite. Genital lesions also need to be treated.

Table 5: Treatment of STD's

STD	Treatment	Eye treatment
Syphilis Early Early latent Late latent /tertiary Neurosyphilis	 Benzathine penicillin G 2.4 MUIM single dose Benzathine penicillin G 2.4 MU IM in a single dose Benzathine penicillin G 7.2 MU total, administered as three doses of 2.4 MU IM eachat 1-week intervals Aqueous crystalline penicillin G 18–24 MU perday, administered as 3 - 4 MU IV every 4 h	Topical steroid for anterior segment complications (interstitial keratitis and anterior uveitis) ?cycloplegics Systemic steroids for posterior segment complications (postuveitis, optic neuritis) andscleritis.
Gonorrhoea	Ceftriaxone 125 mg IM in a single dose or Cefixime 400 mg orally in a single dose or Ciprofloxacin 500 mg orally in a single dose or Ofloxacin 400 mg orally in a single dose Levofloxacin 250 mg orally in a single dose	
Chlamydia	Tab Azithromycin 1 gm single dose or Doxycycline 100mg twice a day for 7 days	Topically with tetracycline, erythromycin, or fluoroquinolones
Herpes simplex	Acyclovir 400 mg orally three times a day for 7–10 days	Keratitis: topical antiviral agents (acycolvir 3%) Anterior uveitis: topical steroid

Sources of support nil

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