Syphilis

97

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Contents

Core Messages

- Syphilis is a sexually transmitted disease caused by a gram-negative bacterium, *Treponema pallidum.*
- Syphilitic uveitis most often presents in the secondary stage. Timely diagnosis and adequate treatment will protect against morbidity and even mortality associated with the advanced stage of the disease.
- Syphilis causes a wide variety of ocular inflammatory conditions. Typical for the disease but rarely observed are vascular tufts (roseolae) on the iris of patients with anterior uveitis. Posterior involvement typically presents as acute posterior placoid chorioretinitis or as acute necrotizing retinitis mimicking herpetic retinal necrosis.
- Ocular syphilis is treated the same way as neurosyphilis: 18–24 million units of aqueous penicillin per day for 2 weeks. Ceftriaxone is the first choice in patients allergic to penicillin.
- Early diagnosis followed by prompt and effective antibiotic treatment results in a cure in the majority of patients.

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97.1 Definition

Syphilis, a sexually transmitted disease, is a systemic infection caused by *Treponema pallidum subsp. pallidum*, a member of the order *Spirochaetales*, family *Spirochaetaceae*, and genus *Treponema.*

The World Health Organization (WHO) estimated that there were approximately 12 million new cases of syphilis among adults in 1999 [1]. Although the disease is present in all parts of the globe, the highest incidence is recorded in the developing world with four million new cases in sub-Saharan Africa, four million in South and Southeast Asia, and three million in Latin America and the Caribbean. Data on the prevalence of the disease are gathered from studies of genital ulcerative diseases (GUD), from serological screening of pregnant women in antenatal clinics, and from screening of blood donors and different populations at risk (truck drivers, commercial sex workers) [14]. The incidence rate in most industrialized countries has substantially declined since the peak after the Second World War with incidence rates below 5 per 100,000 in most countries. In contrast with the decline observed in Western Europe, there has been an alarming increase of the incidence in the independent states of the former Soviet Union with incidence rates as high as 120–170 per 100,000 of population.

Syphilis is responsible for less than 5 % of all cases of uveitis.

97.2 Clinical Manifestations

97.2.1 General Disease

T. pallidum enters the body through small abrasions on the skin or mucous membranes. After local multiplication, the treponemes will spread to the regional lymph nodes and from there to the whole body. Vertical transmission via transplacental infection from the infected mother to the unborn child occurs after the first 3 months of pregnancy and may result in intrauterine death or give rise to congenital syphilis [36].

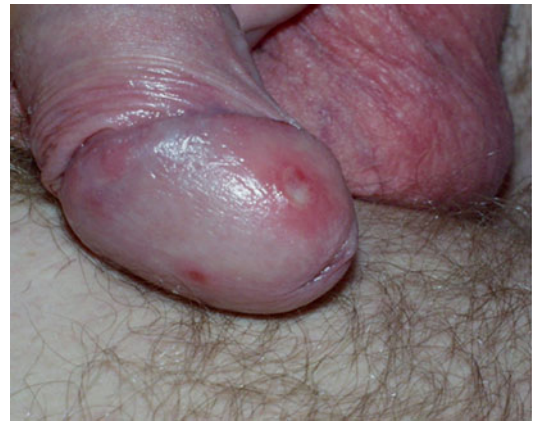

Fig. 97.1 Syphilitic chancre

The natural history of untreated acquired syphilis has been divided into four stages: primary syphilis, secondary syphilis, the latent stage, and tertiary syphilis [31, 36, 40].

Primary syphilis is characterized by the presence of a single, painless, nonsuppurative ulcer with a hard base, the syphilitic chancre (Fig. 97.1). This highly infectious lesion appears 2–6 weeks after exposure and heals within 3–6 weeks. Proliferation and spread to regional lymph nodes causes painless lymphadenopathy. Most chancres are located in the genital area, but extragenital chancres on sites such as the conjunctiva and the eyelids have been reported.

If no appropriate antibiotic treatment is given, the treponemes disseminate in the blood and signs of *secondary syphilis* appear about 6 weeks after the appearance of the primary chancre. Secondary syphilis is characterized by a flu-like illness with sore throat, arthralgias, myalgias, headache, fever, and very often a painless, maculopapular skin rash (Fig. 97.2). The rash disappears spontaneously after some weeks. Invasion of the central nervous system occurs in about 40 % of patients with secondary syphilis . Acute meningitis is observed in only 1–2 % of patients. Neuro-ophthalmological manifestations of secondary syphilis include optic neuritis, optic perineuritis, or cranial nerve palsy. Anterior uveitis is the most common eye finding in this stage and was reported to occur in about 5 % of syphilitic patients before the introduction of penicillin.

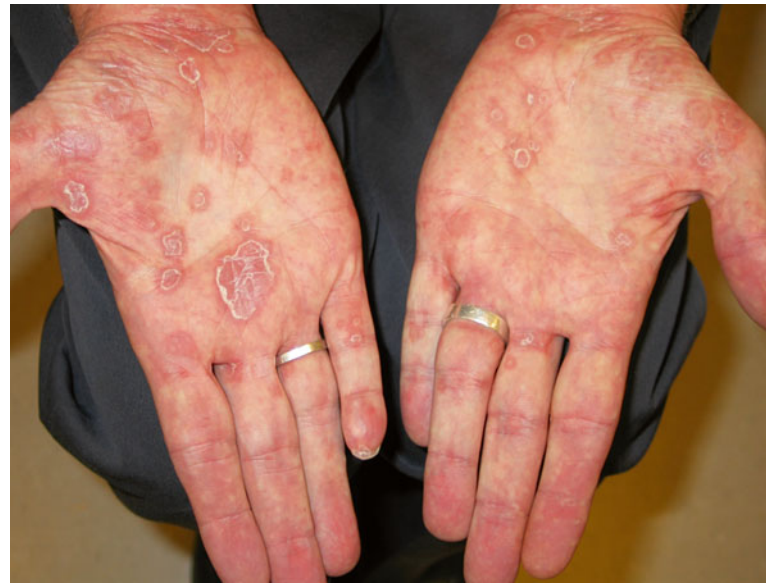

Fig. 97.2 Maculopapular rash in secondary syphilis

The *latent stage* is divided in the early latent stage, the first year following infection, and the late latent stage, the subsequent period. During the early latent stage, relapses of secondary syphilis are still possible. In the late latent stage, clinical disease is no longer detectable and the patient is no longer contagious, although dormant treponemes may be present in liver and spleen. Reawakening and multiplication of dormant treponemes in one third of the patients sets the stage for the development of tertiary syphilis. This may happen from several years to several decades after the secondary stage. Tertiary syphilis is divided in three groups: benign tertiary syphilis, cardiovascular syphilis, and neurosyphilis.

Benign *tertiary syphilis* is characterized by gumma formation. Gummas are granulomatous lesions mainly found in skin and mucous membranes but also described in the uveal tract. Cardiovascular syphilis is the result of an obliterative endarteritis of the vasa vasorum of the aorta and can cause aortitis, aortic aneurysms, and aortic valvular insufficiency.

Neurosyphilis includes meningovascular syphilis and parenchymatous neurosyphilis. Meningovascular syphilis is the result of small-vessel endarteritis and vascular occlusion leading to stroke syndromes or seizures. Visual field defects due to vascular occlusions affecting the visual pathways are commonly seen at this stage. Parenchymatous neurosyphilis is the end result of postinflammatory neuronal degeneration: general paresis, tabes dorsalis, optic atrophy, and pupillary disturbances (Argyll Robertson pupil) are all manifestations of parenchymatous neurosyphilis.

Congenital syphilis causes intrauterine death in one half of infected fetuses. In children who survive, congenital abnormalities may be obvious at birth (early congenital syphilis), mainly mucocutaneous lesions and osteochondritis. In other survivors, congenital infection may not be apparent until about 2 years of age (late congenital syphilis) when facial and tooth deformities develop.

97.2.2 Ocular Disease

Ocular involvement in primary syphilis is rare and mainly limited to chancres of the eyelids and the conjunctiva due to direct inoculation from contaminated fingers or secretions. The protean manifestations of ocular syphilis affecting all structures of the eye occur mainly in secondary and in tertiary syphilis. Despite the widespread but erroneous belief that ophthalmic lesions

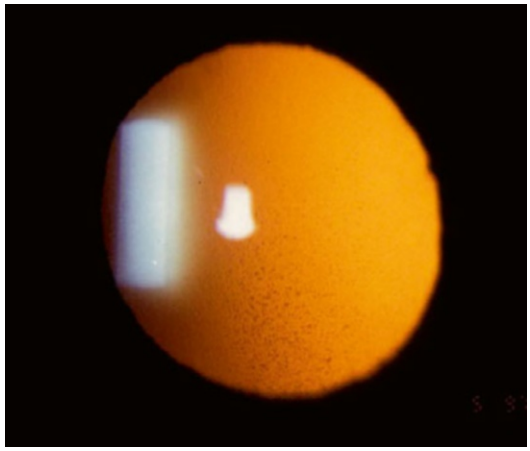

Fig. 97.3 Syphilitic anterior uveitis

are mainly manifestations of tertiary syphilis, corneoscleral, uveal, retinal, and optic nerve inflammation may be observed as well in secondary as in tertiary syphilis. There are however differences: chronic gummatous or granulomatous inflammation of the ocular structures is typical of late-stage disease, whereas more aggressive inflammation (iridocyclitis with vascularized nodules or roseolae and necrotizing retinitis) is associated with secondary syphilis. It is important to stress that many patients who present with ocular signs of syphilis do not have systemic signs of the disease. In fact the ocular manifestations in secondary syphilis often occur up to 6 months after the initial infection when most systemic manifestations such as the skin rash have already resolved. Likewise, only half of the patients with ocular manifestations in the tertiary stage have concomitant non-ocular signs of disease [40].

Anterior Uveitis

Anterior uveitis in secondary syphilis starts as an acute unilateral iridocyclitis. The severity may range from mild nongranulomatous to severe, granulomatous disease (Fig. 97.3). The second eye becomes involved in about one half of the patients. Typical of secondary syphilis but rarely observed are the iris roseolae which are vascular tufts in the middle third of the iris surface, corresponding to the infectious mucocutaneous lesions [32]. In tertiary syphilis, the anterior uveitis may be chronic and granulomatous (with Koeppe and Busacca nodules). Gummas of the uveal tract can mimic iris tumours and even erode through the sclera. Poor response to topical steroid treatment and a history of a skin rash in the recent past should alert the clinician to the possibility of syphilitic anterior uveitis [38].

Intermediate Uveitis

Syphilitic eye disease may lead to intermediate uveitis especially if mild inflammation of the anterior segment is associated with a more pronounced vitreal reaction. Other signs often associated with intermediate uveitis are retinal vasculitis, cystoid macular edema, and/or a hot disk. A frank pars plana exudate is not present in syphilitic intermediate uveitis [22].

Posterior Uveitis

Unlike other infectious agents that have a predilection either for the retina (cytomegalovirus) or for the choroid (*M. tuberculosis*), treponemes seem to be able to thrive in all the layers of the eye, resulting in a wide variety of clinical manifestations: focal/multifocal chorioretinitis, acute posterior placoid chorioretinitis, necrotizing retinitis, retinal vasculitis, intermediate uveitis, and panuveitis [22, 31, 40]. An important distinction is made between acute and chronic syphilitic posterior uveitis [28]. Acute syphilitic uveitic syndromes are usually florid, rapidly progressive, and associated with secondary syphilis and syphilitic meningitis. Retinal involvement is a predominant feature and may lead to chorioretinitis, retinochoroiditis, neuroretinitis, and retinal necrosis. Vitritis is prominent, and associated optic nerve swelling is seen in the majority of patients. Progressive visual loss is the rule, unless penicillin treatment is initiated that will clear inflammation in most patients. Chronic syphilitic posterior uveitis, a manifestation of tertiary

syphilis, is often insidious and associated with subclinical neurosyphilis. Features common to all patients with chronic syphilitic posterior uveitis are a mild vitritis and a low-grade pigment epitheliitis. Multifocal choroiditis seen in some patients and mild retinal vasculitis observed in the majority are superimposed on this pattern.

Deep chorioretinitis used to be considered the most common form of posterior segment involvement. Focal syphilitic chorioretinitis presents as a deep, yellow-grey lesion often with a shallow serous retinal detachment and inflammatory cells in the vitreous. Multifocal lesions from one half to one disk diameter can coalesce to become confluent. Fluorescein angiography shows a pattern of early hypofluorescence of the lesion followed by late staining.

Since the original description by Gass of a specific entity referred to as acute syphilitic posterior placoid chorioretinitis (ASPPC) in six patients with secondary syphilis [12], several case series are reported in the literature [5, 18]. These patients present with large, solitary, placoid, pale-yellowish subretinal lesions with vitreous cell infiltration, usually in both eyes. The lesions show evidence of central fading and a pattern of coarsely stippled hyperpigmentation of the pigment epithelium. The placoid lesions in ASPPC are larger in size and often solitary which differentiates them from the lesions observed in acute posterior multifocal placoid pigment epitheliopathy (APMPPE). The pattern of small leopard-spot alterations of the pigment epithelium seen on fluorescein 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 (Fig. 97.4). A recent study of 30 eyes with ASPPC showed characteristic outer retina abnormalities on SD OCT: disruption of the inner segment/outer segment band, nodular thickening of the retinal pigment epithelium, and punctate choroidal hyperreflectivity. After treatment, these abnormalities reversed and then improved in most of the patients [26].

Necrotizing retinitis mimicking herpetic retinal necrosis has been reported in the recent literature with increasing frequency [8, 23, 37]. This

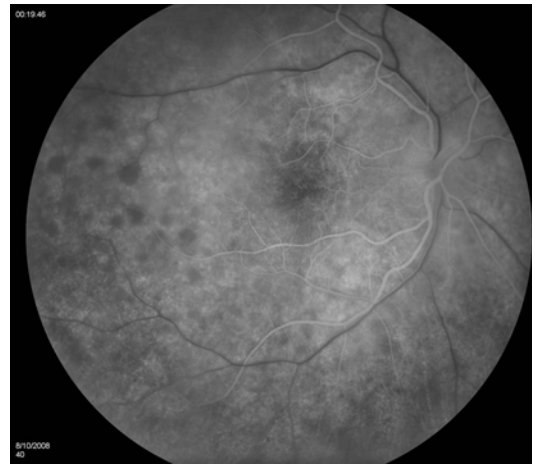

Fig. 97.4 Leopard-spot alterations of the pigment epithelium in the cicatricial phase of ASPPC

form of syphilitic retinitis presents as one or more yellow-white patches of necrosis, often associated with vasculitis, vitreous cells, and discrete anterior segment inflammation, imitating closely the acute retinal necrosis syndrome (ARN) of herpetic origin (Fig. 97.5a, b). In the absence of adequate antibiotic therapy, the lesions will progress and cause serious visual disability in a matter of weeks. The tendency for bilateral disease and the more aggressive course observed in immunodeficient patients dictate the need for prompt diagnosis and effective treatment in this patient group. The response to intravenous penicillin in syphilitic necrosis is excellent and halts further progression. The necrotic areas heal with scarring of the retinal pigment epithelium resulting in the picture of pseudo-retinitis pigmentosa (Fig. 97.6).

Recently, Wickremasinghe and co-workers described the features of an unusual syphilitic uveitis syndrome in five homosexual men: All patients had acute retinal arteriolitis with distinctive inner retinal and preretinal dots [39]. Although this particular pattern was already described previously [30, 33], this report is the first to draw attention to the diagnostic value of this clinical appearance to help differentiate syphilis from other causes of retinitis. We observed an identical case in a patient with syphilitic posterior placoid chorioretinitis who received

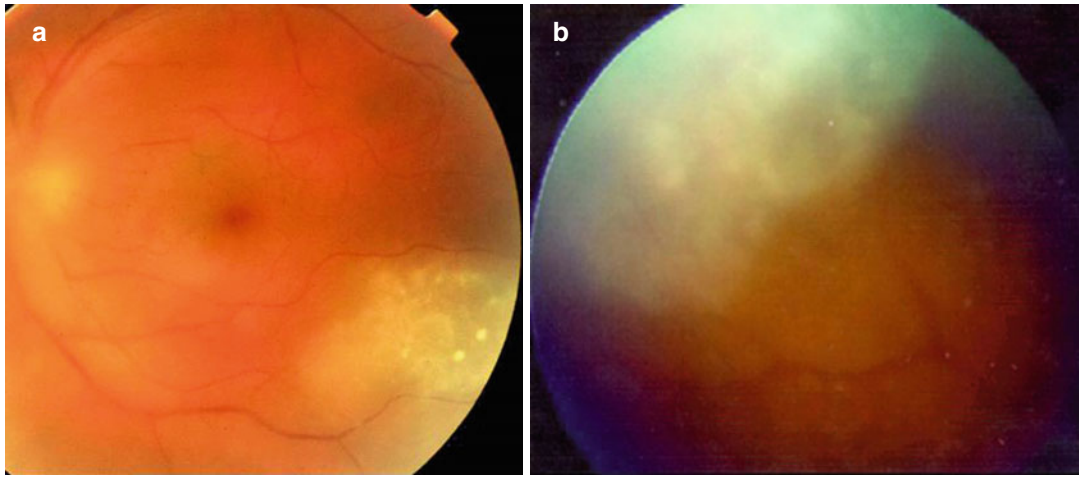

Fig. 97.5 (**a**, **b**) Foci of syphilitic retinitis in an immunocompetent patient

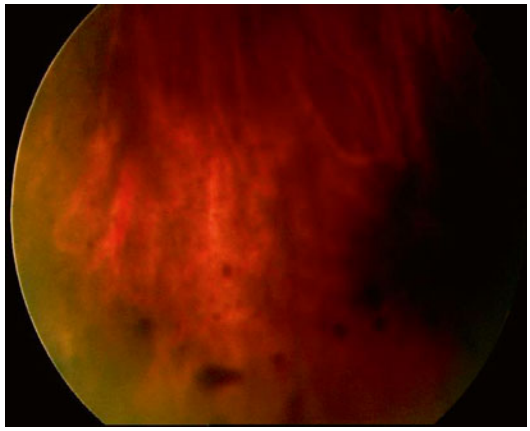

Fig. 97.6 Healed syphilitic retinitis presenting as pseudo-retinitis pigmentosa

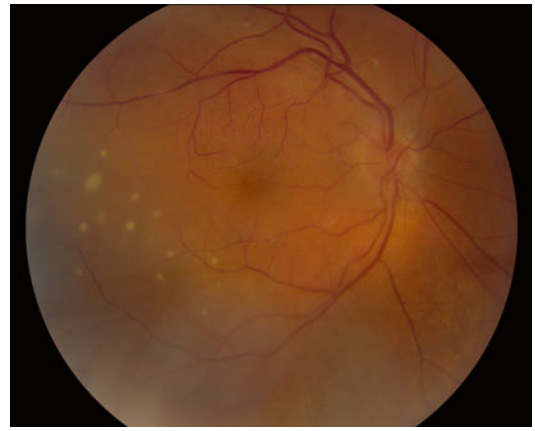

Fig. 97.7 Syphilitic inner punctate retinitis

steroids before the diagnosis of syphilitic uveitis was made (Fig. 97.7).

The reported prevalence of panuveitis is highly variable and ranges from 27 to 66 % [2, 8, 34].

Optic Nerve Inflammation

Acute meningitis occurs in 1–2 % of patients with secondary syphilis, and this can cause increased intracranial pressure and papilledema [21]. In pure papilledema, there is 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, or neuroretinitis [24]. The latter patients have marked loss of visual acuity and display central and coecocentral, 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. When the inflammatory changes extend into the peripapillary retina resulting in hard exudates, the condition qualifies as neuroretinitis. Optic perineuritis is a distinct entity due to an inflammation of the meningeal sheaths of the optic nerve and causes mild swelling of the optic disk, without affecting its function. This condition should be suspected in patients with normal visual acuity and colour vision who seem to have papilledema but in whom lumbar puncture

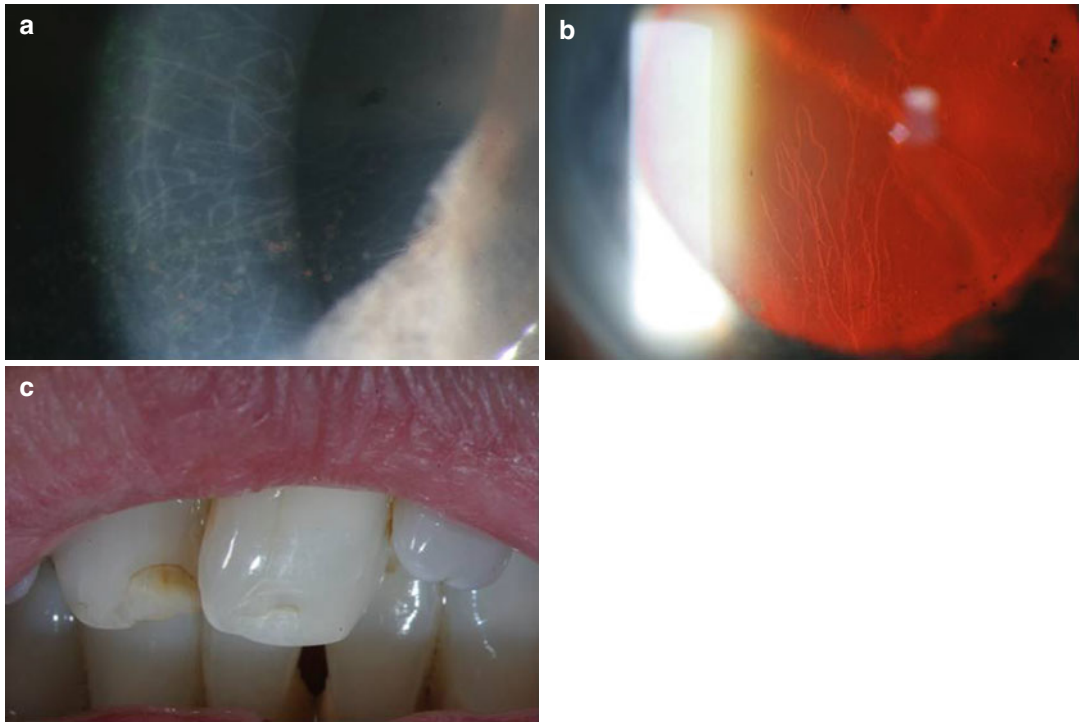

Fig. 97.8 (**a**, **b**) Interstitial keratitis with ghost vessels in a patient with congenital syphilis. (**c**) Peg-shaped central incisors in congenital syphilis

reveals normal cerebrospinal fluid pressure and the presence of inflammatory cells or increased protein. Although inflammatory conditions of the optic nerve are more common in the secondary stage, they may occur in tertiary syphilis as well. Optic atrophy is however the prevailing pathology in this stage and is present in 5 % of patients with symptomatic parenchymatous neurosyphilis [16].

Syphilitic Uveitis in HIV-Infected Patients

Coinfection with HIV and syphilis is common due to shared risk factors related to sexual behaviour. Syphilitic chancres like any genital ulceration increase the risk of acquiring and transmitting HIV [6]. HIV-infected patients with syphilis have a higher treponemal load and are more prone to develop neurosyphilis [17]. Ophthalmic involvement in these patients is often bilateral and several reports suggest that syphilitic uveitis in HIV-infected patients tends to run a more aggressive course and may relapse despite adequate treatment [27, 37]. Moreover, the serological diagnosis of syphilis is more challenging in HIV-infected patients, and depending on the stage of the disease, more false-positive (early stage of HIV) or more false-negative results (advanced immune dysfunction) may be encountered [9, 15].

Congenital Syphilis

Interstitial keratitis is a common inflammatory sign of untreated late congenital syphilis (Fig. 97.8a, b) It is part of the so called classic triad of Hutchinson together with peg-shaped upper incisors (Fig. 97.8c) and sensory deafness [40].

97.3 Etiology and Pathogenesis

Syphilis is caused by the spirochete *Treponema pallidum*, a gram-negative bacterium that does not secrete toxins and is not intrinsically cytotoxic. Tissue destruction in primary disease is mainly due to a massive influx of mononuclear inflammatory cells as a response to the invasion

of spirochetes. Obliterative endarteritis of small vessels will lead to ulceration [10]. The host immune response in syphilis is not entirely understood, but two important observations deserve emphasis. First, a previous episode of syphilitic infection does not protect a patient against subsequent reinfection, indicating that there is no long-term immunity against syphilis. Second, approximately one third of patients, if untreated, will develop lifelong chronic disease, indicating that the body is unable to eradicate the spirochetes, despite high circulating antibody titers and intact cellular immune mechanisms. A switch from the Th1-mediated pathway to a Th2-mediated type has been proposed to explain the chronicity of the infection [31].

Autoimmunity certainly plays a role in secondary and tertiary syphilis, as evidenced by the presence of antitreponemal antibodies within glomerular deposits in patients with nephrotic syndrome secondary to syphilis [11]. Likewise, autoimmune phenomena may be part of the picture in ocular and neurological disease. However, the rapid clinical improvement observed after administration of penicillin in late syphilitic disease is a strong argument in favour of a bacterial cause rather than an autoimmune induced phenomenon. There is only limited information available on the histopathologic findings in syphilitic chorioretinitis. On the basis of four histologically examined eyes, Blodi and Hervouet concluded that the invasion of the choroid by retinal elements (glia, retinal pigment epithelium) through large breaks in Bruch's membrane is a finding characteristic for syphilitic chorioretinitis [3].

97.4 Diagnosis

Because of the wide variety of syphilitic ocular manifestations and the fact that this disease may mimic other etiologic entities, routine use of serologic tests for syphilis in adult patients with intraocular inflammation of unknown origin is mandatory, unless the diagnosis is quite obvious or a well-known systemic disease is present and can explain the ocular inflammation. Although the cost of this approach is high, since syphilis has a low prevalence in the population, even in the selected population of uveitis patients, it is justified in view of the serious implications of undetected disease. Moreover, testing for syphilis is essential in the following situations: if the history or the presentation are suggestive, if the inflammation has unusual characteristics or if it fails to respond to the usual treatment (often steroids), and if the patient belongs to a high-risk group for sexually transmitted diseases (HIV-positive patients, men having sex with men, commercial sex workers) [31, 36, 40].

Laboratory confirmation of syphilis can be obtained via direct detection of *Treponema pallidum* (dark field microscopy, silver staining, direct fluorescent antibody stains), but this method is of little use in ocular syphilis. Serologic testing that includes nontreponemal tests and treponemal tests is considered the standard detection method [20]. The term "nontreponemal" is used because the antigens are not treponemal in origin, but are extracts of normal mammalian tissues. Cardiolipin from beef heart allows the detection of anti-lipid IgG and IgM formed in the patient in response to lipoidal material released from cells damaged by the infection, as well as to lipids in the surface of *T. pallidum*. The two tests commonly in use are the VDRL (Venereal Disease Research Lab) and the RPR (rapid plasma reagin). Nontreponemal antibody titers decline as a result of treatment. A fourfold reduction in antibody titer of the same nontreponemal test is considered a significant response to treatment. Lack of expected reduction in titer or an increase in titer suggests treatment failure or reinfection. Nontreponemal tests may give false-positive results in conditions other than syphilis (viral infection, pregnancy, post-immunization). Moreover, they may be negative in as many as 30 % of patients during the late latent or tertiary stages. Therefore, a specific treponema antibody assay is needed to supplement the nontreponemal tests in all cases of suspected disease. Two commonly used specific tests are the FTA-abs (fluorescent treponemal antibody absorption test) and the TP-PA (*T. pallidum* particle agglutination). These tests have a high sensitivity and specificity and are said to stay positive throughout life, although seroreversion may occur in a small

number of patients, mainly in those treated for early disease [19].

The CDC recommends lumbar puncture in all patients with ocular syphilis to detect neurosyphilis [4], but there is debate whether this procedure is justified in patients with isolated anterior segment inflammation [13]. The diagnosis of neurosyphilis is based upon the cerebrospinal fluid leukocytosis, protein changes, and the presence of a positive VDRL. The VDRL test unfortunately has low sensitivity to detect syphilis in the cerebrospinal fluid and therefore a negative VDRL does not rule out neurosyphilis. Specific treponemal tests are not very useful to detect neurosyphilis because antitreponemal IgG antibodies pass the intact blood-brain barrier and hence a positive result is no proof of neurosyphilis.

Whereas the usefulness of PCR in the diagnosis of non-ocular syphilis is well established, only few reports on the detection of treponemal DNA in ocular fluids are published. However, in a patient with uveitis and atypical clinical signs or equivocal syphilis serology, PCR on intraocular fluid may confirm the diagnosis [38].

97.5 Differential Diagnosis

Syphilis, the great imitator, is able to affect almost all the layers of the eye and hence the differential diagnosis of syphilitic intraocular inflammation is extraordinarily wide. Moreover, many different patterns of intraocular inflammation are described, adding to the difficulty of establishing the diagnosis of syphilis on clinical grounds alone.

Syphilitic anterior uveitis may present as unilateral nongranulomatous or granulomatous uveitis in which case the differential diagnosis with herpetic anterior uveitis should be considered. Unlike herpetic iridocyclitis, syphilitic anterior uveitis is less likely to produce iris atrophy and transillumination defects, less likely to be accompanied by intraocular pressure rise, and more likely to cause posterior synechiae, and it will not respond favourably to topical steroids as herpetic uveitis does. Bilateral granulomatous syphilitic anterior uveitis evokes the possibility of sarcoidosis. Normal ACE levels, normal X-ray of the lungs, normal CT sections of the mediastinum, absence of respiratory symptoms, presence of a skin rash some months ago, and poor response to topical steroids should raise the possibility of luetic anterior uveitis. The differential diagnosis of iris nodules associated with infectious disease should include tuberculosis, leprosy, coccidioidosis, and candidiasis [25].

Intermediate uveitis due to syphilis has no particular distinguishing features, and the differential diagnosis includes the well-known entities associated with this type of inflammation: Lyme disease, sarcoidosis, Whipple's disease, and multiple sclerosis.

Posterior uveitis may present as deep chorioretinitis, as posterior placoid chorioretinitis involving primarily the pigment epithelium, as retinal vasculitis, or as necrotizing retinitis.

Acute posterior syphilitic uveitis will not often create serious differential diagnostic dilemmas: multifocal chorioretinitis with prominent vitreous inflammation and retinal involvement causing progressive visual loss in the course of a few weeks should raise a high index of suspicion for infectious disease and especially syphilis. Chronic posterior syphilitic uveitis may mimic uveitis due to sarcoidosis or to tuberculosis: multifocal choroiditis, moderate vitreous inflammation, and retinal vasculitis can all be observed in any of these entities. Although the differential diagnosis with ARN may be difficult, careful observation of the lesions may yield a clue to the diagnosis of syphilitic retinal necrosis. In ARN the necrotic lesions start in the periphery, whereas in syphilitic retinitis they often are located in the posterior pole. In syphilitic retinal necrosis, one has the impression that the surface of the lesion is somewhat indistinct, as if a layer of exudate obscures the underlying retina from view, whereas in ARN one can clearly identify the surface of the lesions as the surface of the thickened, necrotic retina. The retinal necrotic tissue tends to be homogeneous in ARN, whereas the areas of necrosis in syphilitic retinitis have a mottled aspect that becomes even more obvious in the healing phase.

Although certain clinical characteristics described above (iris roseolae in anterior uveitis, leopard-spot changes in syphilitic posterior placoid chorioretinitis, syphilitic inner punctate

retinitis) are suggestive of syphilitic uveitis, they present only in a small fraction of the total number of patients with ocular syphilis and hence are of limited importance in the differential diagnosis.

Important clues in the differential diagnosis pointing towards the possibility of syphilis include the following:

- The presence of a skin rash or a genital lesion in the past months in patients with suggestive ocular lesions, since most patients with ocular syphilis present in the secondary stage
- Failure to respond to the prescribed treatment (e.g. anterior uveitis unresponsive to topical steroid therapy, presumed viral necrotizing retinitis unresponsive to antiviral treatment, aggravation of presumed autoimmune intraocular inflammation upon administration of steroids)
- The fact that the patient belongs to a high-risk group for sexually transmitted diseases

97.6 Treatment

Ocular syphilis is treated in exactly the same way as neurosyphilis. Since benzathine penicillin does not penetrate the blood ocular barrier, aqueous penicillin G or procaine penicillin G plus probenecid should be given. For patients with ocular syphilis in the tertiary stage, a 3-week course of benzathine penicillin should be added [4].

Stage	Patients not allergic to penicillin	Patients allergic to penicillin
Neurosyphilis (any stage)	Aqueous crystalline penicillin G 3–4 million units IV every 4 h or 18–24 million units/day for 10–14 days	Ceftriaxone 2 g IV or IM daily for 10–14 days
	Procaine penicillin 2.4 million units IM once daily plus probenecid 500 mg PO 4 times daily for 10–14 days	
Neurosyphilis (late stage)	Above regimen followed by benzathine penicillin G 2.4 million units IM every week for up to 3 weeks	

There is certainly a place for adjunctive corticosteroid therapy in the management of syphilitic eye disease. Topical steroids are of benefit as an adjunctive treatment in syphilitic keratitis, scleritis, and anterior uveitis [40]. Systemic steroids always in combination with appropriate antibiotic therapy have a role in the treatment of posterior uveitis and optic nerve inflammation [7, 35]. The Jarisch-Herxheimer reaction is an acute febrile illness with headache, myalgia, chills, and rigours occurring typically within a few hours after the initiation of treatment, probably as a result of endotoxin release and cytokine elevation. The extra inflammation might be particularly harmful in patients with ocular and neurological involvement. Systemic steroids may dampen but not completely prevent the Jarisch-Herxheimer reaction. Antitumour necrosis factor antibodies seem to be more effective than steroids [29].

97.7 Prognosis

Syphilis is a treatable cause of uveitis. Prompt recognition and effective antibiotic treatment in an early stage will result in a cure of the disease. Since many patients with syphilitic uveitis present in the secondary stage and are otherwise asymptomatic, the ophthalmologist has a major responsibility at this point: timely diagnosis and adequate antibiotic treatment will prevent not only further ocular damage but will also protect the patient against morbidity and even mortality associated with the advanced stage of the disease, occurring in one third of untreated patients.

Take-Home Pearls

- Consider the possibility of syphilis in patients with uveitis unresponsive to therapy (steroids, antivirals).
- Nontreponemal tests (VDRL and RPR) are used for screening and quantitation of antibody titer (therapeutic response); treponemal tests are used for diagnostic confirmation of active or prior syphilis;

order both HIV and syphilis serology in patients belonging to risk groups for STD's: coinfection is common and a risk for bilateral blinding retinitis.
- Syphilitic retinal necrosis has a mottled aspect whereas viral retinitis tends to be homogeneous; the surface of syphilitic retinal necrosis is somewhat hazy due to inflammatory exudate in the overlying vitreous, whereas the surface of the thickened necrotic retina in viral retinal necrosis is clearly visible and distinct from the overlying vitreous.
- Hutchinson's triad, a late sequel of congenital syphilis, includes interstitial keratitis, peg-shaped upper incisors, and neurosensory deafness; active disease occurs at 5–10 years of age.
- Treat ocular syphilis as neurosyphilis.

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