

Management of Adult Syphilis between Gynecology and Urology

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ABSTRACT

Syphilis is a sexually transmitted disease found only in humans, which is caused by a spirochete (*Treponema pallidum*). It infects the genital area, lips, mouth, or anus of both men and women. Patients usually get syphilis from sexual contact with someone who has it. It can also pass from mother to baby during pregnancy. The early stage of syphilis usually causes a single, small, painless sore. Sometimes it causes swelling in nearby lymph nodes. If you do not treat it, syphilis usually causes a non-itchy skin rash, often on your hands and feet. Many people do not notice symptoms for years. Symptoms can go away and come back. The sores caused by syphilis make it easier to get or give someone HIV during sex. If you are pregnant, syphilis can cause birth defects, or you could lose your baby. In rare cases, syphilis causes serious health problems and even death. Syphilis is easy to cure with antibiotics if you catch it early. Correct usage of latex condoms greatly reduces, but does not completely eliminate, the risk of catching or spreading syphilis.

Keywords: Syphilis, Infectious Diseases, Prevention, Penicillin, *Treponema pallidum*.

INTRODUCTION

Syphilis is a sexually transmitted disease found only in humans, which is caused by a spirochete (*Treponema pallidum*). Infection is categorized by a wide symptomatology, which makes the diagnosis hard when based exclusively on the clinical picture^[1]. The infection continues to be a significant epidemiological problem^[2, 3]. The World Health Organization estimate that each year in the world there are about 11 million new cases^[4]. Since the year 2000 in most European countries and the North America a steady increase in the occurrence of syphilis has been witnessed^[5]. *Treponema pallidum* is a fragile spiral bacterium 6-15 micrometers long by 0.25 micrometers in diameter. Its small size makes it unseen on light microscopy; consequently, it should be recognized by its distinctive undulating movements on dark field microscopy. It can survive only momentarily outside of the body; accordingly, transmission nearly always necessitates direct contact with the infectious lesion. Syphilis is regularly classified into 4 stages: primary, secondary, latent, and tertiary. It can be either attained or congenital. Explicitly, it can be transmitted either by intimate contact with infectious lesions (most common) or via blood transfusion (if blood has been collected during early syphilis), and it could correspondingly be transmitted transplacentally from a diseased mother to her fetus^[6]. The syphilitic penetrate reflects a delayed-type hypersensitivity reaction to *T pallidum*, and in certain individuals with tertiary syphilis, this

reaction by sensitized T lymphocytes and macrophages results in gummatous ulcerations and necrosis. Antigens of *T pallidum* persuade host production of treponemal antibodies and nonspecific antibodies. Immunity to syphilis is incomplete. For instance, host humoral and cellular immune responses might avert the formation of a primary lesion on consequent contaminations with *T pallidum*, but they are inadequate to clear the organism. This can be because the outer sheath of the spirochete is lacking immunogenic molecules, or it might be as a result of down-regulation of helper T cells of the TH1 class^[7, 8].

The study was done after approval of ethical board of King Abdulaziz university.

Primary syphilis

Primary syphilis ensues 10-90 days after interaction with a diseased individual. It manifests mostly on the glans penis in males and on the vulva or cervix in females. 10 % of syphilitic lesions are found on the fingers, anus, nipples, oropharynx, tongue, or other extragenital sites. Regional nontender lymphadenopathy follows incursion. Lesions (chancres) typically begin as solitary, firm, raised, red papules that can be numerous centimeters in diameter. The chancre erodes to produce an ulcerative crater within the papule, with slightly prominent edges around the central ulcer. It regularly heals within 4-8 weeks, with or without treatment. Even though genital chancres are regularly solitary, they might be multiple in few

patients^[9]. Every so often they seem as kissing lesions on contrasting skin surfaces such as the labia.

Secondary syphilis

Secondary syphilis establishes in several ways. It frequently presents with a cutaneous eruption within 2-10 weeks after the primary chancre and is most florid 3-4 months after infection. The eruption might be refined; twenty-five percent of patients might be unacquainted of skin changes. A localized or rambling mucocutaneous rash (commonly nonpruritic and bilaterally symmetrical) with generalized nontender lymphadenopathy is typical. Patchy alopecia and condylomata lata might likewise be witnessed^[10].

Mild constitutional symptoms of headache, disease, nausea, anorexia, aching pains in the bones, and fatigue frequently are present, in addition to fever and neck stiffness. A small number of patients progress acute syphilitic meningitis and present with headache, facial numbness or weakness, neck stiffness, and deafness^[11]. Other less-common manifestations contain hepatitis, GI involvement, proctitis, nephropathy, optic neuritis, and arthritis.

Latent syphilis

Latency might last from a few years to upwards of 25 years before the damaging lesions of tertiary syphilis manifest. Influenced patients might review symptoms of primary and secondary syphilis. They are asymptomatic throughout the latent phase, and the disease is noticed only by serologic tests. Latent syphilis is allocated into early latent and late latent. The distinction is significant as treatment for each is different. The early latent period is the first year after the resolution of primary or secondary syphilis^[12]. Asymptomatic patients who have a recently active serologic test after having a serologically negative test result within 1 year are correspondingly reflected to be in the early latent period. Late latency syphilis is not infectious; nevertheless, women in this stage can spread the infection in utero.

Tertiary syphilis: Tertiary (late) syphilis is slowly progressive and might affect any organ.

The infection is commonly not assumed to be infectious at this stage. Manifestations might comprise the following:

- Chest pain, stridorm, back pain, or other symptoms related to aortic aneurysms
- Dementia
- Incontinence, impaired balance, paresthesias, and impotence
- Focal neurologic findings, including sensorineural hearing and vision loss

The lesions of gummatous tertiary syphilis generally improve within 3-10 years of contamination. The patient complaints are commonly secondary to bone pain, which is designated as a deep boring pain characteristically worse at night. Trauma might predispose a precise site to gumma involvement. CNS contribution might arise, with presenting symptoms representative of the area affected (i.e., brain involvement [headache, mood disturbance, dizziness, blurred vision, neck stiffness] and spinal cord involvement [bulbar symptoms, incontinence, impotence, weakness and wasting of shoulder girdle and arm muscles]). Some patients might present up to 20 years after contamination with interactive changes and other signs of dementia, which is suggestive of paresis^[13].

Congenital syphilis

Early congenital syphilis happens within the first 2 years of life. Late congenital syphilis emerges in children older than 2 years. A small percentage of infants infected in utero can have a latent form of infection that becomes apparent during childhood and, in some cases, throughout adult life. The earliest symptom that happens prior to age 2 years is rhinitis (snuffles), presently followed by cutaneous lesions. After age 2 years, parents may note problems with the child’s hearing and language development and with vision. Facial and dental abnormalities might be distinguished^[14].

Management of adult syphilis

Key principles for the management of syphilis comprise the following^[25]:

Table 1: Key principles for the management of syphilis

Penicillin is the drug of choice to treat syphilis.
Doxycycline is the best alternative for treating early and late latent syphilis. Syphilis associated with HIV infection does not require any enhanced antimicrobial therapy.
In the treatment of late syphilis by weekly injections, missing a dose of penicillin for a period of 10-14 days does not require restarting the entire course of injections.
The exception to this is in the case of pregnant women in whom there is no latitude for missing a dose of penicillin.
There is evidence that an interval of 7-9 days between doses may produce better results.
CSF testing to detect neurosyphilis is strongly recommended in patients with tertiary syphilis or with neurological signs or symptoms consistent with neurosyphilis and in patients without symptoms whose serologic titers do not decline appropriately after being treated with recommended therapy.
Reinfection rates among MSM are high, so frequent serological testing in this group is recommended.
CDC recommends the use of the RPR-based screening algorithm. When there is a low epidemiologic risk or clinical probability of syphilis, the positive predictive value of an isolated unconfirmed reactive treponemal chemoluminescence test or enzyme immunoassay is low.

Antibiotic therapy

• Penicillin

Penicillin residues the mainstay of management and the standard by which other modes of therapy are judged ^[15]. The 2015 CDC STD treatment guidelines provision the use of penicillin as the ideal drug for treating all stages of syphilis ^[16]. Penicillin is the only suggested treatment for neurosyphilis, congenital syphilis, or syphilis throughout pregnancy. Not often, *T pallidum* has been found to persevere following suitable penicillin treatment; nevertheless, there is no suggestion that the organism has attained resistance to penicillin. Clinicians ought to be responsive that only benzathine penicillin product (Bicillin L-A) should be used, not benzathine-procaine penicillin (Bicillin C-R). Moreover, oral penicillin is certainly not suitable for the management of syphilis.

Table 2. Regimens are recommended for penicillin treatment
Primary or secondary syphilis - Benzathine penicillin G 2.4 million units intramuscularly (IM) in a single dose
Early latent syphilis - Benzathine penicillin G 2.4 million units IM in a single dose
Late latent syphilis or latent syphilis of unknown duration - Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals
Pregnancy - Treatment appropriate to the stage of syphilis is recommended

If the patient attains late for subsequent doses, clinical experience proposes that an interval of 10-14 days amid doses of benzathine penicillin for latent syphilis might be tolerable before restarting the order of injections; nevertheless, consistent with pharmacokinetics/pharmacodynamics, an interval of 7-9 days amid doses is more ideal ^[17-19]. In pregnancy, missed doses are not tolerable. Pregnant patients should repeat the full course of treatment ^[20]. In patients with a history of penicillin allergy, desensitization might be essential in cases of pregnancy, congenital syphilis, neurosyphilis, or tertiary syphilis.

Consistent with the 2015 CDC STD guidelines, no management regimens for syphilis have been shown to be more operative in avoiding neurosyphilis in patients who are HIV positive than the syphilis regimens suggested for patients who are HIV negative. Careful monitoring after treatment is obligatory, as patients with HIV infection are at higher risk for reinfection and have a slower

serologic response than patients without HIV infection ^[16].

• Alternatives to penicillin

As specified in the year 2015 CDC guidelines, numerous treatments exist that may be effective in nonpregnant, penicillin-allergic patients with primary or secondary syphilis ^[16]. Tetracycline, erythromycin, and ceftriaxone ^[21] have shown antitreponemal activity in clinical trials; nevertheless, they presently are suggested merely as alternative management regimens in patients allergic to penicillin. A 10- to 14-day trial of ceftriaxone is operative for treating early syphilis, though the ideal dose and period have not been established. Doxycycline and tetracycline for 28 days have been used for many years and are the only suitable substitutions to penicillin for the management of latent syphilis. Doxycycline is the favored substitute to penicillin as a result of its tolerability ^[19].

Azithromycin has similarly been studied. A meta-analysis of randomized clinical trials comparing azithromycin to benzathine penicillin G for early syphilis was published in the year 2008 showing favorable results for azithromycin ^[22]. At the year 2010 a study by Hook *et al* showed a single dose of azithromycin (2 g PO) to be equivalent to the treatment of choice, benzathine penicillin G (2.4 million units IM) in patients with early syphilis without HIV. Serological cure after 6 months of follow-up was not significant between the 2 treatments, although azithromycin recipients had a higher incidence of adverse effects (mostly self-limited gastrointestinal symptoms) ^[23]. Although azithromycin is effective, resistance is increasing in the United States, with some areas reporting up to 84% resistance; consequently, azithromycin ought to be used only in parts of low resistance or in early syphilis with close clinical follow-up ^[24].

• Procaine toxicity

A few patients encounter serious nervousness and other mental unsettling influences after the organization of procaine penicillin. Fever, mind flights, hyperventilation, and shakings describe the response. Circulatory crumple is once in a while revealed. Revival and strong care are important in extreme cases; be that as it may, most responses are gentle, requiring just consolation or symptomatic help. Indications for the most part scatter inside 30 minutes.

• Jarisch-Herxheimer reaction

Following the start of treatment, the withering treponemes discharge incendiary atoms that trigger a cytokine course conceivably prompting a reaction known as the Jarisch-Herxheimer response. Side effects incorporate myalgias, fever, migraine, and

tachycardia, now and again with intensification of whatever present syphilitic injuries are showed (eg, rash or chancre). The response is normal, creates inside a few hours in the wake of starting anti-microbial treatment, and for the most part clears inside 24 hours after the beginning. Its correct etiology is indistinct, in spite of the fact that it might be because of an immunological response to the burst of spirochetes. Administration of this response regularly includes symptomatic treatment (eg, with antipyretics and analgesics) and perception. In pregnant ladies, treatment may incite early work or cause fetal misery.

Patients ought to be educated of the likelihood of this response before experiencing anti-infection treatment. As expressed in the CDC 2015 STD treatment rules, despite the fact that the Jarisch-Herxheimer response may incite obstetric difficulties, for example, early work or fetal trouble, this hazard ought not block or defer treatment for syphilis. Ladies are encouraged to look for obstetric care after treatment on the off chance that they see any fever, uterine compressions, or a lessening in fetal development ^[9].

Drug	Dose, administration	Treatment duration
Benzathine penicillin	2.4 million units, IM	Single dose
Procaine penicillin	600 000 units once daily, IM	10–14 days
Alternatives		
Doxycycline	200 mg once daily, PO	14 days
Tetracycline	500 mg 4× daily, PO	14 days
Erythromycin	500 mg 4× daily, PO	14 days
Azithromycin*	2 g, PO	Single dose
Ceftriaxone*	500 mg once daily, IM	10 days

Surgical care

Surgical care is reserved for treating the complications of tertiary syphilis (eg, aortic valve replacement).

Prevention of Syphilis

The essential objective of avoidance is to restrain the spread of syphilis. This involves guiding patients to utilize safe sex rehearses and prompting patients who manhandle intravenous (IV)

medications to never share needles and to utilize clean needles. Notice and treatment of sexual accomplices and uncovered medication accomplices are central. Counteractive action additionally involves teaching medicinal services specialists to utilize widespread precautionary measures while treating all patients. Empiric treatment with one dose of benzathine penicillin G 2.4 million units intramuscularly (IM) is recommended in all patients who have had sexual contact with a partner who has tested positive for primary, secondary, or early latent syphilis within the preceding 90 days ^[9].

Studies of primary screening for syphilis in clinics and emergency departments are favorable for screening of high-risk, urban populations. Routine screening is advocated for all at-risk mothers. Two reports from the year 2009 indicated that circumcision does not help prevent the transmission of syphilis, although circumcision may help reduce the transmission of other STDs such as HIV infection ^[25, 26].

CONCLUSION

Syphilis remains to be a serious epidemiological problem. Advances in medical science obligate doctors to apply proven effective diagnostic and therapeutic procedures. Following the guidelines remains the only line of defense for a doctor in cases of a dispute. Despite a great number of new treponemal tests, non-treponemal tests are still very important. Non-treponemal tests are necessary for the final diagnosis, they are only recommended for the evaluation of treatment response and are of the highest specificity for the diagnosis of neurosyphilis. Penicillin remains the drug of choice in the treatment of all forms of syphilis.

Diagnosis, treatment, and follow-up of neurosyphilis are difficult. It is suggested that such patients should be referred to the tertiary reference centers. The treatment scheme for syphilitic patients with HIV co-infection should be the same as for immunocompetent patients. Special attention should be paid to the notification, diagnosis and treatment of sexual partners of the infected patients.

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