Syphilis is becoming more common in adolescents nowadays, especially in men. Syphilis is caused by Treponema pallidum. The main risk factors for acquiring syphilis are multiple sexual partners, having previous history of syphilis and having a partner with syphilis. Apart from Nontreponemal reactive tests, treponemal specific reactive tests is highly recommendable to confirm the diagnosis. Once the diagnosis is confirmed, penicillin G should be administered. Response to penicillin G is excellent but doxycycline, ceftriaxone or azithromycin might be indicated in selected cases where affected individuals are allergic to penicillin G.

Overview

Syphilis is an infectious condition that is characterized by chronic and systemic pathologies. The condition can be transmitted sexually or via vertical transmission. Vertical transmission can occur during pregnancy or delivery.
Case Definitions of Syphilis

Primary syphilis is characterized by one or more ulcerative lesions. Reactive serologic tests such as VDRL, RPR or treponemal-specific tests need to be positive. The demonstration of the causative organism Treponema pallidum confirms the diagnosis of primary syphilis.

Secondary syphilis is characterized by localized or diffuse mucocutaneous lesions with generalized lymphadenopathy. Condylomalata and alopecia are also commonly seen in secondary syphilis. The diagnostic criteria for secondary syphilis include a positive nontreponemal and positive treponemal serology test with the presence of the clinical features of the stage. The isolation and identification of the organisms is not mandatory but it is done to confirm the diagnosis.

Early latent syphilis is characterized by the detection of the causative organisms in the body of the patient without clinical signs or symptoms of syphilis. Typically, this stage starts within 12 months of acquiring the infection. Patients without a previous history of syphilis who have a positive reactive nontreponemal test and a positive treponemal test are diagnosed with early latent syphilis. Additionally, patients with documented history of previous syphilis infection within the last 12 months who are currently asymptomatic but have a positive reactive nontreponemal test or a positive treponemal test are also diagnosed with early latent syphilis. When the documented history of acquiring syphilis is longer than 12 months, the diagnosis of late latent syphilis is made.

Late syphilis with clinical manifestations is characterized by:

- Presence of inflammatory lesions such as aortitis
- Coronary vessel disease
- Gummatous skin lesions
- Osteitis leading to cardiovascular or organ morbidities

This condition which involves other organ system is also known as tertiary syphilis. The clinical manifestations of late syphilis usually happen after 15 to 30 years of untreated syphilis.

Neurosyphilis is defined as the infection of the central nervous system by Treponema pallidum. Patients might develop syphilitic meningitis, optic involvement with interstitial keratitis and uveitis, dementia and tabes dorsalis. Neurosyphilis can happen at any stage.

Epidemiology of Syphilis in Adolescents

The estimated incidence of primary and secondary syphilis combined in the United States is around 6.3 cases per 100,000 adolescents. Primary and secondary syphilis incidence has been increasing in recent years, especially in men. The estimated incidence of primary and secondary syphilis in men is 11.7 per 100,000 whereas the incidence of syphilis in women is around 1.1 per 100,000.

Primary and secondary syphilis are reportable infections in the United States. Impact of syphilis in the adolescent group is underestimated as some cases may not be reported in certain clinics or places in the United States.

Treatment of syphilis is costly. The direct costs of treating confirmed cases of syphilis are
The main risk factors for acquiring syphilis are the previous history of syphilis infection, having a partner with syphilis, current human immunodeficiency virus infection and having more than 4 sex partners per year. Young adult men, sex workers, individuals of African American ethnicity, and those from the southern and western states are more likely to develop syphilis.

Clinical Manifestations of Syphilis

The main manifestation of primary syphilis is a local painless chancre. This small ulcer usually heals by itself without treatment within few weeks. It may progress to secondary syphilis from 2 to 8 weeks if not healed properly.

Secondary syphilis is characterized by:

- Rash
- Fever
- Headache
- Malaise
- Anorexix
- Arthralgia
- Diffuse lymphadenopathy
- Diminished visual acuity

If left untreated, patients will progress to the early latent syphilis stage. Up to 25% of the patients with early latent syphilis will develop a relapse of secondary syphilis symptoms, i.e., diffuse skin rash and lymphadenopathy.

If the patients are not treated, they will progress to latent syphilis. Patients with late-stage syphilis present with symptoms and signs suggestive of multi-system involvement such as:

- Heart failure
- Cardiac arrhythmias
- Coronary artery disease
- Aortitis
- Skin lesions
- Bone lesions

Symptoms of late-stage syphilis can occur within 1 year up to 30 years after the initial primary disease. Tertiary syphilis include cardiovascular syphilis, gummatous syphilis and a slow progressive disease affecting any organ system.

Neurosyphilis can happen at any stage and presents with symptoms and signs suggestive of focal neurologic deficits.

Diagnostic Workup for Syphilis in Adolescents

Screening for syphilis infection should target individuals at an increased risk because of having one of the previously explained risk factors. The aim of screening for syphilis infection in adolescents is the early detection of primary syphilis and secondary syphilis to prevent the progression to late-stage syphilis.

When an adolescent represents similar symptoms to syphilis, he or she should receive a
nontreponemal reactive test such as the **Venereal Disease Research Laboratory (VDRL)** or the **Rapid Plasma Reagin (RPR) tests**. While these tests are not very specific for syphilis, they are highly sensitive.

If the nontreponemal reactive test result is positive, a confirmatory treponemal specific test is indicated. **Fluorescent treponemal antibody absorbed (FTA-ABS)** or **Treponema pallidum particle agglutination (TPPA)** are very specific for syphilis.

Microscopic examination of samples collected from the skin lesions might reveal the organism and help in confirming the diagnosis.

**Treatment of Syphilis in Adolescents**

The treatment of choice for all stages of syphilis is **penicillin G which should be administered via intramuscular injection**. Benzathine, aqueous procaine or aqueous crystalline penicillin preparations have been all used in the treatment of syphilis with equal efficacy. The duration of the treatment plan is dependent on the presenting stage. Additionally, the choice of preparation should be based on the suspected locations of infection, i.e., some forms of penicillin have a poor penetrance of the blood-brain barrier and will not reach a syphilis focus in the central nervous system.

<table>
<thead>
<tr>
<th>Penicillin</th>
<th>Re-examine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic of choice (doxycycline if allergic)</td>
<td>(Nontreponemal test)</td>
</tr>
<tr>
<td>• Dose and duration depends on the stage</td>
<td>• Repeat nontreponemal tests every 3 months</td>
</tr>
<tr>
<td>• 1 dose IM for early disease if otherwise</td>
<td>• Ensure titers are falling (4 fold decrease</td>
</tr>
<tr>
<td>healthy</td>
<td>within 6 months</td>
</tr>
<tr>
<td>• Weekly for three weeks IM for tertiary</td>
<td></td>
</tr>
<tr>
<td>disease</td>
<td></td>
</tr>
</tbody>
</table>

Patients who are nonpregnant and are allergic to penicillin might be treated with **doxycycline or tetracycline**. Ceftriaxone might be effective in the primary syphilis stage. A single oral dose of azithromycin has been shown to be effective in the treatment of early syphilis. Unfortunately, azithromycin resistance is becoming more common in *Treponema pallidum*. Azithromycin efficacy in pregnant women is decreased.

Response to treatment is confirmed by repeating the nontreponemal reactive tests 6 months and 12 months after the initiation of treatment. Patients with relapse of symptoms, worsening of symptoms or a significant increase in the nontreponemal reactive titers should be re-evaluated and the possibility of treatment failure should be addressed.

Patients with neurosyphilis should get a **cerebrospinal fluid examination**. If the cerebrospinal fluid assessment is abnormal, follow-up cerebrospinal fluid examinations are indicated to monitor response to treatment.

Treatment of early syphilis might be associated with an increased risk of anaphylactic reactions to penicillin. Jarisch-Herxheimer reaction is a febrile reaction that is commonly seen within the first 24 hours of the initiation of antibiotic therapy for early syphilis. The administration of antipyretics is usually sufficient in the management of this reaction.
References


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