Syphilis in Adolescents — Diagnosis and Treatment

Syphilis is becoming more common in adolescents, especially in men. The disease is caused by *Treponema pallidum*. The main risk factors for acquiring syphilis are multiple sexual partners, a previous history of syphilis, and having a sexual partner with syphilis. Apart from nontreponemal reactive tests, treponemal-specific reactive tests are recommended to confirm the diagnosis. Penicillin G is the most effective treatment. However, doxycycline, ceftriaxone, or azithromycin may also be indicated in select 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 the venereal disease research laboratory (VDRL), rapid plasma reagin
(RPR), or treponemal-specific tests need to be positive. The presence of the causative organism \textit{T. pallidum} confirms the diagnosis of primary syphilis.

Secondary syphilis is characterized by \textbf{localized or diffuse mucocutaneous lesions with generalized lymphadenopathy}. Condyloma lata and alopecia are also commonly seen in secondary syphilis. The diagnostic criteria for secondary syphilis include a positive non-treponemal and positive treponemal serology test with the presence of clinical features characteristic of this stage. The isolation and identification of the organism is not mandatory but does confirm the diagnosis.

Early latent syphilis is characterized by \textbf{detection of the causative organisms in a 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 non-treponemal test and a positive treponemal test are diagnosed with early latent syphilis. Additionally, patients with a documented history of previous syphilis infection within the last 12 months who are currently asymptomatic but have a positive reactive non-treponemal 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.

\textbf{Late syphilis with clinical manifestations is characterized by:}

- The 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 systems, is also known as tertiary syphilis. The clinical manifestations of late syphilis usually begin after 15 to 30 years of untreated syphilis.

Neurosyphilis is defined as an \textbf{infection of the central nervous system by \textit{T. pallidum}}. Patients may develop syphilitic meningitis, optic involvement with interstitial keratitis and uveitis, dementia, and tabes dorsalis. Neurosyphilis can happen at any stage.

\textbf{Epidemiology of Syphilis in Adolescents}

The estimated combined incidence of primary and secondary syphilis in adolescents in the United States is approximately 6.3 cases per 100,000 adolescents. The 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 approximately 1.1 per 100,000.

Primary and secondary syphilis are reportable infections in the United States. The impact of syphilis in adolescents is underestimated, as some cases may not be reported in certain clinics or places in the country.

The direct cost of treating syphilis is high, at approximately $39.3 million.

The main risk factors for acquiring syphilis are a previous history of syphilis infection, having a sexual partner with syphilis, current human immunodeficiency virus infection, and having more than 4 sex partners per year. Young adult men, sex workers, African Americans, 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 a few weeks. It may progress to secondary syphilis from 2 to 8 weeks after infection if not healed properly.

**Secondary syphilis is characterized by:**

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

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

If 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 or up to 30 years after the initial primary disease. Tertiary syphilis includes cardiovascular syphilis, gummatous syphilis, and a slow, progressive disease affecting any organ system.

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

**Diagnostic Workup for Syphilis in Adolescents**

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

When an adolescent presents with symptoms suggestive of syphilis, they should receive a nontreponemal reactive test such as VDRL or RPR. While these tests are not 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 skin lesions may reveal the organism
and also 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 (IM) injection. Benzathine, aqueous procaine, or aqueous crystalline penicillin preparations have also all been 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 penetration 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>
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<tbody>
<tr>
<td>Antibiotic of choice (doxycycline if allergic)</td>
<td>(Nontreponemal test)</td>
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<tr>
<td>• Dose and duration depends on the stage</td>
<td>• Repeat nontreponemal tests every 3 months</td>
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<tr>
<td>• 1 dose IM for early disease if otherwise healthy</td>
<td>• Ensure titers are falling (4 fold decrease within 6 months)</td>
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<tr>
<td>• Weekly for 3 weeks IM for tertiary disease</td>
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Patients who are not pregnant and are allergic to penicillin can be treated with **doxycycline or tetracycline**. Ceftriaxone may 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 *T. pallidum*. Azithromycin efficacy in pregnant women is also decreasing.

Response to treatment is confirmed by repeating the nontreponemal reactive tests 6 months and 12 months after the initiation of treatment. Patients with a relapse or 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 receive a **cerebrospinal fluid examination**. If this assessment is abnormal, follow-up cerebrospinal fluid examinations are indicated to monitor response to treatment.

Treatment of early syphilis may 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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