



PHARMACOTHERAPEUTIC MANAGEMENT OF SECONDARY SYPHILIS IN PREGNANCY: A COMPREHENSIVE REVIEW

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ABSTRACT

Secondary syphilis is a systemic stage of infection caused by the spirochete bacterium *Treponema pallidum* and remains a significant global public health concern, particularly among pregnant women. If left untreated, maternal syphilis may lead to severe complications including miscarriage, stillbirth, preterm delivery, and congenital infection in newborns. The diverse clinical manifestations of secondary syphilis often mimic other dermatological conditions, which may delay accurate diagnosis and treatment. Early detection through appropriate serological testing such as the Venereal Disease Research Laboratory test and the *Treponema pallidum* hemagglutination assay is essential for effective disease management. Pharmacological treatment plays a crucial role in preventing disease progression and vertical transmission. Long-acting Benzathine Penicillin G remains the first-line therapy due to its high efficacy, safety profile during pregnancy, and ability to eliminate the causative organism effectively. This review summarizes the epidemiology, pathophysiology, clinical manifestations, diagnostic approaches, and pharmacotherapeutic management of secondary syphilis in pregnancy. Special emphasis is placed on antibiotic therapy, therapeutic monitoring, and the role of healthcare professionals in optimizing patient outcomes. The findings highlight that early screening, prompt antimicrobial therapy, and appropriate follow-up significantly reduce maternal complications and prevent congenital transmission. Strengthening prenatal screening programs and improving awareness regarding sexually transmitted infections are essential strategies for reducing the global burden of maternal syphilis.

KEYWORDS: Secondary syphilis; maternal infection; pharmacotherapy; benzathine penicillin; congenital syphilis; antimicrobial therapy; sexually transmitted infections; pregnancy management.

INTRODUCTION

Syphilis is a chronic systemic infectious disease caused by the spirochete bacterium *Treponema pallidum*. Despite the availability of effective antimicrobial therapy, syphilis remains a significant global public health problem, particularly in low- and middle-income countries. The disease is primarily transmitted through sexual contact and is classified among the most important sexually transmitted infections affecting

reproductive-age populations. If untreated, the infection progresses through several clinical stages including primary, secondary, latent, and tertiary syphilis, each characterized by different pathological and clinical manifestations.

The transmission of syphilis occurs mainly through direct contact with infectious lesions during sexual activity, including vaginal, anal, and oral intercourse.

The bacterium enters the body through microscopic abrasions in the skin or mucous membranes and subsequently disseminates through the lymphatic system and bloodstream. In addition to sexual transmission, vertical transmission from mother to fetus during pregnancy is a major concern in clinical medicine. Transplacental transmission can occur at any stage of pregnancy and may lead to congenital syphilis, which is associated with severe neonatal morbidity and mortality. Therefore, early detection and timely pharmacological intervention are critical to prevent disease progression and reduce transmission risks.

Secondary syphilis represents the systemic stage of infection that typically occurs several weeks after the initial primary infection. During this stage, the pathogen spreads throughout the body, resulting in a wide range of clinical manifestations including generalized rash, mucocutaneous lesions, lymphadenopathy, and systemic symptoms. Dermatological manifestations are particularly characteristic of this stage and may present as macular, papular, or annular lesions. However, these skin findings often resemble other dermatological disorders, making clinical diagnosis challenging. As a result, laboratory confirmation using serological tests such as the Venereal Disease Research Laboratory test and the *Treponema pallidum* hemagglutination assay is essential for accurate diagnosis and management.

Syphilis during pregnancy represents a significant medical concern because of the risk of maternal complications and vertical transmission to the fetus.

Untreated maternal infection can lead to adverse pregnancy outcomes including miscarriage, stillbirth, preterm delivery, low birth weight, and congenital infection in newborns. Congenital syphilis remains one of the leading preventable causes of neonatal morbidity worldwide. Consequently, global health organizations strongly recommend routine screening for syphilis during antenatal care to ensure early diagnosis and treatment.

Pharmacological therapy plays a crucial role in the effective management of syphilis. Long-acting Benzathine Penicillin G remains the first-line treatment due to its proven efficacy, minimal resistance, and well-established safety profile in pregnant women. Early antibiotic therapy not only resolves maternal infection but also prevents fetal transmission and improves pregnancy outcomes. In addition, appropriate clinical monitoring and follow-up serological testing are necessary to ensure treatment success and prevent reinfection.

Given the increasing global incidence of sexually transmitted infections and the continuing burden of maternal syphilis, a comprehensive understanding of disease epidemiology, pathophysiology, diagnostic strategies, and pharmacological management is essential for healthcare professionals. This review aims to provide an updated overview of secondary syphilis in pregnancy with a particular focus on pharmacotherapeutic management and strategies to prevent congenital transmission.

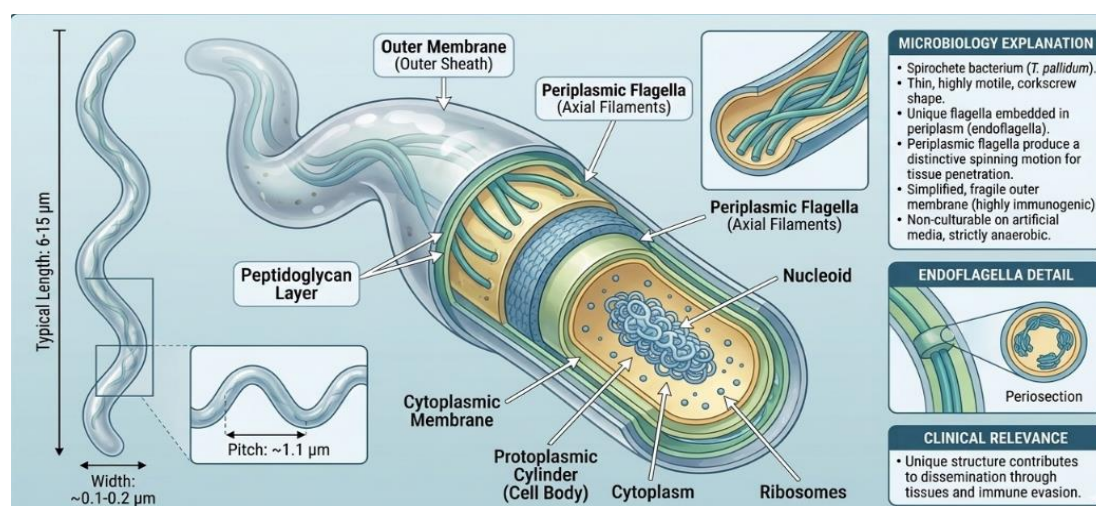


Figure 1: *Treponema pallidum* structure.

Global Epidemiology of Maternal Syphilis

Syphilis remains a significant global public health concern despite the availability of effective diagnostic tools and antimicrobial therapy. The infection caused by the spirochete bacterium *Treponema pallidum* continues to affect millions of individuals worldwide, particularly in low- and middle-income countries where access to early screening and healthcare services may be limited. Maternal syphilis is of particular concern because it is

strongly associated with adverse pregnancy outcomes and congenital infections.

According to global reports published by the World Health Organization, approximately 7 million new cases of syphilis occur annually among individuals aged 15 - 49 years. Among these cases, a considerable proportion occurs among pregnant women. It is estimated that nearly 1 million pregnant women worldwide are infected

with syphilis each year. Untreated maternal infection can result in severe pregnancy complications such as miscarriage, stillbirth, preterm delivery, and congenital infection in newborns.

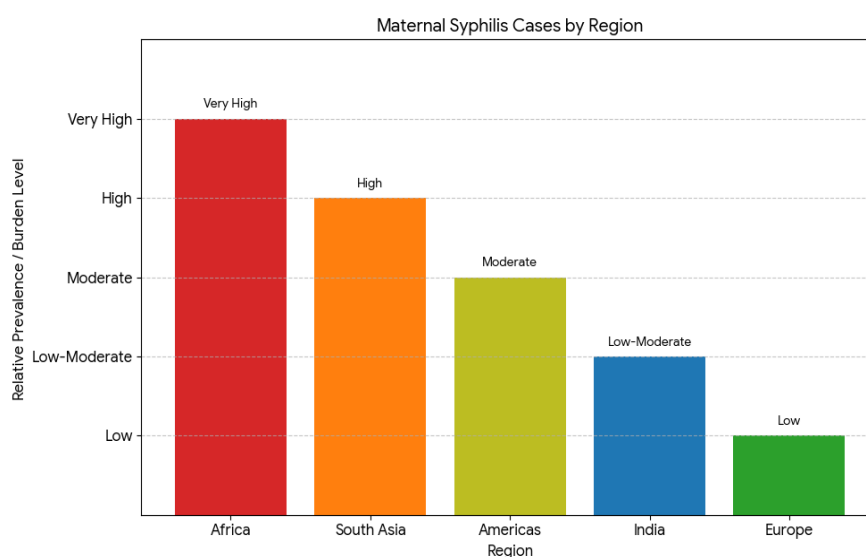
The distribution of maternal syphilis varies significantly across geographical regions. Sub-Saharan Africa reports the highest prevalence due to limited antenatal screening programs and reduced access to healthcare services. Several countries in Asia and Latin America demonstrate moderate levels of infection, while most European countries report relatively lower prevalence rates because of improved healthcare infrastructure and routine prenatal screening programs.

India also contributes to the global burden of maternal syphilis, although the prevalence among antenatal women is lower compared with several African countries. According to reports from the National AIDS Control Organisation, the prevalence of syphilis among pregnant women attending antenatal clinics in India generally ranges from 0.1% to 0.5% depending on regional healthcare accessibility and surveillance programs. Routine screening using the Venereal Disease Research Laboratory test during the first antenatal visit has been implemented in national maternal health

programs. Confirmatory testing using the *Treponema pallidum* hemagglutination assay helps establish an accurate diagnosis and guide treatment decisions.

Vertical transmission of syphilis from mother to fetus represents a major global health challenge. Transplacental infection may occur at any stage of pregnancy and the risk of transmission increases significantly if the maternal infection remains untreated. Studies indicate that the risk of congenital transmission may reach 60–80% in untreated early-stage syphilis. Congenital infection can lead to severe neonatal complications including stillbirth, premature birth, low birth weight, and congenital abnormalities.

Global health organizations have emphasized the importance of universal antenatal screening and early antibiotic therapy in order to prevent congenital syphilis. Early diagnosis followed by appropriate treatment with long-acting penicillin has been shown to significantly reduce the risk of fetal transmission and improve maternal and neonatal outcomes. Strengthening antenatal screening programs, improving healthcare accessibility, and enhancing public awareness remain essential strategies for reducing the global burden of maternal syphilis.



Graph 1.

Title: Maternal Syphilis Cases by Region

- X-axis → Regions
- Y-axis → Relative prevalence / cases

Table: Global Burden of Maternal and Congenital Syphilis.

Indicator	Global Estimate	India Estimate
Maternal syphilis cases annually	~1 million	~0.1–0.5% prevalence among antenatal women
Total global syphilis cases	~7 million	Moderate burden
Risk of congenital transmission (untreated)	60–80%	Similar risk if untreated
Screening method	VDRL	VDRL (antenatal screening)
Confirmatory test	TPHA	TPHA

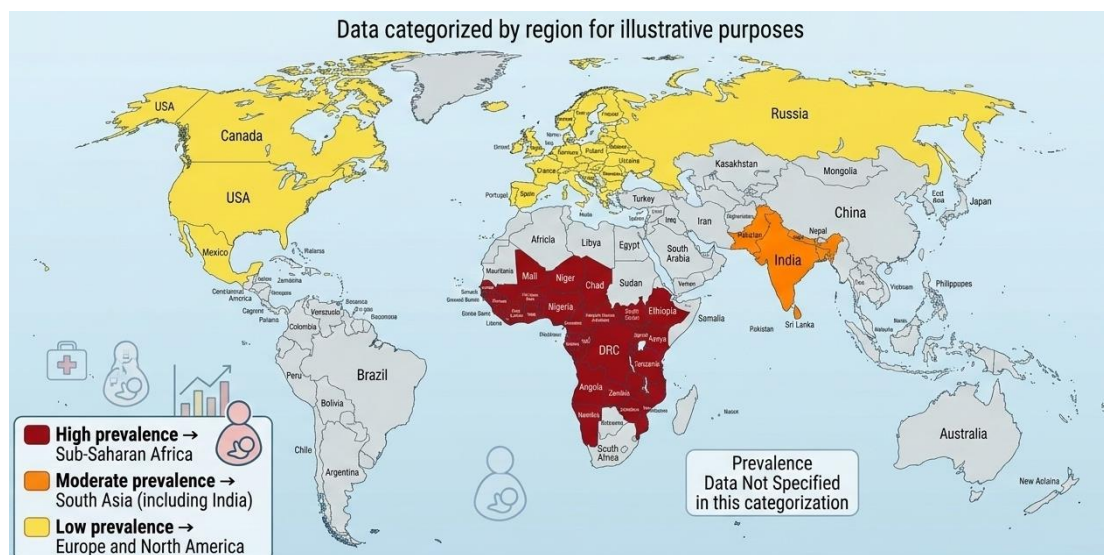


Figure 2: Global distribution of maternal syphilis highlighting high-risk regions including Sub-Saharan Africa and South Asia.

Pathophysiology of Secondary Syphilis

Secondary syphilis represents the disseminated stage of infection caused by the spirochete bacterium *Treponema pallidum*. Following the initial primary infection, the pathogen spreads systemically through hematogenous and lymphatic routes, resulting in widespread clinical manifestations involving the skin, mucous membranes, and multiple organ systems. The pathophysiology of secondary syphilis involves complex interactions between bacterial invasion, host immune response, and systemic dissemination of the pathogen.

Bacterial Invasion

The infection begins when *Treponema pallidum* enters the host through microscopic abrasions in the skin or mucosal surfaces during sexual contact. The bacterium possesses several structural and biological features that facilitate tissue invasion and immune evasion. Due to its corkscrew-shaped morphology and motility, the organism can penetrate epithelial barriers and migrate through connective tissues.

After initial entry, the pathogen multiplies locally at the site of infection, leading to the development of the primary lesion known as a chancre. During this early phase, the bacterium invades regional lymphatic vessels and subsequently enters the bloodstream. The ability of *Treponema pallidum* to adhere to host cells and evade immune recognition allows it to disseminate efficiently throughout the body.

Several outer membrane proteins expressed by the bacterium contribute to host cell attachment and immune modulation. These virulence factors enable the organism to persist within the host for prolonged periods without immediate immune clearance.

Host Immune Response

The host immune system plays a critical role in determining the clinical manifestations of syphilis. Both innate and adaptive immune responses are activated following infection. Macrophages, dendritic cells, and neutrophils participate in the early immune response by recognizing pathogen-associated molecular patterns and initiating inflammatory signalling pathways.

As the infection progresses, T-cell mediated immune responses become increasingly important. CD4⁺ T lymphocytes stimulate macrophage activation and promote phagocytosis of the invading bacteria. However, *Treponema pallidum* has evolved several mechanisms that allow it to evade immune detection, including a relatively low density of surface antigens and antigenic variation of outer membrane proteins.

The inflammatory response generated during secondary syphilis contributes significantly to the development of dermatological manifestations. Immune-mediated damage to small blood vessels and surrounding tissues results in characteristic skin rashes and mucocutaneous lesions observed during this stage of infection.

Systemic Dissemination

Secondary syphilis develops several weeks after the initial infection when the pathogen spreads throughout the body via the bloodstream and lymphatic circulation. At this stage, the bacterium can invade multiple organs including the skin, liver, lymph nodes, and central nervous system.

The systemic spread of the organism leads to widespread clinical symptoms such as generalized rash, lymphadenopathy, fever, malaise, and mucosal lesions. Dermatological manifestations are particularly prominent during this stage and may present as macular, papular or annular lesions affecting various parts of the body.

including the trunk, extremities, palms, soles, and genital region.

In pregnant women, systemic dissemination of *Treponema pallidum* is of particular concern because the bacterium can cross the placental barrier and infect the developing fetus. This transplacental transmission may result in congenital syphilis, which is associated with severe neonatal complications.

Understanding the pathophysiological mechanisms underlying secondary syphilis is essential for accurate diagnosis, effective pharmacological management, and prevention of disease progression. Early antimicrobial therapy with long-acting penicillin can successfully eliminate the pathogen and prevent further systemic complications.

Table: Key Pathophysiological Mechanisms in Secondary Syphilis.

Mechanism	Description
Bacterial invasion	Entry through mucosal surfaces or skin abrasions
Immune response	Activation of macrophages and T-cells
Systemic spread	Dissemination via bloodstream and lymphatics
Tissue inflammation	Immune-mediated skin lesions

Stages of Syphilis

Syphilis is a chronic sexually transmitted infection caused by the spirochete bacterium *Treponema pallidum*. The disease progresses through four distinct clinical stages if untreated: primary, secondary, latent and tertiary syphilis. Each stage has characteristic clinical manifestations and varying degrees of infectivity.

Understanding these stages is crucial for early diagnosis, appropriate pharmacotherapy, and prevention of congenital infection during pregnancy.

1. Primary Syphilis

Primary syphilis is the initial stage of infection and usually occurs 3–6 weeks after exposure to the bacterium. The hallmark feature is the formation of a chancre a painless ulcer at the site where the bacterium entered the body.

Pathogenesis

After entering the body through microabrasions in mucous membranes or skin the bacterium multiplies locally. The infection causes local tissue inflammation and endothelial damage leading to the development of a chancre.

Clinical Features

Typical symptoms include

- Painless ulcer (chancre) at infection site
- Firm, round lesion with clean base
- Regional lymphadenopathy
- Lesions may appear on:
- Genitalia
- Cervix
- Rectum
- Oral cavity

The chancre typically heals spontaneously within 3–6 weeks, even without treatment. However, the infection remains in the body and progresses to the next stage.

Importance in Pregnancy

In pregnant women, untreated primary infection can allow bacterial dissemination through the bloodstream, increasing the risk of transplacental transmission to the fetus.

2. Secondary Syphilis

Secondary syphilis develops 4–10 weeks after the appearance of the primary chancre and represents the systemic dissemination phase of the infection.

During this stage, the bacteria spread throughout the body via bloodstream and lymphatic circulation, producing widespread clinical manifestations.

Clinical Features

Common symptoms include

- Maculopapular rash, especially on palms and soles
- Condylomata lata (moist wart-like lesions in genital areas)
- Fever and malaise
- Lymphadenopathy
- Headache and sore throat
- Alopecia (patchy hair loss)

The rash is considered a classic diagnostic sign of secondary syphilis and may involve trunk, extremities, palms, and soles.

Infectivity

Secondary syphilis is highly contagious, as lesions contain large numbers of bacteria.

Importance in Pregnancy

Maternal infection at this stage significantly increases the risk of congenital syphilis, which may lead to:

- Miscarriage
- Stillbirth
- Neonatal infection
- Developmental abnormalities

Therefore, early screening and treatment during pregnancy are essential.

3. Latent Syphilis

Latent syphilis occurs when clinical symptoms disappear but the bacterium remains in the body. This stage can last months to several years.

Latent syphilis is classified into two subtypes

Early Latent Syphilis

Occurs within the first year after infection.

Characteristics

- No clinical symptoms
- Serological tests remain positive
- Infection is still potentially transmissible

Late Latent Syphilis

Occurs after one year of untreated infection.

Characteristics

- No symptoms
- Lower infectivity
- Bacteria remain dormant in tissues

Clinical Significance

Although patients appear healthy, the infection can reactivate and progress to tertiary syphilis if untreated.

Pregnancy Risk

Even during the latent stage, vertical transmission to the fetus can occur, especially in early latent infection.

4. Tertiary Syphilis

Tertiary syphilis is the late destructive stage of the disease and may occur 10–30 years after the initial infection in untreated individuals.

This stage is characterized by chronic inflammatory damage to multiple organs, including the cardiovascular system, nervous system, and bones.

Table 1: Clinical Stages of Syphilis.

Stage	Symptoms	Duration
Primary	Painless chancre at infection site	3–6 weeks
Secondary	Skin rash, fever, lymphadenopathy	Weeks to months
Latent	No clinical symptoms	Months to years
Tertiary	Organ damage, neurological complications	Years to decades

Clinical Manifestations

The clinical manifestations of Secondary Syphilis occur due to the hematogenous dissemination of the bacterium *Treponema pallidum* throughout the body. During this stage, the organism spreads to multiple organs and tissues resulting in a wide variety of dermatological, mucosal, and systemic symptoms.

Secondary syphilis is characterized by polymorphic clinical presentations meaning the symptoms can vary widely among patients. However, skin lesions, mucosal lesions, and systemic manifestations are the most commonly observed clinical findings. These symptoms usually appear 4–10 weeks after the primary chancre

Major Clinical Forms

1. Cardiovascular Syphilis

Damage to the aorta and large blood vessels leading to:

- Aortic aneurysm
- Aortic valve insufficiency

2. Neurosyphilis

Involvement of the central nervous system causing:

- Meningitis
- Stroke
- Cognitive impairment
- Paralysis

3. Gummatous Syphilis

Formation of granulomatous lesions (gummas) in organs such as:

- Liver
- Skin
- Bones

These lesions can cause severe tissue destruction.

Clinical Importance

Although tertiary syphilis is less infectious it is associated with high morbidity and irreversible organ damage.

Pregnancy Considerations

Pregnant women with untreated infection at any stage may transmit the bacterium to the fetus, leading to congenital syphilis which can cause:

- Skeletal deformities
- Neurological damage
- Neonatal death
-

heals and represent the most infectious stage of the disease.

Clinical manifestations are particularly important in pregnant women as untreated infection during this stage significantly increases the risk of vertical transmission which may result in congenital infection, fetal complications, or neonatal morbidity.

1 Skin Lesions

Skin lesions are the most characteristic and frequently observed manifestation of secondary syphilis. The rash is typically generalized, non-pruritic (non-itchy), and symmetrical affecting multiple parts of the body.

The lesions occur due to immune-mediated inflammatory reactions triggered by the presence of *Treponema pallidum* in the skin tissues.

Types of Skin Lesions

1. Maculopapular Rash

The most common dermatological manifestation is a maculopapular rash, which consists of both flat (macules) and raised (papules) lesions.

Common characteristics include

- Reddish-brown lesions
- Symmetrical distribution
- Non-itchy appearance
- Involvement of palms and soles

The presence of rash on palms and soles is considered a classic diagnostic feature of secondary syphilis and helps differentiate it from many other dermatological diseases.

2. Condylomata Lata

Another characteristic lesion is condylomata lata which are broad-based, moist, wart-like lesions typically found in warm and moist areas of the body.

Common locations include

- Genital region
- Perianal area
- Inner thighs
- Axilla

These lesions contain high concentrations of spirochetes and are therefore highly infectious.

3. Patchy Alopecia

Secondary syphilis may also cause syphilitic alopecia, often described as “moth-eaten” hair loss.

Characteristics include

- Irregular patches of hair loss
- Involvement of scalp, beard, and eyebrows
- Non-scarring alopecia

Although not always present, this sign is considered highly suggestive of secondary syphilis.

2 Mucosal Lesions

Mucosal involvement is another common manifestation during secondary syphilis. The lesions occur due to **bacterial invasion of mucous membranes**, resulting in inflammatory responses.

1. Mucous Patches

Mucous patches are **superficial erosions or ulcerative lesions** that develop on mucosal surfaces.

Typical features include:

- Painless lesions
- Grayish-white plaques
- Highly infectious surface

Common sites include

- Oral cavity

- Tongue
- Lips
- Pharynx
- Genital mucosa

These lesions contain **large numbers of *Treponema pallidum*** and therefore play a major role in **disease transmission**.

2. Oral Lesions

Oral manifestations may appear as:

- Erythematous patches
- Ulcerative lesions
- Mucous plaques

Patients may experience **sore throat, difficulty swallowing, or mild oral discomfort**.

3 Systemic Symptoms

Secondary syphilis is often accompanied by **systemic manifestations** due to the **widespread dissemination of the pathogen in the bloodstream**.

These symptoms resemble **viral or flu-like illness**, which may sometimes delay accurate diagnosis.

Common Systemic Symptoms

Patients may experience

- Fever
- Malaise
- Fatigue
- Headache
- Sore throat
- Muscle pain
- Weight loss

Lymphadenopathy

Generalized **lymph node enlargement** is a common finding during secondary syphilis.

Characteristics include

- Painless lymph node swelling
- Symmetrical involvement
- Commonly affected nodes: cervical, axillary, and inguinal

Hepatosplenomegaly

In some cases, secondary syphilis may involve **internal organs**, leading to enlargement of:

- Liver (hepatomegaly)
- Spleen (splenomegaly)

Although uncommon, these findings indicate **systemic disease progression**.

Clinical Significance in Pregnancy

Secondary syphilis during pregnancy poses a **significant risk to fetal health**. Because the bacterium can **cross the placental barrier**, maternal infection may result in:

- Congenital syphilis
- Miscarriage
- Stillbirth
- Premature birth

- Neonatal infection

Therefore, **early detection and treatment with penicillin therapy** are essential to prevent **maternal and fetal complications**.



Figure 3: Pretreatment lesion: Multiple erythematous annular plaques with central umbilication on bilateral inguinal folds with multiple macerated papules on bilateral labia minora.



Figure 4: Dermoscopy (DermLite DL4 40X): Showing dotted and glomerular vessels with a collarette of scalesClinical photographs showing.



Figure 5: Posttreatment (1 week): Resolving annular plaques after treatment with benzathine penicillin G.

Table 2: Clinical Manifestations of Secondary Syphilis.

Category	Clinical Manifestations
Skin lesions	Maculopapular rash, condylomata lata, patchy alopecia
Mucosal lesions	Mucous patches, oral lesions
Systemic symptoms	Fever, malaise, lymphadenopathy, headache

Differential Diagnosis

The clinical presentation of Secondary Syphilis can mimic several dermatological conditions, which often makes **accurate diagnosis challenging**. Because secondary syphilis produces **polymorphic skin eruptions**, clinicians may initially confuse the lesions with **fungal infections, inflammatory skin disorders, or granulomatous diseases**.

Misdiagnosis can delay appropriate treatment, increasing the risk of **disease progression and vertical transmission during pregnancy**. Therefore, **differential diagnosis is essential** to distinguish syphilitic lesions from other similar dermatological conditions.

Secondary syphilis should be suspected particularly when **skin lesions are accompanied by systemic symptoms such as fever, lymphadenopathy, and mucosal lesions**, and when lesions involve **palms and soles**, which is relatively uncommon in many other skin disorders.

Laboratory investigations such as **serological testing** play a crucial role in confirming infection caused by *Treponema pallidum*.

Common Conditions Confused with Secondary Syphilis

1. Fungal Infection (Tinea Corporis)

Tinea corporis is a superficial fungal infection of the skin caused by dermatophytes such as *Trichophyton*, *Microsporum*, and *Epidermophyton* species.

Similar Features

- Ring-shaped lesions
- Red circular plaques
- Peripheral spreading rash

These lesions may resemble the **annular lesions of secondary syphilis**, leading to diagnostic confusion.

Key Differences

Unlike syphilis

- Lesions are usually **itchy**
- Central clearing is common
- Diagnosis confirmed by **positive fungal microscopy or culture**

A **potassium hydroxide (KOH) test** can detect fungal elements, confirming dermatophyte infection.

2. Psoriasis

Psoriasis is a chronic inflammatory skin condition characterized by **hyperproliferation of keratinocytes and immune-mediated inflammation**.

Similar Features

Psoriasis lesions may resemble syphilitic rashes due to:

- Erythematous plaques
- Widespread skin involvement
- Symmetrical distribution

Key Differences

However, psoriasis typically shows:

- **Thick silvery scaling**
- Chronic recurrent course
- Strong genetic association

In contrast, secondary syphilis lesions are generally **less scaly and more polymorphic**, and patients often show **systemic symptoms such as fever and lymphadenopathy**.

3. Granuloma Annulare

Granuloma annulare is a chronic dermatological disorder characterized by **annular plaques and dermal inflammation**.

Similar Features

Granuloma annulare may resemble syphilitic lesions because of:

- Ring-shaped lesions
- Annular plaque formation
- Localized skin involvement

Key Differences

Important distinguishing features include

- Lesions are **asymptomatic**
- Absence of systemic symptoms
- Negative serological tests for syphilis

Diagnosis is usually confirmed by **skin biopsy**, showing **granulomatous inflammation**.

Importance of Serological Testing

Because clinical appearance alone may be misleading, **laboratory confirmation is essential**. The most commonly used diagnostic methods include:

- **Non-treponemal tests** (VDRL, RPR)
- **Treponemal tests** (FTA-ABS, TPHA)

Positive serological tests confirm infection caused by *Treponema pallidum* and help distinguish syphilis from other dermatological disorders.

Table 2: Differential Diagnosis of Secondary Syphilis.

Disease	Similar Feature	Difference
Tinea corporis	Ring-shaped lesion	Fungal test positive
Psoriasis	Erythematous plaques	Thick silvery scaling
Granuloma annulare	Annular lesions	No systemic symptoms
Syphilis	Annular lesions, rash	Serology positive

Diagnostic Methods

Accurate diagnosis of Syphilis is essential for early treatment and prevention of complications, particularly in pregnant women where untreated infection can lead to **congenital transmission and severe fetal outcomes**. Because the causative organism *Treponema pallidum* cannot be easily cultured in routine laboratory conditions, diagnosis primarily relies on **serological testing and clinical evaluation**.

Diagnostic testing for syphilis generally involves a **two-step approach**:

1. **Screening tests (non-treponemal tests)**
2. **Confirmatory tests (treponemal tests)**

This combination improves **diagnostic accuracy, sensitivity, and specificity**

Early detection is particularly important during **antenatal screening**, as recommended by organizations such as the World Health Organization and the Centers for Disease Control and Prevention.

1 Non-Treponemal Tests (Screening Tests)

Non-treponemal tests detect **non-specific antibodies produced by the host immune system** in response to cellular damage caused by *Treponema pallidum*. These

tests are commonly used for **initial screening** because they are inexpensive, rapid, and widely available.

However, they may sometimes produce **false-positive results** in conditions such as pregnancy, autoimmune disorders, or viral infections. Therefore, positive screening tests must always be **confirmed using treponemal tests**.

VDRL Test

Venereal Disease Research Laboratory Test is one of the most widely used screening tests for syphilis.

Principle

The VDRL test detects **reagin antibodies**, which react with cardiolipin antigen released from damaged host cells.

Key Features

- Inexpensive and simple laboratory procedure
- Useful for **screening large populations**
- Antibody titers correlate with disease activity
- Useful for **monitoring treatment response**

A decrease in VDRL titers after therapy indicates **successful treatment**.

RPR Test

Rapid Plasma Reagin Test is another non-treponemal screening test similar to VDRL.

Advantages include

- Rapid results
- No need for microscopy
- Suitable for **point-of-care screening**

RPR is widely used in **antenatal screening programs** to detect maternal infection.

2 Treponemal Tests (Confirmatory Tests)

Treponemal tests detect **antibodies specifically directed against *Treponema pallidum* antigens**. These tests are more **specific** than non-treponemal tests and are used to **confirm the diagnosis of syphilis**.

Unlike screening tests, treponemal tests usually remain **positive for life**, even after successful treatment.

TPHA Test

Treponema pallidum Hemagglutination Assay is a widely used confirmatory test.

Principle

The test detects antibodies against *Treponema pallidum* using **red blood cells coated with treponemal antigens**.

Advantages

- High specificity

- Reliable confirmation of infection
- Widely used in clinical laboratories

FTA-ABS Test

Fluorescent Treponemal Antibody Absorption Test is another confirmatory test used in specialized laboratories.

Principle

This test detects **fluorescent antibodies bound to treponemal antigens** using immunofluorescence microscopy.

Clinical Use

- Confirmatory diagnosis
- Detection of early infection
- Evaluation of congenital syphilis

3 Diagnostic Screening in Pregnancy

Routine **antenatal screening for syphilis** is strongly recommended because early treatment can prevent **mother-to-child transmission**.

Screening is typically performed

- During the **first prenatal visit**
- In the **third trimester** in high-risk populations
- At **delivery in high prevalence regions**

Positive cases require **immediate treatment with penicillin therapy** to prevent congenital infection.

Table 3: Diagnostic Tests for Syphilis.

Test	Type	Purpose
VDRL	Screening (Non-treponemal)	Detect antibodies produced during infection
RPR	Screening (Non-treponemal)	Rapid detection of antibodies
TPHA	Confirmatory (Treponemal)	Detect antibodies specific to <i>Treponema pallidum</i>
FTA-ABS	Confirmatory (Treponemal)	Confirm infection using immunofluorescence

Pharmacological Management

The pharmacological management of Syphilis primarily focuses on **eliminating the causative organism *Treponema pallidum*** and preventing disease progression and complications. Effective treatment is particularly important in **pregnant women**, as early therapy can significantly reduce the risk of **congenital syphilis and adverse pregnancy outcomes**.

According to treatment guidelines from the World Health Organization and the Centers for Disease Control and Prevention, **penicillin remains the drug of choice for all stages of syphilis**, including infections occurring during pregnancy.

Antibiotic therapy works by **inhibiting bacterial growth, preventing systemic spread, and promoting immune clearance of the pathogen**. Among available agents, penicillin demonstrates **high efficacy, excellent safety profile, and minimal resistance**, making it the preferred first-line therapy.

1 First-Line Therapy: Penicillin

Penicillin G is the most effective and widely recommended treatment for syphilis. It is particularly effective against *Treponema pallidum* because the bacterium has **limited resistance mechanisms and high susceptibility to beta-lactam antibiotics**.

Penicillin therapy is capable of

- Rapidly eliminating the pathogen
- Preventing disease progression
- Reducing transmission risk
- Preventing congenital infection during pregnancy

For **secondary syphilis**, the recommended treatment regimen is a **single intramuscular injection of benzathine penicillin G**.

Recommended Dosage

- **Benzathine Penicillin G: 2.4 million units (MIU)**
- Administered **intramuscularly (IM)** as a single dose

In certain cases, such as late latent infection or unknown duration of infection, **additional weekly doses may be required**.

2 Mechanism of Action of Penicillin

Penicillin belongs to the **β -lactam class of antibiotics**, which exert bactericidal activity by **interfering with bacterial cell wall synthesis**.

Mechanism

1. Penicillin binds to **penicillin-binding proteins (PBPs)** in the bacterial cell wall.
2. This inhibits the **transpeptidation reaction** required for peptidoglycan cross-linking.
3. Disruption of cell wall synthesis weakens the bacterial structure.
4. Osmotic pressure causes **cell lysis and bacterial death**.

Because *Treponema pallidum* relies heavily on **cell wall integrity for survival**, it is highly susceptible to penicillin therapy.

3 Safety of Penicillin in Pregnancy

Penicillin is considered **safe for use during pregnancy** and remains the **only recommended therapy for maternal and congenital syphilis**.

Advantages include

- Minimal fetal toxicity
- Effective placental transfer
- Prevention of vertical transmission
- Extensive clinical evidence supporting safety

Even in pregnant women with **penicillin allergy**, desensitization protocols are recommended because **alternative antibiotics are less effective in preventing congenital infection**.

4 Alternative Antibiotics (When Penicillin Cannot Be Used)

Although penicillin is the preferred therapy, alternative antibiotics may be considered in **non-pregnant patients** with penicillin hypersensitivity.

Examples include

- Doxycycline
- Ceftriaxone

However, these drugs are **not preferred during pregnancy**, as they may pose risks to fetal development.

Table 4: Pharmacological Treatment for Syphilis.

Drug	Dose	Route	Safety in Pregnancy
Penicillin G	2.4 MIU	Intramuscular (IM)	Safe
Doxycycline	100 mg twice daily	Oral	Not recommended
Ceftriaxone	1 g daily	IM/IV	Limited data

Clinical Importance

Timely pharmacological therapy offers several benefits:

- Prevents disease progression
 - Reduces systemic complications
 - Eliminates infectious lesions
 - Protects fetal health during pregnancy
- Delayed treatment may increase the risk of **congenital syphilis, stillbirth, or neonatal complications**.

Role of Clinical Pharmacist

Clinical pharmacists play an essential role in the **management, monitoring, and prevention** of complications associated with Syphilis. Their involvement is particularly important in **pregnant patients**, where safe and effective pharmacotherapy is required to prevent **maternal complications and congenital transmission**.

With the increasing emphasis on **multidisciplinary healthcare**, clinical pharmacists contribute significantly to optimizing drug therapy, improving medication adherence, and ensuring patient safety. By collaborating with physicians, nurses, and laboratory specialists, pharmacists help ensure that **appropriate treatment protocols are followed** and that medications such as Penicillin G are used effectively.

Clinical pharmacists also play a crucial role in **patient counselling, medication management,**

pharmacovigilance, and public health education, all of which contribute to improved treatment outcomes.

1 Drug Counselling

One of the primary responsibilities of a clinical pharmacist is **patient counselling regarding medication therapy**.

Patients diagnosed with syphilis often require detailed information about:

- The importance of completing antibiotic therapy
- Expected therapeutic outcomes
- Possible side effects of medications
- Prevention of disease transmission

For example, when administering **benzathine penicillin G**, pharmacists counsel patients regarding:

- Injection procedure
- Potential mild reactions such as pain at injection site
- Importance of follow-up testing

Effective counselling improves **patient adherence to treatment**, which is critical for eliminating the infection.

2 Dosage Verification

Clinical pharmacists are responsible for **reviewing and verifying medication doses** prescribed for patients.

This includes:

- Confirming the correct dosage regimen
- Verifying frequency and route of administration

- Checking patient-specific factors such as pregnancy status, allergies, and comorbidities

For instance, the recommended treatment for secondary syphilis is:

- **Benzathine penicillin G 2.4 million units intramuscularly**

Pharmacists ensure that the **correct dosage and formulation** are used, thereby reducing medication errors.

3 Monitoring Adverse Drug Reactions

Pharmacists play a key role in **monitoring and reporting adverse drug reactions (ADRs)** associated with antibiotic therapy.

Common reactions related to penicillin therapy include:

- Injection site reactions
- Mild allergic responses
- Fever or malaise

In rare cases, patients may develop **severe allergic reactions or anaphylaxis**, which require immediate medical intervention.

Another reaction associated with syphilis treatment is the **Jarisch–Herxheimer reaction**, a temporary inflammatory response occurring after antibiotic therapy due to rapid bacterial destruction.

Clinical pharmacists help identify and manage these reactions, ensuring **safe continuation of therapy**.

4 Patient Education

Patient education is another critical responsibility of clinical pharmacists. Educating patients helps prevent **reinfection and disease transmission**.

Pharmacists provide guidance on:

- Safe sexual practices
- Importance of screening and follow-up tests
- Partner notification and treatment
- Prevention of congenital infection during pregnancy

Educational interventions improve **public awareness and early detection of the disease**, contributing to better healthcare outcomes.

Complications of Untreated Infection

Untreated infection with Syphilis during pregnancy can lead to severe maternal and fetal complications. The causative bacterium *Treponema pallidum* has the ability to cross the **placental barrier** and infect the developing fetus. This process is known as **vertical transmission** or **mother-to-child transmission**.

The risk of fetal infection is particularly high during the **primary and secondary stages** of syphilis, when the bacterial load in the maternal bloodstream is elevated. If left untreated, maternal infection may result in

congenital syphilis, stillbirth, premature delivery, or neonatal infection.

According to reports from the World Health Organization, untreated maternal syphilis is one of the leading preventable causes of **adverse pregnancy outcomes worldwide**. Early detection and treatment with appropriate antibiotics significantly reduce these complications.

1 Congenital Syphilis

Congenital Syphilis occurs when *Treponema pallidum* is transmitted from an infected mother to her fetus through the placenta during pregnancy.

The infection can occur **at any stage of pregnancy**, although the risk is highest during the **early stages of maternal infection**.

Clinical Features in Infants

Infants born with congenital syphilis may present with a wide range of symptoms, including:

- Skin rashes and lesions
- Hepatosplenomegaly (Enlarged Liver And Spleen)
- Bone deformities
- Anemia
- Jaundice
- Neurological abnormalities

In some cases, newborns may appear **asymptomatic at birth**, but develop clinical signs later in infancy if the infection is untreated.

Long-Term Effects

Untreated congenital syphilis can lead to serious complications such as:

- Hearing loss
- Dental abnormalities
- Skeletal deformities
- Neurological impairment

These long-term effects highlight the importance of **prenatal screening and early treatment**.

2 Stillbirth

Maternal syphilis infection significantly increases the risk of **stillbirth**, which refers to fetal death occurring after **20 weeks of pregnancy**.

The infection can cause

- Placental inflammation
- Reduced blood supply to the fetus
- Fetal growth restriction

These pathological changes can ultimately lead to **fetal demise before delivery**.

Studies indicate that untreated maternal syphilis is responsible for **a substantial proportion of preventable stillbirths globally**, particularly in regions with limited access to antenatal care.

3 Neonatal Infection

Neonatal infection occurs when the infant acquires syphilis **before or during birth**.

Clinical manifestations may appear **immediately after birth or within the first few weeks of life**.

Common Symptoms in Neonates

- Nasal discharge (“snuffles”)
- Skin rashes
- Fever
- Enlarged liver and spleen
- Bone inflammation (osteochondritis)

Without appropriate treatment, neonatal infection can lead to **severe systemic disease or death**.

Early diagnosis and treatment using **penicillin therapy** are essential to prevent these complications.

Clinical Importance

Recognizing and managing maternal infection early provides several benefits:

- Prevention of congenital syphilis
- Reduction in stillbirth rates
- Improved neonatal survival
- Better long-term health outcomes for infants

Routine antenatal screening programs recommended by the World Health Organization and the Centers for Disease Control and Prevention play a vital role in **preventing these complications**.

Future Research Directions

Despite significant progress in the diagnosis and treatment of Syphilis, the disease continues to remain a major public health concern in many regions of the world. Persistent challenges such as **late diagnosis, limited access to screening programs, and rising infection rates** highlight the need for continued research and innovation.

The causative organism, *Treponema pallidum*, possesses unique biological characteristics that make it difficult to culture and study in laboratory conditions. As a result, researchers are focusing on **new preventive strategies, improved diagnostic technologies, and novel therapeutic options**.

Future research is expected to focus on several key areas, including **vaccine development, advanced diagnostic tools, and improved antimicrobial therapies**.

1 Vaccine Development

One of the most promising research areas is the development of an effective **syphilis vaccine**.

Currently, no licensed vaccine exists for preventing infection caused by *Treponema pallidum*. Developing a vaccine would significantly reduce the global burden of the disease and prevent **maternal and congenital infections**.

Researchers are investigating

- Identification of protective antigens
- Immune response mechanisms
- Protein-based vaccine candidates

A successful vaccine could provide **long-term immunity** and significantly reduce transmission rates worldwide.

2 Rapid Diagnostic Tests

Early detection is essential for effective disease control. Traditional laboratory tests may require **specialized equipment and trained personnel**, which can limit access in resource-limited settings.

Future diagnostic research focuses on

- **Point-of-care testing technologies**
- Portable diagnostic devices
- Multiplex testing for multiple infections

Rapid tests that deliver **accurate results within minutes** could greatly improve **screening programs in antenatal clinics and community healthcare settings**.

Improved diagnostic technologies would allow healthcare professionals to **identify infection earlier and initiate prompt treatment**, reducing complications.

3 Development of New Antibiotics

Although antibiotics such as Penicillin G remain highly effective, there is growing concern regarding the **potential emergence of antimicrobial resistance**.

Future pharmaceutical research aims to

- Develop new antimicrobial agents
- Explore alternative drug targets in *Treponema pallidum*
- Investigate combination therapy approaches

New antibiotics could provide alternative treatment options for patients with severe penicillin allergies or treatment failures.

4 Molecular and Genomic Research

Advances in **genomics and molecular biology** are helping scientists better understand the biology of *Treponema pallidum*.

Current research includes

- Genome sequencing studies
- Identification of virulence factors
- Molecular mechanisms of immune evasion

These studies may help identify **new diagnostic biomarkers and therapeutic targets**, improving future treatment strategies.

5 Digital Health and Public Health Strategies

Another emerging research area is the use of **digital health technologies** to improve disease surveillance and prevention.

Examples include

- Mobile health applications for screening programs
- Digital contact tracing systems

- Artificial intelligence–based diagnostic tools

Such innovations may enhance **public health interventions and disease monitoring**, particularly in high-risk populations.

Table: Future Research Areas in Syphilis Management.

Research Area	Future Focus
Vaccines	Prevention of infection
Rapid diagnostic tests	Faster and accessible diagnosis
New antibiotics	Control of potential antimicrobial resistance
Genomic research	Identification of new drug targets
Digital health	Improved surveillance and screening

Importance of Continued Research

Future research will play a crucial role in:

- Reducing the global burden of syphilis
- Preventing congenital infections
- Improving early diagnosis
- Enhancing treatment outcomes

Collaborative efforts between **research institutions, healthcare organizations, and public health agencies** such as the World Health Organization are essential to achieve these goals.

CONCLUSION

Syphilis remains a significant global public health concern, particularly among **pregnant women**, where untreated infection can result in severe maternal and fetal complications. The disease, caused by the bacterium *Treponema pallidum*, progresses through multiple clinical stages and may lead to **congenital infection, stillbirth, and neonatal morbidity** if not diagnosed and treated promptly.

Early and accurate diagnosis plays a critical role in effective disease management. Screening tests such as the Venereal Disease Research Laboratory Test followed by confirmatory tests like the *Treponema pallidum* Hemagglutination Assay enable healthcare professionals to identify infection at an early stage and initiate timely treatment.

Pharmacological therapy remains the cornerstone of disease management. The use of Penicillin G continues to be the most effective treatment option for all stages of syphilis, including infections during pregnancy. Appropriate antibiotic therapy eliminates the pathogen, prevents disease progression, and significantly reduces the risk of vertical transmission.

Prevention strategies, including **routine antenatal screening, early treatment, patient education, and multidisciplinary healthcare involvement**, are essential to control the spread of infection. Clinical pharmacists, physicians, and public health professionals play a key role in improving treatment outcomes and ensuring medication safety.

In conclusion, strengthening **diagnostic programs, pharmacological management, and preventive**

healthcare strategies is essential to reduce the burden of syphilis and prevent congenital infections worldwide. Collaborative efforts by healthcare systems and global organizations such as the World Health Organization remain crucial for achieving long-term disease control and improving maternal and neonatal health outcomes.

REFERENCES

1. World Health Organization. Global progress report on HIV, viral hepatitis and sexually transmitted infections. Geneva: WHO, 2022.
2. Centers for Disease Control and Prevention. Sexually transmitted infections treatment guidelines. Atlanta: CDC, 2021.
3. Hook EW, Peeling RW. Syphilis control — a continuing challenge. *New England Journal of Medicine*, 2004; 351: 122–124.
4. Peeling RW, Mabey D, Kamb ML, et al. Syphilis. *Nature Reviews Disease Primers*, 2017; 3: 17073.
5. Rac MW, Revell PA, Eppes CS. Syphilis during pregnancy: diagnosis and management. *Obstetrics and Gynecology Clinics of North America*, 2014; 41: 601–614.
6. World Health Organization. Global progress report on HIV, viral hepatitis and sexually transmitted infections. Geneva: WHO, 2022.
7. National AIDS Control Organisation. National guidelines for prevention and management of sexually transmitted infections. New Delhi: NACO, 2022.
8. Newman L, Kamb M, Hawkes S, et al. Global estimates of syphilis in pregnancy and associated adverse outcomes. *PLoS Medicine*, 2013; 10: e1001396.
9. Korenromp EL, Rowley J, Alonso M, et al. Global burden of maternal and congenital syphilis. *PLoS Medicine*, 2019; 16: e1002771.
10. Bala M, Ray K, Gupta SM. Changing trends in sexually transmitted infections in India. *Indian Journal of Medical Research*, 2015; 141: 281–289.
11. Peeling RW, Mabey D. Syphilis. *Nature Reviews Disease Primers*, 2017; 3: 17073.
12. Radolf JD, Deka RK, Anand A, et al. *Treponema pallidum*, the syphilis spirochete: making a living as a stealth pathogen. *Nature Reviews Microbiology*, 2016; 14: 744–759.

13. Lafond RE, Lukehart SA. Biological basis for syphilis. *Clinical Microbiology Reviews*, 2006; 19: 29-49.
14. Hook EW, Marra CM. Acquired syphilis in adults. *New England Journal of Medicine*, 1992; 326: 1060-1069.
15. Centers for Disease Control and Prevention. Sexually transmitted infections treatment guidelines. Atlanta: CDC, 2021.
16. World Health Organization. *Global health sector strategy on sexually transmitted infections*. Geneva: WHO, 2022.
17. Centers for Disease Control and Prevention. *Sexually Transmitted Infections Treatment Guidelines*. Atlanta, 2021.
18. Peeling RW, Mabey D, Kamb ML, et al. Syphilis. *Nature Reviews Disease Primers*, 2017; 3: 17073.
19. Hook EW, Marra CM. Acquired Syphilis in Adults. *New England Journal of Medicine*, 1992; 326(16): 1060–1069.
20. World Health Organization. *Global Health Sector Strategy on Sexually Transmitted Infections*. Geneva, 2022.
21. Centers for Disease Control and Prevention. *Sexually Transmitted Infections Treatment Guidelines*. Atlanta, 2021.
22. Peeling RW, Mabey D. Syphilis. *Nature Reviews Disease Primers*, 2017; 3: 17073.
23. Hook EW, Marra CM. Acquired Syphilis in Adults. *New England Journal of Medicine*, 1992; 326: 1060–1069.
24. World Health Organization. *Global Health Sector Strategy on Sexually Transmitted Infections*. Geneva, 2022.
25. Centers for Disease Control and Prevention. *Sexually Transmitted Infections Treatment Guidelines*. Atlanta, 2021.
26. Peeling RW, Mabey D. Syphilis. *Nature Reviews Disease Primers*, 2017; 3: 17073.
27. James WD, Berger TG, Elston DM. Andrews' Diseases of the Skin: Clinical Dermatology, 13th ed.
28. World Health Organization. *WHO guidelines for the treatment of sexually transmitted infections*. Geneva, 2022.
29. Centers for Disease Control and Prevention. *Sexually Transmitted Infections Treatment Guidelines*. Atlanta, 2021.
30. Peeling RW, Mabey D. Syphilis. *Nature Reviews Disease Primers*, 2017; 3: 17073.
31. Hook EW, Marra CM. Acquired Syphilis in Adults. *New England Journal of Medicine*, 1992; 326: 1060–1069.
32. World Health Organization. *WHO guidelines for the treatment of sexually transmitted infections*. Geneva, 2022.
33. Centers for Disease Control and Prevention. *Sexually Transmitted Infections Treatment Guidelines*. Atlanta, 2021.
34. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines. *MMWR Recommendations and Reports*.
35. Peeling RW, Mabey D. Syphilis. *Nature Reviews Disease Primers*, 2017.
36. World Health Organization. *Global Health Sector Strategy on Sexually Transmitted Infections*. Geneva, 2022.
37. Centers for Disease Control and Prevention. *Sexually Transmitted Infections Treatment Guidelines*. Atlanta, 2021.
38. Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. *American Journal of Hospital Pharmacy*.
39. World Health Organization. *Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of syphilis*. Geneva.
40. Centers for Disease Control and Prevention. *Sexually Transmitted Infections Treatment Guidelines*. Atlanta, 2021.