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Diagnosis, Treatment, and Prognosis of Syphilis in HIV Patient

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ABSTRACT

Syphilis is a sexually transmitted infection caused by the bacterium *Treponema pallidum* (T. Palladium). Human Immunodeficiency Virus (HIV) is a virus that attacks the body's immune system, decreased the number of CD4 cells that makes the immune system decrease, and facilitates syphilis infection. Syphilis increased the risk of spreading HIV infection with skin barrier destruction. The diagnosis of syphilis is made based on a complete history, including sexual history, clinical manifestations, and examination. The treatment of syphilis with HIV and without HIV similar, penicillin is still the gold standard for syphilis treatment with HIV. Prevention of syphilis with HIV are educated, screening for syphilis and other sexually transmitted infections, as well as early detection and therapy of partners. The prognosis for syphilis in HIV is worse than for syphilis without HIV.

1. Introduction

Syphilis is a sexually transmitted disease that is chronic or chronic, can attack all organs of the body, resembles various diseases (great imitator disease), has an asymptomatic latent period, and can recur.^{1,2} Human immunodeficiency virus (HIV) is a virus that attacks the immune system. HIV infection causes a decrease in the body's immunity so it is very easy to be infected with various other diseases.³ Syphilis also increase the risk of HIV transmission, because HIV can enter through genital ulcers (disorders of the skin barrier) in syphilis.¹ Syphilis with HIV infection has an increase in HIV viral load and a decrease in CD4 T cell counts.^{1,4} Syphilis infection can increase the risk of HIV transmission by 3-5 times.⁵ The incidence of primary

and secondary syphilis in the United States by the Centers for Disease Control (CDC) increased during 2000-2016, mainly due to the increase in MSM cases. In 2016, 47.0% of cases of syphilis with HIV infection were MSM, 10.7% of men had sex with women, and 4.1% of women.⁶ Cases of primary and secondary syphilis with HIV positive status in 2017 were identified, 45.5% of cases were HIV-positive MSM, 8.8% of cases where men having sex with women, and 4.5% cases were women.⁷ Penicillin is still the gold standard for the treatment of syphilis, with or without HIV coinfection. Serological tests for patients with HIV infection should be repeated at 1, 2, 3, 6, 9, and 12 months.⁴ This literature review will discuss diagnosis,

management, prevention, and prognosis of syphilis in HIV patients.

Diagnosis

The diagnosis of syphilis is based on a complete history, including sexual history, clinical manifestations, and examination. Direct examination to see the bacteria *T. pallidum* using a dark field microscope is the most sensitive and specific examination when there are durum ulcers and condylomata lata, but this examination is difficult because it is an invasive procedure.⁸ Specimens for syphilis examination were obtained from ulcerated lesions or erosions of the skin or mucosa, blood, and CSF. Polymerase chain reaction (PCR) and nucleic acid amplification test (NAAT) methods have now been

developed to detect *T. pallidum* bacteria using fluid from skin lesions, blood, or CSF.^{8,9}

HIV infection complicates the serological diagnosis of syphilis and the evaluation of the patient because there are differences in serological values for syphilis and HIV infection.¹⁰ All syphilis patients should be tested for HIV infection. In primary and secondary syphilis, if the results of the first HIV test are negative, they should be tested again for HIV 3 months later.¹¹ The definitive diagnosis of syphilis is made if *T. pallidum* is found on dark-field microscopy or PCR examination. A presumptive diagnosis of syphilis is made if the results of nontreponemal and treponemal examinations are reactive. The interpretation of the results of the syphilis examination can be seen in Figure 6.²

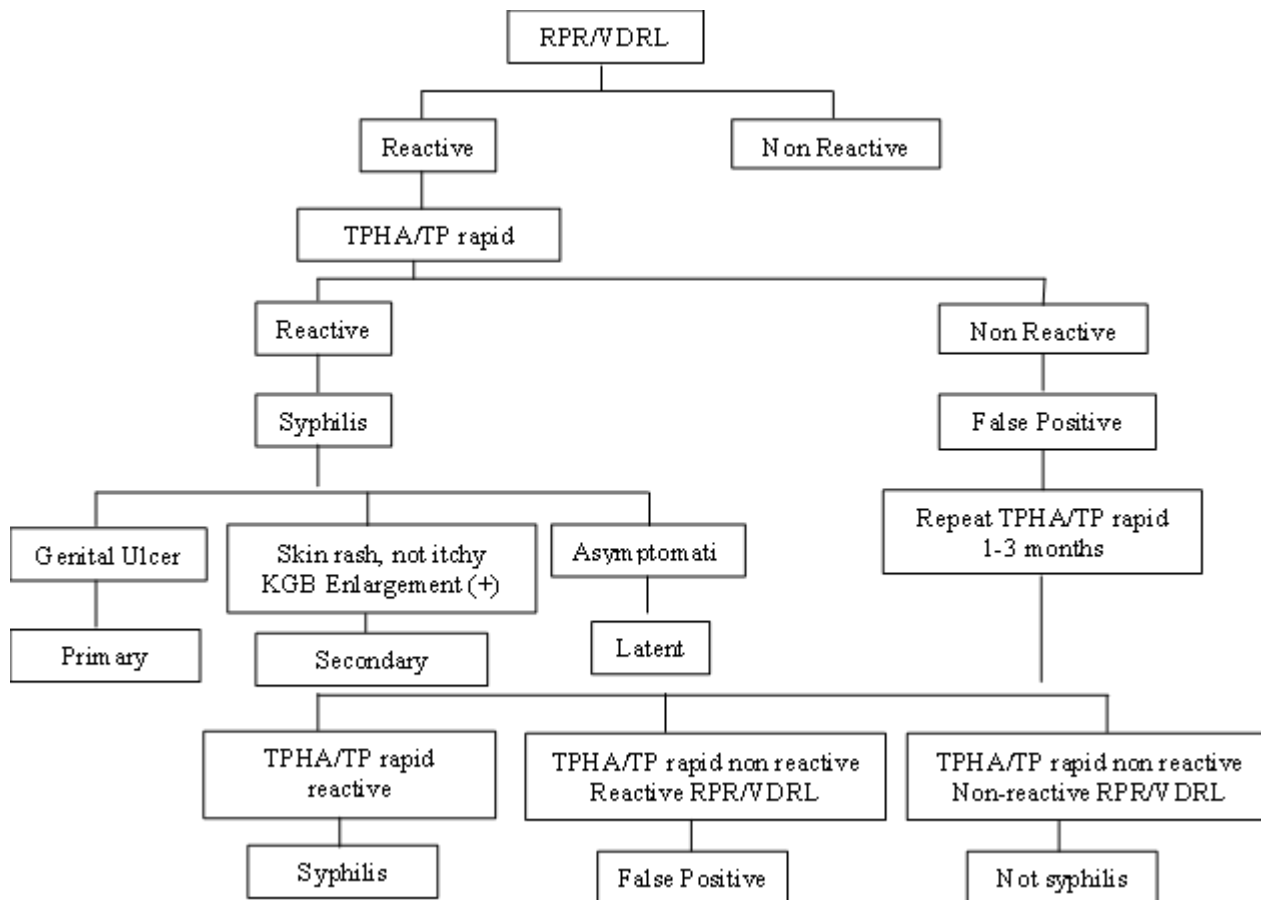


Figure 6. Algorithm interpretation of syphilis serology results.²

A serological examination is a tool for the diagnosis of syphilis in syphilis patients with HIV infection and without HIV infection. In the majority of syphilis patients with HIV infection can be diagnosed by serology examination, but there are differences in VDRL results in syphilis with HIV infection and without HIV infection.¹² Standard examinations nontreponemal are VDRL and rapid plasma reagin (RPR) examinations. Nontreponemal antibody titers correlate with disease activity and are used to assess response to treatment. Reactive nontreponemal examinations must be confirmed by treponemal tests such as *Treponema Pallidum* Hemagglutination Assay (TPHA) or syphilis rapid examination (TP Rapid) to establish the diagnosis of syphilis. Nontreponemal antibodies that persist after therapy may indicate a failure of immune tolerance.^{12,9}

False-negative serological results may occur in prozone phenomena and seronegative syphilis due to a serofast reaction ie, persistent reactive nontreponemal test results, even after treatment.^{1,2,10} The prozone phenomenon occurs because the nontreponemal antibody titer is very high, above the antigen level so that the antigen-antibody reaction does not occur.² Serofast occurs in patients with appropriate management who achieve clinical recovery and no nontreponemal antibodies are found.¹¹ Biological false-positive results were found in 1% of cases and most of the titers were 1:8.^{1,2} False-positive results can be

acute if they last less than six months and chronic if they last more than six months.¹³ False-positive nontreponemal test results can be associated with a variety of medical conditions and factors not associated with syphilis such as HIV infection, autoimmune conditions, immunization, pregnancy, injecting drug use, and old age.^{2,9} The interpretation of nontreponemal tests in syphilis patients with HIV infection and without HIV infection is generally not different. However, false-negative and false-positive results, prozone and serofast phenomena were found more frequently in patients with HIV infection than in patients without HIV infection.²

The cerebrospinal fluid examination was performed on syphilis patients with neurological disorders, visual impairment, hearing loss, cardiovascular symptoms, gumma, failure of serological therapy, advanced syphilis patients on tetracycline therapy, and HIV coinfecting patients with advanced syphilis stage and CD4 count 350/mm³ and/ or serum VDRL/RPR > 1:32.^{2,11} The white blood cell count, protein, RPR/VDRL and TPHA on CSF examination of syphilis patients with HIV infection and without HIV infection were different. The results of CSF examination support the diagnosis of neurosyphilis in patients with HIV infection and without HIV infection can be seen in table 4.²

Table 4. The criteria for the diagnosis of neurosyphilis are based on the examination of the cerebrospinal fluid.²

CSF Parameters	HIV (-)	HIV (+)
White blood cell	>5 ul	>20 ul or 6-20 ul
Protein	>0.45g/l	>0.45g/l
RPR/VDRL	+	+
TPHA	>1:320	>1:320

Syphilis with unreactive clinical and serological features of unclear interpretations may require skin biopsy, dark-field microscopy, or *T. pallidum* PCR to confirm the diagnosis.^{1,12} Skin biopsy of secondary syphilitic lesions has a variety of histopathological appearances related to the clinical picture.^{12,9} The basic feature of histopathological changes in syphilis is a perivascular infiltrate consisting of lymphocytes and

plasma cells, which is a specific but not pathognomonic sign for syphilis. Histopathologic features include endarteritis obliterans and endophlebitis, endothelial proliferation, and thickening of blood vessel walls surrounded by infiltrates.^{8,14} Histopathological features in syphilitic roseola are psoriasiform hyperplasia often accompanied by spongiosis, parakeratosis, dermal papillary, and perivascular or periadnexal edema,

infiltrates dominated by lymphocytes and plasma cells, and thickening of the vascular endothelium (Figure

7).¹⁴

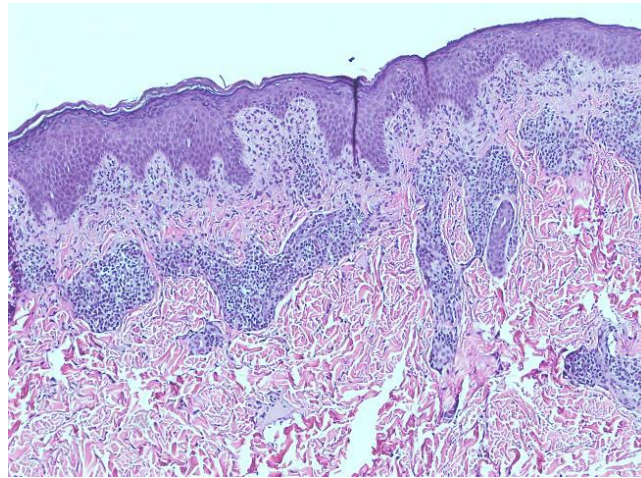


Figure 7. Histopathological appearance of an erythematous patch lesion in the posterior trunk region of a syphilitic patient with HIV infection, showing powdered inflammatory cells in the epidermis, dermis, and around the sebaceous glands (Fig.), impression benign skin lesions consistent with secondary syphilis (syphilitic roseola).

(Source: Photo collection of Departement of Dermatology and Venereology, Faculty of Medicine, Universitas Sriwijaya /Dr. Mohammad Hoesin, General Hospital, Palembang-Indonesia)

Treatment

Penicillin is still the gold standard for the treatment of syphilis, with or without HIV coinfection. Serological tests for patients with HIV infection should be repeated at 1, 2, 3, 6, 9, and 12 months.⁴ Primary or secondary syphilis with HIV infection is treated the same as for syphilis without HIV infection. The drug of choice for all stages of secondary syphilis is benzathine penicillin G (BPG) 2.4 million units IM in a single dose.^{1,15,10} Primary or secondary syphilis infection with HIV infection without neurologic involvement at least three doses of benzathine penicillin 2.4 million units IM at one-week intervals.¹³ Procaine penicillin (PP) 1.2

million units can be an alternative therapy in the absence of BPG.^{15,16} Penicillin-allergic syphilis patients were given a regimen of doxycycline 100 mg orally twice daily for 14 days and tetracycline 500 mg four times a day for 14 days. All syphilis with HIV infection should undergo a neurologic examination.^{15,10,17} Primary or secondary syphilis with HIV infection should be evaluated for clinical and serological management failure at 3, 6, 9, 12, and 24 months after therapy.^{12,10} Patients with penicillin allergies should be desensitized.^{15,10} Syphilis treatment algorithm can be seen in Figure 8.¹⁸

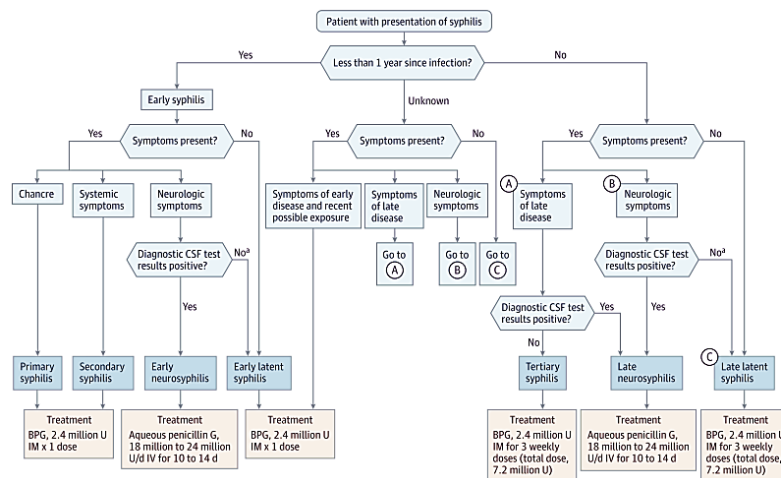


Figure 8. Syphilis treatment algorithm.¹⁸

The CDC's management recommendations for syphilis are independent of HIV infection status.¹⁰ Titers decreased more slowly in syphilis with HIV infection with appropriate treatment than in those without HIV infection, especially in patients with low initial

diagnosis titers. Primary or secondary syphilis with HIV infection should be evaluated more frequently than syphilis without HIV infection.^{1,10} Management of primary and secondary syphilis can be seen in table 5.^{16,15,10}

Table 5. Syphilis management in primary and secondary syphilis.^{16,15,10}

Syphilis Stadium	WHO (2016) ¹⁵	Indonesian Ministry of Health (2016) ¹⁶	CDC(2015) ¹⁰
Primary and secondary syphilis	<ul style="list-style-type: none"> • BPG G 2.4 million units IM, single dose or • PP 1.2 million units IM, 10 -14 days <p>Alternative:</p> <ul style="list-style-type: none"> • Doxycycline 100 mg PO for 30 days or • Ceftriaxone 1g IM once daily, for 10-14 days, or • Azithromycin 2 g single dose PO <p>Pregnant mother:</p> <ul style="list-style-type: none"> • BPG 2.4 million units IM single dose or • PP 1.2 million IM units once a day for 10 days <p>Alternative:</p> <ul style="list-style-type: none"> • Erythromycin 4x500 mg PO for 14 days or • Ceftriaxone 1 g IM once daily for 10-14 days or • Azithromycin 2 g PO single dose 	<p>BPG G 2.4 million units IM, single dose</p> <p>Alternative:</p> <ul style="list-style-type: none"> • PP 1.2 million units IM, 10 -14 days • Doxycycline 2x100 mg PO for 14 days <p>Pregnant Women and Penicillin Allergy:</p> <ul style="list-style-type: none"> • Decentitisation • Erythromycin 4x500 mg PO for 30 days 	<p>BPG 2.4 million units IM single dose</p> <p>Alternative:</p> <ul style="list-style-type: none"> • PP 600,000 IM units per day for 10-14 days • Ceftriaxone 1 g-2 g SC/IV per day for 10 days • Doxycycline 2x100 mg per day PO for 14 days • Azithromycin 2 g PO single dose <p>Pregnancy and Penicillin Allergy:</p> <p>Azithromycin 2 g PO single dose</p> <p>Infants and children:</p> <p>BPG 50,000 units/kg IM single dose, maximum 2.4 million units</p>

The management of syphilis according to the 2017 Perdoski PPK is divided into education and drug administration. In education, sexual partners were told that they had to be treated, counseling about syphilis, modes of transmission, prevention, management, and the risk of being easily infected with HIV.¹⁹ The treatment of choice for the primary and secondary stages is benzyl benzathine penicillin G (BBPG), with a single dose of 2.4 million units of intramuscular injection, while in the latent stage 2.4 million units of BBPG are given an intramuscular injection every week on day 1, 8 and 15 according to WHO guidelines.^{15,19} Patients were asked to wait for 30 minutes after the injection of BBPG.¹⁹ Alternative medicine if allergic to penicillin, the patient refuses injection or BBPG is not

available is doxycycline 2x100 mg orally for 14 days for primary and secondary syphilis or 28 days for latent syphilis according to WHO guidelines.^{15,19} Doxycycline according to the Indonesian Ministry of Health can be given 2x100 mg orally for 30 days in primary and secondary syphilis and more than 30 days in latent syphilis. Pregnant women can be given erythromycin 4x500 mg orally for 30 days in primary and secondary syphilis, or more than 30 days in latent syphilis according to the Indonesian Ministry of Health.^{16,19} Clinical and serological evaluation of therapy was performed at 1, 3, 6 and 12 months with criteria for recovery if VDRL or RPR titers decreased 4-fold within 6 months after treatment.¹⁹

Table 6. Syphilis management in advanced syphilis.^{16,15,10}

Syphilis Stadium	WHO (2016) ¹⁵	Indonesian Ministry of Health (2016) ¹⁶	CDC(2015) ¹⁰
Advanced syphilis	<ul style="list-style-type: none"> BPG 2.4 million units IM at 1-week intervals for 3 weeks (3 doses) PP 1.2 million units IM, 20 days <p>Alternative:</p> <ul style="list-style-type: none"> Doxycycline 100 mg PO for 30 days or <p>Pregnant mother:</p> <ul style="list-style-type: none"> BPG 2.4 million units IM per week for 3 weeks (3 doses, maximum injection distance of 14 days) PP 1.2 million IM units once a day for 20 days <p>Alternative:</p> <ul style="list-style-type: none"> Erythromycin 4x500 mg PO for 30 days 	<p>BPG 2.4 million units IM at 1-week intervals for 3 weeks (3 doses)</p> <p>Alternative:</p> <ul style="list-style-type: none"> PP 600,000 million units IM, 10 -14 days Doxycycline 2x100 mg PO for 30 days Ceftriaxone 1 g IM once daily for 10-14 days <p>Pregnant Women and Penicillin Allergy:</p> <ul style="list-style-type: none"> desensitization Erythromycin 4x500 mg PO for 30 days 	<p>BPG 2.4 million units IM at 1-week intervals for 3 weeks (3 doses)</p> <p>Penicillin allergy:</p> <ul style="list-style-type: none"> PP 600,000 million units once a day for 10-14 days Doxycycline 100 mg 2x for 28 days Tetracycline 500 mg for 28 days <p>Pregnant mother: BPG 2.4 million units IM administered 1 week after an initial dose</p> <p>Infants and children: BPG 50,000 units/kg IM in 3 doses at 1-week intervals (total 150,000 units/kg, maximum dose 7.2 million units)</p>

A fourfold increase in titer after treatment indicates reinfection or treatment failure. Re-infection should be assessed by clinical history and physical examination. Patients should be treated with benzathine penicillin G 7.2 million units (divided into 3 doses per week) if treatment fails. A CSF examination should be

performed to determine if neurosyphilis is present and if any the patient should be treated for neurosyphilis.¹⁰ Management of neurosyphilis can be seen in table 7.^{16,15,10}

Table 7. Management of neurosyphilis.^{16,15,10}

Syphilis Stadium	WHO (2016) ¹⁵	Indonesian Ministry of Health (2016) ¹⁶	CDC(2015) ¹⁰
Neurosyphilis	<ul style="list-style-type: none"> BPG 2.4 million units IM at 1-week intervals for 3 weeks (3 doses) PP 1.2 million units IM, 20 days <p>Alternative:</p> <ul style="list-style-type: none"> Doxycycline 100 mg PO for 30 days or <p>Pregnant mother:</p> <ul style="list-style-type: none"> BPG 2.4 million IM units per 851can for 3 weeks (3 doses, maximum injection distance 14 days) PP 1.2 million IM units once a day for 20 days <p>Alternative:</p> <ul style="list-style-type: none"> Erythromycin 4x500 mg PO for 30 days 	desensitization	<p>Penicillin G Crystal in aqua, dose 18-24 million units per day, IV dose 3-4 million units every 4 hours for 10-14 days</p> <p>Alternative:</p> <p>PP 2.4 million units IM once a day plus Probenecid 4x 500mg PO for 10-14 days</p>

Management evaluation

Treatment success was defined as a fourfold decrease in nontreponemal serological titers (or return to nonreactive results) after appropriate treatment, without signs or symptoms of persistent syphilis, and over a period of time according to the stage of syphilis infection and HIV status. fold is the 1:64 titer decreased to 1:16, or the 1:16 titer decreased to 1:4.1,¹⁰ Centers for Disease Control recommend evaluation of management at 6-month intervals until the titer decreases fourfold, unless primary or secondary syphilis patients with HIV infection are recommended for evaluation at 3, 6, 9, 12, and 24 months, and congenital syphilis is recommended for evaluation every 2 to 3 months .1,¹⁰Patients with latent syphilis fail treatment if there are clinical signs or symptoms of syphilis, a fourfold increase in serum nontreponemal test titer or no serological response (less than fourfold decrease in nontreponemal test titer) at 6, 12, and 24 months evaluation in 12-24 months after treatment

with high initial titers (> 1:32). The patient should be re-examined CSF, if the CSF examination reveals CNS involvement, re-treatment should be according to the management of neurosyphilis.²⁰

Primary and secondary syphilis with proper management of about 15% to 20% serofast will persist and not achieve a fourfold decrease in titer. The CDC guidelines recommend an additional clinical examination and re-evaluation or examination of the CSF to rule out CNS infection.¹⁰Patients with a CSF profile without CNS disease were re-treated with benzathine penicillin, 2.4 million units IM weekly for 3 weeks, although some were treated for neurosyphilis. Re-treatment of neurosyphilis was given if the CSF white blood cell count did not decrease 6 months after re-treatment or if the CSF-VDRL remained reactive after 2 years of treatment.²⁰ Evaluation of the management of syphilis in patients with HIV and without HIV can be seen in table 8¹¹

Table 8.Time to evaluate the management of syphilis in HIV patients and without HIV.¹¹

Syphilis stage	Syphilis titer re-evaluation time		Initial 4 times titer reduction time limit
	HIV (+)	HIV(-)	
Primary and secondary syphilis	3, 6, 9, 12, and 24 months	6 and 12 months	6 to 12 months
Early latent syphilis	6, 12, 18, and 24 months	6, 12 and 24 months	12 to 24 months
Advanced latent syphilis or unknown duration	6, 12, 18, and 24 months	6, 12, and 24 months	12 to 24 months
Gummatous tertiary syphilis	6, 12, 18, and 24 months	6, 12, and 24 months	12 to 24 months
Cardiovascular tertiary syphilis	6, 12, 18 and 24 months	6, 12 and 24 months	12 to 24 months
Neurosyphilis	3, 6, 9, 12 and 24 months	6, 12, 18 and 24 months	12 to 24 months

Evaluation of nontreponemal antibody serologic titers in congenital or pediatric syphilis should be performed during routine follow-up at 2, 4, 6, 12 and 15 months. Nontreponemal serological tests will become non-reactive within 6-12 months of adequate therapy.²¹ Treatment failure in congenital syphilis is characterized by a fixed or increasing nontreponemal titer at 6-12 months of age. Children with seropositive treponemal or non-treponemal titers at 18 months of age should be evaluated (eg, CSF examination) and reconsidered with parenteral penicillin for 10 days.^{21,20}

Prophylaxis or long-term maintenance management to prevent recurrence of syphilis in children with HIV

infection does not exist.²⁰All seroreactive infants (or infants of seroactive mothers at delivery) should undergo evaluation and serological tests (ie, nontreponemal testing) every 2–3 months until the test becomes nonreactive or the titer has decreased fourfold. Nontreponemal antibody titers should decrease by 3 months of age and should be nonreactive by 6 months of age in infants not infected or infected but well treated. Serological response after treatment may be slower in infants treated after the neonatal period.^{11,10,20}

Treponemal testing in children is not used to evaluate response to treatment because results remain

positive despite effective treatment. Treponemal antibodies from the mother can be found in infants up to 15 months of age. A reactive treponemal test after 18 months of age is diagnostic of congenital syphilis. A nonreactive nontreponemal test at 18 months of age does not require further evaluation or treatment, whereas if the nontreponemal test is reactive the infant should be reevaluated and treated for congenital syphilis.²⁰ Failure to treat syphilis in children and adolescents is similar to that in adults i.e., there is no fourfold decrease in serum nontreponemal test titer for 6–12 months after therapy, a fourfold increase in serum nontreponemal test titer after initial reduction in treatment or clinical signs/symptoms of persistent disease or repeated. If the CSF examination does not confirm the diagnosis of neurosyphilis, the patient should be treated with benzathine penicillin G 2.4 million units IM at 1-week intervals for 3 weeks.^{10,20}

In congenital syphilis with abnormal CSF, if Initial CSF examination shows pleocytosis, repeat lumbar puncture 6 months after therapy until the cell count is normal.^{21,20} Follow-up CSF examination can be used to evaluate changes in VDRL-CSF or CSF protein levels after therapy, but in HIV the parameter changes are slower than changes in CSF cell numbers. Neurosyphilis patients with HIV infection have long-lasting CSF abnormalities and should be closely evaluated clinically.^{10,20}

Drug resistance

The use of penicillin in the treatment of syphilis has not been reported to be resistant for more than 60 years. Syphilis patients with HIV only one patient reported failing penicillin therapy. Research with other alternative drugs is still limited with small samples, uncontrolled, and retrospective studies although there are studies of randomized trials. Erythromycin is not recommended because of drug resistance and tolerance, while doxycycline is a potential substitute for penicillin.²²

Doxycycline (100 mg orally twice daily for 14 days) is effective for the treatment of early syphilis with penicillin allergy. In a failure of treatment with doxycycline, syphilitic patients should be desensitized

to penicillin and receive penicillin treatment.^{4,11} Doxycycline response to the treatment of syphilis with HIV is 73-88%, while in syphilis without HIV the average serological response is 83-100%.²²

The use of ceftriaxone for the treatment of latent syphilis and neurologic failure has been reported in several cases.¹¹ Ceftriaxone response to serological mean is 65-100%. Response rates were lower in syphilis patients with HIV, especially patients with incomplete HIV suppression. Treatment failure was most commonly noted in patients with latent syphilis with HIV infection.²²

The use of azithromycin (2 g orally in a single dose) in early syphilis has been reported to be resistant and treatment failure. Azithromycin should be used with caution and only used when treatment with penicillin or doxycycline is not possible.^{4,11} Azithromycin should not be used in patients with HIV.¹⁰ Azithromycin-resistant strains are more common in the male population who have sex with men; azithromycin-resistant syphilis during pregnancy increases the risk of congenital syphilis.¹¹

Treatment complications

Complications of syphilis management can be in the form of a Jarisch-Herxheimer reaction and anaphylactic shock, therefore, after the injection of penicillin the patient was observed for 30 minutes.² The Jarisch-Herxheimer reaction is a syndrome that occurs 12 hours after therapy, then resolves spontaneously within 24-36 hours. The Jarisch-Herxheimer reaction occurs in 1/3 to 2/3 of primary and secondary syphilis patients treated with penicillin.¹ The Jarisch-Herxheimer reaction is not a hypersensitivity reaction but rather the presence of cytokines triggered by dead lipoprotein T. pallidum, so penicillin therapy does not need to be discontinued.^{1,2,22}

This reaction is thought to result from the release of lipoproteins, cytokines, and immune complexes from dead organisms.²² Clinical manifestations of fever, rash, malaise, headache, mucocutaneous lesions, lymphadenopathy tender to pressure, sore throat, malaise, and myalgia are seen in 10% to 35% of patients and are self-limiting.¹ Treatment of syphilis in

pregnant women can trigger the Jarisch-Herxheimer reaction. This reaction can trigger uterine contractions, premature birth, and impaired fetal heart rate, but the risk of a Jarisch-Herxheimer reaction is not a contraindication to the administration of penicillin in pregnant women.²¹ Acetaminophen or ibuprofen can be given to treat complaints.^{1,2}

Penicillin allergic reactions may include urticaria, angioedema, or anaphylactic shock. Anaphylactic shock has symptoms of upper airway obstruction, bronchospasm, or hypotension. Treatment is epinephrine (adrenaline) 1:1000 IM, 0.5 mL followed by an IM/IV antihistamine (eg diphenhydramine 10 mg) and hydrocortisone IM/IV 100 mg.^{2,10} Penicillin desensitization is an option in the following situations: (1) neurosyphilis in persons with a history of severe hypersensitivity reactions to penicillins; (2) tertiary syphilis in all penicillin-allergic patients; (3) all stages of syphilis in penicillin-allergic pregnant women; and (4) congenital syphilis in penicillin-allergic infants.^{10,22}

Prevention

Prevention of syphilis with HIV infection can be done by education, screening for syphilis and other sexually transmitted infections, as well as early detection of partners and therapy. Education in the form of not having sex before marriage, being faithful to a partner, using condoms, not consuming narcotics, psychotropic substances, and addictive substances (Drugs).² The use of condoms and abstaining from risky sex is very important to prevent the transmission of syphilis and HIV.^{23,10} Screening for syphilis and other sexually transmitted infections is carried out in high-risk groups and pregnant women.² Screening is also important in identifying asymptomatic patients. Sexually active MSM patients should be screened at least annually and every 3 to 6 months if at high risk (eg, the patient or sexual partner has multiple partners).¹

Pregnant women are screened at the first prenatal visit, with re-examination early in the third trimester and at delivery if at high risk for syphilis. Screening of syphilis patients with sexually active HIV infection should be carried out at the first subsequent HIV evaluation at least annually, screening more frequently

depending on individual risk behavior and local epidemiology.^{1,10} Early detection and therapy of sexual partners with syphilis is carried out if sexual intercourse occurs within 3 months after the onset of primary syphilis symptoms, 6 months after the onset of secondary syphilis symptoms, 12 months in patients with early latent syphilis and 24 months in patients with latent syphilis. Examination and laboratory results suggest syphilis in sexual partners can be given therapy.²

In communities and populations at high risk of congenital syphilis, serologic tests and sexual history should be checked at 28 weeks gestation and delivery. This examination as part of the management of pregnant women with syphilis, information about the treatment of sexual partners should be known to assess the risk of reinfection.^{21,20} Routine screening of serum from newborns or cord blood is not recommended. Maternal serum serologic tests are preferred over infant serum tests because serologic tests of infant serum may become nonreactive if the mother's serologic test results are low or the mother is infected with syphilis in late pregnancy. Infants with HIV infection in a population at high risk for congenital syphilis should not leave the hospital unless the mother's serologic status is at least once during pregnancy and at delivery.²⁰

Prognosis

The prognosis for syphilis in HIV is worse than for syphilis without HIV. Neurosyphilis is more common in syphilis patients with HIV infection, clinical manifestations such as uveitis or meningitis are more common.⁴ *Treponema pallidum* remains sensitive to penicillin despite its use for decades. Treatment failure can occur and more often in syphilis patients with HIV infection, penicillin treatment is very effective for treating the infection at all stages of syphilis. Primary and secondary syphilis mostly have a resolution of symptoms, without sequelae even without treatment. In tertiary syphilis, there can be permanent damage to vital organs such as gumma, cardiovascular or CNS involvement.¹ In a 2016 study by Sophie et al., two patients from 12 cases of ocular syphilis experienced

sequelae of permanent blindness despite treatment.²⁴ The prognosis of the fetus depends on the diagnosis of syphilis in the pregnant woman at the time of presentation for antenatal care. Congenital syphilis is a disease that can be prevented through antenatal services to reach pregnant women with syphilis.²¹

2. Conclusion

Syphilis and HIV have a reciprocal relationship, HIV infection causes a decrease in the body's immunity so it is very easy to be infected with various other diseases such as syphilis, while syphilis also increases the risk of HIV transmission. The prevalence of syphilis in HIV was greater than that of syphilis without HIV and was more common in the MSM group. Patients with syphilis should be tested for HIV infection and HIV patients should be tested for syphilis infection. The diagnosis of syphilis is based on a complete history including sexual history, clinical manifestations, and examination. Serological examination is a tool for the diagnosis of syphilis in syphilis patients with HIV infection and without HIV infection. Penicillin is still the gold standard for the management of syphilis with or without HIV infection, there is no difference in therapy between syphilis patients with HIV infection and without HIV infection. Prevention of syphilis in HIV can be done by education, screening for syphilis and other STIs, as well as early detection and therapy in partners. Syphilis patients with HIV infection are more at risk of developing neurosyphilis.

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