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2023 Korean sexually transmitted infections guidelines for non-gonococcal bacterial infection (chlamydia, syphilis, etc.) by the Korean Association of Urogenital Tract Infection and Inflammation

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Non-gonococcal sexually transmitted infections (STIs) include chlamydia, syphilis, and chancroids. Chlamydia is the most common STI caused by *Chlamydia trachomatis* and is mainly transmitted through sexual intercourse or vertical transmission at birth. Although symptoms are mostly absent or mild, untreated chlamydial infections in females can lead to pelvic inflammatory disease, chronic pelvic pain, and infertility due to the narrowing of fallopian tubes. Syphilis is caused by *Treponema pallidum* and is divided into phase I, phase II, latent syphilis, and phase III. The incidence of syphilis, including congenital syphilis, has significantly increased in the United States in recent years. The chronic status of this disease can significantly increase morbidity and potentially affect almost all body organs, which, in rare cases, can lead to death. Additionally, untreated maternal syphilis can lead to fetal death and fatal congenital infections in newborns. Chancroid is an STI caused by *Haemophilus ducreyi,* and its prevalence is gradually decreasing in Korea and worldwide. The symptoms include shallow genital ulcers with suppurative granulomatous inflammation and tender inguinal lymphadenopathy. Chancroids can be differentiated from syphilitic chancres based on their appearance. In contrast to painless chancres, chancroids are painful. *Ureaplasma urealyticum, Ureaplasma parvum,* and *Mycoplasma hominis* are considered symbiotic bacteria. Infections caused by these bacteria are usually not considered STIs and do not require treatment unless they are suspected of being associated with infertility. This article presents the 2023 Korean STI guidelines for non-gonococcal bacterial infections.

Keywords: Chancroid; Chlamydia; Guideline; Sexually transmitted infection; Syphilis

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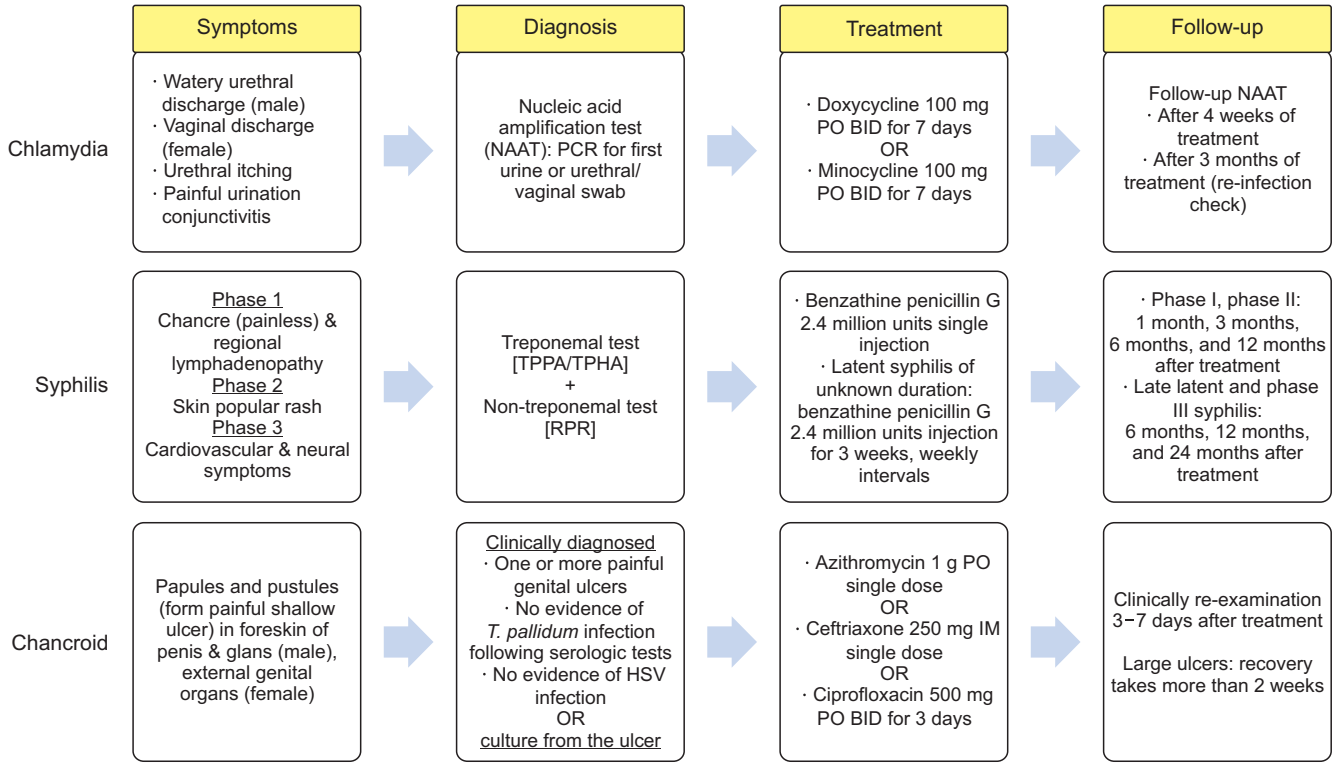

Fig. 1. Schematic flowchart of the overall diagnostic and treatment. PCR, polymerase chain reaction; PO, orally; BID, twice daily; TPPA, *Treponema pallidum* particle agglutination assay; TPHA, *Treponema pallidum* hemagglutination assay; RPR, rapid plasma reagin; *T. pallidum*, *Treponema pallidum*; HSV, herpes simplex virus; IM, intramuscularly.

SUMMARY OF RECOMMENDATIONS

The overall diagnostic and treatment flowchart is schematically represented in Fig. 1.

1. Chlamydia

1) Diagnosis

(1) Sample collection
- i. Male: urethral secretions or a first-catch urine specimen
- ii. Female: vaginal swab, cervical swab, or endometrial biopsy

(2) Nucleic acid amplification tests (NAATs)
- i. Polymerase chain reaction (PCR), real-time PCR, strand displacement assay (SDA), transcription-mediated amplification (TMA), and nucleic acid sequence-based amplification (NASBA)

2) Treatment

(1) Adolescents and adults with chlamydial infections
- i. Doxycycline 100 mg orally 2×/day for 7 days
- OR minocycline 100 mg orally 2×/day for 7 days
- ii. Alternatives: azithromycin 1 g orally as a single dose
- OR levofloxacin 500 mg orally 1×/day for 7 days

(2) Chlamydial infections during pregnancy
- i. Azithromycin 1 g orally as a single dose
- ii. Alternative: amoxicillin 500 mg orally 3×/day for 7 days

(3) Infants and children with chlamydial infections (weight <45 kg)
- i. Erythromycin base, 50 mg/kg body weight/day orally, divided into four doses daily for 14 days
- OR erythromycin ethylsuccinate, 50 mg/kg body weight/day orally, divided into four doses daily for 14 days

(4) Children with chlamydial infections (weight ≥45 kg, age <8 years)
- i. Azithromycin 1 g orally as a single dose

(5) Children and adolescents with chlamydial infections (age ≥8 years)
- i. Azithromycin 1 g orally as a single dose
- OR doxycycline 100 mg orally 2×/day for 7 days
- OR minocycline 100 mg orally 2×/day for 7 days

(6) Neonates with ophthalmia neonatorum/pneumonia due to chlamydial infections
- i. Erythromycin base, 50 mg/kg body weight/day orally, divided into four doses daily for 14 days

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OR erythromycin ethylsuccinate, 50 mg/kg body weight/day orally, divided into four doses daily for 14 days

ii. Alternative: azithromycin suspension, 20 mg/kg body weight/day orally 1×/day for 3 days

3) Follow-up and monitoring

(1) Test-of-cure after completing therapy

i. Routine test-of-cure is not recommended.

ii. Recommended for pregnant females.

iii. Retesting may be necessary if symptoms persist or recur despite treatment.

iv. NAATs should be performed after 4 weeks of treatment (due to false positives owing to dead microorganisms).

(2) Follow-up for 3 months after treatment

i. All females and males should return for follow-up and repeat testing because of the substantial risk of re-infection.

2. Syphilis

1) Diagnosis

(1) PCR analysis of ulcer exudate or tissue

(2) Serum rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL)+enzyme immunoassay (EIA), *Treponema pallidum* hemagglutination assay (TPHA), *T. pallidum* particle agglutination assay (TPPA), *T. pallidum* latex agglutination assay (TPLA), or fluorescent treponemal antibody absorbed test (FTA-ABS tests)

2) Treatment

(1) Phase I/II syphilis or early latent syphilis in adult/adolescent/pregnant or HIV-infected individuals

i. Benzathine penicillin G 2.4 million units intramuscularly (IM) as a single dose

(2) Late latent syphilis in adults/adolescents/pregnant females or HIV-infected individuals

i. Benzathine penicillin G, 7.2 million units in total, administered as three doses of 2.4 million units IM each at 1-week intervals.

(3) Neurosyphilis

i. Aqueous crystalline penicillin G 18–24 million units per day (administered as 3–4 million units intravenously [IV] every 4 hours or continuous infusion) for 10–14 days

ii. Alternatives: procaine penicillin G 2.4 million units IM 1×/day plus probenecid 500 mg orally 4×/day, both for 10–14 days

OR ceftriaxone 1–2 g IV daily for 10–14 days

3) Follow-up and monitoring

(1) Follow-up of non-treponemal tests until a negative result or consistently low threshold (1:4 or less) is observed.

i. Phase I, phase II, and early latent syphilis: 1 month, 3 months, 6 months, and 12 months after treatment

ii. Late latent and phase III syphilis: 6 months, 12 months, and 24 months after treatment

iii. Neurosyphilis: 6 months, 12 months, and 24 months after treatment

3. Chancroid

1) Diagnosis

(1) Clinical diagnosis

i. One or more painful genital ulcers and regional lymphadenopathy

ii. No evidence of *T. pallidum* infection following darkfield examination.

iii. No evidence of *T. pallidum* infection following serological tests for syphilis performed at least 7 days after the onset of the ulcers.

iv. No evidence of herpes simplex virus (HSV) infection.

(2) Culture

i. Collected from the base of the genital ulcer.

ii. Culture is required for differential diagnosis from *T. pallidum* or HSV.

(3) NAAT

i. PCR analysis for *Haemophilus ducreyi*

2) Treatment

(1) Azithromycin 1 g orally as a single dose

OR ceftriaxone 250 mg IM as a single dose

OR ciprofloxacin 500 mg orally 2×/day for 3 days

OR erythromycin base 500 mg orally 3×/day for 7 days

3) Follow-up and monitoring

(1) Re-examination 3–7 days after treatment

i. Improve symptomatically within 3 days and objectively within 7 days after treatment.

ii. Large ulcers: recovery takes more than 2 weeks

iii. Ulcers under the foreskin in uncircumcised males: slower recovery

iv. Fluctuant lymphadenopathy: slower recovery than an ulcer

(2) No improvement after treatment

i. Check for diagnosis, presence of another sexually transmitted infection (STI), HIV infection, compliance with treatment, resistance to antimicrobial agent.

(3) Management of sex partners

i. All sexual partners in the 2 weeks preceding symptom onset should be examined and treated.

4. *Ureaplasma urealyticum*, *Ureaplasma parvum*, and *Mycoplasma hominis* infections

1) Diagnosis

(1) These bacteria are regarded as symbiotic, and their infections are not considered STIs. Therefore, treatment is not necessary. Treatment is only considered if a connection with pregnancy-related complications is suspected.

(2) NAATs (e.g., multiplex PCR) can be performed on various samples, including male first-voided urine and female vagina or endocervix swabs.

2) Treatment

(1) Doxycycline 100 mg orally 2×/day for 7 days
OR minocycline 100 mg orally 2×/day for 7 days

INTRODUCTION

Chlamydia, caused by *Chlamydia trachomatis*, is the most common bacterial sexually transmitted infection (STI), accounting for approximately 20%–50% of non-gonococcal STIs [1]. Because symptoms are usually absent or mild, chlamydia is often not properly diagnosed and treated. Therefore, the actual number of chlamydial infections is expected to be higher than reported. Untreated chlamydia causes complications, such as pelvic inflammatory disease, chronic pelvic pain, and infertility, due to the narrowing of the fallopian tubes. Rectal chlamydial infections increase the risk of HIV infection [2].

Syphilis is a systemic infection mainly caused by the transmission of *Treponema pallidum* through sexual activity or vertical transmission through pregnancy. The incidence of syphilis infections, including congenital syphilis, has significantly increased in the United States (US) in recent years [3]. Patients with syphilis may develop chronic clinical symptoms if treatment is not administered properly. Characteristically, syphilis progresses in stages (phase I, phase II, latent period, and phase III), and disease activity stops during the incubation period. However, neurological symptoms can occur at any stage [4]. The chronic status of this disease can significantly increase morbidity and potentially affect almost all body organs, which, in rare cases, can lead to death. Untreated maternal syphilis can lead to fetal death and fatal congenital infections in newborns.

Chancroid is a disease caused by *Haemophilus ducreyi* and is characterized by painful purulent ulcers in the genital area accompanied by inguinal lymphadenitis called buboes. Although the incidence of chancroids is declining worldwide, they mainly occur in developing countries in Africa, the Caribbean Basin, and Southwest Asia.

Ureaplasma urealyticum, *Ureaplasma parvum*, and *Mycoplasma hominis* are considered symbiotic bacteria. Infections caused by these bacteria are usually not considered sexually transmitted infections and do not require treatment unless they are suspected of being associated with infertility. This article presents the 2023 Korean sexually transmitted infection guidelines for non-gonococcal bacterial infections.

DEVELOPMENT OF THE KOREAN GUIDELINES

The Korea Centers for Disease Control and Prevention (currently the Korea Disease Control and Prevention Agency, KDCA) and the Korean Association of Urogenital Tract Infection and Inflammation (KAUTII) developed the first Korean STI guidelines (2011) in 2009–2010. In 2016, STI guidelines (2016) were published as the first revision. Six years later, in 2022, the KDCA and the KAUTII conducted a second revision of their guidelines from July 2022 to April 2023.

The development committee consisted of a steering committee, a development committee, a writing committee, an internal review committee, and an external review committee. The writing committee included an insurance team for insurance-related reviews, similar to the first revision of the guidelines. The external review committee consisted of the Korean Urological Association, the Association of Korean Urologist, the Korean Society of Obstetricians and Gynecology, the Korean Association of Obstetricians and Gynecologists, the Korean Society for Laboratory Medicine, the Korean Society of Clinical Microbiology, the Korean Society of Infectious Diseases, and AIDS at the Korea Centers for Disease Control and Prevention. No conflicts of interest were reported during the development.

We adopted a local adaptation to accommodate and develop foreign guidelines to suit the Korean situation following the recommendations of the Clinical Practice Guidelines Executive Committee of the Korean Medical Association (KMA). Data sources, including PubMed, NICE (National Institute for Health and Care Excellence), KoreaMed, a trial

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register (https://clinicaltrials.gov/), SciELO, Scopus, Embase, Google Scholar, the Cochrane Library, the National Guideline Clearinghouse, and the CMA (Canadian Medical Association) Infobase Clinical Practice Guideline database were searched for existing treatment recommendations for acceptance development. The search index words were sexually transmitted infection index words ("sexually transmitted infection" OR "sexually transmitted disease") and treatment guideline index words ("guideline" OR "national guideline" OR "practice guideline" OR "management guideline" OR "consensus" OR "recommendation"). The range of publication dates was limited to January 2017 to December 2022, and the latest edition was selected if there was a revision. The ten foreign STI guidelines were searched based on the topics or formats.

Five guidelines were evaluated after excluding guidelines that were not developed based on evidence or were published without references: the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC) in the US, BASHH (British Association for Sexual Health and HIV) in the UK, IUSTI (International Union against Sexually Transmitted Infections) in Europe, and JSSTI (Japanese Society for Sexually Transmitted Infections) in Japan. The Korean version of the AGREE 2.0 (K-AGREE 2.0) evaluation development scale distributed by the Clinical Practice Guideline Expert Committee of the KMA was used for quality evaluation. Four members of the development committee evaluated six areas to obtain standardized scores for each area. After comparing the scores of each area, two guidelines (CDC and WHO) were finally selected with a standardization score for development rigor and an applicability score of 50% or higher.

Domestic data were searched and analyzed in all fields to adapt to the domestic situation. Key questions were derived using the PICO (Population or Patient problem, Intervention, Comparison, Outcome) technique and presented in the literature search process, evidence table, and meta-analysis. PubMed (http://www.pubmed.gov) and KoreaMed (http://www.koreamed.org) were searched for evidence. Papers published in Korean were first searched, and in cases that lacked evidence, evidence was obtained by re-searching without limiting the year. In cases where there was a recently published systematic review or meta-analysis, previously published literature with a low level of evidence was excluded. Case reports were also excluded.

The Delphi technique was applied to derive and adopt the draft recommendations. Seventeen panels were created to ensure the representativeness and expertise of the recommendation development group.

DIAGNOSIS

1. Chlamydia

The incubation period for chlamydia is 2–3 weeks and can last up to 6 weeks. If not treated, the infection can persist for several months. Co-infection with *Neisseria gonorrhoeae* is common.

Approximately 50% of males with chlamydial infections are asymptomatic. However, these infections can cause symptoms such as:

- Urethral discharge (watery)
- Urethral itching
- Painful urination
- Testicular pain
- Conjunctivitis
- Proctitis (mostly asymptomatic)

Approximately 70%–80% of females with chlamydial infections are asymptomatic. However, these infections can cause symptoms such as:

- Vaginal discharge
- Painful urination
- Lower abdominal pain
- Abnormal vaginal bleeding
- Dyspareunia
- Conjunctivitis
- Proctitis (mostly asymptomatic)

In infants, chlamydia can cause symptoms such as:

- Conjunctivitis
- Pneumonia (within 6 months of age)

Chlamydia is diagnosed using nucleic acid amplification tests (NAATs), which include polymerase chain reaction (PCR), real-time PCR, strand displacement assay (SDA), transcription-mediated amplification (TMA), and nucleic acid sequence-based amplification (NASBA). NAATs have higher sensitivity and specificity than culture tests, enzyme immunoassays (EIA), or direct fluorescent antibody assays (DFA). Samples should be collected from the first urine or urethra in males and from the endometrium or vagina during colposcopy in females. If colposcopy is difficult, testing should be performed on a vaginal swab or the first urine sample. Combination or multiplex methods can be used to diagnose gonorrhea or other causative bacteria simultaneously.

2. Syphilis

Syphilis can cause symptoms such as:

- Phase 1: chancre and regional lymphadenopathy
- Phase 2: papular rash on the skin (body, palm, and sole), fever, boredom, lymphadenopathy, mucosal lesions, alopecia with rash, meningitis, headache, uveitis, and

Table 1. Result of treponemal/non-treponemal test and interpretations

Treponemal test	Non-treponemal test	RPR titer	Translation
Negative	Negative		• When medical history and clinical symptoms exist, the early stage of syphilis cannot be excluded (window period). • Other treponemal tests (FTA-ABS) should be conducted and confirmed.
Positive	Positive	≥1:16	• Phase 1, phase 2, or early latent syphilis (active syphilis)
		<1:8	• Treat syphilis (serofast state). However, if the patient has a history of treatment, the patient does not need treatment.
Positive	Negative		Usually treated syphilis • If the history of treatment is unclear, treatment is performed for late latent syphilis without knowing the duration of the disease. • Early stage of syphilis (window period). If this cannot be ruled out, re-examination should be conducted after 3–4 weeks.
Negative	Positive		Biological false positivity • Early stage of syphilis (window period) • Re-examination after 3–4 weeks

RPR, rapid plasma reagin; FTA-ABS, fluorescent treponemal antibody absorbed test.

retinitis
- Latent phase: asymptomatic
- Phase 3:
  - Cardiovascular syphilis: aortic aneurysm, aortic regurgitation, and coronary artery ostial stenosis
  - Neurosyphilis: Range varies from asymptomatic to symptomatic, headaches, vertigo, personality changes, delirium, ataxia, and Argyll Robertson pupil
  - Gumma: Symptoms vary depending on the affected area
- Serum tests (treponemal test [*T. pallidum* particle agglutination assay (TPPA)/*T. pallidum* hemagglutination assay (TPHA)]+non-treponemal test [rapid plasma reagin (RPR)])
- A non-treponemal test should be performed before treatment and follow-up with titer afterward.
- The treponemal test remains positive for life after a syphilis infection, and the titer is clinically meaningless because it is not related to syphilis activity.
- If appropriate treatment is performed, a non-treponemal test result can convert to negative. However, if treated late, the titer decreases, but a lower titer can persist (≤1:8) (serofast state).

Detailed interpretations of treponemal/non-treponemal test results are described in Table 1.

3. Chancroid

The chancroid incubation period is 5–14 days, during which papules and pustules develop and rupture to form shallow ulcers with granulomatous inflammation. In males, ulcers occur mainly on the foreskin of the penis, the coronal sulcus of the glans, and the body of the penis. In females, ulceration may occur widely in the external genital organs, and multiple ulcers are commonly observed, but rarely occur in the vagina or cervix. Painful inguinal lymphadenitis develops in 30% of patients and may spontaneously rupture. A chancroid has a pattern similar to that of other genital ulcers, especially a chancre in the primary stage of syphilis. However, a chancroid is painful, whereas a chancre is painless. Chancroids rarely extend from the genital tract and do not cause systemic disease. Most diagnoses are based on clinical symptoms, as it is difficult to definitively diagnose *H. ducreyi* by culturing.

Chancroid is clinically diagnosed when there is:
- One or more painful genital ulcers and regional lymphadenopathy
- No evidence of *T. pallidum* infection following darkfield examination.
- No evidence of *T. pallidum* infection following serologic tests for syphilis performed at least 7 days after onset of ulcers.
- No evidence of HSV infection.

TREATMENT

1. Chlamydia

Patients with chlamydial infections must be treated to reduce complications and prevent the spread of the infection to others. Chlamydial infections are treated according to the target patients as described in the Summary of Recommendations.

There are two key questions about the treatment of chlamydia.

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■ Is doxycycline 100 mg orally twice daily for 7-day treatment more effective than azithromycin 1 g orally single dose as the primary treatment for chlamydial infection in adolescents and adults?

This guideline recommends a 7-day course of doxycycline as the first-line treatment for chlamydia for several reasons. First, the recently reported macrolide resistance of *Mycoplasma genitalium* has greatly increased because of the widespread use of azithromycin for STIs [5]. Thus, azithromycin should be used in a limited manner. In addition, several clinical studies reported that a 7-day course of doxycycline was more effective than a single dose of azithromycin for rectal chlamydial infections in men who have sex with men (MSM) and females [6-10] and pharyngeal chlamydial infections [11].

1A	Doxycycline 100 mg orally twice daily for 7 days is recommended for the treatment of uncomplicated chlamydial infections in genital, pharyngeal, and rectal areas.

■ Is amoxicillin more effective than erythromycin as an alternative chlamydia treatment in pregnant females if azithromycin is not available?

Doxycycline and quinolone cannot be used to treat chlamydial infections during pregnancy because they are contraindicated in pregnancy. Therefore, azithromycin is recommended as a first-line drug. Erythromycin was recommended as an alternative in previous guidelines. However, several studies reported that erythromycin reduced drug adherence owing to gastrointestinal side effects and the possibility of adverse child outcomes. Therefore, it is no longer recommended in these guidelines [12,13]. In a meta-analysis, amoxicillin showed a therapeutic effect similar to erythromycin and had a favorable adverse event profile [14]. However, *in vitro* studies reported that amoxicillin may be associated with infection recurrence. Therefore, amoxicillin is not recommended as a first-line treatment for chlamydia in pregnant females and should be used as an alternative therapy only when azithromycin cannot be used [15].

1A	Azithromycin 1 g orally as a single dose is recommended for the treatment of uncomplicated chlamydial infections during pregnancy.
1A	If azithromycin is not available, amoxicillin 500 mg 3 times daily for 7 days is recommended as an alternative to treat uncomplicated chlamydial infections during pregnancy.

2. Syphilis

The following is a key question about syphilis treatment.

■ Is there a difference in treatment effectiveness when alternative therapy is administered in adult patients initially diagnosed with syphilis who cannot undergo penicillin therapy due to allergies?

Penicillin is the treatment of choice for syphilis, and if patients are treated with drugs other than penicillin, treatment failure is highly likely.

1B	For the treatment of primary, secondary, or early latent syphilis, a single intramuscular injection of benzathine penicillin G 2.4 million units is recommended.
1C	For the treatment of late latent syphilis or latent syphilis of unknown duration, a regimen of 3 intramuscular injections of benzathine penicillin G 2.4 million units at weekly intervals is recommended.
1C	As an alternative therapy for patients with primary, secondary, or early latent syphilis and penicillin allergies, an oral administration of doxycycline 100 mg twice daily for 14 days is recommended.
2D	For patients with late latent syphilis or latent syphilis of unknown duration and penicillin allergies, an oral administration of doxycycline 100 mg twice daily for 28 days is recommended.
1B	In pregnant females with primary, secondary, or early latent syphilis, a single intramuscular injection of benzathine penicillin G 2.4 million units is recommended. Desensitization, followed by penicillin treatment, is recommended for patients with penicillin allergies.
1C	For pregnant females with late latent syphilis or latent syphilis of unknown duration, 3 intramuscular injections of benzathine penicillin G 2.4 million units at weekly intervals are recommended. Desensitization, followed by penicillin treatment, is recommended for patients with penicillin allergies.

After treatment of syphilis, follow-up must be provided for a sufficient period of time as suggested in the recommendations. Generally, it takes 1–2 years to reduce the titer to complete a cure. The longer the patient has been infected with syphilis, as in patients with late latent syphilis, the longer it takes to decrease titers. If treatment failure is suspected, a cerebrospinal fluid test must be considered to exclude neurosyphilis [16]. It is important to distinguish between the "serofast state" and treatment failure. However, if this is difficult to distinguish, the recommended treatment modality is benzathine penicillin G 2.4 million units intramuscularly (IM) 3 times every week [17]. A cerebrospinal fluid test should also be considered to exclude neurosyphilis [18].

In the case of latent syphilis or in cases where treatment is performed according to latent syphilis because the treatment history is unclear, the standard titer before treatment is often as low as 1:2 or 1:4, and it takes a long time to reduce the titer by more than 4 times, which is the standard for

complete recovery [19]. Furthermore, titers often remain at 1:1 or 1:2 without a decrease of more than 4 times, even after 24 months. Since appropriate treatment for this situation has not yet been established, an expert should be consulted for continuous follow-up, or, if necessary, the patient should be re-treated with benzathine penicillin G 2.4 million units IM 3 times a week.

3. Chancroid

See the Summary of Recommendations.

FOLLOW-UP AND MONITORING

1. Chlamydia

See the Summary of Recommendations.

2. Syphilis

- Syphilis treatment response can be seen as a decrease in treponemal test (RPR or venereal disease research laboratory [VDRL]).
- Follow-up treponemal tests should be conducted until a negative result or consistently low threshold (1:4) is achieved.
- In cases of latent syphilis or unclear treatment history, the treponemal test titer before treatment is often as low as less than 1:4, and the titer may not be sufficiently reduced even after treatment.
- An increase in the treponemal test titer after treatment may indicate treatment failure or re-infection. Further investigation, including cerebrospinal fluid testing, is required if the treatment is presumed to be a failure.
- Abstinence after syphilis treatment
  - Phase I or phase II syphilis is not contagious within a few days after proper treatment (especially when treated with benzathine penicillin G). The recommended abstinence period is from the completion of treatment until the lesion is completely healed, or approximately 1 month.
  - Late latent syphilis is not transmitted through sexual contact. Therefore, no specific abstinence period is required.
- Monitoring with non-treponemal tests
  - Tests are recommended to be conducted in the same method by the same hospital according to the following guidelines.
  - Phase I, phase II, and early latent syphilis: 1 month, 3 months, 6 months, and 12 months after treatment
  - Late latent and phase III syphilis: 6 months, 12 months, and 24 months after treatment
  - Neurosyphilis: 6 months, 12 months, and 24 months after treatment
  - HIV-infected individuals: 1 month, 3 months, 6 months, 12 months, 24 months after treatment, and every year thereafter
  - Newborns born to mothers who tested positive for syphilis: 3 months and 6 months after childbirth
  - Congenital syphilis: 0 months, 3 months, 6 months, 12 months, and 18 months after childbirth
- A titer change is considered to indicate successful treatment
  - Phase I syphilis
    i. 6 months: 4× reduction in titer (e.g., 1:32 to 1:8)
    ii. 12 months: 8× reduction in titer
    iii. 24 months: 16× reduction in titer
  - Phase II syphilis
    i. 6 months: 8× reduction in titer
    ii. 12 months: 16× reduction in titer
  - Phase III syphilis
    i. 12 months: 4× reduction in titer
- Suspected re-infection or failure of treatment indicated for re-treatment
  - Non-treponemal test (RPR or VDRL) with 4× increase in titer
  - Non-treponemal test (RPR or VDRL) titer does not decrease by 4× within 12–24 months.
  - Symptoms or signs of syphilis occur

3. Chancroid

See the Summary of Recommendations.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

Research conception and design: Seung-Ju Lee and Kyu Won Lee. Data analysis and interpretation: Joongwon Choi and Sangrak Bae. Drafting of the manuscript: Joongwon Choi and Kyu Won Lee. Critical revision of the manuscript: Dalsan You, Chan Ho Lee, Jin Bong Choi, Yu Seob Shin, and Seung-Ju Lee. Obtaining funding: Seung-Ju Lee. Administrative, technical, or material support: Sangrak Bae. Supervision: Joo Yong Lee. Approval of the final manuscript: Seung-Ju Lee and Kyu Won Lee.

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