2019 Chinese expert consensus statement on diagnosis and treatment of syphilis

National Center for Sexually Transmitted Disease Control, China Centers for Disease Control and Prevention; Committee of Sexually Transmitted Disease, Branch of Dermatovenereology, Chinese Medical Association; Committee of Sexually Transmitted Disease, Branch of Dermatologists, Chinese Medical Doctor Association

Syphilis, caused by *Treponema pallidum* subsp *pallidum* (*T. pallidum*), is a chronic, systemic human disease transmitted through sexual contact. The incidence and prevalence of syphilis is still high in China.[1] To guide the prevention measures and management of this disease, we renew the guidelines on diagnosis and treatment of syphilis [Supplementary file, http://links.lww.com/CM9/A292]. Manifestations and diagnosis of all stages of syphilis are presented in Table 1, and management in Table 2.

In addition, after recommended treatment, regular follow-up should be performed, including clinical and serological evaluation. The assessment criteria of effective treatment include disappear of the skin lesion and clinical symptoms, and the titer of a non-treponemal serological test (NTT) should decline by more than or equal to four-fold within 3 to 6 months after treatment. If the NTT reverts from negative to positive or the titer is increased by four-fold, it is defined as serological reactivation. If clinical symptoms reappear (usually accompanied by increased NTT titer), it is defined as clinical reactivation. All patients with serological or clinical reactivation should receive treatment again. In a few syphilis patients, the titer of NTT may decline, but it usually does not return to negative, and remain positive within certain period (even through life), in which case, defined as serofast.

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Table 1: Manifestations and diagnosis of all stages of syphilis.

Stages	Clinical features	Diagnostic classification	
		Probable case	Confirmed case
Primary syphilis	1. Chancre; 2. Indolent enlargement of lymph nodes.	With epidemiological history and clinical features and positive NTT or positive TT	With epidemiological history and clinical features and positive DFME; Or with both positive NTT and positive TT
Secondary syphilis	1. Cutaneous or mucosal lesions; 2. Generalized lymphadenopathy.	With epidemiological history and clinical features and positive NTT or positive TT	With epidemiological history and clinical features and positive DFME or both of positive NTT and TT
Tertiary syphilis (late syphilis)	1. "Benign" late syphilis; 2. Cutaneous or mucosal lesions; 3. Syphilis of bone; 4. Syphilis of other viscera; 5. Cardiovascular syphilis.[2]	With epidemiological history and clinical features and positive NTT or positive TT;	With epidemiological history and clinical features and both of positive NTT and TT
Neurosyphilis	1. Asymptomatic neurosyphilis; 2. Syphilitic meningitis; 3. Meningovascular syphilis[3]; 4. Parenchymatous neurosyphilis[4]; 5. Ocular syphilis[5]; 6. Auricular syphilis.[6]	With epidemiological history and clinical features and positive NTT or positive TT	With epidemiological history and clinical features and both of positive NTT and TT
Latent syphilis	No clinical manifestation of syphilis	With positive NTT or positive TT	With both of positive NTT and TT
Congenital syphilis	Early congenital syphilis: Rhinitis, laryngitis, osteomyelitis, osteochonitis, and ossitis. Late congenital syphilis: Saddle-nose, Hutchinson teeth, and skin radially chapped around mouth, and so on.[7] Latent congenital syphilis: No clinical manifestation of syphilis.	All the infants born by the mother with syphilis but untreated before. Or all the stillbirth and abortion cases without enough evidence to confirm fetal transmission of syphilis.	With one of the below tests or follow-up scenarios: 1. Positive DFME or positive argentic staining; 2. Positive sera IgM test; 3. NTT titer by fourfold or greater than the mother's serum, and positive TT; 4. Negative NTT at birth; 5. TT remains positive at 18 months.

Epidemiological history, the patients usually have unprotected sex contact with the sex partner, and either of several sex partners or sex partner who had been infected with syphilis in the past or history of blood transfusion. DFME: Darkfield microscopy examination; NTT: Non-treponemal serological tests; TT: Treponemal test.

Table 2: Managements of all stages of syphilis.

Stages	Recommended regimen	Penicillin allergy
Early syphilis*	Benzathine penicillin G 2.4 million units IM in both buttocks, one dose or two doses of 2.4 million units each at 1-week intervals. Or procaine penicillin 800,000 units IM daily for 15 days.[8]	Doxycycline 100 mg twice daily, orally for 15 days.
Late syphilis	Benzathine penicillin G 2.4 million units IM in both buttocks separately, three doses in total, once weekly. Or procaine penicillin 800,000 units IM daily for 20 days (defined as a course of treatment), when it is necessary, repeating a course of treatment after a 2-week interval.	Doxycycline 100 mg twice daily, orally for 30 days.
Cardiovascular syphilis	Aqueous crystalline penicillin G 100,000 units IM at first day, one time. Aqueous crystalline penicillin G 100,000 units IM at secondary day, two times. Aqueous crystalline penicillin G 200,000 units IM at third day, two times. From forth day, following the below regimens: procaine penicillin 800,000 units IM daily for 20 days, repeating a course of treatment after a 2-week interval. Or Benzathine penicillin G 1.2 million units IM in each buttock, total three doses, once weekly.[9]	Doxycycline 100 mg twice daily, orally for 30 days

(*continued*)

Table 2
(continued).

Stages	Recommended regimen	Penicillin allergy
Neurosyphilis, ocular, and auricular syphilis	Aqueous crystalline penicillin G 18 to 24 million units daily IV for 10 to 14 days, if necessarily, following with Benzathine penicillin G 2.4 million units IM weekly, total three doses. Or Procaine penicillin 2.4 million units IM once daily and Probenecid 500 mg orally four times a day, for 10 to 14 days, if necessarily, following with Benzathine penicillin G 2.4 million units IM weekly, total three doses.[10]	Doxycycline 100 mg twice daily, orally for 30 days.
Congenital syphilis	Early congenital syphilis: Aqueous crystalline penicillin G 100,000–150,000 units/kg intravenously daily, administered as 50,000 units/kg per dose intravenously every 12 h during the first 7 days of life and every 8 h thereafter for 10 to 14 days. Or procaine penicillin G 50,000 units/kg IM in a single daily dose for 10 to 14 days.[11] Late congenital syphilis: Procaine penicillin 50,000 units/kg IM daily for 10 days defined as a course of treatment (the dose of penicillin should be less than that of adults in the same stage of syphilis).	No best alternative treatment so far, if without a history of ceftriaxone allergy, ceftriaxone (normal examination of cerebrospinal fluid 125 mg, abnormal examination of cerebrospinal fluid 250 mg) IM daily for 10 to 14 days, be aware of possible cross-allergic reactions with penicillin.

Early syphilis*, alternative regimen is ceftriaxone 500 mg to 1 g, IM or intravenously daily for 10 days. Early congenital syphilis: <2 years of age; Late congenital syphilis: ≥2 years of age. IM: Intramuscularly.

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Conflicts of interest

None.

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