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## SPECIAL ARTICLE

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# Elimination of Congenital Syphilis in Thailand: What can be done during antenatal period?

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### ABSTRACT

Congenital syphilis (CS) is an infection in infants born to mothers infected by *Treponema pallidum*. It is transmitted via placenta or direct exposure to vaginal secretion during vaginal birth. World Health Organization aims to eliminate CS by 2015, which is defined as an incidence of 0.5 cases or fewer per 1,000 births. Thailand has already achieved the goal for many years. However, new syphilis cases have been increasingly reported, especially among young people. The National Guideline on the management for the elimination of congenital syphilis in Thailand, 2015 has been developed to tackle the problem and enhance the healthcare system for this preventable condition. The optimal goal is to reduce the incidence of CS to less than 0.05 per 1,000 livebirths by 2020. For early detection and early treatment, the guideline focuses on the early ANC and the same-day-result testing of syphilis for pregnant women with late or no ANC. We, obstetricians, can play essential roles in this mission.

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Congenital syphilis (CS) is an infection in infants born to mothers infected by *Treponema pallidum* (Tp). It is transmitted via placenta or direct exposure to vaginal secretion during vaginal birth. CS can cause permanent damages in a variety of organs such as brain and bone, as well as some fatal conditions such as miscarriage, stillbirth and even neonatal death. World Health Organization aims to eliminate CS by 2015, which is defined as an incidence of 0.5 cases or fewer per 1,000 births (including stillbirths). Thailand has

already achieved the goal for many years. In a survey of eight provinces in 2009 (n=118,948), the incidence of CS is 0.1 per 1,000 livebirths. Moreover, the prevalence of syphilis was quite stable at the rate of 2.8-3.6 per 100,000 population during 2009-2012.

Despite the well-controlled situation in Thailand, new syphilis cases have been increasingly reported in young people, aged 15-24, since 2009 as well as teenage pregnancy has become one of the national concerns. Accordingly, the incidence of CS appears

more prominent each year. The National Guideline on the management for the elimination of congenital syphilis in Thailand, 2015 has been developed to tackle the problem and enhance the healthcare system for this preventable condition. The optimal goal is to reduce the incidence of CS to less than 0.05 per 1,000 livebirths by 2020. As known, the consequences of CS can be substantially compromised by proper antenatal care (ANC). Thus, obstetricians can play essential roles in this mission.

## Syphilis

Syphilis is caused by a spirochete called Tp. The first manifestation, primary syphilis, is a clean, isolated, painless genital lesion, which is self-limited within 2-3 weeks. Then, Tp enters the bloodstream and causes secondary syphilis, which can present as generalized rash, alopecia or multiple lesions on the genital area called condyloma lata. The Tp then re-enters the bloodstream and becomes asymptomatic. This period is called 'latent syphilis' and is divided into early and late latent using a cut-point time at 2 years. Without the treatment, Tp can stay life-long in the body and lodge in blood vessel. This stage is called tertiary syphilis. Neurosyphilis is a feature of syphilis which involves central nervous system.

As most patients are asymptomatic, serological tests are commonly used. Positive results from both treponemal and nontreponemal tests indicate syphilis. Nontreponemal test is a serological test for tissue lipid which is resulted from the infection. Many conditions can also give positive non-treponemal test such as yaws, pinta, old age or even pregnancy itself etc. Therefore, the acceptable cut-off titer indicating Tp infection in this guideline is 1:8 or more. The non-specific tests include Venereal Disease Research Laboratory (VDRL) and Rapid Plasma Reagin (RPR). Treponemal test is a serological test for antibody to Tp. Although there are also false positive results from many conditions, the specificity of these tests is very high (99-100%). At present, TPHA is the most widely used. Other treponemal tests include Fluorescent treponemal antibody-absorption test (FTA-Abs), Microagglutination test (Treponemal pallidum hemagglutination test

(TPHA); Treponemal pallidum particle agglutination test (TPPA)), Immunochromatography test (rapid test), Enzyme-linked immunosorbent assay (ELISA) and Chemiluminescent immunoassay (CMIA).

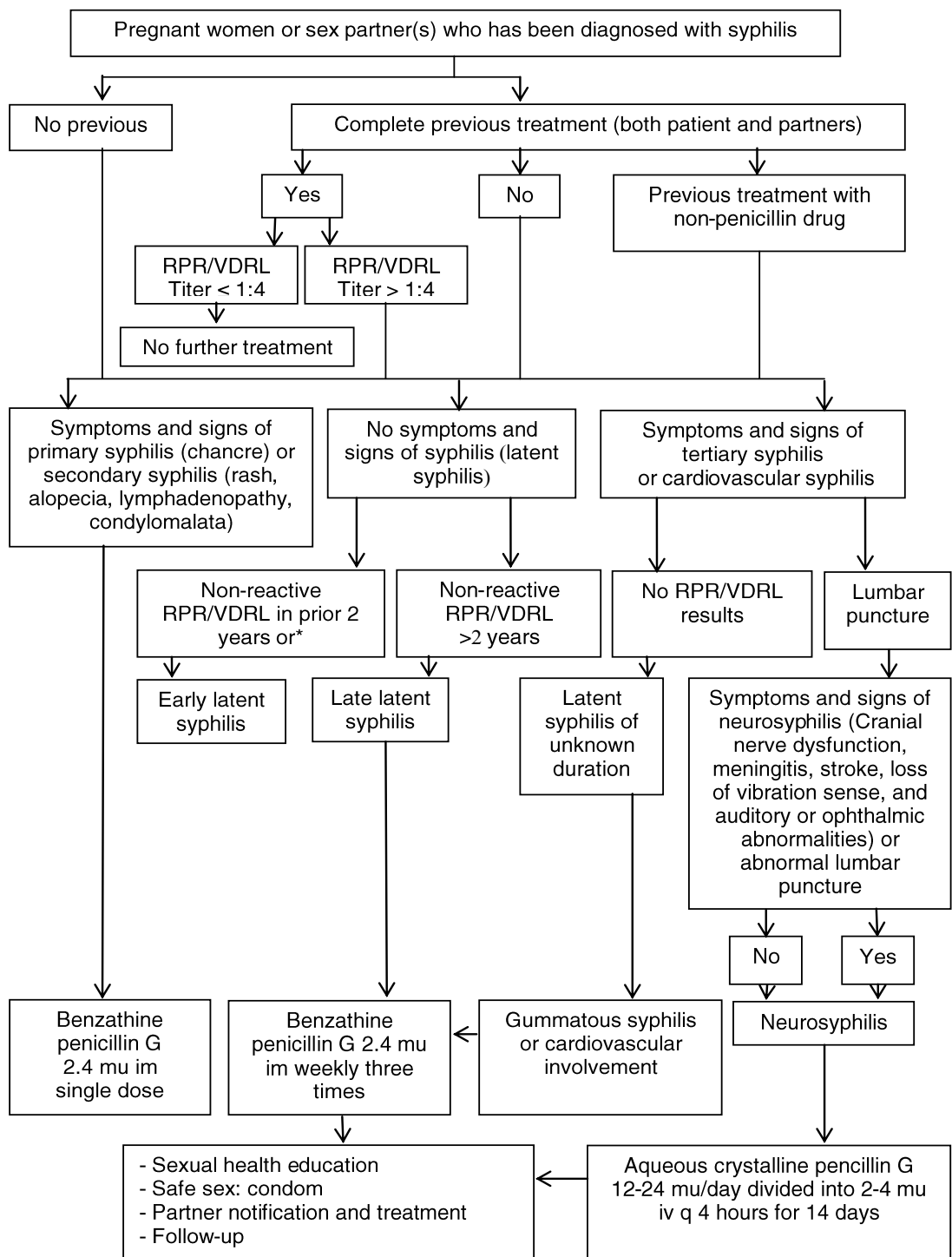
The treatment of choice for syphilis is penicillin which acts by lysing cell wall of Tp. Primary, secondary and early latent syphilis can be treated by a single dose of intramuscular benzathine penicillin G 2.4 million units while late latent syphilis and tertiary syphilis must be treated by intramuscular benzathine penicillin G 2.4 million units weekly for 3 weeks. Patients with neurosyphilis should be admitted for intravenous aqueous crystalline penicillin G 18-24 million per day for 10-14 days. (Algorithm 1) The alternative antibiotics schemes include doxycycline, tetracycline, azithromycin and ceftriaxone but none of them evidently prevents intrauterine infection of Tp.

Other considerations are treatment of sex partner(s) and follow-up. Sex partner(s) should be invited to have blood test and treated accordingly. Post-treatment follow-up is done using serological tests (VDRL/RPR titre). The definition of treatment failure includes no clinical improvement/ recurrence of clinical symptoms and signs; increasing VDRL/RPR titer  $\geq 4$  folds during follow-up or declining of VDRL/RPR titer less than 4 folds at one year after completing the treatment or VDRL/ RPR titer persists at 1:8 or more.

### **Syphilis during pregnancy**

Tp can be transmitted through placenta at all stages. The vertical transmission rates vary with each stage of syphilis in pregnant women as the followings: 70-100% in primary syphilis; 90% in secondary syphilis; 30% in latent syphilis and 10% in tertiary syphilis. Early ANC before GA 12 weeks is strongly recommended as an early treatment can minimize morbidity and mortality to the fetus. Permanent damage to fetus' vital organs is believed to be after 16 weeks of gestation onwards because of the increasing development of fetal immune system. Nonetheless, severe spirochetemia of Tp in early pregnancy can also result in miscarriage.

**Algorithm 1: Stages of syphilis and management**



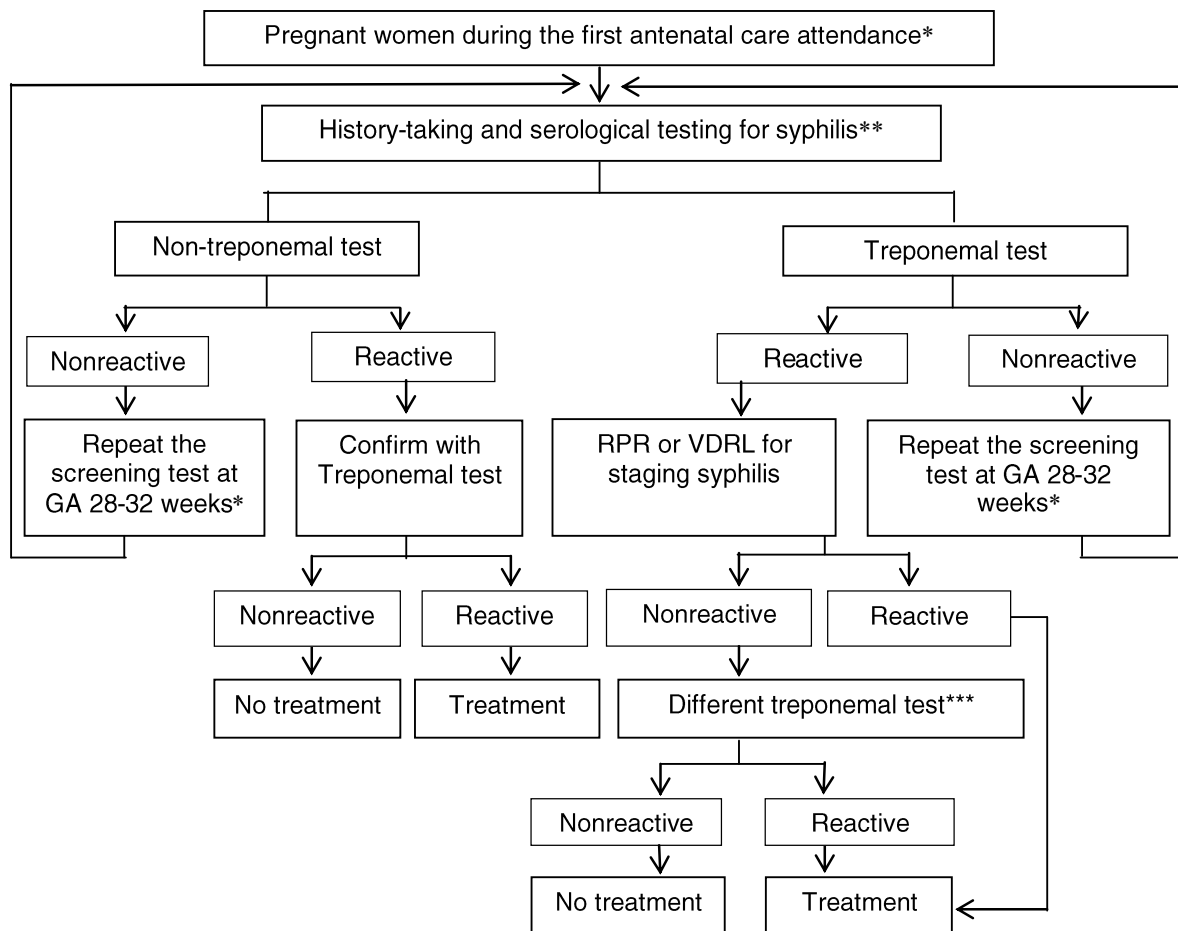
\*Or the following conditions;

1. Increased RPR/VDRL  $\geq 4$  folds from the previous titers which was performed within prior 2 years.
2. Sex partners have been diagnosed as having syphilis stage 1, 2 or early latent syphilis.
3. Having symptoms and signs of primary or secondary syphilis within prior 2 years.

Nontreponemal test (VDRL/RPR) is widely used for screening at the first ANC and repeated during GA 28-32 weeks. The Thai new guideline suggests using either non-treponemal or treponemal tests. The reactive result of nontreponemal test must be confirmed by a treponemal test and vice versa. Among women with no ANC or ANC later than GA 32 weeks, the same-day-result testing by either treponemal or nontreponemal

test is highly recommended; and immediate treatment should be initiated once any tests become reactive. The positive result must be then confirmed to guide the continuation of the treatment. Those who are positive for Tp but absent from the clinic need to be efficiently traced and brought to any medical clinic where penicillin is available. (Algorithm 2)

**Algorithm 2:** Screening for syphilis during pregnancy



\* Serological screening for syphilis should be performed at the first antenatal care attendance and during GA 28-32 weeks. Among women with late attendance, same-day-result testing should be done for the screening and immediate treatment should be commenced once any tests are reactive. Pregnant women with no attendance should be given serological testing for syphilis, human immunodeficiency virus and hepatitis B at labor room.

\*\* Serological screening for syphilis can be done by using either treponemal test (TPHA, CMAI, EIA etc) or nontreponemal test (RPR, VDRL).

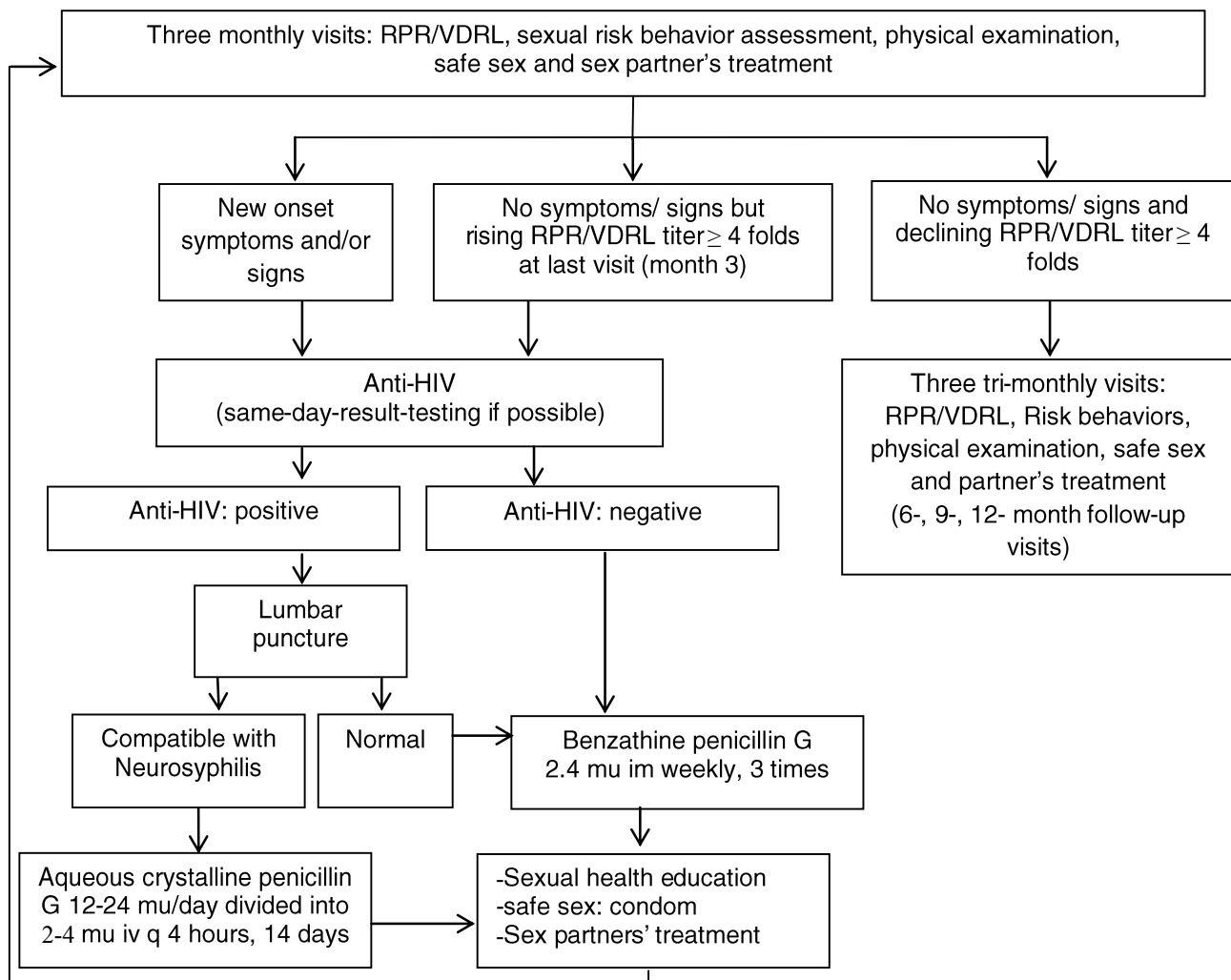
\*\*\* If different treponemal test is not available, sexual risk behaviors should be fully assessed. Pregnant women with sexual risk behaviors and have no previous treatment should be given treatment as women with late latent syphilis.

Penicillin, azithromycin and ceftriaxone can be safely used during pregnancy as they are classified in Category B (=no proven risk in human). However, only penicillin can prevent CS. Thus, in case of hypersensitivity to penicillin, desensitization is suggested. The principle of the process is to increasingly administer penicillin to patients until they can tolerate therapeutic dose of penicillin. This needs close monitoring and, in some cases, the patients should be admitted to the hospital. Treatment for sex partner(s) and post-treatment follow-

up are similar to syphilis in non-pregnant patients.

For the early detection of treatment failure, the guideline suggests three monthly visits after completion of treatment. If the patient has new onset symptoms and/or signs of syphilis or rising RPR/VDRL titre  $\geq 4$  folds at 3 months, her HIV status should be re-tested. Neurosyphilis should be excluded by lumbar puncture. The total follow-up period is two years as follow: 1-, 2-, 3-, 6-, 9-, 12-, 18-, 24-month visits. (Algorithm 3)

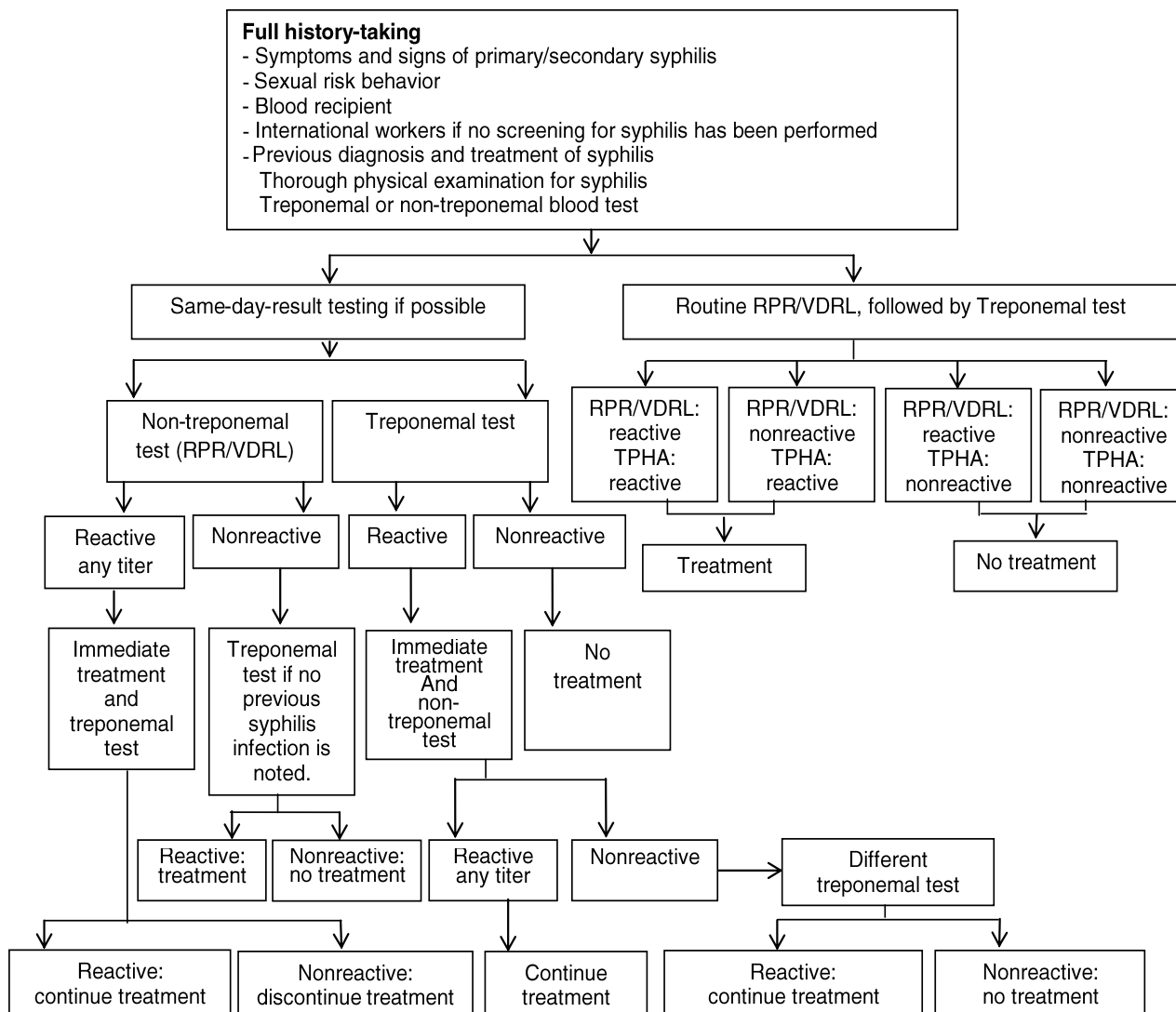
**Algorithm 3:** Follow-up scheme after the completion of treatment



Treatment of sex partners is mandatory as reinfection is common. The critical contact periods are as follow: 3 months in primary syphilis, 6 months in secondary syphilis and 2 years in other stages of

syphilis. For an early treatment, the same-day-result testing by either treponemal or non-treponemal test should be performed if possible. (Algorithm 4)

**Algorithm 4:** Approach to sex partner(s)



## Conclusion

Despite the achievement in the elimination of CS in Thailand according to WHO's definition, the increasing incidence of syphilis, especially in young people, is an alarming sign that our healthcare system should be reinforced with the Thai new guidance. For early detection and early treatment, the National Guideline

on the management for the elimination of congenital syphilis in Thailand, 2015 focuses on the early ANC and the same-day-result testing of syphilis for pregnant women with late or no ANC. This article is only an antenatal section of the guideline. Further reading is suggested to understand the project of CS elimination as a whole, including pediatricians' role, medical

statistics, and medical personnel at different levels in the Ministry of Public Health. We, all obstetricians, should realize that we are working in the crucial part to prevent those innocent babies from congenital syphilis and preparing Thailand to be zero birth of CS in the near future.

## **References**

1. The National Guideline on the management for the elimination of congenital syphilis in Thailand, 2015.