Syphilis

Stage it, then treat by stage · penicillin is the only drug that works in pregnancy, and the dose is decided by duration

Stage decides *the regimen*

STAGE IT FIRST *the stage sets the dose, the follow-up and the CSF question*

Stage	Features	Notes
Primary	**Painless, indurated chancre** with a clean base, appearing about 3 weeks after exposure, plus regional lymphadenopathy	**Painless is the discriminator**: a painful ulcer suggests HSV or chancroid. It heals on its own, so the patient may not report it
Secondary	**Diffuse rash including palms and soles, condylomata lata**, mucous patches, patchy alopecia, fever, malaise, generalized lymphadenopathy	**The great imitator**, and the most infectious stage. Any rash on palms and soles should prompt an RPR
Early latent	Seroreactive, no symptoms, **infection acquired within the past 12 months**	Requires documented evidence: a negative test or a fourfold lower titer within the year, or a clear recent exposure
Late latent or unknown duration	Seroreactive, no symptoms, acquired more than 12 months ago **or duration cannot be established**	**Unknown duration is treated as late latent**, which is the commonest real-world situation and the reason 3 weekly doses are so often needed
Tertiary	**Gummas**, cardiovascular syphilis with **aortitis and aortic regurgitation**	Now uncommon. Evaluate for neurosyphilis before treating
Neurosyphilis *at ANY stage*	**Not a late stage.** Early: meningitis, **ocular syphilis**, **otosyphilis**, stroke. Late: tabes dorsalis, general paresis, **Argyll Robertson pupil**	**Ocular or auditory symptoms at any stage mean neurosyphilis treatment**, and ocular syphilis needs same-day ophthalmology. **Do not wait for a lumbar puncture to treat**

TESTING *two different antibody types, and each can mislead*

Test	What it does
Non-treponemal *RPR, VDRL*	**Quantitative and used to follow treatment.** Becomes negative or falls after cure. **False positives** occur with pregnancy, autoimmune disease including antiphospholipid syndrome, older age, IV drug use and other infections
Treponemal *FTA-ABS, TP-PA, EIA*	**Confirms exposure and usually stays positive for life**, so it cannot distinguish treated from active infection and cannot be used to judge response
⚠ The prozone phenomenon	**A very high antibody titer can make the RPR read falsely NEGATIVE** because there is too much antibody for the assay. It matters most in **secondary syphilis and in pregnancy**, exactly where you can least afford to miss it. **Ask the laboratory to dilute the sample** when the clinical picture is convincing and the test is negative
Lumbar puncture	Indicated for **neurological, ocular or auditory symptoms**, tertiary disease, or serological failure after adequate treatment. **Ocular and otosyphilis are treated as neurosyphilis regardless of CSF findings**

TREATMENT BY STAGE *benzathine penicillin G, and the dose follows the duration*

Stage	First-line	Penicillin allergy, NOT pregnant
Primary, secondary, early latent	**Benzathine penicillin G 2.4 million units IM, single dose**	**Doxycycline 100 mg orally twice daily for 14 days**
Late latent or unknown duration	**Benzathine penicillin G 2.4 million units IM weekly for 3 weeks** (7.2 million units total)	**Doxycycline 100 mg orally twice daily for 28 days.** Tetracycline 500 mg four times daily is the alternative
Neurosyphilis, ocular or otosyphilis	**Aqueous crystalline penicillin G 18 to 24 million units per day IV**, as 3 to 4 million units every 4 hours or by continuous infusion, **for 10 to 14 days**	**Desensitize and give penicillin.** There is no acceptable oral alternative here
⚠ Pregnancy, any stage	**Penicillin only.** It is the sole regimen with documented efficacy for preventing congenital syphilis	**Doxycycline is contraindicated. Desensitize and treat with penicillin.** A second dose one week later is used in early syphilis in pregnancy
Sexual contacts	**Treat empirically** anyone exposed within the preceding **90 days** to a partner with primary, secondary or early latent syphilis, without waiting for their serology	Same alternatives apply if penicillin allergic and not pregnant

PREGNANCY & CONGENITAL DISEASE *the highest-stakes part of the topic, and almost entirely preventable*

SCREEN, AND SCREEN AGAIN

Test every pregnant patient at the first prenatal visit. Retest at **28 weeks and at delivery** where prevalence is high, the patient is at ongoing risk, or she was untested earlier. **No mother should deliver with unknown syphilis status.**

TREAT EARLY, AND ADEQUATELY

Congenital syphilis is prevented by **maternal penicillin given at least 30 days before delivery**. Treatment that is late, incomplete, or with any non-penicillin drug counts as **inadequate**, and the neonate is then evaluated and treated.

WHAT THE BABY LOOKS LIKE

Often **asymptomatic at birth**, which is why maternal screening rather than newborn examination is the safeguard. Early signs: **snuffles**, hepatosplenomegaly, rash including palms and soles, jaundice, long-bone changes. Late: **Hutchinson teeth, interstitial keratitis, deafness, saber shins**.

FOLLOW-UP, PREVENTION & PEARLS

- **Follow the RPR, and define success numerically.** Repeat titers at **6 and 12 months** (more often in HIV and in pregnancy). An adequate response is a **fourfold fall**, which is two dilutions, for example 1:32 down to 1:8. **Failure to fall, or a fourfold rise, means treatment failure or reinfection**: re-treat and evaluate for neurosyphilis. Always compare titers run by the same test and ideally the same laboratory.
- **Warn about the Jarisch-Herxheimer reaction.** Fever, chills, myalgia and headache within **24 hours** of the first dose, from released treponemal antigen. It is **not an allergy** and is not a reason to stop or avoid re-treatment. Antipyretics suffice, but in pregnancy it can precipitate **uterine contractions and fetal distress**, so treat pregnant patients where fetal monitoring is available.
- **Doxy-PEP is now recommended prevention.** CDC 2024 guidance: for **men who have sex with men and transgender women who have had syphilis, chlamydia or gonorrhea in the past 12 months**, offer **doxycycline 200 mg within 72 hours after sex**, not exceeding 200 mg in 24 hours. It cut syphilis and chlamydia by more than 70% and gonorrhea by roughly half. Continue screening for gonorrhea and chlamydia at all exposure sites, and for syphilis, **every 3 to 6 months**.
- **Test for HIV in everyone with syphilis, and repeat it.** The two travel together, and syphilis increases HIV transmission. Also screen for other STIs, and remember **benzathine penicillin must never be given intravenously**: it is intramuscular only, and inadvertent IV administration can be fatal. Report cases as required.

References: CDC Sexually Transmitted Infections Treatment Guidelines (syphilis, latent syphilis and syphilis in pregnancy sections) · CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial STI Prevention, United States, 2024 (MMWR).

Educational aid; verify against current guidance, local formulary and patient factors.