

Syphilis

General observations on HIV-infected patients with syphilis:

- Case reports suggest that the unusual clinical manifestations of syphilis may be more common (e.g. overlap of primary & secondary manifestations) and the course more rapid in patients with HIV infection.
- Though above not corroborated in prospective studies, case reports have largely driven the hypotheses that among patients coinfecting with HIV and *T pallidum*:
 - Mucocutaneous lesions may be more severe or numerous,
 - Symptomatic neurosyphilis may be more likely to develop,
 - Latency period before the development of meningovascular syphilis may be shorter,
 - Efficacy of standard therapy for early syphilis may be reduced.
- HIV-infected patients can have atypical serologic responses. More typical is higher-than-expected RPR titers (e.g. 1:128). More rare: false negative and delayed onset of seroreactivity. Biologic false positives can occur (treponemal test negative), esp. if polyclonal gammopathy present.
 - The “serofast” state is not uncommon among HIV-infected persons. It is the persistence of a reactive nontreponemal syphilis test, usually 1:16 or less, with variation no greater than 1 to 2 dilutions over time, despite adequate therapy and no evidence of reexposure.
 - NOTE: Reinfection may be difficult to rule out in some patients, and reactivation or relapse of a previously treated infection is also possible in a person with HIV infection.

General treatment principles – areas of consensus [**CDC STD 2006 Guidelines**: add hyperlink: <http://www.cdc.gov/std/treatment/2006/genital-ulcers.htm#genulc6>]

- Long-acting penicillin G is treatment of choice:
 - Benzathine penicillin G (Bicillin LA) 2.4 million U intramuscularly x 1 should be used in all cases for incubating, primary, secondary or early latent syphilis with no evidence of neurologic involvement.
 - For late latent or syphilis of unknown duration:
 - Careful clinical evaluation & CSF examination should precede any treatment decision
 - If CSF without evidence of neurosyphilis (CSF WBC>20/μL or reactive CSF VDRL), then benzathine PCN G should be given as 7.4 million IU IM as 3 doses of 2.4 million IU in successive weeks.
 - Neurosyphilis (or syphilitic eye or auditory disease):
 - Aqueous crystalline penicillin G 18-24 million U per day, dosed as continuous infusion or q4h, x 14 days, followed
- Doxycycline is an oral alternative and reserved only for patients who are truly penicillin-allergic – oral agents should *never* be used for neurosyphilis or pregnant patients with syphilis.

- Azithromycin, though it has shown promise in early syphilis, should not be used because of reported resistance.
- Confirmation of post-treatment serologic response:
 - NOTE: Nontreponemal test antibody titers (RPR or VDRL) usually correlate with disease activity. Sequential serologic tests should be performed by same testing method (RPR or VDRL) & preferably by same lab.
 - Follow-up of RPR titer recommended at 1, 3, 6, 12 for early syphilis & additional check at 24 months for late latent syphilis, tertiary syphilis or syphilis of unknown duration.
 - Appropriate response to treatment = 4-fold decrease in titer (2 dilutions) in 6 months.
- When do you perform a lumbar puncture to examine CSF?
 - Any patient with syphilis who has neurologic complaints (includes ophthalmic or otologic complaints).
 - HIV-infected pt with syphilis of unknown duration or duration >1 year
 - All patients with treatment failure defined as:
 - Recurrence or persistence of symptoms
 - Lack of a 4-fold decrease in RPR titers after 12 months in early syphilis, 24 months in late syphilis
 - 4-fold increase in RPR titers at any time after treatment
 - More controversial: any asymptomatic HIV+ patient with RPR titer >1:32 or CD4 count <350.

Reference

Zetola, NM and Klausner JD. Syphilis and HIV infection: an update. *Clin Infect Dis* 2007; 44:1222-8.
Workowski KA, Berman SM. Sexually transmitted diseases treatment guidelines, 2006. *MMWR Recomm Rep* 2006; 55:1–94.