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To: San Francisco Medical Providers

From: Jeffrey D. Klausner, MD, MPH
Director, STD Prevention and Control Services

Re: Screening and Management of Syphilis in HIV-infected Patients

The syphilis epidemic continues in San Francisco. There were 522 early syphilis cases in 2003, up from 41 cases in 1998; 94% of cases were among gay and bisexual men, and 62% were HIV-infected. The following recommendations, based on the STD Treatment Guidelines 2002 from CDC (www.cdc.gov/std) and the San Francisco Department of Public Health, are provided to assist clinicians in the screening and management of syphilis infection in HIV-infected patients.

SCREENING
Screening for syphilis using the Rapid Plasma Reagin (RPR) or the Venereal Disease Research Laboratory (VDRL) test is recommended for all sexually active HIV-infected men at least every 6 months. More frequent screening is suggested for HIV-infected men who have multiple sexual partners, who meet partners at commercial sex venues (sex clubs, bathhouses, or adult bookstores), on the Internet, or who use methamphetamine.

DIAGNOSTIC CONSIDERATIONS
While unusual serologic responses have been observed among HIV-infected patients with syphilis, the results are generally reliable. Syphilis in HIV-infected patients may present atypically, with for example, multiple chancres or the presence of a generalized body rash concurrent with a syphilitic chancre. All patients with syphilis should be assessed with a thorough clinical neurological evaluation. See box below for indications for CSF examination. Neurosyphilis should be considered in the differential diagnosis of neurologic disease.

Indications for CSF Examination in HIV-infected Persons, 2002

1. Neurologic signs or symptoms, including meningitis
2. Ophthalmic signs or symptoms
3. Late-latent syphilis or syphilis of unknown duration
4. Tertiary syphilis
5. Syphilis treatment failure

TREATMENT
Benzathine penicillin G 2.4 million units IM in a single dose is recommended for the treatment of primary, secondary, and early latent syphilis in HIV-infected patients. Alternative therapeutic options for treatment of primary, secondary, and early latent syphilis include: doxycycline 100 mg PO BID x 2 weeks or tetracycline 500 mg PO QID x 2 weeks. Patients with late latent syphilis or syphilis of unknown duration and a normal CSF examination can be treated with benzathine

penicillin G 2.4 million units weekly for 3 weeks. Alternative regimens for late-latent and latent syphilis unknown duration include: doxycycline 100 mg PO BID x 4 weeks or tetracycline 500 mg PO QID x 4 weeks. HIV-infected patients who have syphilis may be at increased risk for neurologic complications and may have higher rates of treatment failure with currently recommended regimens. Careful follow-up after therapy is essential.

FOLLOW-UP

HIV-infected patients should be evaluated clinically and serologically for treatment failure at 3, 6, 9, 12 and 24 months after therapy. Patients who have signs or symptoms that persist or recur or whose titers (RPR or VDRL) do not decrease fourfold within 12 months compared with the maximum or baseline titer at the time of treatment probably failed treatment or were re-infected. HIV-infected patients who failed treatment should be evaluated with a CSF examination and re-treated for syphilis infection. If CSF examinations are normal, most specialists would re-treat patients with benzathine penicillin G 2.4 million units IM weekly for 3 weeks.

NEUROSYPHILIS

CNS disease can occur during any stage of syphilis. A patient who has clinical evidence of neurologic involvement with syphilis (e.g. cognitive dysfunction, motor or sensory deficits, ophthalmic or auditory symptoms, cranial nerve palsies, and symptoms or signs of meningitis) should undergo CSF examination. In addition, a patient with late latent syphilis or latent syphilis of unknown duration should undergo CSF examination. Patients diagnosed with neurosyphilis are recommended to receive aqueous crystalline penicillin G 24 million units per day, administered as 4 million units IV every 4 hours or continuous infusion for 14 days followed by benzathine penicillin G, 2.4 million units IM once upon completion of IV therapy. If CSF pleocytosis was present initially, a CSF examination should be repeated every 6 months until the cell count is normal. If the cell count has not decreased after 6 months, or if the CSF is not normal after 2 years, re-treatment for neurosyphilis should be considered.

MANAGEMENT OF SEX PARTNERS

All persons potentially exposed* to syphilis should be treated presumptively with benzathine penicillin G 2.4 million units IM in a single dose. Doxycycline 100 mg PO BID x 2 weeks may be used as an alternative prophylaxis. All persons receiving prophylactic antibiotics should be evaluated with a clinical examination and a serologic test for syphilis.

* For primary syphilis, sex partners within the past 3 months; secondary, 6 months; latent syphilis, 1 year.

CONSULTATION

Syphilis can be difficult to diagnose and manage for the busy clinician. Please contact Dr. Joseph Engelman at City Clinic (487-5595, Joseph.Engelman@sfdph.org) or myself (355-2000, Jeff.Klausner@sfdph.org) for any questions.

REFERENCES

1. CDC. *Sexually Transmitted Diseases Treatment Guidelines, 2002*. MMWR Vol. 51, 2002.

2. Rompalo AM, Lawlor J, Seaman P, et al. *Modification of syphilitic genital ulcer manifestations by coexistent HIV Infection.* Sexually Transmitted Diseases, 2001. **28**(8): p. 448-454.

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