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MMWR

Weekly

October 07, 1988 / 37(39);600-602,607-608

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# Current Trends -- Recommendations for Diagnosing and Treating Syphillis in HIV-Infected Patients

The clinical manifestations, serologic responses, efficacy of treatment, and occurrence of complications of syphilis may be altered in patients coinfected with human immunodeficiency virus (HIV). Because syphilis is a disease with a broad range of manifestations and variable course, assessing reports of unusual clinical or laboratory findings in HIV-coinfected patients is difficult (1). On March 21 and 22, 1988, experts* from academic medical centers and state and local health departments met at CDC to discuss the diagnosis and treatment of syphilis in HIV-infected patients. The following recommendations were developed based on these discussions.

DIAGNOSIS OF SYPHILIS IN HIV-INFECTED PATIENTS Most HIV-infected patients appear to have a normal serologic response to Treponema pallidum infection (2). However, in some HIV-infected patients with biopsy- confirmed secondary syphilis, both nontreponemal and treponemal tests for syphilis are negative (3). In addition, some patients infected with both T. pallidum and HIV have had unusually high titers on nontreponemal serologic tests for syphilis (CDC, unpublished data, 1987-88), possibly because of HIV-related polyclonal B-cell stimulation. The frequency of unusual clinical and laboratory manifestations of syphilis in patients coinfected with HIV is unknown. Recommendations

1. Persons with HIV infection acquired through sexual contact or intravenous (IV)- drug abuse should be tested for syphilis, and all sexually active persons with syphilis should be tested for HIV (with the informed consent of the patient). HIV test results are clinically important in managing patients with syphilis and, with appropriate confidentiality safeguards, should be made available to medical per- sonnel who care for these patients.

2. When clinical findings suggest syphilis is present, but serologic tests are negative, other tests should be used to determine if syphilis is present. These tests include dark-field microscopy and direct fluorescent antibody for T. pallidum (DFA-TP) staining of lesion exudate and examination of biopsy tissue using DFA-TP or Steiner stain (4).**

3. Laboratories should titrate nontreponemal tests to a final endpoint, rather than reporting results as greater than an arbitrary cutoff (e.g.,greater than 1:512). Specific results permit more accurate determination of response to therapy and also help identify unusual serologic responses to syphilis.

4. Neurosyphilis should be considered in the differential diagnosis of neurologic disease in HIV-infected persons.

5. Consultation should be obtained to evaluate unusual serologic test results in patients suspected of having

syphilis or in those being followed for response to treatment.

TREATMENT AND FOLLOW-UP Case reports have suggested that treatment failures, including progression to neurosyphilis, may occur more frequently in patients coinfected with HIV than in those with syphilis alone (5,6). This has not yet been confirmed, but because an intact cellular immune response is important in the host response to T. pallidum infection (7) and because HIV infection impairs cellular immune response in some patients, an increased frequency of treatment failure is plausible.

Recommended treatment schedules for neurosyphilis have included benzathine penicillin (8), although treatment with benzathine penicillin in currently recommended dosages does not achieve treponemicidal antibiotic levels in the cerebrospinal fluid (CSF) of most patients with syphilis, and rare treatment failures have been reported (9-11). Recommendations

1. No change in therapy for early syphilis for HIV-coinfected patients is recommended. However, there is disagreement on this issue, and some authorities have advised CSF examination and/or treatment with a regimen appropriate for neurosyphilis for all patients coinfected with syphilis and HIV, regardless of the clinical stage of syphilis (12). In all cases, careful follow-up is necessary to assure adequacy of treatment.

2. Serologic testing after treatment for early syphilis is important for all patients, regardless of HIV infection status. In patients coinfected with HIV, quantitative nontreponemal tests should be repeated at 1, 2, and 3 months and at 3-month intervals thereafter until a satisfactory serologic response to treatment occurs. If the titer does not decrease appropriately (two-dilution decrease by 3 months for primary syphilis or by 6 months for secondary syphilis) (13) or if a sustained two-dilution or greater increase occurs, the patient should be reevaluated to consider the possibility of treatment failure or reinfection, and CSF should be examined. Sexually transmitted disease (STD) clinics and others providing STD treatment should assure adequate follow-up.

3. A CSF examination should precede and guide treatment of HIV-infected patients with latent syphilis present for longer than 1 year or for unknown duration. If an examination is not possible, patients should be treated for presumed neuro- syphilis.

4. Benzathine penicillin regimens should not be used to treat either asymptomatic or symptomatic neurosyphilis in HIV-infected patients. Patients should be treated for at least 10 days with either aqueous crystalline penicillin G, 2-4 million units IV every 4 hours (12-24 million units each day), or aqueous procaine penicillin G, 2.4 million units intramuscularly daily, plus probenecid 500 mg orally 4 times daily (8). Reported by: Div of Sexually Transmitted Diseases, Center for Prevention Svcs; AIDS Program and Sexually Transmitted Diseases Laboratory Program, Center for Infectious Diseases, CDC.

## Editorial Note

Editorial Note: The expert consultants also highlighted the following research priorities related to the diagnosis and treatment of syphilis in HIV-coinfected patients:

1. The effect of HIV infection on initial clinical and laboratory manifestations of syphilis and on the efficacy of current syphilis therapy should be prospectively studied.

2. A surveillance system should be developed to detect complications of syphilis, especially neurosyphilis, and unusual clinical and laboratory manifestations of syphilis in patients with and without HIV-coinfection.

3. The importance of CNS involvement in early syphilis should be determined in patients with and without HIV coinfection.

4. Better laboratory methods should be developed for detecting T. pallidum or T. pallidumantigens in CSF,

blood, and lesions.

5. A better animal model of T. pallidum infection is needed to examine the effect of immunosuppression on the course of syphilis.

So that the frequency of unusual manifestations of syphilis can be determined, health-care providers are requested to notify their state epidemiologists of HIV- infected patients who meet one of the following conditions:

1. Neurosyphilis confirmed by CSF examination or histopathology;

2. Negative serologic tests for syphilis (nontreponemal (VDRL, RPR) or treponemal (FTA-ABS, MHA-TP, HATTS) tests) during secondary syphilis diagnosed by dark- field microscopy or histopathology of lesion material.

The state epidemiologists will forward these reports without personal identifiers to the Division of Sexually Transmitted Diseases, Center for Prevention Services, CDC.

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13. Brown ST, Zaidi A, Larsen SA, Reynolds GH. Serological response to syphillis treatment: a new analysis of old data. JAMA 1985;253:1296-9. *Expert consultants: M Rein, MD, Univ of Virginia School of Medicine; G Bolan, MD, San Francisco Dept of Public Health; W Boyd, Georgia Dept of Human Resources; D Burke, Tennessee Dept of Health and Environment; W Greaves, MD, Howard Univ Hospital; V Mesa, MD, Detroit Dept of Health; E Hook, III, MD, Johns Hopkins Univ School of Medicine; J Hadler, MD, Connecticut State Dept of Health Svcs; D Des Jarlais, PhD, State of New York Div of Substance Abuse Svcs; S Lukehart, PhD, Univ of Washington School of Medicine; M Lovett, MD, Univ of California, Los Angeles, School of Medicine; R Magana, PhD, Orange County (California) Health Dept; W McCormack, MD, Downstate Medical Center, Brooklyn, New York; S Schultz, MD, New York City Dept of Health; E Tramont, MD, Walter Reed Army Medical Center; H Jaffe, MD, CDC. **In evaluating biopsy specimens, histologic stains (Warthin Starry Silver, Steiner) must be interpreted with caution since other spirochetes and artifacts may be misidentified as T. pallidum with these silver stains.





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This page last reviewed 5/2/01