Update on Syphilis

As you continue to observe in your own practices, syphilis infections are on the rise again. From 2006 to 2007, there was a 12% increase in primary and secondary syphilis. In March, the CDC reported the following increases:

<table>
<thead>
<tr>
<th>Gender</th>
<th>Data (cases per 100,000)</th>
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The CDC is still examining the reasons for the third consecutive annual increase among females. After seeing a decline in female syphilis cases for more than a decade, this emerging trend might result in increases in congenital syphilis.

For more information on the Syphilis Education Today program please contact meded@csimeded.com.
Serological Response to Treatment

During a recent audio conference conducted by Dr. Klausner, the most pressing concern raised by listeners was how to interpret serologic test results.

Following effective syphilis treatment, the RPR* or VDRL* titer (non-treponemal test) declines and may become non-reactive or negative. In treating early syphilis such a response can occur in 6 months. In treating late syphilis that response can occur in 12 months or more.1 HIV-infected patients generally have a slower decline in titers than HIV-uninfected patients.2,3,4 As a result, most experts recommend determining the serological response to treatment at 6 and 12 months in HIV-uninfected patients in early and late syphilis respectively. Because of the slower serological response in HIV-infected patients some experts recommend determining treatment outcomes at 12 months in early syphilis and 24 months in late syphilis.1,2,3,4 The CDC guidelines recommend clinical and serological post-therapy follow-up at 3, 6, 9, 12 and 24 months in HIV-infected patients.

However, a reactive serologic titer may persist after the titer declines in up to 20% of patients. A persistently reactive non-treponemal (RPR or VDRL) serologic test for syphilis after treatment for syphilis may represent treatment failure or a "serofast" reaction.1,2

One of the most challenging aspects in syphilis management is determining whether a persistently reactive titer represents treatment failure or a serofast reaction.

A 4-fold decrease in non-treponemal titer post-treatment demonstrates a therapeutic response. In some patients, after the initial 4-fold decline, a low, serofast (less than or equal to 1:8) will remain for a long period or for life.

Rising or persistent titers greater than or equal to 1:32 are problematic and raise concerns about treatment failure, but in some cases could be a serofast reaction, in particular if the prior titer was substantially elevated (greater than 1:256) and the 1:32 represents at least a 4-fold decline.1,2,6

The following are some additional tips on interpreting syphilis test results:

- Allow an adequate amount of time for follow-up of syphilis tests.
- Syphilis titers represent an immunologic reaction to infection and may take 1-2 years to decline.
- Titer response in long-standing infection usually takes longer to decline than the titer response in recently acquired infection.
- If treatment failure is a consideration, CSF analysis should be considered to rule out neurosyphilis.1,3
- If there is doubt about whether the persistent titer represents treatment failure or a serofast response, many experts would recommend re-treating the patient with a repeat course of therapy, usually a series of 3 injections of penicillin G benzathine (Bicillin® L-A) 2.4 MU intramuscular weekly for 3 weeks. Again, CSF analysis should be considered to rule out neurosyphilis, a cause of treatment failure.

In the case of late syphilis, which is usually diagnosed as late latent syphilis detected through a routine screening test and the non-treponemal serologic test titer is low (e.g., 1:2), a 4-fold decline in titer may take years. At 24 months should the titer not have declined 4-fold, and persists at 1:2 or 1:1, there are no clinical data to dictate best practice. Some experts would recommend continuing observation and others would re-treat with penicillin G benzathine 2.4 MU intramuscular once weekly for 3 weeks.1

(CONTINUED)
New STD Resource

McGraw-Hill recently added a new title to its well-known Current Diagnosis and Treatment series entitled Sexually Transmitted Diseases. Edited by the internationally renown STD experts Jeffrey D. Klausner, MD, MPH (San Francisco Department of Public Health and University of California, San Francisco) and Edward W. Hook, III, (University of Alabama Birmingham), the easy-to-read and practical text contains over 30 chapters with 3 specifically focused on syphilis (syphilis, neurosyphilis and interpretation of syphilis tests) for the practicing clinician. A recent review of the book in Clinical Infectious Diseases, stated "It is highly recommended reading for clinicians as an excellent and authoritative overview in terms of diagnostic, management, and treatment considerations for STDs."

The book is available on www.amazon.com and from your local medical bookstore.

Serological Response to Treatment (CONTINUED)

The Treatment Response Chart on page 3 is a helpful resource when treating syphils in all patient types.

Remember that the syphilis titers one follow over time to evaluate the response to treatment are the non-treponemal test titers, the RPR or VDRL. The treponemal test titers (TPPA* or FTA-ABS*) once reactive usually remain reactive for the life of the patient. Although in primary syphilis, treponemal titers can become non-reactive (after 2-3 years) in about 15%-25% of patients after successful treatment.

REFERENCE

1 Centers for Disease Control and Prevention, 2006 STD Treatment Guidelines. Syphilis Section. Available at www.cdc.gov/std.
6 Zetola MZ, Klausner JD. Syphilis and HIV Infection: An Update. CID 1007:44 (1 May), HIV/AIDS.

Important STD Meetings, 2008

OCTOBER 24-25
National Coalition of STD Directors
Phoenix AZ
ncsddc.org

OCTOBER 25-29
Infectious Disease Society of America (IDSA) and (ICAAC)
Washington DC
www.idsociety.org

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Treatment Response Algorithm

by Dr. Jeffrey Klausner, Director of STD Prevention and Control Services of the San Francisco Department of Public Health

**HIV-UNINFECTED**

Early Syphilis  
< 1 year duration

4-fold titer decline  
at 6 months

Yes  
No

- Yes  
  Cure
- No  
  Treatment failure*  
or re-infection†

**HIV-INFECTED**

Early Syphilis  
< 1 year duration

4-fold titer decline  
at 12 months

Yes  
No

- Yes  
  Cure
- No  
  Treatment failure*  
or re-infection†

Late Syphilis  
> 1 year duration

4-fold serologic titer decline  
at 12 months

Yes  
No

- Yes  
  Cure
- No  
  Treatment failure*  
or re-infection†

Late Syphilis  
> 1 year duration

4-fold titer decline  
at 24 months

Yes  
No

- Yes  
  Cure
- No  
  Treatment failure*  
or re-infection†

If treatment failure, CSF analysis to rule out neurosyphilis

Neurosyphilis

- Yes  
  Treat with penicillin G IV 18-24 MU qD (3-4 MU q 4°) x 10-14 days; followed by penicillin G benzathine (Bicillin® L-A) 2.4 MU IM weekly x 1-3.
- No  
  Treat with penicillin G benzathine (Bicillin® L-A) 2.4 MU IM once weekly x 3.

* Treatment failure may be caused by untreated neurosyphilis.
† Reinfection may be consistent with a 4-fold serologic titer decline followed by a 4-fold serologic titer increase and re-exposure. Treat with penicillin G benzathine (Bicillin® L-A) 2.4 MU IM once.