

### Answer to Dermacase *continued from page 409*

#### 4. Secondary syphilis

This patient presented with multisystem disease consistent with secondary syphilis. Diagnosis was confirmed histopathologically by the presence of spirochetes and based on positive serology results (rapid plasma regain [RPR] test result of 1:256 and a positive result on *Treponema pallidum* particle agglutination assay). Syphilis can be grouped into primary, secondary, and tertiary stages, each with clinically distinct features. Primary syphilis can present with a single chancre, secondary syphilis as multiple cutaneous lesions, and tertiary syphilis with systemic involvement and myriad symptoms.<sup>1</sup> Primary disease is most frequently acquired through vaginal, anal, or oral sexual contact but it can also be vertically transmitted.<sup>2</sup> Secondary syphilis results from the progression of primary syphilis by intravascular spread of *T pallidum* from the site of infection. *T pallidum* is a microaerophilic spirochete that is strictly a human pathogen.<sup>1</sup> Progression of the infection can take 4 to 8 weeks before the appearance of secondary symptoms.<sup>2</sup> Clinical presentations of secondary syphilis can include fever, lymphadenopathy, genital condyloma latum, and, most commonly, cutaneous eruption.<sup>3</sup>

#### Epidemiology

Syphilis has been increasing in both men and women in many parts of Canada and the United States over the past decade. Many outbreaks have been described among men who have sex with men, often associated with anonymous sex and encounters facilitated through the Internet.<sup>4,5</sup> However, there have been well-described outbreaks from predominately heterosexual contact in some areas of Canada.<sup>6</sup>

#### Diagnosis

Initial suspicion of secondary syphilis often arises with the presentation of cutaneous findings, which develop in 80% to 95% of cases.<sup>1</sup> Lesions can be macular, papular, papulosquamous, lenticular, annular, follicular, pustular, or nodular.<sup>1,7</sup> It is important to note that at the onset of secondary syphilis, the eruption is generalized and symmetric in distribution, but as the secondary stage progresses, distribution can become asymmetric.<sup>8</sup> Although lesions are classically associated with the palms and the soles, they commonly occur on the proximal extremities and trunk and can progress to involve all skin surfaces.<sup>3</sup>

Clinical diagnosis of secondary syphilis can be difficult owing to its range of presentations; therefore, serologic testing is important. Traditionally, specimens are screened with a nontreponemal test (NTT) such as the RPR test or the Venereal Disease Research

Laboratory test. Positive reactions are confirmed using specific treponemal tests such as the fluorescent treponemal antibody absorption test or *T pallidum* particle agglutination test. However, many laboratories are now using treponemal-specific enzyme immune assays as their primary method for syphilis serology. It is important to note that in early primary and late latent syphilis, the NTT results can be negative. In these circumstances the treponemal-specific test must also be requested. In addition, histopathologic examination might be required.<sup>7</sup>

#### Progression

Secondary syphilis is a progression of the primary disease, but it can further develop into latent or tertiary syphilis if left untreated. Latent syphilis can be further divided into an early and late stage.<sup>3</sup> Early latent syphilis comprises the first year after the onset of the initial infection, and late latent syphilis fills the remainder of the latent period, often lasting for several years.<sup>3</sup> During the latent phase, patients remain seropositive for *T pallidum* but show no signs of the secondary rash or other earlier symptoms.<sup>3</sup> Tertiary syphilis develops in only one-third of untreated cases. The tertiary disease most commonly presents as reoccurring symptoms, cardiovascular disease, and neurosyphilis.<sup>1</sup>

#### Complications

The most serious complication associated with secondary syphilis is progression to tertiary syphilis and development of cardiovascular (cardiovascular syphilis) or neurologic (neurosyphilis) disease. In cardiovascular syphilis the presentation can include aortitis, aortic aneurysm, aortic valve incompetence, coronary ostial stenosis, and myocardial gummatous disease.<sup>1,3</sup> Neurosyphilis is a complication that occurs in 10% of untreated cases<sup>9</sup> and it can occur at any of the 3 clinical stages. Neurosyphilis most commonly presents asymptotically,<sup>10</sup> but can result in seizures, ataxia, aphasia, paresis, hyperreflexia, visual changes, hearing loss, neuropathy, and personality and cognitive changes.<sup>1,3</sup> Some experts suggest that patients presenting with RPR results of 1:32 or higher should be offered lumbar puncture to rule out the possibility of central nervous system involvement.<sup>11,12</sup>

#### Treatment and follow-up


Treatment regimens vary depending on the stage of the disease. Recommendations are summarized in **Table 1**.<sup>12</sup> Treatment regimens for pregnant women and for patients who are allergic to penicillin are outlined in the Canadian Guidelines on Sexually Transmitted Infections,<sup>12</sup> but consultation with a local sexual health clinic or infectious disease physician is recommended.

**Table 1. Recommended treatment regimens for adults with syphilis**

STAGE	TREATMENT	RECOMMENDED DOSAGE
Primary syphilis	Benzathine penicillin G	2.4 million units IM (single dose)
Secondary syphilis	Benzathine penicillin G	2.4 million units IM (single dose)
Early latent syphilis (< 1 y)	Benzathine penicillin G	2.4 million units IM (single dose)
Late latent syphilis or latent syphilis of unknown duration	Benzathine penicillin G	3 doses of 2.4 million units IM each, at 1-wk intervals
Neurosyphilis or syphilitic eye disease	Aqueous crystalline penicillin G	18-24 million units/d (3-4 million units IV every 4 h or continuous infusion for 10-14 d)

IM—intramuscularly, IV—intravenously.  
Data from the Public Health Agency of Canada.<sup>12</sup>

To assess response to therapy, NTT results should be monitored regularly until the patient is seronegative or remains at a stable low titre (1:8). Frequency of monitoring and expected serologic response depends on the stage of infection. Patients with primary, secondary, or early latent syphilis should have follow-up serologic testing at 1, 3, 6, and 12 months after treatment to ensure they have had adequate serologic response.

Syphilis is a notifiable infectious disease, and local public health should be informed of the case to allow for appropriate contact tracing and follow-up. Given the increasing incidence, the variable clinical presentation, and the potential for the primary chancre to go unnoticed (as illustrated by this case), it is important for family physicians to maintain a high index of suspicion for secondary syphilis. 

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#### Competing interests

None declared

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