stable in recent years, with approximately 14,000 being reported in 2010.

Pathogenesis. Proliferative endarteritis affecting small vessels with a surrounding plasma cell-rich infiltrate is characteristic of all stages of syphilis. Much of the pathology of syphilis can be ascribed to the ischemia produced by the vascular lesions. The pathogenesis of endarteritis is unknown.

The immune response to *T. pallidum* reduces the burden of bacteria and can lead to resolution of local lesions but does not reliably eliminate the systemic infection. Superficial sites of infection (chancres and rashes) have an intense inflammatory infiltrate that includes T cells, plasma cells and macrophages that surround the bacteria. The infiltrating CD4+ T cells are T_H1 cells that may activate macrophages to kill the bacteria. Treponeme-specific antibodies are detectable and these activate complement in the lesion and opsonize the bacteria for phagocytosis by macrophages. In many patients, the organism persists despite these host responses. A protein in the outer membrane of *T. pallidum*, TprK, accumulates structural diversity during the course of infection through gene conversion (recombination) between silent donor sites and the *tprK* gene and this might contribute to antigenic diversity that allows the organism to persist.

Syphilis is divided into three stages, with distinct clinical and pathologic manifestations (Fig. 8-34).

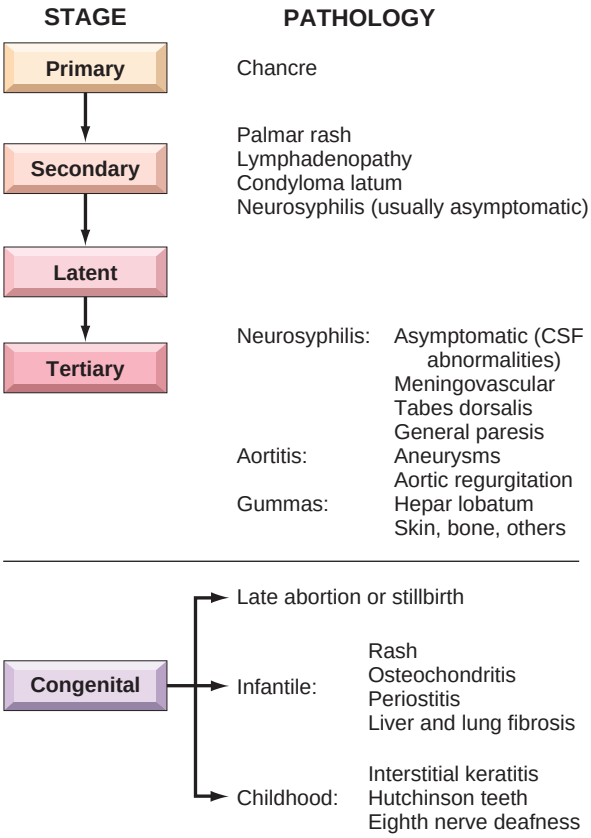

Figure 8-34 Protean manifestations of syphilis.

Primary Syphilis. This stage, occurring approximately 3 weeks after infection, features a single firm, nontender, raised, red lesion (chancre) located at the site of treponemal invasion on the penis, cervix, vaginal wall, or anus. The chancre heals with or without therapy. Spirochetes are plentiful within the chancre and spread from there throughout the body by hematologic and lymphatic dissemination.

Secondary Syphilis. This stage is marked by painless, superficial lesions of the skin and mucosal surfaces. It occurs 2 to 10 weeks after the primary chancre in approximately 75% of untreated people. Skin lesions frequently occur on the palms or soles of the feet, may be maculopapular, scaly, or pustular. Moist areas of the skin, such as the anogenital region, inner thighs, and axillae, may have *condylomata lata*, which are broad-based, elevated plaques. Silvery-gray superficial erosions may form on the oral, pharyngeal and genital mucous membranes. Lymphadenopathy, mild fever, malaise, and weight loss are also common in secondary syphilis. Asymptomatic neurosyphilis (discussed below) occurs in 8-40% of patients and symptomatic neurosyphilis, with meningitis, visual changes or hearing changes, occurs in 1-2%. Secondary syphilis lasts several weeks and then the person enters the latent stage of the disease.

Tertiary Syphilis. Tertiary syphilis has three main manifestations: cardiovascular syphilis, neurosyphilis, and so-called *benign tertiary syphilis.* These may occur alone or in combination. Tertiary syphilis occurs in one third of untreated patients, usually after a latent period of 5 years or more.

- *Cardiovascular syphilis*, in the form of syphilitic aortitis, accounts for more than 80% of cases of tertiary disease. The pathogenesis of this vascular lesion is not known, but the scarcity of treponemes and the intense inflammatory infiltrate suggest that the immune response plays a role. The aortitis leads to slowly progressive dilation of the aortic root and arch, which causes aortic valve insufficiency and aneurysms of the proximal aorta (Chapter 11).
- *Neurosyphilis* may be symptomatic or asymptomatic. Symptomatic neurosyphilis is discussed in Chapter 28. Asymptomatic neurosyphilis, which accounts for about one third of neurosyphilis cases, is initially suspected on detection of CSF abnormalities such as pleocytosis (increased numbers of inflammatory cells), elevated protein levels, or decreased glucose, and is confirmed by detection of antibodies stimulated by the spirochetes (discussed later) in the CSF. Antibiotics are given for a longer time if the spirochetes have spread to the CNS, so patients with tertiary syphilis should be tested for neurosyphilis even if they do not have neurologic symptoms.
- *Benign tertiary syphilis* is characterized by the formation of *gummas* in bone, skin, and the mucous membranes of the upper airway and mouth. Gummas are nodular lesions probably related to the development of delayed hypersensitivity to the bacteria. Skeletal involvement characteristically causes pain, tenderness, swelling, and pathologic fractures. Gummas in the skin and mucous membranes may produce nodular lesions or, rarely,