207e Endemic Treponematoses

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The endemic treponematoses are chronic diseases that are transmitted by direct contact, usually during childhood, and, like syphilis, can cause severe late manifestations years after initial infection. These diseases are caused by very close relatives of *Treponema pallidum* subspecies *pallidum*, the etiologic agent of venereal syphilis (Chap. 206). Yaws, pinta, and endemic syphilis are traditionally distinguished from venereal syphilis by mode of transmission, age of acquisition, geographic distribution, and clinical features; however, there is some overlap for each of these factors. Generally, yaws flourishes in moist tropical areas of several regions, endemic syphilis is found primarily in arid climates, and pinta is found in temperate foci in the Americas (Fig. 207e-1). These infections are usually limited to rural areas of developing nations and are seen in developed countries only among recent immigrants from endemic regions. Our "knowledge" about the endemic treponematoses is based on observations by health care workers who have visited endemic areas; virtually no well-designed studies of the natural history, diagnosis, or treatment of these infections have been conducted. The treponemal infections are compared and contrasted in Table 207e-1.

EPIDEMIOLOGY

In a World Health Organization (WHO)–sponsored mass eradication campaign from 1952 to 1969, more than 160 million people in Africa, Asia, and South America were examined for treponemal infections, and more than 50 million cases, contacts, and persons with latent infections were treated. This campaign reduced the prevalence of active yaws from >20% to <1% in many areas. In recent decades, lack of focused surveillance and diversion of resources have resulted in documented resurgence of these infections in some regions. The most recent WHO global estimate (1995) suggested that there are 460,000 new cases per year (mostly yaws) and a prevalence of 2.5 million infected persons; during subsequent years, an increased incidence was documented in some countries. Recent areas of resurgent yaws morbidity include West Africa (Ivory Coast, Ghana, Togo, Benin), the Central African Republic, Nigeria, and rural Democratic Republic of the Congo. The prevalence of endemic syphilis is estimated to be >10% in some regions of northern Ghana, Mali, Niger, Burkina Faso, and Senegal. In Asia and the Pacific Islands, reports suggest active outbreaks of yaws in Indonesia, Papua New Guinea, the Solomon Islands, East Timor, Vanuatu, Laos, and Kampuchea. India actively renewed its focus on yaws control in 1996, achieved zero-case status in 2003, and declared elimination in 2006. In the Americas, foci of yaws are thought to persist in Haiti and other Caribbean islands, Peru, Colombia, Ecuador, Brazil, Guyana, and Surinam, although recent data are lacking. Pinta is limited to Central America and northern South America, where it is found rarely and only in very remote villages. Evidence of yaws-like and venereal diseases, with treponemal seroreactivity, in wild gorillas and baboons in Africa has led to speculation that there may be an animal reservoir for yaws.

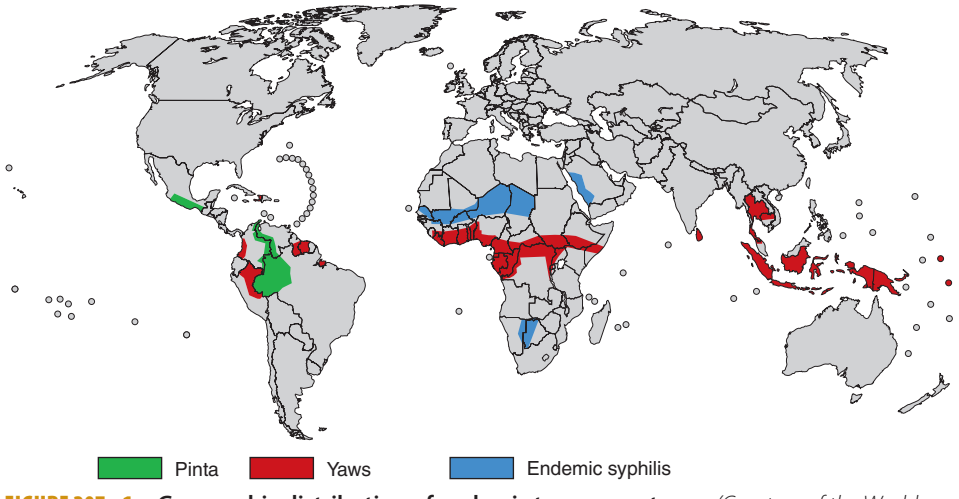

FIGURE 207e-1 Geographic distribution of endemic treponematoses. *(Courtesy of the World Health Organization; updated from www.who.int/yaws/epidemiology/Map_yaws_90s.jpg.)*

MICROBIOLOGY

The etiologic agents of the endemic treponematoses are listed in Table 207e-1. These little-studied organisms are morphologically identical to *T. pallidum* subspecies *pallidum* (the agent of venereal syphilis), and no definitive antigenic differences among them have been identified to date. A controversy has existed about whether the pathogenic treponemes are truly separate organisms, as genome sequencing indicates that yaws and syphilis treponemes are 99.8% identical. Three of the four organisms are classified as subspecies of *T. pallidum*; the fourth (*T. carateum*) remains a separate species simply because no organisms have been available for genetic studies. Based on analysis of the small number of strains currently available, molecular signatures—assessed by polymerase chain reaction (PCR) amplification of *tpr* genes and restriction digestion—have been identified that can differentiate the *T. pallidum* subspecies. Whether these genetic differences are related to distinct clinical characteristics of these diseases has not been determined. Full genome sequencing of an unclassified strain (Fribourg-Blanc) isolated from a baboon in 1966 shows a very high degree of homology with available strains of *T. pallidum* subspecies *pertenue*. This observation is consistent with an earlier report that the Fribourg-Blanc strain can cause experimental infection of humans. Molecular analyses of additional samples from affected baboons suggests that the nonhuman primate samples diverge from the evolutionary tree prior to the clade that contains the human isolates, but uncertainty remains about the importance of the nonhuman primate reservoir for human infection.

CLINICAL FEATURES

All of the treponemal infections, including syphilis, are chronic and are characterized by defined disease stages, with a localized primary lesion, disseminated secondary lesions, periods of latency, and possible late lesions. Primary and secondary stages are more frequently overlapping in yaws and endemic syphilis than in venereal syphilis, and the late manifestations of pinta are very mild relative to the destructive lesions of the other treponematoses. The current preference is to divide the clinical course of the endemic treponematoses into "early" and "late" stages.

The major clinical distinctions made between venereal syphilis and the nonvenereal infections are the apparent lack of congenital transmission and of central nervous system (CNS) involvement in the nonvenereal infections. It is not known whether these distinctions are entirely accurate. Because of the high degree of genetic relatedness among the organisms, there is little biological reason to think that *T. pallidum* subspecies *endemicum* and *T. pallidum* subspecies *pertenue* would be unable to cross the blood-brain barrier or to invade the placenta. These organisms are like *T. pallidum* subspecies *pallidum* in that they obviously disseminate from the site of initial infection and can persist for decades. The lack of recognized congenital infection may be due to the fact that childhood infections often reach the latent stage (low bacterial load) before girls reach sexual maturity. Neurologic involvement may go unrecognized because of the lack of trained medical personnel in endemic regions, the delay of many years between infection