tissues other than the skin. The initial papule is most often located on the extremities or face and is pruritic. After one to many months of infection, numerous disseminated secondary lesions (*pintides*) appear. These lesions are initially red but become deeply pigmented, ultimately turning a dark slate blue. The secondary lesions are infectious and highly pruritic and may persist for years. Late pigmented lesions are called *dyschromic macules* and contain treponemes. Over time, most pigmented lesions show varying degrees of depigmentation, becoming brown and eventually white and giving the skin a mottled appearance. White achromic lesions are characteristic of the late stage.

DIAGNOSIS

Diagnosis of the endemic treponematoses is based on clinical manifestations and, when available, dark-field microscopy and serologic testing. The same serologic tests that are used for venereal syphilis **(Chap. 206)** become reactive during all treponemal infections. Although several targets have been evaluated for specific serodiagnosis, to date there is no antibody test that can discriminate among the different infections. The nonvenereal treponemal infections should be considered in the evaluation of a reactive syphilis serology in any person who has emigrated from an endemic area. Sensitive PCR assays can be used to confirm treponemal infection and to identify the etiologic agent in research laboratories.

TREATMENT ENDEMIC TREPONEMATOSES

The WHO-recommended therapy for patients and their contacts is benzathine penicillin G (1.2 million units IM for adults; 600,000 units for children <10 years old). This dose is half of that recommended for early venereal syphilis, and no controlled efficacy studies have been conducted. Definitive evidence of resistance to penicillin is lacking, although relapsing lesions have been reported after penicillin treatment in Papua New Guinea. A recent study in that nation demonstrated equivalence between IM benzathine penicillin G and a single oral dose of azithromycin (30 mg/kg, up to a maximum of 2 g). This finding provided the WHO's revitalized yaws eradication program with a much easier regimen for use in mass treatment. Although macrolide resistance mutations are common in circulating strains of *T. pallidum* subspecies *pallidum* in many parts of the world, analysis of a limited number of yaws samples from Papua New Guinea has yielded no evidence of resistance mutations to date. Limited data suggest the efficacy of tetracycline for treatment of yaws, but no data exist for other endemic treponematoses. Solely on the basis of experience with venereal syphilis, it is thought that doxycycline or tetracycline (at doses appropriate for syphilis; **Chap. 206**) are alternatives for patients allergic to penicillin. A Jarisch-Herxheimer reaction **(Chap. 206)** may follow treatment of endemic treponematoses. Nontreponemal serologic titers (in the Venereal Disease Research Laboratory [VDRL] slide test or the rapid plasma reagin [RPR] test) usually decline after effective therapy, but patients may not become seronegative.

CONTROL

Buoyed by the successful elimination of yaws in India in 2006 and the availability of an inexpensive, single-dose oral drug for treatment, in 2012 the WHO renewed its efforts to eradicate yaws globally by 2020. Enthusiasm is high; several planning meetings have been held to develop country-specific plans of action; and resources are being sought. Some caution is warranted: The possible animal reservoir will need to be evaluated. There may be only a window of time during which countries can successfully use azithromycin for yaws eradication before resistance begins to appear in yaws organisms. Given the ongoing lower-dose azithromycin mass treatment campaigns against trachoma, often in populations also at high risk for yaws, development of macrolide resistance is likely at some point. Complete drug coverage and continued careful surveillance by health centers (the weak link in prior control efforts) will be essential for success.