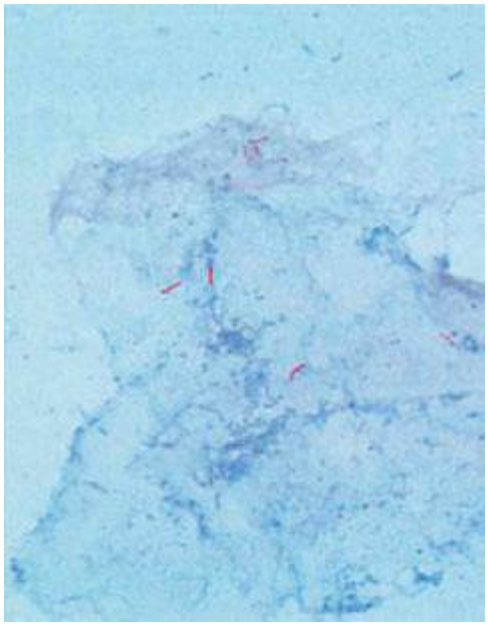

FIGURE 202-1 Acid-fast bacillus smear showing *M. tuberculosis* bacilli. *(Courtesy of the Centers for Disease Control and Prevention, Atlanta.)*

complex includes *M. bovis* (the bovine tubercle bacillus—characteristically resistant to pyrazinamide, once an important cause of TB transmitted by unpasteurized milk, and currently the cause of a small percentage of human cases worldwide), *M. caprae* (related to *M. bovis*), *M. africanum* (isolated from cases in West, Central, and East Africa), *M. microti* (the "vole" bacillus, a less virulent and rarely encountered organism), *M. pinnipedii* (a bacillus infecting seals and sea lions in the Southern Hemisphere and recently isolated from humans), *M. mungi* (isolated from banded mongooses in southern Africa), *M. orygis* (described recently in oryxes and other Bovidae in Africa and Asia and a potential cause of infection in humans), and *M. canetti* (a rare isolate from East African cases that produces unusual smooth colonies on solid media and is considered closely related to a supposed progenitor type).

M. tuberculosis is a rod-shaped, non-spore-forming, thin aerobic bacterium measuring 0.5 μm by 3 μm. Mycobacteria, including *M. tuberculosis*, are often neutral on Gram's staining. However, once stained, the bacilli cannot be decolorized by acid alcohol; this characteristic justifies their classification as acid-fast bacilli (AFB; Fig. 202-1). Acid fastness is due mainly to the organisms' high content of mycolic acids, long-chain cross-linked fatty acids, and other cell-wall lipids. Microorganisms other than mycobacteria that display some acid fastness include species of *Nocardia* and *Rhodococcus*, *Legionella micdadei*, and the protozoa *Isospora* and *Cryptosporidium*. In the mycobacterial cell wall, lipids (e.g., mycolic acids) are linked to underlying arabinogalactan and peptidoglycan. This structure results in very low permeability of the cell wall, thus reducing the effectiveness of most antibiotics. Another molecule in the mycobacterial cell wall, lipoarabinomannan, is involved in the pathogen–host interaction and facilitates the survival of *M. tuberculosis* within macrophages. The complete genome sequence of *M. tuberculosis* comprises 4043 genes encoding 3993 proteins and 50 genes encoding RNAs; its high guanine-plus-cytosine content (65.6%) is indicative of an aerobic "lifestyle." A large proportion of genes are devoted to the production of enzymes involved in cell wall metabolism.

EPIDEMIOLOGY

More than 5.7 million new cases of TB (all forms, both pulmonary and extrapulmonary) were reported to the World Health Organization (WHO) in 2013; 95% of cases were reported from developing countries. However, because of insufficient case detection and incomplete notification, reported cases may represent only about two-thirds of the total estimated cases. The WHO estimated that 9 million (range, 8.6–9.4 million) new cases of TB occurred worldwide in 2013, 95% of them in developing countries of Asia (5 million), Africa (2.6 million), the Middle East (0.7 million), and Latin America (0.3 million). It is further estimated that 1.49 million (range, 1.32–1.67 million) deaths from TB, including 0.36 million among people living with HIV infection, occurred in 2013, 96% of them in developing countries. Estimates of TB incidence rates (per 100,000 population) and numbers of TB-related deaths in 2013 are depicted in Figs. 202-2 and 202-3, respectively. During the late 1980s and early 1990s, numbers of reported cases of TB increased in industrialized countries. These increases were related largely to immigration from countries with a high incidence of TB; the spread of the HIV epidemic; social problems, such as increased urban poverty, homelessness, and drug abuse; and dismantling of TB services. During the past few years, numbers of reported cases have begun to decline again or have stabilized in most industrialized nations. In the United States, with the re-establishment of stronger control programs, the decline resumed in 1993 and has since been maintained. In 2013, 9582 cases of TB (3.0 cases/100,000 population) were reported to the Centers for Disease Control and Prevention (CDC).

In the United States, TB is uncommon among young adults of European descent, who have only rarely been exposed to *M. tuberculosis* infection during recent decades. In contrast, because of a high risk of transmission in the past, the prevalence of latent *M. tuberculosis* infection (LTBI) is relatively high among elderly whites. In general, adults ≥65 years of age have the highest incidence rate per capita (4.9 cases/100,000 population in 2013) and children <14 years of age the lowest (0.8 case/100,000 population). Blacks account for the highest proportion of cases (37%; 1257 cases in 2013) among U.S.-born persons. TB in the United States is also a disease of adult members of the HIV-infected population, the foreign-born population (64.6% of all cases in 2013), and disadvantaged/marginalized populations. Of the 6193 cases reported among foreign-born persons in 2013, 37% occurred in persons from the Americas and 32% occurred in persons born in the Western Pacific region. Overall, the highest rates per capita were among Asian Americans (18.7 cases/100,000 population). A total of 536 deaths were caused by TB in the United States in 2011. In Canada in 2013, 1638 TB cases were reported (4.7 cases/100,000 population); 70% (1145) of these cases occurred in foreign-born persons and 19% (309 cases) occurred in members of the Canadian aboriginal peoples, whose per capita rate is disproportionately high (23.4 cases/100,000 population) with a peak in the Nunavut territory of 143 cases/100,000 population—a rate similar to that in many highly endemic countries. Similarly, in Europe, TB has reemerged as an important public health problem, mainly as a result of cases among immigrants from high-incidence countries and among marginalized populations, often in large urban settings like London; in 2013, 41% of all cases reported from the United Kingdom occurred in London, and the rate per capita (36 cases/100,000 population) was similar to that in some middle-income countries. In most Western European countries, there are more cases annually among foreign-born than native populations.

Recent data on global trends indicate that in 2013 the TB incidence was stable or falling in most regions; this trend began in the early 2000s and appears to have continued, with an average annual decline of 2% globally. This global decrease is explained largely by the simultaneous reduction in TB incidence in sub-Saharan Africa, where rates had risen steeply since the 1980s as a result of the HIV epidemic and the lack of capacity of health systems and services to deal with the problem effectively, and in Eastern Europe, where incidence increased rapidly during the 1990s because of a deterioration in socioeconomic conditions and the health care infrastructure (although, after peaking in 2001, incidence in Eastern Europe has since declined slowly).

Of the estimated 9 million new cases of TB in 2013, 13% (1.1 million) were associated with HIV infection, and 78% of these HIV-associated cases occurred in Africa. An estimated 0.36 million persons with HIV-associated TB died in 2013. Furthermore, an estimated 480,000 cases (range, 350,000–610,000) of multidrug-resistant TB (MDR-TB)—a form of the disease caused by bacilli resistant at least to isoniazid and rifampin—occurred in 2013. Only 28% of these