nasopharyngeal areas and, with progression, may be highly destructive and disfiguring. Microscopic examination reveals a mixed inflammatory infiltrate composed of parasite-containing macrophages with lymphocytes and plasma cells. Later, the tissue inflammatory response becomes granulomatous, and the number of parasites declines. Eventually, the lesions remit and scar, although reactivation may occur after long intervals by mechanisms that are not currently understood.

Diffuse cutaneous leishmaniasis is a rare form of dermal infection found in Ethiopia and adjacent East Africa and in Central and South America. Diffuse cutaneous leishmaniasis begins as a single skin nodule, which continues spreading until the entire body is covered by nodular lesions. Microscopically, they contain aggregates of foamy macrophages stuffed with leishmania.

African Trypanosomiasis

African trypanosomes are kinetoplastid parasites that proliferate as extracellular forms in the blood and cause sustained or intermittent fevers, lymphadenopathy, splenomegaly, progressive brain dysfunction (sleeping sickness), cachexia, and death. *Trypanosoma brucei rhodesiense* infection, which occurs in East Africa and is often acute and virulent, is a zoonotic infection that is best combated by reducing infected fly populations. *Trypanosoma brucei gambiense* infection occurring in West Africa tends to spread from human to human via fly bites and requires active case detection and treatment. Tsetse flies (genus *Glossina*) transmit African *Trypanosoma* to humans either from the reservoir of parasites found in wild and domestic animals *(T. brucei rhodesiense)* or from other humans *(T. brucei gambiense)*. Within the fly, the parasites multiply in the stomach and then in the salivary glands before developing into nondividing trypomastigotes, which are transmitted to humans and animals with the next blood meal.

Pathogenesis. African trypanosomes are covered by a single, abundant, glycolipid-anchored protein called the *variant surface glycoprotein (VSG)*. As parasites proliferate in the bloodstream, the host produces antibodies to the VSG, which, in association with phagocytes, kill most of the organisms, causing a spike of fever. A small number of parasites, however, undergo a genetic rearrangement and produce a different VSG on their surface and so escape the host immune response. These successor trypanosomes multiply until the host mounts a new anti-VSG response and kills most of them, but then another clone with a distinct VSG takes over. In this way, African trypanosomes cause waves of fever before they finally invade the CNS. Trypanosomes have many VSG genes, only one of which is expressed at a time. The parasite uses an elegant mechanism to turn VSG genes on and off. Although VSG genes are scattered throughout the trypanosome genome, only VSG genes found within *bloodstream expression sites* near the ends of chromosomes (the telomeres) are transcribed. New VSG genes are periodically moved into the bloodstream expression sites, mainly by homologous recombination. A specialized RNA polymerase that transcribes VSG genes associates with only a single bloodstream expression site, limiting expression to one VSG gene at a time.

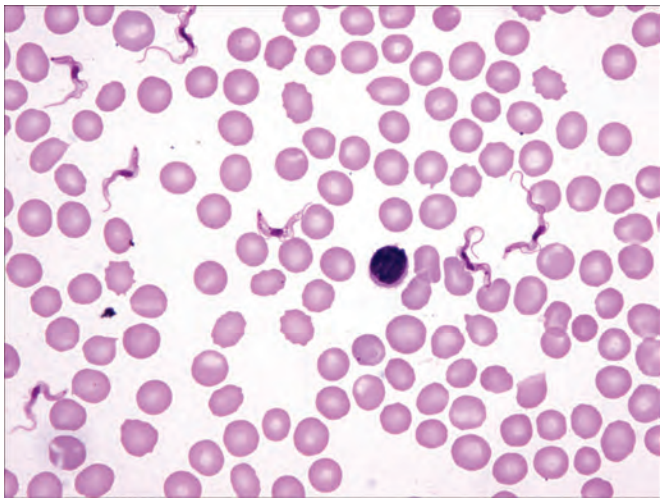

Figure 8-50 Slender bloodstream parasites of African trypanosomiasis.

MORPHOLOGY

A large, red, rubbery chancre forms at the site of the insect bite and contains numerous parasites surrounded by a dense, predominantly mononuclear, inflammatory infiltrate. With chronicity, the lymph nodes and spleen enlarge due to infiltration by lymphocytes, plasma cells, and macrophages, which are filled with dead parasites. Trypanosomes, which are small and difficult to visualize (Fig. 8-50), concentrate in capillary loops, such as the choroid plexus and glomeruli. When parasites breach the blood-brain barrier and invade the CNS, a leptomeningitis develops that extends into the perivascular Virchow-Robin spaces, and eventually a demyelinating panencephalitis occurs. Plasma cells containing cytoplasmic globules filled with immunoglobulins are frequent and are referred to as **Mott cells**. Chronic disease leads to progressive cachexia; patients, devoid of energy and normal mentation, literally waste away.

Chagas Disease

***Trypanosoma cruzi* is a kinetoplastid, intracellular protozoan parasite that causes American trypanosomiasis (Chagas disease).** Chagas disease occurs rarely in the United States and Mexico but is more common in South America, particularly Brazil. *T. cruzi* parasites infect many animals, including cats, dogs, and rodents. The parasites are transmitted between animals and to humans by triatomine bugs (also known as kissing bugs or reduviids), which hide in the cracks of loosely constructed houses, feed on the sleeping inhabitants, and pass the parasites in the feces; the infectious parasites enter the host through damaged skin or through mucous membranes. At the site of skin entry there may be a transient, erythematous nodule. Another important route of infection is oral ingestion of the parasites due to contamination of food products with triatomine bugs and/or their feces. Once in the host, *T. cruzi* invades human cells through interaction with a variety of molecules including TLRs, kinins, and receptors for TGF, EGF, tyrosine kinases, and LDL.

Pathogenesis. While most intracellular pathogens avoid the toxic contents of lysosomes, *T. cruzi* actually requires brief exposure to the acidic phagolysosome for development of amastigotes, the intracellular stage of the parasite.