To ensure exposure to lysosomes, *T. cruzi* trypomastigotes elevate the concentration of cytoplasmic calcium in host cells, which promotes fusion of the phagosome and lysosome. In addition to enhancing amastigote development, the low pH of the lysosome activates pore-forming proteins that disrupt the lysosomal membrane, releasing the parasite into the cell cytoplasm. Parasites reproduce as rounded amastigotes in the cytoplasm of host cells and then develop flagella, lyse host cells, enter the bloodstream, and penetrate smooth, skeletal, and heart muscles.

Chagas disease primarily affects the heart and in endemic areas, it is a major cause of sudden death due to cardiac arrhythmia. In acute Chagas disease, which is mild in most individuals, cardiac damage results from direct invasion of myocardial cells by the organisms and the subsequent inflammation. Rarely, acute Chagas disease presents with high parasitemia, fever, or progressive cardiac dilation and failure, often with generalized lymphadenopathy or splenomegaly. In chronic Chagas disease, which occurs in 20% of people 5 to 15 years after initial infection, the mechanism of cardiac damage has two components.

- The presence of persistent *T. cruzi* parasites leads to a continued immune response with a striking inflammatory infiltration of the myocardium, even though only scant organisms may be present.
- The parasite also may induce autoimmune responses, such that antibodies and T cells that recognize parasite proteins cross-react with host myocardial cells, nerve cells, and extracellular proteins such as laminin. For example, cross-reactive antibodies may induce electrophysiologic dysfunction of the heart.

Damage to myocardial cells and to conductance pathways causes a dilated cardiomyopathy and cardiac arrhythmias. In addition, damage to the myenteric plexus causes dilation of the colon (megacolon) and esophagus. This is particularly common in Brazilian endemic areas where as many as 50% of the patients with lethal carditis have colonic and esophageal disease.

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In lethal **acute myocarditis**, the changes are diffusely distributed throughout the heart. Clusters of amastigotes cause swelling of individual myocardial fibers and create intracellular pseudocysts. There is focal myocardial cell necrosis accompanied by extensive, dense, acute interstitial inflammatory infiltration throughout the myocardium, often associated with four-chamber cardiac dilation (Chapter 12).

In **chronic Chagas disease** the heart is typically dilated, rounded, and increased in size and weight. Often, there are mural thrombi that, in about half of autopsy cases, have given rise to pulmonary or systemic emboli or infarctions. On histologic examination, there are interstitial and perivascular inflammatory infiltrates composed of lymphocytes, plasma cells, and monocytes. There are scattered foci of myocardial cell necrosis and interstitial fibrosis, especially toward the apex of the left ventricle, which may undergo aneurysmal dilation and thinning. Even with dilation of the esophagus and colon, parasites cannot be found within ganglia of myenteric plexus. Chronic Chagas cardiomyopathy is often treated by cardiac transplantation.

Metazoa

Metazoa are multicellular, eukaryotic organisms. The parasitic metazoa are contracted by consuming the parasite, often in undercooked meat, or by direct invasion of the host through the skin or via insect bites. Metazoa dwell in many sites of the body, including the intestine, skin, lung, liver, muscle, blood vessels, and lymphatics. The infections are diagnosed by microscopic identification of larvae or ova in excretions or tissues, and by serology.

Strongyloidiasis

Strongyloides stercoralis infects tens of million people worldwide and is endemic in the southeastern United States, South America, sub-Saharan Africa, and Southeast Asia. **The worms live in the soil and infect humans when larvae penetrate the skin, travel in the circulation to the lungs, and then travel up the trachea to be swallowed.** Female worms reside in the mucosa of the small intestine, where they produce eggs by asexual reproduction (parthenogenesis). Most of the larvae are passed in the stool and then may contaminate soil to continue the cycle of infection.

In immunocompetent hosts, *S. stercoralis* may cause diarrhea, bloating, and occasionally malabsorption. Unlike other parasitic worms, *S. stercoralis* larvae hatched in the gut can invade the colon mucosa and reinitiate infection (autoinfection). Immunocompromised hosts, particularly people on prolonged corticosteroid therapy, can have very high worm burdens (hyperinfection) due to uncontrolled autoinfection, leading to fatal disease. Corticosteroids inhibit the functions of eosinophils that accumulate in tissues in response to infection, induce apoptosis in immune cells, and stimulate female *Strongyloides* directly to increase infective larvae production. In addition, other disease states which perturb immune control mechanisms (e.g., organ transplantation, lymphoma, HIV/AIDS, HTLV-1) have increased risks. Hyperinfection can be complicated by sepsis caused by intestinal bacteria, which enter the blood following damage to the intestinal wall by the invading larvae.

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In mild strongyloidiasis, worms, mainly larvae, are present in the duodenal crypts but are not seen in the underlying tissue. There is an eosinophil-rich infiltrate in the lamina propria with mucosal edema. Hyperinfection with *S. stercoralis* results in invasion of larvae into the colonic submucosa, lymphatics, and blood vessels, with an associated mononuclear infiltrate. There are many adult worms, larvae, and eggs in the crypts of the duodenum and ileum (Fig. 8-51). Worms of all stages may be found in other organs, including skin and lungs, and may even be found in large numbers in sputum.

Tapeworms (Cestodes): Cysticercosis and Hydatid Disease

Taenia solium and *Echinococcus granulosus* are cestode parasites (tapeworms) that cause cysticercosis and hydatid infections, respectively. Both diseases are caused by larvae that develop after ingestion of tapeworm eggs. These tapeworms have a complex life cycle requiring two mammalian hosts: a definitive host, in which the worm reaches sexual