animals (usually pigs, boars, or horses) that have themselves been infected by eating rats or meat products containing *T. spiralis*, *T. nativa,* or *T. britovi*. In the United States the number of *T. spiralis*–infected pigs has been greatly reduced by laws requiring proper cooking of food fed to hogs; the number of reported human infections in the United States is now less than 20 cases each year. Still, trichinosis remains widespread in other parts of the world, where undercooked meat, including noncommercial livestock and game (e.g., bear), is commonly eaten.

The life cycle of *T. spiralis* begins in the human intestine but ends within muscle as humans are dead-end hosts. In the human gut, *T. spiralis* larvae develop into adults that mate and release new larvae, which penetrate into the tissues. Larvae disseminate hematogenously and penetrate muscle cells, causing fever, myalgias, marked eosinophilia, and periorbital edema. Less commonly, the larvae lodge in the heart, lungs, and brain, and patients can develop dyspnea, encephalitis, and cardiac failure. In striated skeletal muscle, *T. spiralis* larvae become intracellular parasites, increase dramatically in size, and modify the host muscle cell (referred to as the *nurse cell*) so that it loses its striations, gains a collagenous capsule, and develops a plexus of new blood vessels around itself. The nurse cell-parasite complex is largely asymptomatic, and the worm may persist for years before it dies and calcifies. Antibodies to larval antigens, which include an immunodominant carbohydrate epitope called *tyvelose*, may reduce reinfection and are useful for serodiagnosis of the disease.

***Trichinella spiralis* and other invasive nematodes stimulate a T_H2 response,** with production of IL-4, IL-5, IL-10, and IL-13. The cytokines produced by T_H2 cells activate eosinophils and mast cells, both of which are associated with the inflammatory response to these parasites. In animal models of *T. spiralis* infection, the T_H2 response is associated with increased contractility of the intestine, which expels adult worms from the gut and subsequently reduces the number of larvae in the muscles. While the T_H2 response indirectly reduces the number of larvae in muscle by eliminating adults from the intestine, it is not clear whether the intramuscular inflammatory response, which is composed of mononuclear cells and eosinophils, is effective against the larvae.

MORPHOLOGY

During the invasive phase of trichinosis, cell destruction can be widespread with heavy infections and may be lethal. In the heart there is a patchy interstitial myocarditis characterized by many eosinophils and scattered giant cells. The myocarditis can lead to scarring. Larvae in the heart do not encyst and are difficult to identify, because they die and disappear. In the lungs, trapped larvae cause focal edema and hemorrhages, sometimes with an allergic eosinophilic infiltrate. In the CNS, larvae cause a diffuse lymphocytic and eosinophilic infiltrate, with focal gliosis in and about small capillaries of the brain.

Trichinella spiralis preferentially encysts in striated skeletal muscles with the richest blood supply, including the diaphragm and the extraocular, laryngeal, deltoid, gastrocnemius, and intercostal muscles (Fig. 8-53). Coiled larvae are approximately 1 mm long and are surrounded by membrane-bound vacuoles within nurse cells, which in turn are surrounded by new blood vessels and an eosinophil-rich mononuclear cell infiltrate. This infiltrate is greatest around dying parasites, which eventually calcify and leave behind scars that are sufficiently characteristic to suggest the diagnosis of trichinosis.

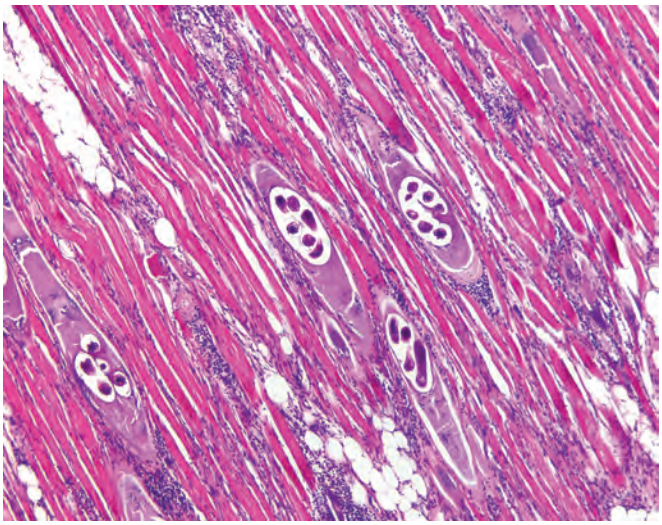

Figure 8-53 Multiple coiled *Trichinella spiralis* larvae within skeletal muscle cells.

Schistosomiasis

Schistosomiasis infects approximately 230 million persons and kills more than 200,000 individuals annually. The affected organs and hence the site of major disease vary with the species. *Shistosoma* mansoni and *S. japonicum* affect the liver and the gut predominantly. Most deaths are due to hepatic cirrhosis, which is caused by *S. mansoni* in Latin America, Africa, and the Middle East and by *S. japonicum* and *S. mekongi* in East Asia. By contrast, *S. haematobium*, found in Africa, causes chronic granulomatous bladder inflammation that may lead to hematuria, obstructive uropathy, and carcinoma. *Schistosoma* flukes, like all trematodes, require passage through freshwater snails that live in the slow-moving water of tropical rivers, lakes, and irrigation ditches, ironically linking agricultural development with spread of the disease. Acute schistosomiasis in humans can be a severe febrile illness that peaks about 2 months after infection. Severe hepatic fibrosis is a serious manifestation of chronic schistosomiasis (see later).

Pathogenesis. **Much of the pathology of schistosomiasis is caused by host inflammatory reactions to different stages of the parasite.** The life cycle of *Schistosoma* involves stepwise infection of several human tissues, each associated with host inflammatory responses. After release from snails, ciliated miracidium larvae mature into infectious schistosome larvae (cercariae) that swim through fresh water and penetrate human skin with the aid of powerful proteolytic enzymes that degrade the keratinized layer. There is minimal skin reaction. Schistosomes migrate through the skin into the peripheral vasculature and lymphatics, travel to the lungs and heart, from where they are disseminated widely, including the mesenteric, splanchnic and portal circulation, ultimately reaching the hepatic vessels where they mature (*S. mansoni* and *S. japonicum*).