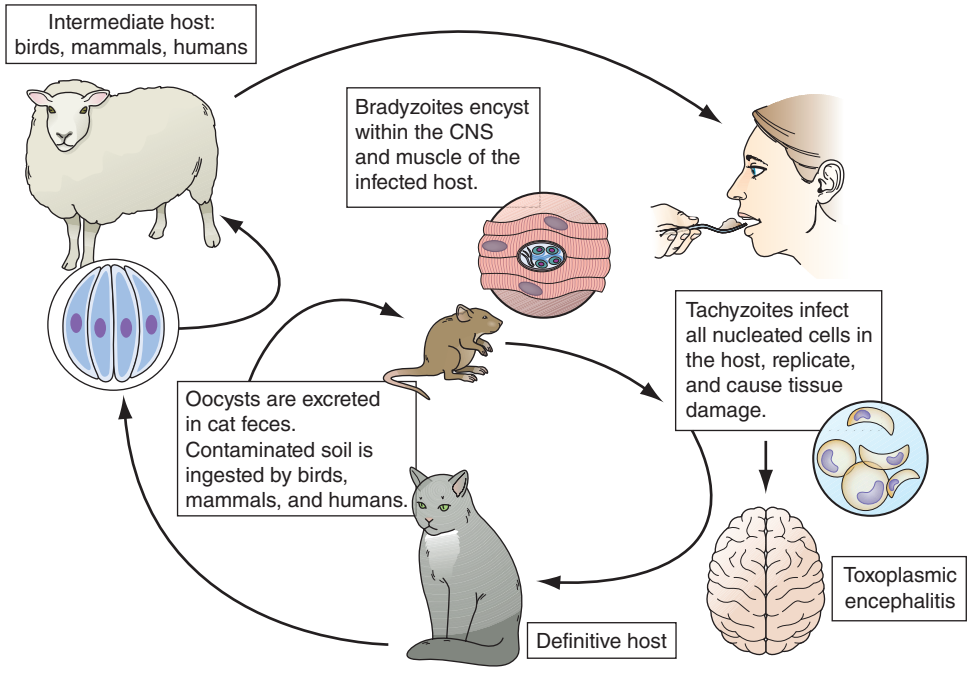

FIGURE 253-1 Life cycle of *Toxoplasma gondii*. The cat is the definitive host in which the sexual phase of the cycle is completed. Oocysts shed in cat feces can infect a wide range of animals, including birds, rodents, grazing domestic animals, and humans. The bradyzoites found in the muscle of food animals may infect humans who eat insufficiently cooked meat products, particularly lamb and pork. Although human disease can take many forms, congenital infection and encephalitis from reactivation of latent infection in the brains of immunosuppressed persons are the most important manifestations. CNS, central nervous system. *(Courtesy of Dominique Buzoni-Gatel, Institut Pasteur, Paris; with permission.)*

acidic-pH gastric secretions. Bradyzoites or sporozoites are released, enter the small-intestinal epithelium, and transform into rapidly dividing tachyzoites. The tachyzoites can infect and replicate in all mammalian cells except red blood cells. The parasite actively penetrates the cell and forms a parasitophorous vacuole. Parasite replication continues within the vacuole. After the parasites reach a critical mass, intracellular signaling within the host and the parasite, including calcium fluxes, result in parasite egress from the vacuole. The host cell is destroyed, and the released tachyzoites infect adjoining cells. The tachyzoite replication cycle within an infected organ causes cytopathology. Most tachyzoites are eliminated by the host's humoral and cell-mediated immune responses. Tissue cysts containing many bradyzoites develop 7–10 days after systemic tachyzoite infection. These tissue cysts occur in various host organs but persist principally within the central nervous system (CNS) and muscle. The development of this chronic stage completes the asexual portion of the life cycle. Active infection in the immunocompromised host is most likely to be due to the spontaneous release of encysted parasites that undergo rapid transformation into tachyzoites within the CNS and are not contained by the immune system.

The *sexual* stage in the life cycle takes place in the cat (the definitive host). The parasite's sexual phase is defined by the formation of oocysts within the feline host. This enteroepithelial cycle begins with the ingestion of the bradyzoite tissue cysts and, after several intermediate stages, culminates in the production of gametes. Gamete fusion produces a zygote, which envelops itself in a rigid wall and is secreted in the feces as an unsporulated oocyst. After 2–3 days of exposure to air at ambient temperature, the noninfectious oocyst sporulates to produce eight sporozoite progeny. The sporulated oocyst can be ingested by an intermediate host, such as a person emptying a cat's litter box or a pig rummaging in a barnyard. It is in the intermediate host that *T. gondii* completes its life cycle.

Sporulated oocysts are environmentally hardy and very infectious; they are thought to be sources of waterborne outbreaks such as those reported in Victoria (British Columbia, Canada) and in South America.

EPIDEMIOLOGY

T. gondii infects a wide range of mammals and birds. Its seroprevalence depends on the locale and the age of the population. Generally, hot arid climatic conditions are associated with a low prevalence of infection. In the United States and most European countries, the seroprevalence increases with age and exposure. For example, in the United States, 5–30% of individuals 10–19 years old and 10–67% of those >50 years old have serologic evidence of exposure. In Central America, France, Turkey, and Brazil, the seroprevalence is higher. Because of increased awareness of foodborne infections, the prevalence of seropositivity has decreased worldwide.

TRANSMISSION

Oral Transmission Most cases of human *Toxoplasma* infection are thought to be acquired by the oral route. Transmission can be attributable to ingestion of sporulated oocysts from contaminated soil, food, or water. During acute feline infection, a cat may excrete as many as 100 million parasites per day. These very stable sporozoite-containing oocysts are highly infectious and may remain viable for many years in soil or water. Humans infected during an oocyst-transmitted infection develop stage-specific antibodies to the oocyst/sporozoite.

Children and adults also can acquire infection from tissue cysts containing bradyzoites. The ingestion of a single cyst is all that is required for human infection. Undercooking or insufficient freezing of meat is an important source of infection in the developed world. In the United States, lamb products and pork products may yield evidence of cysts that contain bradyzoites, but the overall prevalence of *T. gondii* has been gradually decreasing. The incidence in beef is much lower—perhaps as low as 1%. Direct ingestion of bradyzoite cysts in these various meat products leads to acute infection.

Transmission via Blood or Organs In addition to being transmitted orally, *T. gondii* can be transmitted directly from a seropositive donor to a seronegative recipient in a transplanted heart, heart-lung, kidney, liver, or pancreas. Viable parasites can be cultured from refrigerated anticoagulated blood, which may be a source of infection in individuals receiving blood transfusions. *T. gondii* reactivation has been reported in bone marrow, hematopoietic stem cell, and liver transplant recipients as well as in individuals with AIDS. Although antibody titers generally are not useful in monitoring *T. gondii* infection, individuals with higher antibody titers may be at relatively high risk for reactivation after hematopoietic stem cell transplantation; thus routine polymerase chain reaction (PCR) screening of blood from these patients may be in order. Finally, laboratory personnel can be infected after contact with contaminated needles or glassware or with infected tissue.

Transplacental Transmission On average, about one-third of all women who acquire infection with *T. gondii* during pregnancy transmit the parasite to the fetus; the remainder give birth to normal, uninfected babies. Of the various factors that influence fetal outcome, gestational age at the time of infection is the most critical (see below). Few data support a role for recrudescent maternal infection as the source of congenital disease, although rare cases of transmission by immunocompromised women (e.g., those infected with HIV or those receiving high-dose glucocorticoids) have been reported. Thus, women who are seropositive before pregnancy usually are protected against acute infection and do not give birth to congenitally infected neonates.