sometimes complicated by cerebral infarctions when fungi invade arteries and induce thrombosis.

Lung involvement with Mucormycotina may be secondary to rhinocerebral disease, or it may be primary in people with severe immunodeficiency. The lung lesions combine areas of hemorrhagic pneumonia with vascular thrombi and distal infarctions.

Dimorphic Fungi

The medically important dimorphic fungi are discussed in Chapter 15 and include blastomyces, histoplasma, and coccidioidomyces. Suffice it to say that **they grow as yeast in human tissue but as a hyaline mold under some laboratory culture conditions, typically at room temperature.** On histological examination, the organisms have characteristic yeast appearances but can be somewhat difficult to speciate if organisms are rare. The immune response can range from suppurative to granulomatous depending on the organism and stage of disease. If concurrent cultures from a sample begin to demonstrate hyaline mold, this indicates that the organism is dimorphic and specific treatment can be started.

Parasitic Infections

Protozoa

Protozoa are unicellular eukaryotic organisms. The parasitic protozoa are transmitted by insects or by the fecal-oral route and, in humans, mainly reside in the blood or intestine (Table 8-8). Most protozoal infections are diagnosed by microscopic examination of blood smears or lesions.

Malaria

Malaria, caused by the intracellular parasite *Plasmodium*, affects more than 160 million people worldwide and kills more than 500,000 people each year. According to the WHO, 90% of deaths from malaria occur in sub-Saharan Africa, where malaria is a leading cause of death in children younger than 5 years old. *Plasmodium falciparum* (the cause of severe cerebral malaria) and the four other malaria parasites that infect humans (*P. vivax, P. ovale, P. knowlesi,* and *P. malariae*) are all transmitted by female Anopheles mosquitoes, which are widely distributed throughout Africa, Asia, and Latin America. Nearly all of the approximately 1500 new cases of malaria each year in the United States occur in travelers or immigrants. Mass spraying to eliminate the mosquito vectors was successful initially but ultimately failed when DDT was removed from the market due to environmental concerns. Worldwide public health efforts to control malaria today face the challenges of insecticide-resistant mosquitoes and drug-resistant *Plasmodium* species. Currently, a combination of mosquito control and anti-malarial drugs is viewed as the means to decrease the incidence.

Table 8-8 Selected Human Protozoal Diseases

Location	Species	Disease
Luminal or epithelial	*Entamoeba histolytica*	Amebic dysentery; liver abscess
	Balantidium coli	Colitis
	Giardia lamblia	Diarrheal disease, malabsorption
	Isospora belli,	Chronic enterocolitis or
	Cryptosporidium sp.	malabsorption or both
	Trichomonas vaginalis	Urethritis, vaginitis
Central nervous system	*Naegleria fowleri*	Meningoencephalitis
	Acanthamoeba sp.	Meningoencephalitis or ophthalmitis
Bloodstream	*Plasmodium* sp.	Malaria
	Babesia microti, B. bovis	Babesiosis
	Trypanosoma sp.	African sleeping sickness
Intracellular	*Trypanosoma cruzi*	Chagas disease
	Leishmania donovani	Kala-azar
	Leishmania sp.	Cutaneous and mucocutaneous leishmaniasis
	Toxoplasma gondii	Toxoplasmosis

Life Cycle and Pathogenesis. The life cycles of the *Plasmodium* species are similar, although *P. falciparum* differs in ways that contribute to its greater virulence. *P. vivax, P. ovale, P. knowlesi,* and *P. malariae* cause low levels of parasitemia, mild anemia, and, in very rare instances, splenic rupture and nephrotic syndrome. ***P. falciparum* infection is associated with high levels of parasitemia, that may lead to severe anemia, cerebral symptoms, renal failure, pulmonary edema, and death, depending on the susceptibility of the host.**

The life cycle of *Plasmodium* species is simple, as it involves only humans and mosquitoes, but the development of the parasite is complex, as it passes through several morphologically distinct forms. The infectious stage of *Plasmodium*, the *sporozoite*, is found in the salivary glands of female mosquitoes. When the mosquito takes a blood meal, sporozoites are released into the human's blood and, within minutes, attach to and invade liver cells by binding to the hepatocyte receptor for the serum proteins thrombospondin and properdin (Fig. 8-46). Within liver cells, malaria parasites multiply, releasing as many as 30,000 *merozoites* (asexual, haploid forms) when each infected hepatocyte ruptures. During *P. falciparum* infection, rupture usually occurs within 8 to 12 weeks. In contrast, *P. vivax* and *P. ovale* form latent *hypnozoites* in hepatocytes, which cause relapses of malaria weeks to months after initial infection. The infection of the liver and development of merozoites is called the *exoerythrocytic* stage. This stage is asymptomatic. Once released from the liver, *Plasmodium* merozoites use a lectin-like molecule to bind to sialic acid residues on glycophorin molecules on the surface of red cells and invade by active membrane penetration. Within the red cells (*erythrocytic* stage) the parasites grow in a membrane-bound digestive vacuole, hydrolyzing hemoglobin through secreted enzymes. The *trophozoite* is the first stage of the parasite in the red cell and is defined by the presence of a single chromatin mass. The next stage, the *schizont*, has multiple chromatin masses, each of which develops into a merozoite. Upon lysis of the red cell, the new merozoites infect additional red cells. Paroxysmal fever, chills, and rigors characteristic of malaria occur when the merozoites are released into the blood. As discussed later, release of merozoites induces the host cells to produce cytokines such as TNF that cause fever. The periodicity of such paroxysms (every 48-72 hours) varies with