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SECTION 18 Protozoal Infections

serum levels of theophylline should be monitored closely in this situation. Tinidazole This nitroimidazole is effective for the treatment of amebiasis, giardiasis, and trichomoniasis. Like metronidazole, tini dazole must undergo reductive activation by the parasite’s metabolic system before it can act on protozoal targets. Tinidazole inhibits the synthesis of new DNA in the parasite and causes degradation of exist ing DNA. The reduced free-radical derivatives alkylate DNA, with consequent cytotoxic damage to the parasite. This damage appears to be produced by short-lived reduction intermediates, resulting in helix destabilization and strain breakage of DNA. The mechanism of action and side effects of tinidazole are similar to those of metronidazole, but adverse events appear to be less frequent and severe with tinidazole. In addition, the significantly longer half-life of tinidazole (>12 h) offers potential cure with a single dose. Tribendimidine Tribendimidine, a diamidine derivative of ami nophenylamidine amidantel, is a cholinergic agonist that is selective for the nicotinic acetylcholine receptors of nematode muscle. This novel agent has a broad spectrum of activity against a wide variety of helminths and is highly effective against food-borne trematodes, with a similar cure rate to praziquantel. Clinical trials have demonstrated efficacy of a single dose alone or in combination with other helminthics against soil-transmitted helminth infections. The drug is an L-type nicotinic acetylcholine receptor agonist and exhibits the same method of action as levamisole and pyrantel; therefore, it may not be effective in regions where resistance to these agents is widespread. It is not avail able in the United States. Triclabendazole In contrast to other benzimidazoles, the antihel minthic activity of triclabendazole is highly specific for Fasciola and Paragonimus species, with little activity against nematodes, cestodes, and other trematodes. Triclabendazole is effective against all stages of Fasciola species. The active sulfoxide metabolite of triclabendazole binds to fluke tubulin by assuming a unique nonplanar configuration and disrupts microtubule-based processes. Resistance to triclaben dazole in veterinary use has been reported in Australia and Europe; however, no resistance has been documented in humans. Triclabendazole is rapidly absorbed after oral ingestion; administra tion with food enhances its absorption and shortens the elimination half-life of the active metabolite. Both the sulfoxide and the sulfone metabolites are highly protein bound (>99%). Treatment with tricla bendazole is typically given in one or two doses. No clinical data are available regarding dose adjustment in renal or hepatic insufficiency; however, given the short course of therapy and extensive hepatic metabolism of triclabendazole, dose adjustment is unlikely to be neces sary. No information exists on drug interactions. Trimethoprim-Sulfamethoxazole See Table 229-1 and Chap.

149. ■ ■FURTHER READING Dziduch K et al: The current directions of searching for antiparasitic drugs. Molecules 27:1534, 2022. Fehintola FA et al: Drug interactions in the treatment and chemo prophylaxis of malaria in HIV infected individuals in sub-Saharan Africa. Curr Drug Metab 12:51, 2011. Keiser J, Häberli C: Evaluation of commercially available anthelmin thics in laboratory models of human intestinal nematode infections. ACS Infect Dis 7:1177, 2021. Keiser J et al: Antiparasitic drugs for paediatrics: Systematic review, formulations, pharmacokinetics, safety, efficacy, and implications for control. Parasitology 138:1620, 2011. Kelesidis T, Falagas ME: Substandard/counterfeit antimicrobial drugs. Clin Microbiol Rev 28:443, 2015. Pink R et al: Opportunities and challenges in antiparasitic drug discovery. Nat Rev Drug Discov 4:727, 2005.

Section 18 Protozoal Infections Rosa M. Andrade, Sharon L. Reed

Amebiasis and Infection

with Free-Living

Amebae AMEBIASIS ■ ■DEFINITION Amebiasis is an infection caused by Entamoeba histolytica, an intestinal protozoan. Its spectrum of clinical syndromes ranges from asymptom atic colonization (90% of cases) to invasive amebiasis, which accounts for 10% of affected individuals. Invasive amebiasis frequently presents as intestinal colitis (dysentery or diarrhea) or as extraintestinal ame biasis, in which abscesses of the liver are more commonly found than involvement of the lungs or brain. ■ ■LIFE CYCLE AND TRANSMISSION E. histolytica is acquired by ingestion of viable cysts from fecally con taminated water, food, or hands (Fig. 230-1). Food-borne exposure is the most prevalent form of transmission. It occurs when food handlers are shedding cysts or food is being grown with feces-contaminated soil, fertilizer, or water. Less common means of transmission include oral and anal sexual practices and, in rare instances, direct rectal inoculation through colonic irrigation devices. Motile trophozoites are released from cysts in the small intestine and, in most patients, remain as harmless commensals in the large bowel. After encystation, infec tious cysts are shed in the stool and can survive for several weeks in a moist environment. In some patients, the trophozoites invade either the bowel mucosa, causing symptomatic colitis, or the bloodstream, causing distant abscesses of the liver, lungs, or brain. The trophozoites may not encyst in patients with active dysentery, and motile hematoph agous trophozoites are frequently present in fresh stools. Trophozoites are rapidly killed by exposure to air or stomach acid and therefore can not transmit infection. CHAPTER 230 Amebiasis and Infection with Free-Living Amebae

■ ■EPIDEMIOLOGY E. histolytica infection typically affects underdeveloped tropical regions with poor sanitation systems and hygiene, occurring often in children <5 years of age. This infection is widespread in the Indian subconti nent and Africa, parts of East Asia (Thailand), and Central and South America (Mexico and Colombia). According to the Global Burden of Disease 2016 study, amebiasis accounts for 26,748 all-age deaths, including 4567 children <5 years old. In contrast, returning travelers, recent immigrants, men who have sex with men (MSM), military personnel, and inmates of institutions are the main groups at risk for amebiasis in developed countries. The GeoSentinel Surveillance Network, which encompasses information from tropical medicine clinics on six continents, showed that, among long-term travelers (trip duration, >6 months), diarrhea due to E. histo lytica was among the most common diagnoses. In countries like Japan and Spain, amebiasis is emerging as a sexually transmitted disease, first reported in HIV-positive MSM. However, in Japan, E. histolytica infec tions, symptomatic or asymptomatic, seem to be steadily

spreading among non-HIV men and women. Worldwide, E. histolytica is the second most common cause of death related to parasitic infection (after malaria). Invasive colitis and liver abscesses are tenfold more common among men than among women; this difference has been attributed to a disparity in complementmediated killing and effects of testosterone on the secretion of inter feron γ. The wide spectrum of clinical disease caused by Entamoeba is due in part to the differences between the two major infecting species,

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