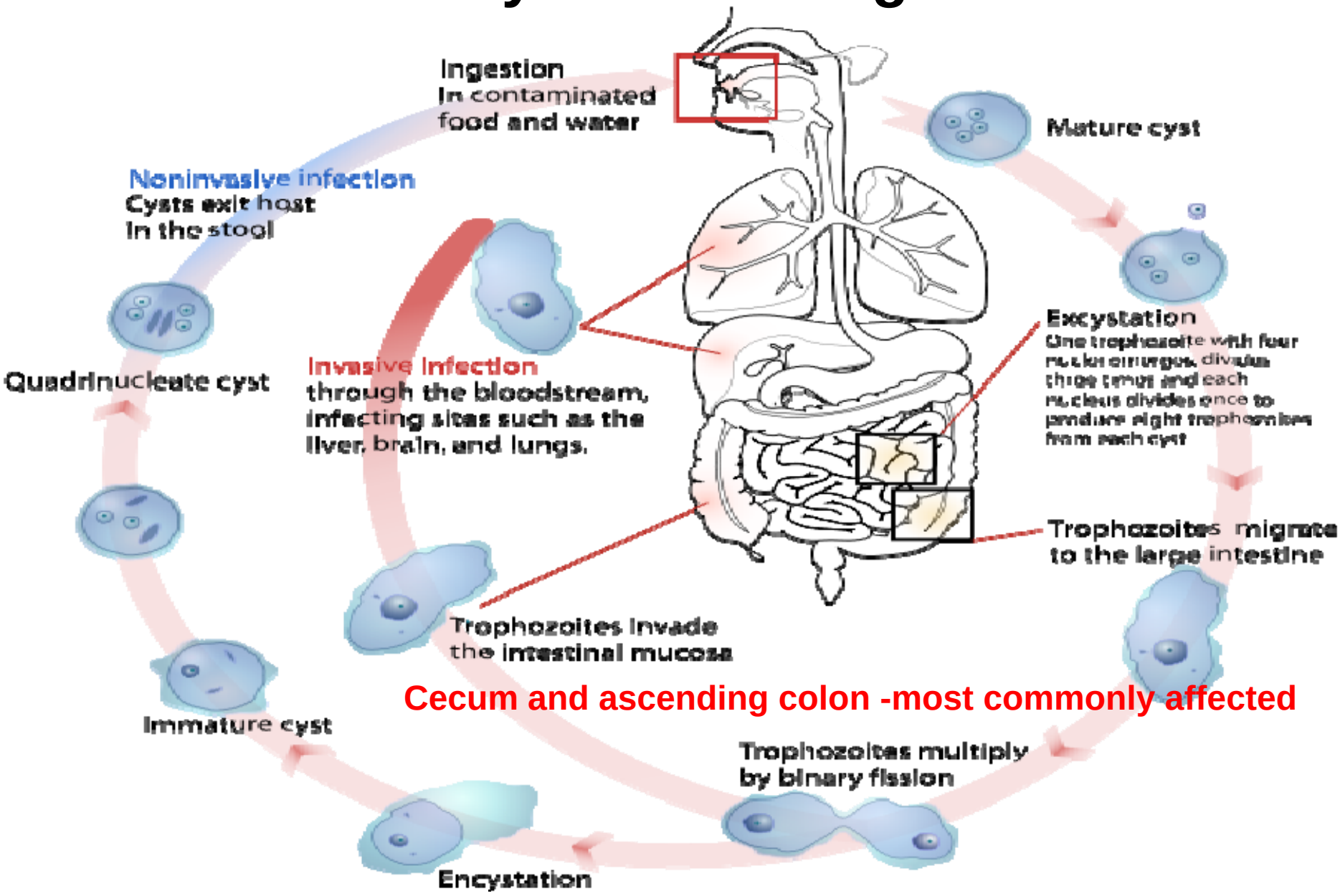
Protozoa

ENTAMOEBA HISTOLYTICA

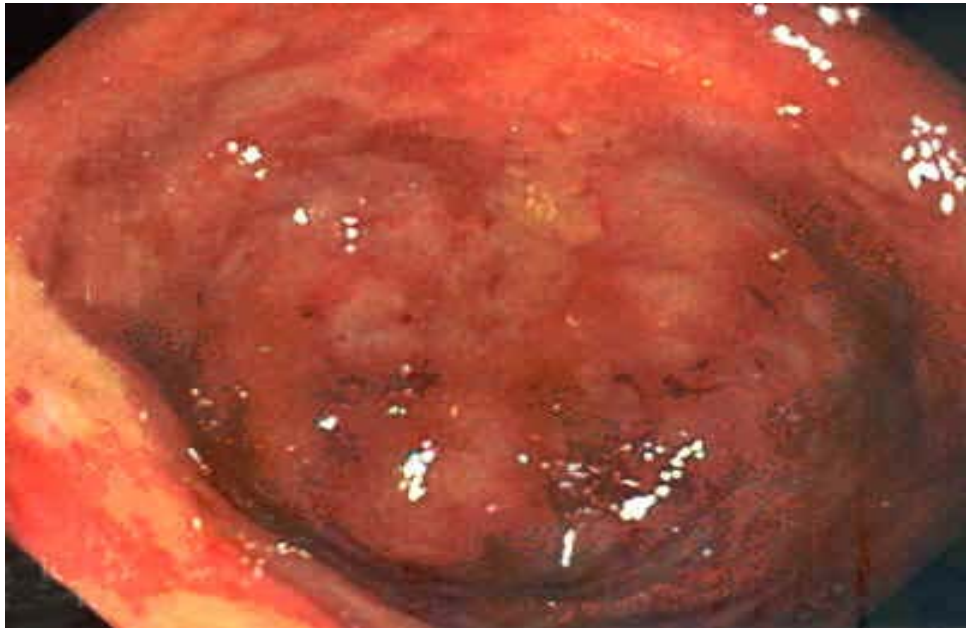
- Global distribution
- Most morbidity and mortality- Central and South America, Africa, and the Indian subcontinent

Life cycle -two-stage



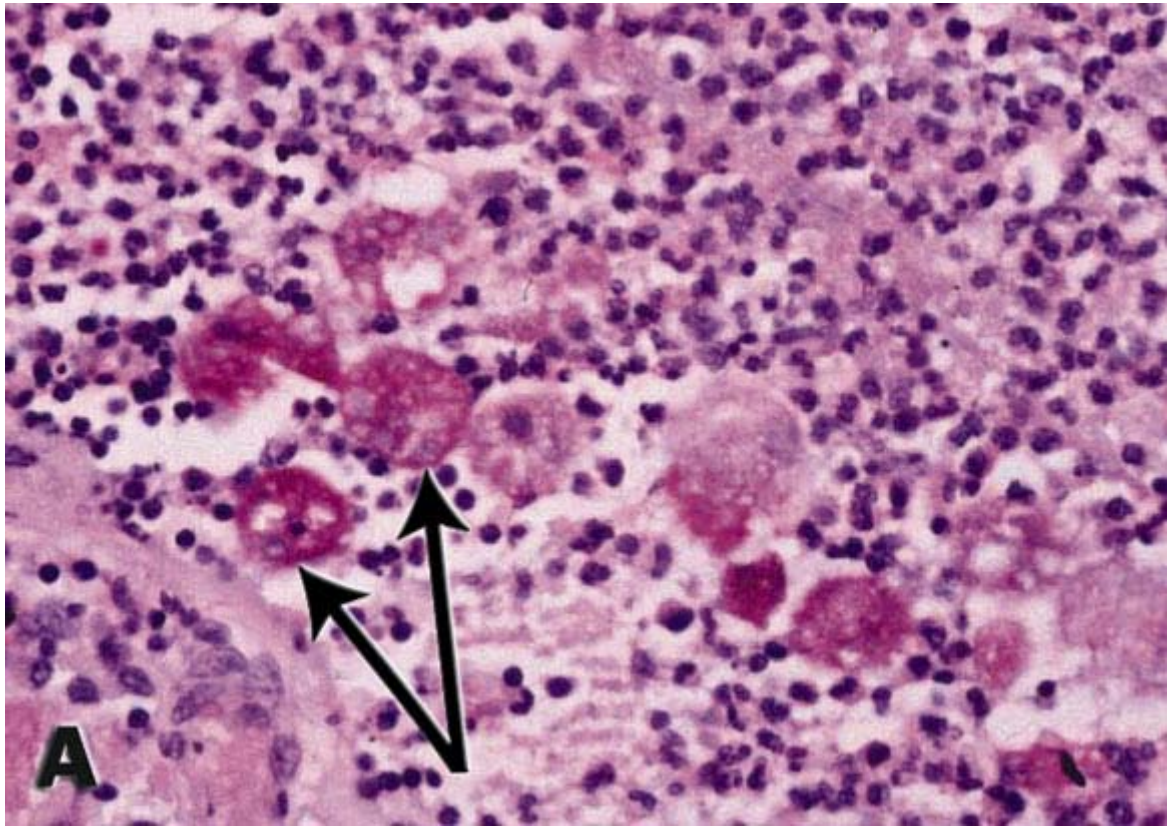
Gross examination

- Cecum and ascending colon -most commonly affected
- Mucosal thickening to multiple punctate ulcers with normal intervening tissue to frank necrosis



Histopathology

- The downward invasion of amebic trophozoites often is halted at the level of the muscularis mucosa.
- Subsequent lateral spread of amebae undermines the overlying epithelium, resulting in the **clean-based, flask-shaped ulcers**
- Early in infection, an influx of neutrophils is typical, but in well-established ulcers, few inflammatory cells are seen.
- Organisms may be seen ingesting red blood cells (erythrophagocytosis)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CLINICAL FEATURES

- 90% of infected persons remain asymptomatic
- 10% of infections result in invasive amebiasis characterized by dysentery (amebic colitis) or, in a minority of cases, extraintestinal disease (most commonly amebic liver abscess

Risk of invasive amebiasis

- Immigrants from or travelers to endemic regions
- Male homosexuals
- Institutionalized persons
- Malnourished patients,
- Infants
- Elderly
- Pregnant women
- Glucocorticoids

Comparison of Amebic Colitis and Invasive Bacterial Dysentery

FEATURE	AMEBIC COLITIS	DYSENTERY* BACTERIAL
Travel to or from an endemic area	Yes	Sometimes
Usual duration of symptoms	>7 days	2-7 days
Diarrhea	100%	100%
Fecal occult blood	94-100%	40%
Abdominal pain	12-80%	~50%
Weight loss	Common	Unusual
Fever >38?C	Minority	Majority

Complication

- Acute necrotizing colitis with toxic megacolon-most feared complication-0.5% of cases
- Enterocutaneous, rectovaginal, and enterovesicular fistulas -Unusual complication
- Ameboma -Unusual complication
- Extraintestinal sites

Complication

- Extraintestinal sites of infection are involved and typically result either from direct extension of liver abscesses (e.g., amebic pericarditis or lung abscess) or from hematogenous spread of disease (e.g., brain abscess)

DIAGNOSIS

- **Stool examination for ova and parasites-**

  The sensitivity - at best 60%
- **Colonoscopy with biopsy** -Gold standard

- **Stool ELISA (to detect the *E. histolytica* adherence lectin)**
- The most specific clinically available test
- Specificity- greater than 90%,
- Sensitivity- greater than 85%
- It also may be possible to use this antigen detection test to diagnose amebic liver abscess, because before treatment is initiated, amebic lectin antigen can be detected in the serum of greater than 90% of patients who have amebic liver abscess.

- **Noninvasive methods to accurately differentiate *E. histolytica* from *E. dispar-*** include stool culture with isoenzyme analysis, serum amebic-antibody titers, PCR, and an enzyme-linked immunosorbent assay (ELISA)

TREATMENT

- Because approximately 10% of asymptomatic cyst passers develop invasive amebiasis, *E. histolytica* carriers should be treated
- For noninvasive disease, treatment with a luminal agent alone is adequate

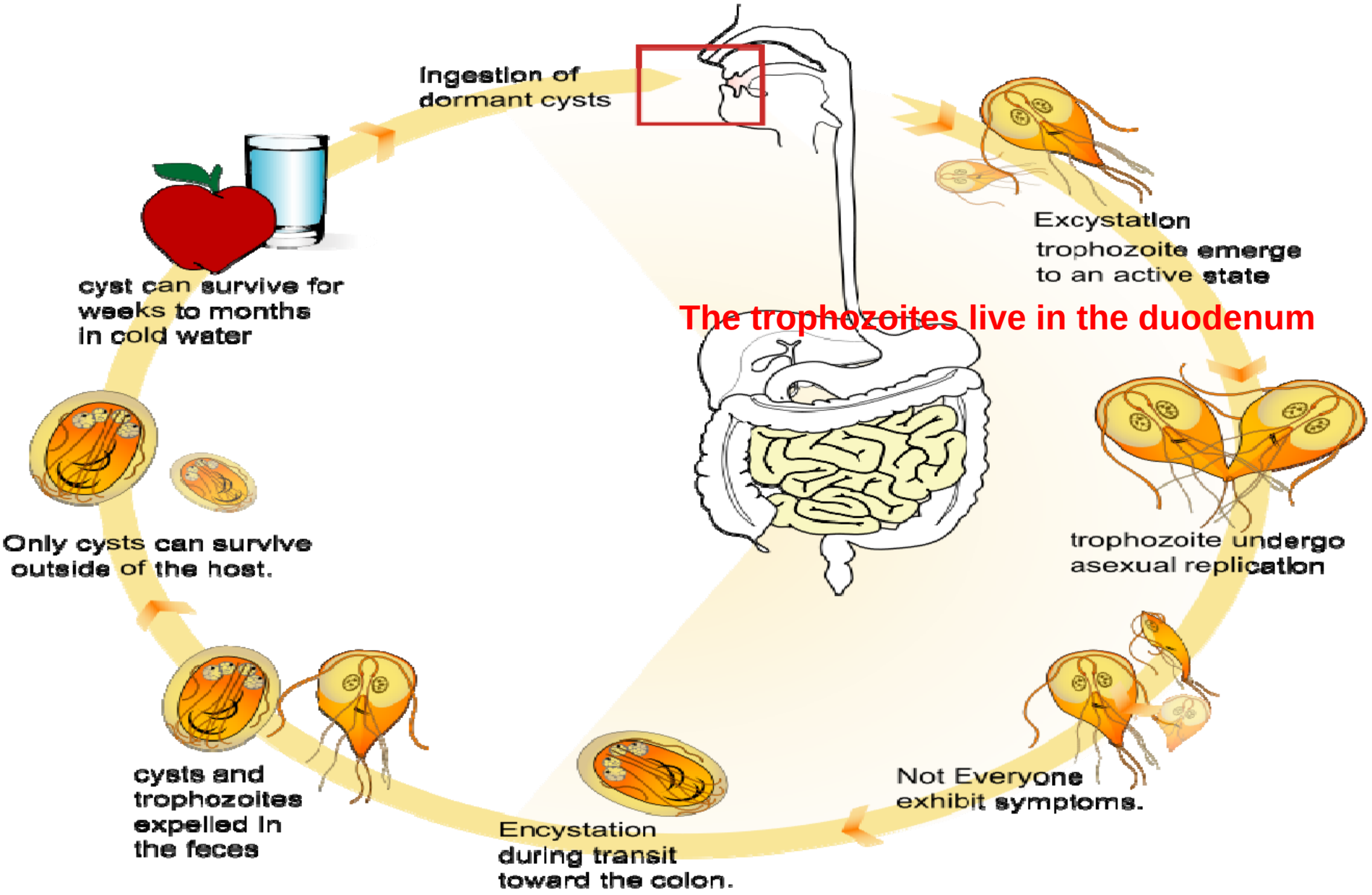
- Amebic colitis –oral nitroimidazole followed by a luminal agent
- Oral nitroimidazole (either metronidazole [500-750 mg three times daily for 10 days] or tinidazole [2 grams once daily for three to five days]) to eliminate invasive trophozoites.
- Metronidazole and tinidazole are believed to be less effective against organisms in the colonic lumen, and subsequent treatment with a luminal agent such as paromomycin is recommended to prevent recurrent disease
- Amebic liver abscess - Metronidazole (750 mg three times a day for 10 days) followed by a luminal agent

- Despite conflicting reports on the safety of the nitroimidazoles for the developing fetus during pregnancy, women with severe disease during pregnancy should probably be treated without delay.

GIARDIA INTESTINALIS (also called *G. lamblia* and *G. duodenalis*)

- Giardiasis occurs in both endemic and epidemic forms via water-borne, food-borne, and person-to-person transmission.
- Worldwide, *Giardia* infects infants more commonly than adults, and in highly endemic regions, essentially all children are infected by two to three years of age
- In the developing world, it is likely that recurrent infantile diarrhea from giardiasis contributes significantly to malnutrition

Life cycle of *Giardia intestinalis*



PATHOGENESIS

- *Giardia* causes malabsorptive diarrhea by an unknown mechanism.
- There is no evidence that trophozoites invade the mucosa, but electron microscopy has shown they damage the mucosal brush border.
- On biopsy, pathologic changes range from an entirely normal-appearing duodenal mucosa (except for adherent trophozoites), as was found in more than 96% of biopsy specimens in one large study, to severe villus atrophy with a mononuclear cell infiltrate that resembles celiac sprue
- The severity of diarrhea appears to correlate with the severity of the pathologic change

CLINICAL FEATURES

- Asymptomatic infection
- Severe, chronic diarrhea with malabsorption
- Children younger than two years and patients with hypogammaglobulinemia, are more likely to develop serious disease
- Not more common, or severe, or resistant to treatment in patients with AIDS

DIAGNOSIS

- **Stool exam** –

  Iodine-stained, wet stool preparations and modified-trichrome-stained permanent smears
- Because cysts and trophozoites are present only intermittently in the stool, however, the sensitivity is only about 50%,

Endoscopic methods

- **String test** -direct sampling of duodenal contents, such as duodenal aspiration sensitivity can be improved to approximately 80%.
- **Small intestinal biopsy-** identification of trophozoites requires careful examination

TREATMENT

- Metronidazole (250 mg orally three times a day for five days) is the preferred treatment for giardiasis
- Nitazoxanide appears to be at least as effective as metronidazole
- The recommended dosage in children is 100 mg (ages 12 to 47 months) or 200 mg (age older than four years) twice daily, and in adults is 500 mg twice daily for three days

- Alternative regimens –
  Tinidazole
  Quinacrine
  Furazolidone
  Paromomycin

- Because paromomycin is not absorbed - especially useful for treatment of giardiasis during pregnancy

DIENTAMOEBA FRAGILIS

- The organism initially was classified as an ameba, but it is more closely related to the flagellates
- Mode of its transmission remains unknown
- Diarrhea, abdominal pain, nausea, weight loss, anorexia, flatus, and malaise

Treatment

- Iodoquinol
- Metronidazole
- Paromomycin

CRYPTOSPORIDIUM SPECIES

- Tiny intracellular protozoan

CLINICAL FEATURES

Immunocompetent hosts –

Following a one-week incubation period (range, 2 to 14 days), a watery, relatively noninflammatory diarrheal illness typically lasts for 10 to 14 days

In immunocompromised patients –

Diarrheal illness with cryptosporidial infection can be cholera-like, protracted (often for the duration of severe immune compromise), and fatal

DIAGNOSIS

- Most important element in diagnosis is to consider it in patients with diarrhea lasting longer than five to seven days and to request the appropriate special fecal studies.
- Cryptosporidial oocysts have been detected with a modified acid-fast stain of the stool

- ELISA or direct fluorescence antibody tests of the stool have replaced microscopy as the diagnostic test of choice

TREATMENT

- Nitazoxanide -only known drug with consistent efficacy for treating cryptosporidiosis in immunocompetent patients
- The recommended dosage in children is 100 mg (ages 12 to 47 months) or 200 mg (age greater than 4 years) twice daily and in adults is 500 mg twice daily for three days.

- Failure is common in immunocompromised patients
- Additional treatment options in immunocompromised patients not responsive to nitazoxanide include the nonabsorbable aminoglycoside paromomycin or paromomycin in combination with azithromycin
- Most important in treating HIV-infected patients with cryptosporidiosis is highly active antiretroviral therapy (HAART)

CYCLOSPORA CAYETANENSIS

- Clinical presentation – similar to *Cryptosporidium*
- More severe generalized fatigue and malaise
- *Cyclospora* diarrhea typically lasts for one to three weeks and may be associated with significant weight loss.
- Also as seen with cryptosporidiosis, protracted diarrhea and acalculous cholecystitis can occur with *Cyclospora* infection in HIV-infected persons

DIAGNOSIS

- Acid-fast stain
- Blue-green autofluorescence when examined under fluorescence microscopy

TREATMENT

- *Cyclospora* infections are readily treatable, even in immunocompromised patients
- Trimethoprim-sulfamethoxazole at a dosage of 160/800 mg twice daily for one week
- Ciprofloxacin /Nitazoxanide -alternative

ISOSPORA BELLI

- Similar to *Cryptosporidium* and *Cyclospora*

DIAGNOSIS

- Associated with peripheral eosinophilia and with Charcot-Leyden crystals in the stool
- Acid-fast staining

TREATMENT

- *Isospora* infections are readily treated with trimethoprim-sulfamethoxazole
- Ciprofloxacin- Alternatives

MICROSPORIDIA

- *Enterocytozoon bieneusi, Encephalitozoon* (old *Septata*) *intestinalis*

PATHOLOGY

- Intestinal pathology is marked by villus atrophy, crypt hyperplasia, and mild inflammation in the lamina propria

CLINICAL FEATURES

- Self-limited diarrhea in travelers or health professionals
- Immunocompromised patients- chronic watery, relatively noninflammatory diarrhea and weight loss
- Acalculous cholecystitis or even sclerosing cholangitis
- *E. intestinalis* also can cause colitis and disseminate especially to the kidneys or less often to sinuses, bronchi, conjunctivae, or prostate

DIAGNOSIS

- Modified trichrome stain
- Screening samples with fluorescent chitin stains such as Fungi-Fluor chitin stain

TREATMENT

- *E. bieneusi* -oral fumagillin
- *E. intestinalis* infections -albendazole
- HAART