 lots of Protozoa

Edward Mitre, MD
Bethesda, MD

Protozoa - Extraintestinal

Apicomplexa
- Plasmodium
- Babesia (Toxoplasma)

Flagellates
- Leishmania
- Trypanosomes (Trichomonas)

Amoebae
- Naegleria
- Acanthamoeba
- Balamuthia

Protozoa - Intestinal

Apicomplexa
- Cryptosporidium
- Cystoisospora

Flagellates
- Giardia
- Dientamoeba

Amoebae
- Entamoeba

Ciliates
- Balantidium

Not Protozoa

Kingdom Fungi: Microsporidiosis agents
Kingdom Chromista: Blastocystis

P. knowlesi

diagnosed in over 120 people in Malaysian Borneo.


morphologically similar to P. malariae

usually a parasite of long-tailed macaques

increasingly recognized in Myanmar, Phillipines, Indonesia, and Thailand.

causes high parasitemia

highly morbid and can be lethal

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MALARIA
one of the most important pathogens in the history of the world

In 1775 the Continental Congress bought quinine for George Washington's troops

MALARIA EPIDEMIOLOGY

In non-immune patients, falciparum malaria is a medical emergency!!

→ most studies find it to be the #1 cause of fever in a returned traveler

→ infected individuals can rapidly progress from appearing well to being critically ill

Family Feud: The Three Most Common Causes of Fever in a Returned Traveler.

1. Malaria
2. Malaria
3. Malaria
Some helpful heuristics—make sure patient doesn’t have:

- Fever and freshwater contact
- Fever and unpasteurized milk
- Fever and undercooked meat
- Fever and raw vegetables
- Fever and untreated water
- Fever and wild dog bite
- Fever and abdominal pain
- Fever and headache
- Fever and diarrhea
- Fever and cough
- Fever and dysuria

Characteristics of human malaria species:

<table>
<thead>
<tr>
<th></th>
<th>P. falciparum</th>
<th>P. knowlesi</th>
<th>P. vivax</th>
<th>P. ovale</th>
<th>P. malariae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation</td>
<td>8 - 25 d</td>
<td>prob 8-25 d</td>
<td>~ 2 wks</td>
<td>~ 2 wks</td>
<td>~ 3-4 wks</td>
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<tr>
<td>Hypnozoite</td>
<td>no</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
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<tr>
<td>RBC age</td>
<td>any</td>
<td>any</td>
<td>young</td>
<td>young</td>
<td>old</td>
</tr>
<tr>
<td>Parasitemia</td>
<td>high</td>
<td>high</td>
<td>&lt; 2%</td>
<td>&lt; 2%</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Morbidity</td>
<td>high</td>
<td>high</td>
<td>high</td>
<td>moderate</td>
<td>low</td>
</tr>
<tr>
<td>Mortality</td>
<td>high</td>
<td>moderate</td>
<td>low</td>
<td>low</td>
<td>low</td>
</tr>
</tbody>
</table>

Possible evolutionary defenses against malaria:

- **Duffy antigen negative** (*P. vivax* uses Duffy Ag to enter RBCs)
- **Sickle cell trait** (increases survival during *P. falciparum* infection, perhaps by selective sickling of infected RBCs)
- **Glucose-6-phosphate dehydrogenase deficiency** (malaria parasites grow poorly in G6PD deficient RBCs, perhaps b/c this results in an overall increase in reactive oxygen species in RBCs)

Uncomplicated (mild) malaria:

- Symptoms: fevers, chills, headache, fatigue
  - *NOTE*: abdominal pain presenting symptom in 20%

- Periodicity of fevers not common when patients seen acutely

- Labs: Thrombocytopenia in 50%
  - mild anemia in 30%
  - typically no leukocytosis
  - may see evidence of hemolysis with mild increase T bill and LDH
Complicated (severe) malaria

- Cerebral malaria (altered mental status, seizures)
- Respiratory distress/pulmonary edema
- Severe anemia (Hct <15% in children, <20% in adults)
- Renal failure
- Hypoglycemia
- Shock (MAP < 80 mm Hg or capillary refill > 3 seconds)
- Acidosis (often lactic acidosis)
- Jaundice (total bilirubin > 3 mg/dL)
- Bleeding disorder (spontaneous bleeding or evidence of DIC)

These complications primarily occur with *Plasmodium falciparum*, usually when parasitemia >2%.

NOTE: in the absence of end organ damage, parasitemia >10% is often used as the cut-off to treat for severe malaria.

P. vivax or ovale

- Both have
  - intracellular Schüffner's dots
  - enlarged infected cells

P. ovale

- elongated or oval
- 6-12 merozoites (vs 12-24 for vivax)

P. malariae

- band form
  (also seen in *P. knowlesi*)

P. falciparum

Banana shaped gametocyte

Diagnosis

- antigen capture
- sensitivity 95% for *P. falciparum* (about 85% for other species)

Malaria Chemoprophylaxis (note: no vac for travelers)

**CENTRAL AMERICA and MIDDLE EAST**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pre-Exposure</th>
<th>During</th>
<th>Post-Travel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine 500mg tabs</td>
<td>1 tab/wk x 2 wks</td>
<td>1 tab/wk</td>
<td>4 weeks</td>
</tr>
<tr>
<td><strong>EVERYWHERE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atovaquone/proguanil</td>
<td>1 tab daily x 2 d</td>
<td>1 daily</td>
<td>7 days</td>
</tr>
<tr>
<td>250/100mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline 100mg tabs</td>
<td>none</td>
<td>1 daily</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Tafenoquine* 10mg tabs</td>
<td>2 tab daily x 3 d</td>
<td>2 tab/wk</td>
<td>2 tab after 1 wk</td>
</tr>
<tr>
<td>Mefloquine (not SE Asia)**</td>
<td>1 tab/wk x 2-3 wks</td>
<td>1 tab/wk</td>
<td>4 weeks</td>
</tr>
<tr>
<td>250mg tabs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Tafenoquine can precipitate severe hemolytic anemia in individuals that are G6PD deficient
** FDA black box warning in 2013 that mefloquine can cause neurologic symptoms, hallucinations, and feelings of anxiety, mistrust, and depression. Can also cause QT prolongation. Thus, many U.S. practitioners now reserve mefloquine for pregnant travelers to areas with chloroquine resistance.

Question 2: A 33-year-old woman is traveling to Uganda to do field studies in anthropology. She is two months pregnant. Which of the following do you prescribe for malaria prophylaxis?

A. Doxycycline
B. Chloroquine
C. Mefloquine
D. Atovaquone/proguanil
E. No prophylaxis
Treatment of *P. falciparum*

**Uncomplicated** (no organ dysfunction, low parasitemia, able to take po)

- If chloroquine sensitive area → chloroquine
- If chloroquine resistant area
  - → artemether/lumefantrine (Coartem) x 3 days
  - → atovaquone/proguanil (Malarone) x 3 days
  - → 2nd line: quinine x 3 days + doxycycline x 7 days

**Severe**

- IV artesunate → FDA approved since May 2020
  (CDC malaria hotline: 770-488-7788 or -7100)

(Note: IV quinidine unavailable in U.S. since 3/2019)

**NOTE:** there is increasing artemisinin resistance in SE Asia but it has not yet emerged in Africa

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Treatment of *P. vivax*

- chloroquine x 3 days and then...
  - primquine – weight based dosing and duration as determined by G6PD activity
    (usually 0.5 mg/kg primquine base x 14 days if normal G6PD activity, if G6PD activity < 30% then can treat with 0.75mg/kg weekly for 8 weeks)
  - or
  - tafenoquine (two 150 mg tabs) FDA-approved 7/2018!

- Need to check G6PD status before administering primquine OR tafenoquine as both can cause severe hemolysis in patients with G6PD deficiency

- Primquine requires cytochrome P450 2D6 to be effective. Therefore, clinical failure to cure *P. vivax* can be due to low host levels of CYP450-2D6.

*Suggestions for all ID practitioners*

1) Make sure the facility where one works has the means to rapidly test for malaria

2) Ensure that hospital pharmacy has access to appropriate medications for treatment of malaria

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**Protozoa**

**Protozoa - Extraintestinal**

- Apicomplexa: Plasmodium, Babesia (Toxoplasma)
- Flagellates: Leishmania, Trypanosomes (Trichomonas)
- Amoebae: Naegleria, Acanthamoeba, Balamuthia

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- Kingdom Chromista: Blastocystis

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**Babesia**

**Transmission**

- Nodules ticks in Northeast and upper midwest → co-infection with Lyme and Anaplasma
- Transmission approx. 1/20k in NE if unscreened...Ab screening tests approved by FDA in 2018

**Symptoms:** fever, headache, chills, myalgias

less common: nausea, dry cough, neck stiffness, vomiting, diarrhea, arthralgias

→ severe disease: in HIV, sepsis

**Labs:** anemia, thrombocytopenia, mild increase LFTs, normal/low/high WBC

**Diagnosis:** small ring forms in RBCs, PCR, Ab

**Treatment:** azithromycin + atovaquone

(clindamycin + quinine is alternative)

→ Exchange transfusion for severe disease

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**Leishmaniasis**

- obligate intracellular protozoan infection
- transmitted by sand flies (noiseless, active in evenings)

- *Lutzomyia* New world leishmaniasis
- *Phlebotomus* Old world leishmaniasis
Leishmania life cycle – Two stages

Promastigote
- extracellular, in sand fly
- 2μm wide x 20μm long
- + flagella
- large central nucleus
- band shaped kinetoplast

Amastigote
- Intracellular (macrophages)
- Round or oval
- Wright-Giemsa:
  - dark-purple nucleus
  - small rod shaped kinetoplast

Leishmania taxonomy and disease simplified

NEW WORLD
- L. mexicana complex X
- L. braziliensis X
- L. infantum chagasi X

OLD WORLD
- L. tropica X
- L. major X
- L. donovani X
- L. Infantum chagasi X

*note: L. braziliensis is in the Viannia subgenus. L. V. guyanensis and L. V. panamensis also cause mucosal disease. L. peruviana DOES NOT

Cutaneous Leishmaniasis – Clinical Presentation

- papule → nodule → ulcerative lesion → atrophic scar
  - ulcerative lesion may have:
    - induration,
    - scaliness
    - central depression
    - raised border
- takes weeks to months to develop
- usually painless, unless superinfected
- most lesions will eventually resolve on their own

Question 3: A 42 yo man from Bolivia presents with nasal stuffiness and is found to have nasal septal perforation. Biopsy demonstrates intracellular amastigotes consistent with Leishmania.

Which is the most likely species?

A. L. mexicana
B. L. braziliensis
C. L. peruviana
D. L. infantum chagasi
E. L. major

Here are some very clear amastigotes → intracellular organisms with nucleus and kinetoplast

http://www.dpd.cdc.gov/dpdx/HTML/Leishmaniasis.htm

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Cutaneous Leishmaniasis – Diagnosis
Definitive diagnosis is very helpful because
1. Allows you to rule out other possibilities
2. May help in deciding whether and how to treat

Diagnostic Tools (edge of ulcer skin: scraping, aspirate, punch)
- Touch prep with examination under oil looking for amastigotes
- Culture on triple N media (may take weeks to grow)
  - (Nicolle's modification of Novy and MacNeal's medium – biphasic)
- Histology
- PCR

Amastigotes in tissue sample
64 – Lots of Protozoa
Speaker: Edward Mitre, MD

**Cutaneous Leishmaniasis – Treatment Recommendations**

- Treat **systemically** if *L. (V.) braziliensis*, *guyanensis*, *panamensis*
- If not, ok to observe if there are:
  - few lesions, they are < 5 cm, not on face/fingers/toes/genitals, normal host, no subcutaneous nodules

**Treatment Options**

- **Local:** heat with radiotherapy (FDA approved), cryotherapy, intralesional therapy
- **Oral:** miltefosine for certain species (2014 FDA approved)
- **Ketoconazole, Fluconazole** (off-label)
- **IV:** liposomal amphotericin B (off-label)
  (June 2021: pentavalent antimony aka stibogluconate no longer available from CDC on IND)

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**Mucosal leishmaniasis**

*Leishmania* (Viannia) *braziliensis*

dissemination to nasal mucosa

- also *L. (V.) guyanensis* and *L. (V.) panamensis*
- Slow, progressive, destructive
- Can occur months or years following cutaneous ulcer

**Treatment:**

- IV liposomal amphotericin (off-label)
- IV antimony (not available)
- Oral miltefosine (FDA approved for *L. braziliensis*)

Note: infection of *Leishmania* organisms with *Leishmaniavirus*, a double-stranded RNA virus, may be associated with increased risk of mucocutaneous disease

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**Visceral Leishmaniasis**

*L. donovani* (South Asia, East Africa)

*L. infantum chagasi* (Middle East, Central Asia, Mediterranean, Central and S. America)

- Amastigotes in macrophages go to local LNs then hematogenously to liver, spleen, bone marrow
- A persistent disease that can reactivate
  - TNF blockade, HIV CD4 < 200
- Weeks/months: fever, chills, fatigue, hepatosplenomegaly
- Pancytopenia & hypergamma globulinemia

**Diagnosis:** intracellular amastigotes in bone marrow or splenic aspirate

**Antibody to rK39 recombinant Ag (dipstick test)**

**Treatment:** liposomal ampho B (FDA approved)

miltefosine (oral) FDA approved for *L. donovani*

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**African Trypanosomiasis**

African Trypanosomiasis – Lab findings

- Non-specific lab findings
  - anemia
  - elevated IgM
  - hypergamma globulinemia

**Diagnostic lab findings**

- Detection of parasite in lymph node, circulating blood, or CSF

  - qPCR of lymph node using nested PCR

  - V. sensitive (94-98%), but poor specificity

  - can get false +s in pts with Schisto, filaria, toxo, malaria

---

**Question 4:** A 41 yo woman presented to a local emergency department with a one day history of fever associated with swelling and redness in her groin four days after returning from safari in Tanzania. Peripheral blood smear is obtained.

What is the most likely diagnosis?

A. *Leishmania* donovani
B. *Plasmodium vivax*
C. *Trypanosoma brucei*
D. *Wuchereria bancrofti*
E. *Leptospira interrogans*

---

**African Trypanosomiasis**

- Vector = tse tse fly (Glossina sp)

  - *Trypanosoma brucei gambiense* (W. Africa)
    - humans as reservoirs
    - progression over many months

  - *Trypanosoma brucei rhodesiense* (E. Africa)
    - cattle and game park animals as reservoirs
    - progression over weeks

**DISEASE**

- within 5 days: chancre at Tse Tse fly bite
- regional lymphadenopathy
- for weeks: fever, hepatosplenomegaly, lymphadenopathy, faint rash, headache
- late: mental status changes, terminal somnolent state

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Q. Why are Trypanosoma brucei infections associated with persistently elevated IgM levels?

A. because they keep changing their outer surface protein

- T. brucei contains as many as 1000 genes encoding different VSGs (VSG = variant surface glycoprotein)
- each trypanosome expresses one, and only one, VSG at a time
- individual parasites can spontaneously switch the VSG they express

African Trypanosomes – The Lady Gaga of the Microbial World

Chagas disease

- transmitted by Trypanosoma cruzi (also blood transfusion and congenitally)
- vector: reduvid (triatomine) bugs
- reservoirs: opossums, rats, armadillos, raccoons, dogs, cats

Chagas – Clinical Disease

Acute (starts 1 week after infection, can persist for 8 weeks)
- fever
  - local lymphadenopathy
  - unilateral, painless peri-orbital edema

Indeterminate stage
- serology positive, no evidence of disease

Chronic
- dilated cardiomyopathy, R-L dilated cardiomyopathy, R-L CHF, syncope, arrhythmia
- megaesophagus

West African (T. gambiense)

If < 6 yo or < 20 kg: lumbar puncture
- CSF < 5 WBC/ul → iv pentamidine
- CSF > 5 WBC/ul → iv eflornithine + nifurtimox

If adult: confusion, ataxia, anxiety, abnl speech, motor weakness, abnl gait?
- no suspicion of late disease → oral fexinidazole
- if suspicion of CNS disease → obtain lumbar puncture
- CSF < 100 cells/ul (non-severe 2nd stage) → oral fexinidazole
- CSF > 100 cells/ul → iv eflornithine + nifurtimox

East African (T. rhodesiense): Rx always guided by lumbar puncture

- CSF < 5 WBC/ul → suramin
- CSF > 5 WBC/ul → melarsoprol

Juy 16, 2021: Oral fexinidazole FDA approved for T. gambiense

Notes: 1) Melarsoprol associated with ~5% death rate due to reactive encephalopathy
      2) This is reduced by co-administration of corticosteroids.
Protozoa

Protozoa - Intestinal

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- Cryptosporidium
- Cyclospora

Flagellates
- Giardia
- Dientamoeba

Amoebae
- Entamoeba

Ciliates
- Balantidium

Chagas Diagnosis & Rx

Acute disease
- identification of parasites in blood

Chronic disease
- T. cruzi specific IgG antibodies in serum
- two antibody tests using different antigens
- different techniques recommended for dx (research: xenodiagnosis, hemoculture, PCR)

NOTE: U.S. blood supply screened for 1st time donors

Treatment

Benznidazole for 30 – 60 d; alternative: Nifurtimox (both FDA approved)

Benznidazole AEs: peripheral neuropathy, granulocytopenia, rash

Nifurtimox AEs: abdominal pain/vomiting, tremors, peripheral neuropathy

Always offer: acute infection, congenital, < 18 yo, reactivation disease

Usually offer: 19-50 years old and no advanced cardiac disease

Individual decision: > 50 years old and no advanced cardiac disease

Chagas in immunosuppressed patients

T. cruzi and AIDS

Primarily reactivation neurologic disease
- acute, diffuse, necrotic meningoencephalitis
- focal CNS lesions (similar to Toxo)**

T. cruzi and solid organ transplant

Recipient of infected organ:
- fevers, hepatosplenomegaly, myocarditis
- disease often does not occur until months after transplant

ALSO… reactivation myocarditis occurs in ~40% of patients that receive heart transplant because of Chagas cardiomyopathy

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Free-living amoebae

Naegleria fowleri
- warm freshwater exposure
- fulminating meningoencephalitis
- immunocompetent children/young adults

Acanthamoeba
- found in soil and water
- enter through olfactory neuroepithelium
- immunocompetent children/young adults
- chronic granulomatous keratitis (contact lens, LASIK)

Balamuthia mandrillaris
- likely enters through lower respiratory tract or broken skin
- subacute granulomatous encephalitis
- immunocompromised hosts
- fulminating meningoencephalitis
- chronic granulomatous keratitis

Outcome → often fatal (amphotericin B, azoles, pentamidine, others tried)

When to suspect an intestinal protozoan infection:

Patient has: Protracted watery diarrhea (weeks to months)

AND/OR:
- history of travel [domestic (esp. camping) or foreign]
- recreational water activities
- altered immunity (esp. HIV infection)
- exposure to group care (daycare)

Note: discussion will focus on intestinal protozoa as they occur in patients seen in the U.S. These are leading causes of diarrhea, morbidity, and mortality worldwide, especially in young children.
Intestinal Apicomplexa parasites

Cryptosporidium
- C. parvum: cows
- C. hominis: humans

Cyclospora cayetanensis
- all have worldwide distribution
- all transmitted by water or food contaminated with oocysts
- organisms invade enterocytes
- all cause watery diarrhea that can be prolonged & severe in immunocompromised

Cystoisospora belli
- no animal reservoirs known
- watery diarrhea
- may be associated with a peripheral eosinophilia
  (the ONLY intestinal protozoa that does this)

Intestinal Coccidia characteristics

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Size</th>
<th>Stain</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptosporidium</td>
<td>4 μm</td>
<td>acid-fast</td>
<td>nitazoxanide or paromomycin</td>
</tr>
<tr>
<td>Cyclospora</td>
<td>10 μm</td>
<td>acid-fast</td>
<td>TMP/SMX</td>
</tr>
<tr>
<td>Cystoisospora</td>
<td>20 μm</td>
<td>acid-fast</td>
<td>TMP/SMX</td>
</tr>
</tbody>
</table>

Molecular tests
- stool multiplex PCR detects cryptosporidium AND Cyclospora but NOT Cystoisospora
- stool Ag tests commercially available for cryptosporidium

Cryptosporidiosis Outbreaks — United States, 2009–2017

"The number of reported outbreaks has increased an average of approximately 13% per year."
Question 5: A 28 year old woman returns after studying mosquito breeding habits in Honduras for one year. She reports intermittent abdominal pain and diarrhea for several months. Stool ova and parasite exam is positive for the presence of a ciliated single cell organism.

What is the most likely diagnosis?

A. Balantidium coli
B. Entamoeba histolytica
C. Giardia lamblia
D. Dientamoeba fragilis
E. Endolimax nana

Entamoeba histolytica

- **Diagnosis**
  - Stool PCR (multiplex or single)
  - close to 100% sensitivity and specificity

- **Stool O/P**
  - only 50% sensitive for colitis and abscess
  - poor specificity (i.e., unable to differentiate E. histolytica from non-pathogenic E. dispar and the diarrhea-only causing E. moshkovskii
  (note: ingested RBCs suggestive of Eh, but not 100%)

- **Stool antigen testing** > 85% sensitive for intestinal disease

- **Serology**
  - helpful in amebic liver abscess (95% sensitive)
  - can be helpful (about 85% sensitive) in intestinal amebiasis

- **Treatment**
  - tinidazole or metronidazole followed by an agent such as paromomycin to eliminate intraluminal cysts

Entamoeba histolytica

- **Symptoms**
  - sharp abdominal pain
  - bloody diarrhea
  - flask-shaped ulcerations
  - onset can occur weeks to months after travel
  - ameboma
  - extraintestinal (liver, brain abscess) in young men

- **Diagnosis**
  - stool PCR
    - close to 100% sensitivity and specificity
  - stool O/P
    - only 50% sensitive for colitis and abscess
    - poor specificity because unable to differentiate E. histolytica from non-pathogenic E. dispar and the diarrhea-only causing E. moshkovskii
  - Stool antigen testing > 85% sensitive for intestinal disease

Giardia duodenalis

- **Flagellated protozoan**
  - fecal/oral via ingestion of cyst form in food/water
  - cyst is chlorine resistant
  - cysts from humans (beavers, muskrats)

- **Disease in U.S.**
  - most common parasitic infection in the U.S (20k cases reported/year, likely 2M)
  - U.S-acquired cases peak in the late summer/early fall
  - a leading cause of traveler’s diarrhea

- **Symptoms**
  - intermittent watery diarrhea weeks to months
  - foul smelling stools, flatulence, “sulfur burps”

- **Diagnosis**
  - stool antigen test
  - stool multiplex PCR

- **Treatment**
  - tinidazole (FDA approved)
  - metronidazole (off-label), nitazoxanide (FDA-approved), and albendazole (off-label)

Other intestinal protozoa

- **Non-pathogens**
  - amoebae
    - Entamoeba dispar
    - Chilomastix mesnili
    - Entamoeba hartmanni
    - Trichomonas hominis
    - Entamoeba coli
    - Endolimax nana
    - Iodamoeba bütschlii

- **Treat if symptomatic:** Dientamoeba fragilis (implicated in IBS)
### Protozoa

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### Microsporidia – obligate intracellular fungi!

- Produce extracellular, 1-2 micron, infective spores
- Spores have a coiled organelle called a polar tubule
- After ingestion, the spore germinates and the polar tubule is used to inject sporoplasm into a host cell

#### Enterocytozoon bieneusi
- watery diarrhea
- biliary disease (choleliths, acalculous cholecystitis)

#### Encephalitozoon intestinalis
- watery diarrhea
- biliary disease
- disseminated disease (liver, kidney, lung, sinuses)

#### Encephalitozoon cuniculi, hellem
- can cause disseminated disease of multiple organs, plus eye disease...
- Many species (including Vittaforma cornea): punctate keratoconjunctivitis

**DIAGNOSIS:** modified trichrome stain, Calcofluor white, IFA

**TREATMENT:** albendazole (not effective for E. bieneusi)

### Blastocystis

**What is it?**
Nobody really knows!!! Might be a protozoa.

Might also be a part of a new kingdom (Chromista!!), with kelp and diatoms!

Forms are 5-40 microns wide. Anaerobic. Eukaryotic.

- cystic, ameboid, granular, and vacuolar forms

**Does it cause disease?**
That’s a good question!!! Maybe.

Associated with watery diarrhea, abdominal discomfort, nausea, and flatulence.

**Diagnosis:** light microscopy of stool samples

**Treatment?**
metronidazole, tinidazole, TMP/SMX, or nitazoxanide (none FDA-approved)

### Protozoan infections that can reactivate in the severely immunocompromised

- Toxoplasmosis
  - encephalitis with mass lesions
  - pneumonitis
  - retinitis
- Leishmania
  - reactivation of visceral and cutaneous reported
  - visceral with fever, hepatosplenomegaly, pancytopenia
- Chagas
  - encephalitis with mass lesions
  - hepatosplenomegaly and fevers
  - myocarditis in 40% that receive heart transplant b/c Chagas disease
- Malaria

### Some other protozoa that can cause severe disease in immunocompromised

- Cryptosporidium
- Giardia
- Microsporidia
- Babesia
- Acanthamoeba

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