Zoonoses of Nonhuman Primates
Enteric Protozoa

Zoonotic Enteric Protozoa

*Entamoeba histolytica*
*Giardia lamblia*
*Cryptosporidium parvum*
*Cyclospora cayetanensis*
*Balantidium coli*

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Zoonoses of Nonhuman Primates
Amoebiasis

Amoebiasis (Amoebic dysentery)
Agent: *Entamoeba histolytica*
Transmission: Fecal-Oral; Food or water
   Infective stage – nonmotile cyst (4 nucleii)
Life cycle: Excystation in small intestine
   Motile trophozoites migrate to colon
   Two forms – commensal and invasive
Amoebiasis

*Entamoeba histolytica* cyst and troph

- **E. histolytica** trophozoite

- **E. histolytica** cyst

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**Amoebiasis**

*Entamoeba* Life Cycle

- Infective stage is mature cyst
- Ingestion begins the cycle
- Excystation in small intestine
  - Trophozoites migrate to colon
- Troph multiplication in colon
  - Invasive or commensal
- Cyst formation
- Cysts passed in feces
- Extra-intestinal disease
  - Liver, brain, lung abscesses

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**Amoebiasis**

*Entamoeba histolytica* cyst and troph

- **E. histolytica** trophozoite

- **E. histolytica** cyst

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**Amoebiasis**

*Entamoeba* Life Cycle

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Amoebiasis

Epidemiology
- Host species – humans, NW and OW monkeys and apes
- Incubation period – variable (1-14 weeks)
- Chronic infection – months to years
- Carriers – excrete millions of cysts per day
- Pathogenicity – strain-specific virulence factors (isoenzymes)

Amoebiasis

Pathogenesis
- Invasion of colonic mucosa
  inflammation, sloughing, ulceration
- Large bowel diarrhea – chronic, intermittent
- “Amoebic dysentery” – blood and mucous
- Subclinical infections common
- Extra-intestinal – liver abscess (lung, CNS)
Amoebiasis

Diagnosis
Cysts or Trophozoites in fecal samples
Multiple stool samples maybe required (4-6)
Invasive forms – Ab production

Treatment
Metronidazole (Flagyl) in combination with Yodoxin

E. Histolytica
Prevalence in NHPs

Prevalence of infection in NHP
Olive baboons (wild) 24/96 26%
African green monkeys 14/55 25%
Hamadryas baboons (wild) 10/76 12%
DeBrazza’s monkey 6/12 50%
**Entamoeba histolytica**

Prevalence in NHP and Human Contact

Prevalence of *E. histolytica* in Hamadryas baboons from three geographic locations -Saudi Arabia

Extent of human contact

<table>
<thead>
<tr>
<th></th>
<th>High  (n=300)</th>
<th>Moderate  (n=186)</th>
<th>Low  (n=90)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>32 (11.0 %)</td>
<td>7 (3.8%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>


**Zoonotic Amoebiasis from NHP**

Reported Human Zoonotic Cases

- Zoo keepers – same isoenzyme pattern in NHP
- Shared pathogenic and nonpathogenic strains
Zoonotic Enteric Protozoa of NHP
Giardiasis

Agent: *Giardia lamblia*; flagellated protozoan

Hosts: Many species of NHP, other mammals

Transmission: Fecal-oral; contaminated food or water

Infective stage: Cyst (4 nuclei)

*Giardia* Trophozoite

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**Giardia lamblia**

*Life Cycle*

Ingestion of infective cyst

4 nuclei

Excystation in small bowel

Trophozoites adhere to mucosal epithelium in duodenum and jejunum

Encystment in lumen of small bowel

Cysts shed in feces
Giardiasis

Epidemiology

- **Incubation period** – 5-20 days (7-10)
- Most common intestinal pathogen in developed countries
- Clinical disease – infants and children
- Inapparent infections are common – intermittent shedding of infectious cysts
- Cysts resistant to chlorine levels of standard water treatment
- Cysts remain viable in environment

Giardiasis

Clinical Disease

- Abdominal cramps, bloat, anorexia, fever
- Watery diarrhea (no blood or mucous)
- No mucosal invasion – may damage villi
- Chronic case – fat malabsorption (mechanical obstruction)
- Self limiting – 1-4 wks (diarrhea 5-7 days)
Giardiasis

Diagnosis
- Cysts or trophozoites in fecal samples
- Fluorescence tagged Dx kits
- Multiple stool exams may be needed

Treatment
- Metronidazole (Flagyl), Quinicrine, Furazolidone
- Drug resistance?

Giardiasis
Prevalence in NHP

<table>
<thead>
<tr>
<th>Species</th>
<th>Prevalence</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamadryas baboon</td>
<td>52/576</td>
<td>9%</td>
</tr>
<tr>
<td>Hamadryas baboon</td>
<td>16/76</td>
<td>19%</td>
</tr>
<tr>
<td>Rhesus macaque</td>
<td>2/100</td>
<td>2%</td>
</tr>
<tr>
<td>Lowland gorilla (wild)</td>
<td>2/100</td>
<td>2%</td>
</tr>
<tr>
<td>Mtn gorilla (wild)</td>
<td>2/70</td>
<td>2.8%</td>
</tr>
<tr>
<td>Common marmoset</td>
<td>5/25</td>
<td>20%</td>
</tr>
</tbody>
</table>
Zoonotic Protozoa of NHP

Cryptosporidiosis

Agent: *Cryptosporidium parvum* (Coccidia)
Transmission: Fecal-oral; food or water
Infectious stage: Sporulated oocyst
Clinical disease: Profuse, watery diarrhea
  - Self-limiting in immune competent host
  - Life-threatening in immune compromised host

Cryptosporidiosis

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  - Life-threatening in immunocompromised host
Cryptosporidium Life Cycle

Ingestion of thick-walled oocyst
Excystation in small bowel release of sporozoites
Sporozoites infect epithelial cells (intracellular, but extracytoplasmic)
Sporozoites trophs in microvilli
Trophs → schizonts → merozoites
Autoinfection
Merozoites → gametocytes
Sexual cycle → Zygote (= oocyst)
Oocyst shed in feces
Cryptosporidiosis

**Epidemiology**
- Many vertebrate host species including NHP
- Cysts extremely resistant to chlorine
- Persist in environment – months
- Low inoculum required for infection
- Clinical disease most common in children
- Largest water-borne outbreak (>400,000 cases)

**Diagnosis**
- Oocysts in fecal sample (fluorescent assay)

**Treatment**
- No effective treatment
### Cryptosporidiosis: Prevalence in NHP

#### Prevalence in NHP

<table>
<thead>
<tr>
<th>Species</th>
<th>Count/Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cynomolgus macaque</td>
<td>10/22</td>
<td>45%</td>
</tr>
<tr>
<td>Pig-tailed macaque</td>
<td>66/128</td>
<td>52%</td>
</tr>
<tr>
<td>Japanese macaque</td>
<td>2/3</td>
<td>67%</td>
</tr>
<tr>
<td>Baboons</td>
<td>3/4</td>
<td>75%</td>
</tr>
<tr>
<td>Mtn gorilla (wild)</td>
<td>7/70</td>
<td>11%</td>
</tr>
<tr>
<td>Common marmoset</td>
<td>4/25</td>
<td>16%</td>
</tr>
<tr>
<td>African green monkey</td>
<td>4/6 (67%)</td>
<td>36/45 (80%)</td>
</tr>
<tr>
<td>Olive baboon</td>
<td>2/3 (66%)</td>
<td>17/60 (28%)</td>
</tr>
</tbody>
</table>

#### Diarrhea and Normal

<table>
<thead>
<tr>
<th>Species</th>
<th>Diarrhea</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>African green monkey</td>
<td>4/6 (67%)</td>
<td>36/45 (80%)</td>
</tr>
<tr>
<td>Olive baboon</td>
<td>2/3 (66%)</td>
<td>17/60 (28%)</td>
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**Figure 1.** Cryptosporidium oocyst passage after primary inoculation with 10 or 2 x 10⁵ oocysts on day 0.

Cyclosporiasis

Agent: *Cyclospora cayetanensis* (Coccidia)  
*Cyclospora spp.*

Transmission: Fecal-oral; food or water

Infectious stage: Oocyst (unsporulated)

Life Cycle: not well characterized
  - Sporozoites released in small intestine
  - Intracellular infection of epithelial cells

Clinical Disease

- Profuse watery diarrhea
- Fatigue, nausea, abdominal cramps, vomiting
- Prodrome – “flu-like” muscle and joint pain
- Self-limiting in immune competent host
- Life-threatening in immunocompromised host
Cyclosporiasis

Diagnosis
- Oocysts in fecal samples (8-10 um)
  - Autofluorescence

Treatment
- Trimethoprim-Sulfamethoxizole

Epidemiology
- Oocysts resistant to chlorine
- Hosts for *Cyclospora* spp.- rodents, reptiles, insectivores
- High prevalence in NHP in East Africa
Zoonoses of Nonhuman Primates
Microsporidiosis

Agent: *Enterocytozoon bieneusi*

Epidemiology
- High prevalence in healthy rhesus macaques (~16%)
- Persistent infection (>260 days)
- Infection localized to hepatobiliary tree
- Zoonotic potential – not well studied
  - Human strains pathogenic for NHP

Microsporidia Life Cycle

- Infective stage – resistant spore
- Transmission – fecal-oral, Ingestion
- Sporoplasm – released from spore, infects mucosal epithelium (Polar filament)
- Intracellular multiplication – fission (sporogony)
  - Microsporidia produced
- Microsporidia develop to mature spores (thick capsule)
- Rupture of cell membrane – spores released
- Free cells can infect new cells (autoinfection) or be shed into the environment