

# Treatment of Parasitic Infections

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## Disclosure Information

I have no financial relationships to disclose.

I will discuss the following FDA off-label use and/or investigational use in my presentation:

- off-label parasitic infection treatments
- non-FDA approved medication use

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## Objectives

- Review the current treatment of parasites within and outside of the US.
- Describe how to control symptoms of a patient with a parasitic infection
- Discuss current research on future treatments of parasitic infections.

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## Parasites

- There are hundreds if not thousands of parasitic diseases that affect humans and all life
- This presentation will focus on:
  - Amebiasis
  - Chagas (American Trypanosomiasis)
  - Giardiasis
  - Leishmaniasis
  - Worms (Hookworms, Pinworms, Roundworms, Tapeworms)

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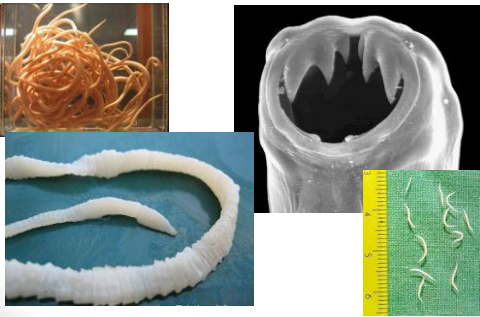
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## Worms



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## Worms - Background

- Roundworms (Ascaris)
  - Transmitted via soil or fecal-oral route
  - Estimated to infect up to 1 billion people in the world
  - Symptoms range from none to intestinal blockage
- Hookworms
  - Transmitted via soil or fecal-oral route
  - Estimated to infect 500-750 million people
  - Symptoms range from none to severe anemia
- Tapeworms
  - Transmitted by eating undercooked meat
  - Symptoms range from none to GI to seizures
- Pinworms
  - Spreads easily through fecal-oral route
  - Symptoms are usually mild - itching



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## Worms - Treatment

- Treatment depends on the type of worm and symptoms
- Treatment may involve supportive care
- Most commonly used medications are:
  - Albendazole
  - Mebendazole
  - Ivermectin
  - Pyrantel pamoate
  - Praziquantel

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## Worms – Treatment (cont)

### Albendazole

- Dose –
  - Adult:
    - Roundworm – 400mg x 1 dose
    - Hookworm – 400mg x 1 dose
    - Tapeworm – varies widely depending on type of tapeworm
    - Pinworm – 400mg x 1 dose and repeat in 2 weeks
  - Peds:
    - Roundworm – 400mg x 1 dose
    - Hookworm – 400mg x 1 dose
    - Tapeworm – varies widely depending on type of tapeworm
    - Pinworm – 400mg x 1 dose and repeat in 2 weeks
- Side effects – Mostly GI, headache
- Pregnancy – No
- Lactation – Use caution
- Availability – US and worldwide

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## Worms – Treatment (cont)

### Mebendazole

- Dose –
  - Adult:
    - Roundworm – 100mg twice daily x 3 days; may repeat in 3 weeks
    - Hookworm – 100mg twice daily x 3 days; may repeat in 3 weeks
    - Tapeworm – 100mg twice daily x 3 days; may repeat in 3 weeks
    - Pinworm – 100mg x 1 dose; repeat in 14 days and 28 days
  - Peds:
    - Roundworm – 100mg twice daily x 3 days; may repeat in 3 weeks
    - Hookworm – 100mg twice daily x 3 days; may repeat in 3 weeks
    - Tapeworm – 100mg twice daily x 3 days; may repeat in 3 weeks
    - Pinworm – 100mg x 1 dose; repeat in 14 days and 28 days
- Side effects – Mostly GI, headache
- Pregnancy – Not recommended in first or second trimester
- Lactation – Use caution
- Availability – US and worldwide

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## Worms – Treatment (cont)

### Ivermectin

- Dose –
  - Adult:
    - Roundworm – 200mcg/kg x 1 dose
  - Peds:
    - Roundworm – 100mg twice daily x 3 days; may repeat in 3 weeks
- Side effects – Rash, itching, fever, GI, headache
- Pregnancy – Not recommended
- Lactation – Not recommended
- Availability – US and worldwide

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## Worms – Treatment (cont)

### Pyrantel pamoate

- Dose –
  - Adult:
    - Hookworm – 11mg/kg x daily x 3 days (max 1gm per day)
    - Pinworm – 11mg/kg x 1 dose (max 1gm); repeat in 2 weeks
  - Peds:
    - Hookworm – 11mg/kg x daily x 3 days (max 1gm per day)
    - Pinworm – 11mg/kg x 1 dose (max 1gm); repeat in 2 weeks
- Side effects – Mostly GI, headache
- Pregnancy – Ok
- Lactation – Ok
- Availability – US and worldwide

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## Worms – Treatment (cont)

### Praziquantel

- Dose –
  - Adult:
    - Tapeworm – 5-25mg/kg x 1 dose
  - Peds:
    - Tapeworm – 5-25mg/kg x 1 dose
- Side effects – Mostly GI, headache, dizziness, malaise
- Pregnancy – Probably Ok, but not known for sure
- Lactation – Not recommended
- Availability – US and worldwide

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## Worms - Future Treatments

- Hookworm – vaccine in development
- Tapeworm – vaccine to treat tapeworms in pigs
  
- Interesting research is also being done in using worms for diseases of endocrinology and inflammatory disease

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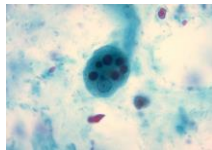
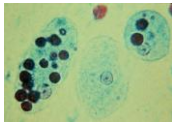
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## Amebiasis



• Images courtesy of CDC

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## Amebiasis - Background

- Caused by the protozoal parasite *Entamoeba histolytica*.
- Transmitted through the fecal-oral route
- Found worldwide, but especially within developing tropical countries
- Presents as a gradual illness with symptoms of cramps, diarrhea (watery or bloody), and weight loss. All of which may last several weeks. May also cause abscesses within the liver.
- Some patients are asymptomatic (up to 90%)
- Prevention is difficult but includes food and water safety precautions as well as good hand hygiene.



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## Amebiasis - Treatment

- For symptomatic (GI or liver) patients is a 2-step process:
  - 1<sup>st</sup> – treatment with tinidazole or metronidazole
  - 2<sup>nd</sup> – treatment with a luminal agent (iodoquinol, paromomycin, or diloxanide)
- For patients who are asymptomatic (carriers):
  - Treatment with a luminal agent only

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## Amebiasis – Treatment (cont)

### Tinidazole

- Dose –
  - Adult:
    - Intestinal: 2gm/d for 3 days
    - Liver abscess: 2gm/d for 3-5 days
  - Peds: (over age of 3 years old)
    - Intestinal: 50mg/kg/day for 3 days
    - Liver Abscess: 50mg/kg/day for 3-5 days
- Side effects – Mostly GI, disulfiram, yeast infections
- Pregnancy – not in the first trimester
- Lactation – not recommended
- Availability – US and worldwide

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## Amebiasis – Treatment (cont)

### Metronidazole

- Dose –
  - Adult:
    - Intestinal or liver: 500-750mg every 8 hours for 5-10 days
  - Peds: (infants and children)
    - Intestinal or liver: 35-50mg/kg/day in divided doses every 8 hours for 10 days
- Side effects – Mostly GI, disulfiram, yeast infections
- Pregnancy – not in the first trimester
- Lactation – not recommended, but risks vs benefits
- Availability – US and worldwide

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## Amebiasis – Treatment (cont)

### Iodoquinol

- Dose –
  - Adult:
    - 650mg 3 times a day (after meals) for 20 days
  - Peds:
    - 30-40mg/kg/day in 3 divided doses for 20 days
- Side effects – Mostly GI, fever, headache,
- Pregnancy – not recommended
- Lactation – not recommended
- Availability – US and worldwide
- Other considerations – take after meals

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## Amebiasis – Treatment (cont)

### Paromomycin

- Dose –
  - Adult:
    - 25-35mg/kg/day in three divided doses for 5-10 days
  - Peds:
    - Same as adult
- Side effects – Mostly GI, *C. difficile* associated diarrhea
- Pregnancy – safe
- Lactation – safe
- Availability – US and worldwide
- Other considerations – take with food

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## Amebiasis – Treatment (cont)

### Diloxanide

- Dose –
  - Adult:
    - 500mg 3 times a day for 10 days
  - Peds:
    - 20mg/kg/day given in 3 divided doses
- Side effects – Mostly GI
- Pregnancy – unknown
- Lactation – unknown
- Availability – Not in the US, but widely available elsewhere
- Other considerations – take with food

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## Amebiasis – The Future

- The World Health Organization is researching a vaccine based on:
  - “Evidence from a cohort of Bangladeshi children suggests that mucosal IgA directed against the major amoebic adherence molecule, a 170 kD lectin, correlates with resistance to reinfection with *E. histolytica*. Gerbils immunized with this lectin antigen were reported to show significant decrease of liver abscesses following parasite challenge, suggesting that a subunit vaccine might elicit protective immunity.”

[http://www.who.int/vaccine\\_research/diseases/oa\\_parasitic/en/index.html](http://www.who.int/vaccine_research/diseases/oa_parasitic/en/index.html)

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## Amebiasis Thinking Question

- We talked about the two-step method of treating amebiasis. Using the tissue amebicide first and then following with the luminal amebicide. So the question is: Could you give both steps at the same time?

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## Chagas Disease



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## Chagas Disease - Background

- Caused by the protozoal parasite *Trypanosoma cruzi*
- Transmitted by the Triatomine bug
- Found only in North and South America
- Estimated 8-10 million people affected
- Presents as a mild infection with fever and swelling at site of infection (acute phase)
- If left untreated can cause severe complications (chronic phase)
  - Arrhythmias
  - Heart failure
  - Esophageal and colon dilation
- Prevention is difficult but includes eliminating areas where triatomine bug lives



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## Chagas Disease - Treatment

- All patients with Chagas disease should be treated
- May also help to treat those with chronic disease
- If patients develop cardiac or GI issues from Chagas disease then symptomatic treatment of those conditions is warranted
- Treatment with antiparasitic medications leads to an estimated 60-85% cure rate, but the longer someone has been infected the less likely a cure will occur
- Antiparasitic medications commonly used are:
  - Benznidazole
  - Nifurtimox

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## Chagas Disease – Treatment (cont)

### Benznidazole

- Dose –
  - Adult:
    - 5-7mg/kg/day divided in 2 doses for 60 days
  - Peds:
    - 5-7.5mg/kg/day divided in 2 doses for 60 days
- Side effects – allergic dermatitis, neuropathy, insomnia, weight loss
- Pregnancy – unknown
- Lactation – unknown
- Availability – Not in the US (except CDC), but widely available elsewhere
- Other considerations – take with food

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## Chagas Disease – Treatment (cont)

### Nifurtimox

- Dose –
  - Adult:
    - 8-10mg/kg/day in 3 or 4 divided doses for 90 days
  - Peds:
    - 15-20mg/kg/day divided in 3 or 4 doses for 90 days
- Side effects – GI, headache, dizziness, polyneuropathy
- Pregnancy – unknown
- Lactation – unknown
- Availability – Not in the US (except CDC), but widely available elsewhere
- Other considerations – take with food

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## Chagas Disease - Future

- There are currently several drugs being researched around the world that are promising
- VNI, an experimental drug from Vanderbilt University, seems very promising with one study in mice exhibiting 100% cure rate and no observable side effects

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## Chagas Disease - Question

- Why should all patients with Chagas disease be treated even if they are currently asymptomatic?
  - A. Prevent spread to others
  - B. Prevent long-term complications
  - C. The treatments are cheap so we may as well use them up
  - D. We don't want it to get into the water supply

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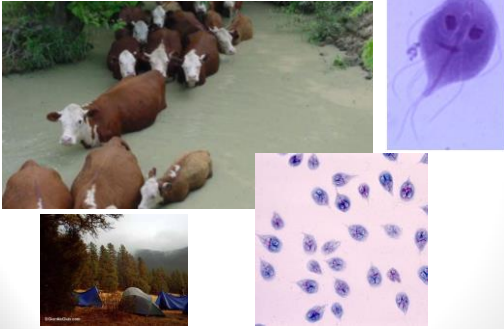
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## Giardiasis



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## Giardiasis - Background

- Caused by the protozoal parasite *Giardia lamblia*
- Transmitted through fecal-oral route
- Infected by *Giardia* cysts
  - An infectious person excretes 1-10 billion cysts per day
  - As few as 10 cysts needed to cause an infection
- Found throughout the world
- Estimated 200 million people infected
- Presents as gastroenteritis (dehydration, diarrhea, cramps, vomiting, gas)
- Causes temporary lactose intolerance
- Many people are asymptomatic
- Without treatment symptoms typically last 4-6 weeks
- Prevention is difficult but proper sanitation is essential

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## Giardiasis - Treatment

- Not all patients will need treated
- Rehydration is essential in all symptomatic patients
- Antiparasitic medications commonly used are:
  - Metronidazole
  - Tinidazole
  - Nitazoxanide
  - Others
    - Paromomycin
    - Furazolidone
    - Quinacrine
    - Albendazole



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## Giardia – Treatment (cont)

### Metronidazole

- Dose –
  - Adult:
    - 500mg twice daily for 5-7 days
  - Peds:
    - 15-30mg/kg/day in divided doses every 8 hours for 7 days
- Side effects – Mostly GI, disulfiram, yeast infections
- Pregnancy – not in the first trimester
- Lactation – not recommended, but risks vs benefits
- Availability – US and worldwide

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## Giardia – Treatment (cont)

### Tinidazole

- Dose –
  - Adult:
    - 2gm x 1 dose
  - Peds: (over age of 3 years old)
    - 50mg/kg x 1 dose (2gm max)
- Side effects – Mostly GI, disulfiram, yeast infections
- Pregnancy – not in the first trimester
- Lactation – not recommended
- Availability – US and worldwide

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## Giardia – Treatment (cont)

### Nitazoxanide

- Dose –
  - Adult:
    - 500mg every 12 hours for 3 days
  - Peds: (over age of 1 year old)
    - 100mg every 12 hours for 3 days
- Side effects – Mostly GI, headache
- Pregnancy – probably ok
- Lactation – use caution
- Availability – US and worldwide

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## Leishmaniasis




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## Leishmaniasis - Background

- Caused by the protozoal parasites of the *Leishmania* genus
- Transmitted by the bite of a sand fly
- Found throughout most of the tropical and sub-tropical world
- Estimated 12 million people infected
- Symptoms are skin sores, fever, splenomegaly
- Four types of leishmaniasis
  - Cutaneous – most common and occurs at bite-site; long time to heal
  - Diffuse cutaneous – resembles leprosy; difficult to heal
  - Mucocutaneous – ulcers spread into nose, mouth, throat
  - Visceral – liver and/or spleen and/or bone marrow involved; fatal if untreated
- Prevention is difficult
- Vaccines in development

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## Leishmaniasis - Treatment

- Treatment depends largely on type of leishmaniasis and genus
- Medications commonly used are:
  - Liposomal amphotericin B
  - Sodium stibogluconate
  - Meglumine antimonate
  - Miltefosine
  - Paromomycin
- Resistance to some medications is an issue in some parts of the world
- Treatment of leishmaniasis should only be done by physicians experienced in the management of the disease

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## Leishmaniasis – Treatment (cont)

### Liposomal Amphotericin B

- Dose –
  - Adult:
    - \*Visceral: 3mg/kg/day IV on days 1-5, repeated on days 14 and 21
    - Mucosal: 3mg/kg/day IV on days 1-5
  - Peds: (over age of 1 month old)
    - \*Visceral: 3mg/kg/day IV on days 1-5, repeated on days 14 and 21
    - Mucosal: 3mg/kg/day IV on days 1-5
- Side effects – LOTS!! Cardio, CNS, Dermatologic, Endocrine, etc
- Pregnancy – probably ok
- Lactation – unknown; not recommended
- Availability – US and worldwide

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## Leishmaniasis – Treatment (cont)

### Sodium Stibogluconate

- Dose –
  - Adult:
    - Visceral: 20mg Sb/kg/day IV or IM x 28 days
    - \*Mucosal: 20mg Sb/kg/day IV or IM x 28 days
    - \*Cutaneous: 20mg Sb/kg/day IV or IM x 20 days
  - Peds:
    - Visceral: 20mg Sb/kg/day IV or IM x 28 days
    - \*Mucosal: 20mg Sb/kg/day IV or IM x 28 days
    - \*Cutaneous: 20mg Sb/kg/day IV or IM x 20 days
- Side effects – aching, arthralgia, GI, QT prolongation (rare)
- Pregnancy – unknown; not recommended
- Lactation – unknown; not recommended
- Availability – US (through CDC) and worldwide

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## Leishmaniasis – Treatment (cont)

### Meglumine antimonate

- Dose –
  - Adult:
    - Visceral: 20mg Sb/kg/day IV or IM x 28 days
    - \*Mucosal: 20mg Sb/kg/day IV or IM x 28 days
    - \*Cutaneous: 20mg Sb/kg/day IV or IM x 20 days
  - Peds:
    - Visceral: 20mg Sb/kg/day IV or IM x 28 days
    - \*Mucosal: 20mg Sb/kg/day IV or IM x 28 days
    - \*Cutaneous: 20mg Sb/kg/day IV or IM x 20 days
- Side effects – aching, arthralgia, GI, QT prolongation (rare)
- Pregnancy – unknown; not recommended
- Lactation – unknown; not recommended
- Availability – Not in the US, but most of the world

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## Leishmaniasis – Treatment (cont)

### Miltefosine

- Dose –
  - Adult:
    - Visceral: 2.5mg/kg/day x 28 days (150mg/day max)
    - \*Mucosal: 2.5mg/kg/day x 28 days (150mg/day max)
    - \*Cutaneous: 2.5mg/kg/day x 28 days (150mg/day max)
  - Peds:
    - Visceral: 2.5mg/kg/day x 28 days (150mg/day max)
    - \*Mucosal: 2.5mg/kg/day x 28 days (150mg/day max)
    - \*Cutaneous: 2.5mg/kg/day x 28 days (150mg/day max)
- Side effects – GI (nausea and vomiting)
- Pregnancy – No! Teratogen
- Lactation – unknown; not recommended
- Availability – In the US (from CDC) and rest of the world

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## Leishmaniasis – Treatment (cont)

### Paromomycin

- Dose –
  - Adult:
    - Visceral: 15mg/kg/day IM x 21 days
    - Cutaneous: Topically 2 times a day for 10-20 days
  - Peds:
    - Visceral: 15mg/kg/day IM x 21 days
    - Cutaneous: Topically 2 times a day for 10-20 days
- Side effects – Mostly GI, *C. difficile* associated diarrhea
- Pregnancy – unknown when given IM
- Lactation – unknown when given IM
- Availability – US and worldwide

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## Leishmaniasis – Future Treatment

- World Health Organization and the Centers for Disease Control are both working on vaccines against leishmaniasis.
- Vaccines are currently in Phase I trials

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# Questions??

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