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

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.
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)

Worms

- 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
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

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

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
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

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

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
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

Amebiasis

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.
Amebiasis - Treatment

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

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

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
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

Amebiasis – Treatment (cont)

Paromomycin
- **Dose**—
  - **Adult:**
    - 25-35mg/kg/day in 3 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

Amebiasis – Treatment (cont)

Diloxanide
- **Dose**—
  - **Adult:**
    - 50mg 3 times a day for 10 days
  - **Peds:**
    - 20mg/kg/day 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
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."


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?

Chagas Disease
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

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

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
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

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

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
Giardiasis

- 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

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
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

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

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
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

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
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

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

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
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

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

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
Questions??

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