

Treatment of Worms and Other Parasitic Infections

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Disclosure Information

Dr. Mosler and Dr. Chancey have no financial relationships to disclose

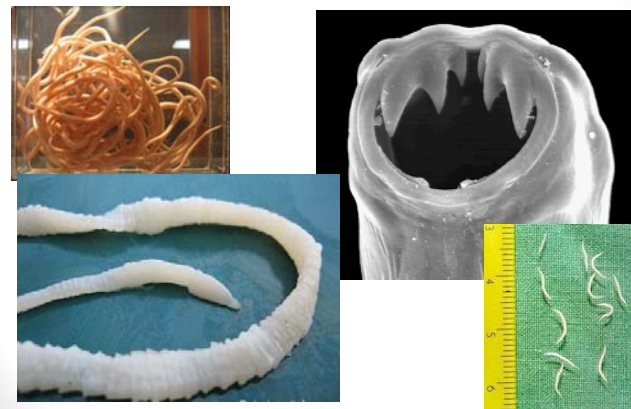
Dr. Mosler and Dr. Chancey will discuss the following FDA off-label use and/or investigational use in the presentation:

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

Objectives

- Review the current treatment of common parasitic infections within and outside of the U.S. including soil transmitted helminths, leishmaniasis, Chagas disease, and Human African Trypanosomiasis.
- Describe epidemiology and symptomatology of these parasitic infections.
- Discuss current research on future treatment options for parasitic infections.

Worms



Worms – Background

- Roundworms (*Ascaris lumbricoides*)
 - 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 (*Ancylostoma duodenale*, *Necator americanus*)
 - Transmitted via soil or fecal-oral route
 - Estimated to infect 500-750 million people
 - Symptoms range from none to severe anemia
- Tapeworms (*Taenia solium*, *Taenia saginata*)
 - Transmitted by eating undercooked meat
 - Symptoms range from none to GI to seizures
- Pinworms (*Enterobius vermicularis*)
 - 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 – U.S. and worldwide

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
 - 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
- Side effects – Mostly GI, headache
- Pregnancy – Not recommended in first or second trimester
- Lactation – Use caution
- Availability – U.S. and worldwide

Worms – Treatment (cont)

Ivermectin

- Dose –
 - Adult:
 - Roundworm – 200mcg/kg x 1 dose
 - Peds:
 - Roundworm – 150-200mcg/kg x 1 dose (use a weight-based table)
- Side effects – Rash, itching, fever, GI, headache
- Pregnancy – Not recommended
- Lactation – Not recommended
- Availability – U.S. 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 – U.S. and worldwide

Worms – Treatment (cont)

Praziquantel

- Dose –
 - Adult:
 - Tapeworm – 5-10mg/kg x 1 dose
 - Peds:
 - Tapeworm – 5-10mg/kg x 1 dose
- Side effects – Mostly GI, headache, dizziness, malaise
- Pregnancy – Probably Ok, but not known for sure
- Lactation – Not recommended
- Availability – U.S. and worldwide

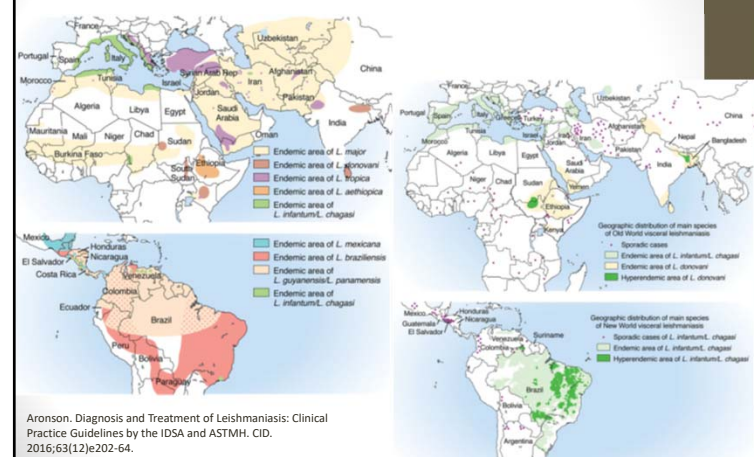
Worms – Future Treatments

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

Leishmaniasis



Geographic Distribution of Leishmaniasis



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 (cutaneous); fever and splenomegaly (visceral)
- Four types of leishmaniasis
 - Cutaneous – most common and occurs at bite-site; variable time to heal
 - Diffuse cutaneous – resembles leprosy; difficult to heal
 - Mucocutaneous – ulcers in mucosal areas of 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, genus and resistance patterns
- 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 be done by physicians experienced in the management of the disease
- Experts at CDC available for consultation

Leishmaniasis – Treatment (cont)

Liposomal Amphotericin B

- Dose –
 - Adult:
 - Cutaneous: 3mg/kg/day on days 1-5 and 10 or on days 1-7 (total dose 18-21 mg/kg)
 - Mucosal: 3mg/kg/day IV for cumulative total of 20-60 mg/kg
 - *Visceral: 3mg/kg/day IV on days 1-5, repeated on days 14 and 21 (total dose 21 mg/kg)
 - Peds: (over age of 1 month old)
 - Cutaneous: 3mg/kg/day on days 1-5 and 10 or on days 1-7 (total dose 18-21 mg/kg)
 - Mucosal: 3mg/kg/day IV for cumulative total of 20-60 mg/kg
 - *Visceral: 3mg/kg/day IV on days 1-5, repeated on days 14 and 21 (total dose 21 mg/kg)
- Side effects – LOTS!! Cardio, CNS, Dermatologic, Endocrine, etc
- Pregnancy – probably ok
- Lactation – unknown; not recommended
- Availability – U.S. and worldwide

* Alternative FDA-approved regimen for Visceral leishmaniasis if immunosuppressed

Leishmaniasis – Treatment (cont)

Sodium Stibogluconate

- Dose –
 - Adult:
 - *Cutaneous: 20mg Sb^v/kg/day IV or IM x 20 days
 - *Mucosal: 20mg Sb^v/kg/day IV or IM x 28 days
 - Visceral: 20mg Sb^v/kg/day IV or IM x 28 days
 - Peds:
 - *Cutaneous: 20mg Sb^v/kg/day IV or IM x 20 days
 - *Mucosal: 20mg Sb^v/kg/day IV or IM x 28 days
 - Visceral: 20mg Sb^v/kg/day IV or IM x 28 days
- Side effects – aching, arthralgia, GI, QT prolongation (rare)
- Pregnancy – unknown; not recommended
- Lactation – unknown; not recommended
- Availability – generic formulations may be available in some countries
 - Pentostam is no longer being manufactured

Leishmaniasis – Treatment (cont)

Meglumine antimonate

- Dose –
 - Adult:
 - Cutaneous: 20mg Sb^v/kg/day IV or IM x 20 days
 - *Mucosal: 20mg Sb^v/kg/day IV or IM x 28 days
 - Visceral: 20mg Sb^v/kg/day IV or IM x 28 days
 - Peds:
 - *Cutaneous: 20mg Sb^v/kg/day IV or IM x 20 days
 - *Mucosal: 20mg Sb^v/kg/day IV or IM x 28 days
 - Visceral: 20mg Sb^v/kg/day IV or IM x 28 days
- Side effects – aching, arthralgia, GI, QT prolongation (rare)
- Pregnancy – unknown; not recommended
- Lactation – unknown; not recommended
- Availability – available in U.S. through Sanofi with individual IND through FDA

Leishmaniasis – Treatment (cont)

Miltefosine

- Dose –
 - Adult:
 - ≥ 45 kg: 50mg three times daily x 28 consecutive days
 - Peds:
 - 30-44 kg: 50 mg twice daily x 28 consecutive days
 - ≥ 45 kg: 50 mg three times daily x 28 consecutive days
- FDA approved for
 - Cutaneous leishmaniasis due to *L. braziliensis*, *L. guyanensis*, *L. panamensis*
 - Mucosal leishmaniasis due to *L. braziliensis*
 - Visceral leishmaniasis due to *L. donovani*
- Side effects – GI (nausea and vomiting). Discuss future fertility issues
- Pregnancy – no! teratogen
- Lactation – unknown; not recommended
- Availability – available in the U.S. from the marketer Profunda

Leishmaniasis – Treatment (cont)

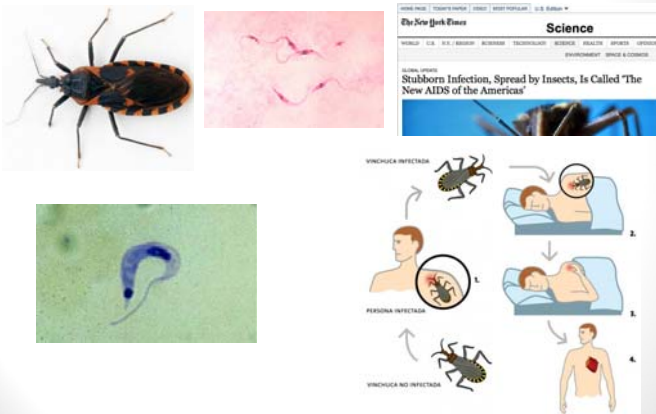
Paromomycin

- Dose –
 - Adult (Cutaneous leishmaniasis):
 - 15% paromomycin and 12% MBCL ointment: Apply twice daily for 10 days, rest for 10 days, and reapply twice daily for 10 days
 - 15% paromomycin and 0.5% gentamicin cream: Apply once per day for 20 days
 - Peds (Cutaneous leishmaniasis):
 - 15% paromomycin and 12% MBCL ointment: Apply twice daily for 10 days, rest for 10 days, and reapply twice daily for 10 days
 - 15% paromomycin and 0.5% gentamicin cream: Apply once per day for 20 days
- Side effects – local irritation, erythema, mild pain
- Pregnancy – unknown when given IM
- Lactation – unknown when given IM
- Availability – U.S. and worldwide

Leishmaniasis – Future Treatment

- Vaccines against leishmaniasis are being studied and developed; currently in Phase I trials
- DNDi (Drugs for Neglected Diseases initiative) evaluating new medications and current medication regimens
- WHO, PAHO, ASTMH, IDSA updating guidelines

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
- Estimated 300,000 persons in the U.S. are infected^{1,2}
- 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
- Eliminate areas where triatomine bugs live



¹ Bern C, Montgomery SP. An estimate of the burden of Chagas disease in the United States. *Clin Infect Dis*. 2009;49(5):e52-e54.

² Irish A, Whittman JD, Clark EH, Marcus R, Bern C. Updated estimates and mapping for prevalence of Chagas disease among adults, United States. *Emerg Infect Dis*. 2022;28(7):1313-1320.

Chagas Disease Map

ENDEMIC IN 21 LATIN AMERICAN COUNTRIES



- Endemic
- Not endemic but present

<https://dndi.org/diseases/chagas/facts/>

Chagas Disease – Treatment

- Treatment for all patients with Chagas disease should be considered
- Benefit of treatment declines as degree of cardiac damage increases
- Treat symptomatic cardiac or GI issues
- Cure rate of 60-85% with antiparasitic medications
 - The longer someone has been infected the less likely a cure will occur
- Side effects are significant, and some patients cannot tolerate
 - Children tend to tolerate the medications better than adults
- Available antiparasitic medications include:
 - Benznidazole – considered first line treatment on basis of more favorable side effect profile and accumulated clinical experience
 - Nifurtimox

Chagas Disease – Treatment (cont)

Benznidazole

- Dose –
 - Adult:
 - 5-8 mg/kg/day divided in 2 doses for 60 days
 - Peds (FDA approved for 2-12 years of age):
 - 5-8 mg/kg/day divided in 2 doses for 60 days
- Side effects – allergic dermatitis, nausea, abdominal pain, peripheral neuropathy, insomnia, weight loss
- Pregnancy – unknown
- Lactation – unknown
- Availability – available in the U.S. through www.benznidazoletablets.com
- Other considerations – take with food

Chagas Disease – Treatment (cont)

Nifurtimox

- Dose –
 - Adult:
 - 8-10mg/kg/day in 3 divided doses for 60 days
 - Peds (< 18 years old):
 - 2.5kg to < 40kg: 10-20mg/kg/day in 3 divided doses for 60 days
 - ≥ 40kg: 8-10mg/kg/day in 3 divided doses for 60 days
- Side effects – nausea, vomiting, abdominal pain, headache, dizziness, peripheral neuropathy
- Pregnancy – unknown
- Lactation – unknown
- Availability – available in the U.S. through www.lampit.com
- 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

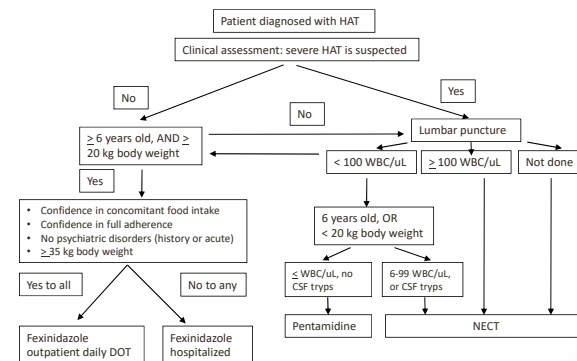
Human African Trypanosomiasis – Background

- Caused by the protozoal parasites of the *Trypanosoma* genus
- Transmitted by the bite of a tsetse fly (*Glossina* species)
- *T. b. gambiense* is endemic in 24 countries in west and central Africa
- *T. b. rhodesiense* is endemic in 13 countries of east and southern Africa
- Reported cases have fallen over the last 20 years from over 27,000 (>90% caused by *T. b. gambiense*) to <1000.
- Symptoms:
 - First stage: Chancre skin lesion at the site of fly bite, fever, headache, weakness, lymphadenopathy, hepatosplenomegaly, weight loss
 - Second stage: increased sleepiness, daytime somnolence, nocturnal insomnia, hallucinations, delirium, anxiety, emotional instability as well as motor, sensory, and neurologic signs and symptoms
- Prevention is avoiding tsetse fly bites

Treatment of African Trypanosomiasis

Species and Stage of Disease	First-line Treatment	Alternative Treatment
<i>T. b. gambiense</i> , first stage	Pentamidine	Fexinidazole*
<i>T. b. gambiense</i> , second stage	Nifurtimox-Eflornithine combination therapy (NECT)	NECT long Eflornithine monotherapy
<i>T. b. rhodesiense</i> , first stage	Suramin	Pentamidine
<i>T. b. rhodesiense</i> , second stage	Melarsoprol	

Algorithm of WHO Recommendations for the Management of Gambiense HAT



Human African Trypanosomiasis – Treatment

Suramin

- Dose –
 - Adult:
 - Day 0: Test dose of 4-5 mg/kg slowly IV
 - Days 1, 3, 7, 14, 21: 20 mg/kg/day (max 1g) IV over several hours
 - Peds:
 - Day 0: Test dose of 2 mg/kg (max 100mg) slowly IV
 - Days 1, 3, 7, 14, 21: 10-20 mg/kg/day (max 1g) IV over several hours
- Used for hemolymphatic (first) stage of *T. b. rhodesiense*
- Side effects – diarrhea, nausea, vomiting, headache, lethargy
- Pregnancy – unknown
- Lactation – unknown
- Availability – available in U.S. only through CDC

Human African Trypanosomiasis – Treatment (cont)

Melarsoprol

- Dose –
 - Adult:
 - 2.2 mg/kg/day (max 180-200 mg/day) IV x 10 days
 - Peds:
 - 2.2 mg/kg/day (max 180-200 mg/day) IV x 10 days
- Used for second stage (CNS stage) of *T. b. rhodesiense* infection
- Corticosteroid pretreatment should be considered to reduce the risk of encephalopathic reaction
- Side effects – diarrhea, vomiting, headache
- Pregnancy – not recommended; Other agents preferred
- Lactation – unknown
- Availability – available in U.S. only through CDC

Human African Trypanosomiasis – Treatment (cont)

Pentamidine

- Dose –
 - Adult:
 - 4 mg/kg/dose once daily IV or IM for 7 days
 - Dilute in saline in 2-hour infusions
 - Peds:
 - 4 mg/kg/dose once daily IV or IM for 7 days
 - Dilute in saline in 2-hour infusions
- Used for hemolymphatic (first) stage *T. b. gambiense* infection
- Side effects – injection reactions, increased sCr, nausea
- Pregnancy – unknown
- Lactation – contraindicated
- Availability – available in U.S. and worldwide

Human African Trypanosomiasis – Treatment (cont)

Fexinidazole

- Dose –
 - Adult:
 - Days 1-4: Loading dose 1,800 mg daily
 - Days 5-10: Maintenance dose 1,200 mg daily
 - Peds >6 years old and ≥ 20 kg to <35 kg:
 - Days 1-4: Loading dose 1,200 mg daily
 - Days 5-10: Maintenance dose 600 mg
 - Peds >6 years old and ≥ 35 kg:
 - Days 1-4: Loading dose 1,800 mg daily
 - Days 5-10: Maintenance dose 1,200 mg
- Used for hemolymphatic (first) stage *T. b. gambiense* infection and CNS (second) stage *T. b. gambiense* infection when CSF WBC < 100 cells/ml
- Side effects – N/V, anorexia, headache, insomnia, dizziness, tremor, weakness
- Pregnancy – may be given after 1st trimester to reduce fetal transmission of disease and prevent maternal death in mod-severe disease
- Lactation – unknown, but WHO 2019 guidelines suggest okay to use
- Availability – Available in U.S. through Sanofi; available in Africa through WHO

Human African Trypanosomiasis – Treatment (cont)

Nifurtimox and Eflornithine Combination Therapy (NECT)

- Dose –
 - Adult:
 - Nifurtimox 15 mg/kg/day orally in three doses x 10 days
 - Eflornithine 400 mg/kg/day IV in two 2-hour infusions x 7 days
 - Alternative NECT long: nifurtimox 15 mg/kg/day in three doses x 10 days and eflornithine 400 mg/kg/day IV in four 2-hour infusions x 14 days
 - Peds:
 - Nifurtimox 15 mg/kg/day orally in three doses x 10 days
 - Eflornithine 400 mg/kg/day IV in two 2-hour infusions x 7 days
 - Alternative NECT long: nifurtimox 15 mg/kg/day in three doses x 10 days and eflornithine 400 mg/kg/day IV in four 2-hour infusions x 14 days
- Used for CNS (second) stage *T. b. gambiense* infection
- Side effects – Eflornithine – headache, arrhythmia, N/V/D, neutropenia, fever, arthralgia, myalgia. Nifurtimox – see Chagas section
- Pregnancy – Eflornithine – Not recommended. Nifurtimox – see Chagas section
- Lactation – Eflornithine – unknown, but WHO 2019 guidelines suggest okay to use. Nifurtimox – see Chagas section
- Availability – in U.S., Eflornithine is only available through CDC
Nifurtimox is available commercially. Both are available worldwide

Parasitic Emergencies and Consults through CDC

- How to reach the Parasitic Inquiries Hotline at CDC:
 - parasites@cdc.gov
 - 404-718-4745
- After hours EOC phone number:
 - 770-488-7100

Worms - Question

- Which type of worm is Praziquantel able to treat?
 - A. Tapeworm
 - B. Pinworm
 - C. Roundworm
 - D. Earthworm

Leishmaniasis - Question

- Which of these treatments for leishmaniasis is safe to use in pregnancy?
 - A. Sodium stibogluconate
 - B. Meglumine antimonate
 - C. Miltefosine
 - D. None of the above

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 Chagas to get into the water supply

HAT - Question

- What is the best way to prevent HAT?
 - A. vaccination
 - B. avoid mosquitoes
 - C. don't drink the water
 - D. avoid tsetse fly bites

Questions??

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