Treatment of Worms and Other Parasitic Infections

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Acknowledgements

Special thanks to Rebecca Chancey, MD, DTMH, Chief, Parasitic Disease Drug Service, Centers for Disease Control and Prevention for her help with this presentation.

Disclosure Information

Dr. Mosler has no financial relationships to disclose

Dr. Mosler 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

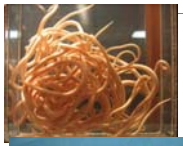
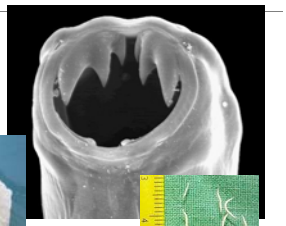
Objectives

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 – 5-25mg/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 – Probably Ok

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

Worms - Question

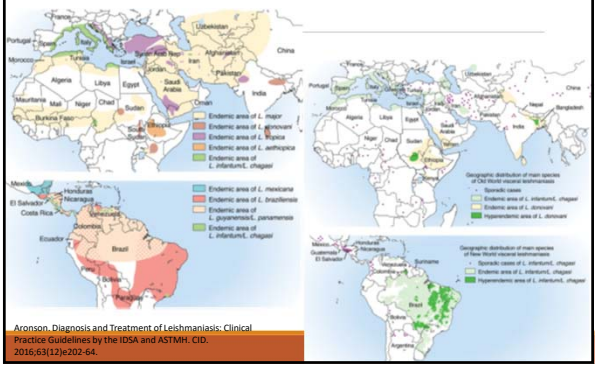
Which type of worm is Praziquantel able to treat?

- A. Tapeworm
- B. Pinworm
- C. Roundworm
- D. Earthworm

Leishmaniasis




Geographic Distribution of Leishmaniasis



Aronson. Diagnosis and Treatment of Leishmaniasis: Clinical Practice Guidelines by the IDSA and ASTMH. CID. 2016;63(12)e202-64.

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; risk vs benefit

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 and not available from CDC anymore

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 (https://www.astmh.org/blog/september-2022/instructions-for-acquiring-glucantime-(meglumine-a)

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. Pharmacy must contact manufacturer Profunda to obtain (https://www.impavido.com/order-page)

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. (but must be compounded) and worldwide

(MBCL = methybenzethonium chloride)

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

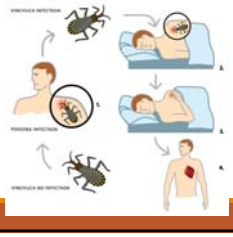
Leishmaniasis - Question

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



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, Whitman 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

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:
  - 5-7 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 – not recommended

Lactation – not recommended

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 3-4 divided doses for 90 days
- Peds (< 18 years old) (FDA approved):
- 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. at pharmacies. More info 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

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

Human African Trypanosomiasis – Background

Caused by the protozoal parasites of the *Trypanosoma brucei* 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:

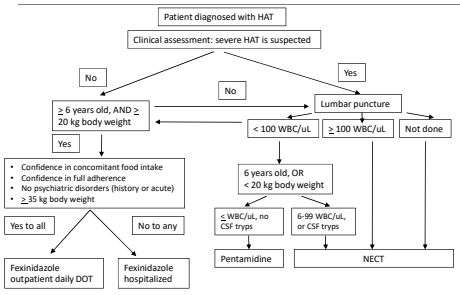
- First stage: Chancre skin lesion at the site of fly bite, fever, headache, weakness, lymphadenopathy, hepatosplenomegaly, weight loss
- Second stage: increased sleepiness, daytime somnolence, nocturnal insomnia, hallucinations, delirium, anxiety, emotional instability as well as motor, sensory, and neurologic signs and symptoms

Prevention is avoiding tsetse fly bites

Treatment of African Trypanosomiasis

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

Algorithm of WHO Recommendations for the Management of Gambiense HAT



(https://www.sciencedirect.com/science/article/pii/S1473309919306127)

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 ≥20kg 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)

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)

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

Human African Trypanosomiasis – Treatment (cont)

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

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

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

Questions??

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