Chagas
African Sleeping Sickness
Leishmaniasis

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Center for Global Health
Outline

• Case seen in Colorado
• American Trypanosomiasis (Chagas)
• African Trypanosomiasis (Sleeping Sickness)
• Leishmaniasis
  • Cutaneous
  • Visceral
Case

• 2 year old girl with a pre-auricular skin lesion x 15 months
• Started off looking like a mosquito bite
• Slowly progressed in size since then
• Non-tender, non-itchy
• Family members w/ similar lesions
Chagas
(American Trypanosomiasis)
Chagas Disease (American Trypanosomiasis)

Is America ready for a new wave of tropical diseases?

The 'new AIDS of the Americas': Experts warn of deadly insect-borne disease that can cause victims' hearts to explode

Northern Virginia: 'Ground Zero' for Kissing Bug Disease

Chagas, a disease common in Latin America, is gaining traction among immigrants in the U.S.
Chagas

- *T. cruzei*
- “Discovered” by Carlos Chagas in 1909
  - Died from Chagas in 1934
- Pleomorphic, spindle-shaped (“C” or “S” in blood)
- Triatomine “kissing” bug
- NTD, but kills up to 10% of adults in some countries
Epidemiology

- Endemic in 21 countries in the W Hemisphere
- 300,000 infected in the US, especially TX
- Up to 10% of adult deaths in parts of LA
- In Bolivia 20% of pregnant women
  - 60% of adults with heart disease

<table>
<thead>
<tr>
<th>Epidemiological parameters</th>
<th>1990</th>
<th>2000</th>
<th>2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual deaths</td>
<td>&gt;45,000</td>
<td>21,000</td>
<td>12,500</td>
</tr>
<tr>
<td>Cases of human infection</td>
<td>30 million</td>
<td>18 million</td>
<td>15 million</td>
</tr>
<tr>
<td>New cases per year</td>
<td>700,000</td>
<td>200,000</td>
<td>41,200</td>
</tr>
<tr>
<td>Population at risk</td>
<td>100 million</td>
<td>40 million</td>
<td>28 million</td>
</tr>
<tr>
<td>Number of countries</td>
<td>21</td>
<td>21</td>
<td>21</td>
</tr>
</tbody>
</table>
Epidemiology

• Transmission: triatomine nighttime blood meal
• Zoonotic (non-human) hosts most common
• Domestic (150 species) and Sylvatic (wild) hosts (opossums, *Didelphis*)
• Rural wooded areas, low SES
• Some triatomines (reduviids) have adapted to household, urban areas
Epidemiology

• Transfusion: 3-15% positive serology, but 99% screened now
  • 1 in 30,000 units in the US
  • Survive refrigeration -> can treat with gentian violet x 24 hours
• Organ donation (9 cases)
• Congenital: 1-10% of infected mothers
• Contaminated food or drink (rare)
  • Caracas outbreak (2010): contaminated guava juice
  • Severe acute disease
Clinical Disease

• Incubation: 1-2 weeks
  • Up to 4 months if transfusion or organ transplant

• Acute Phase: 8-12 weeks
  • Circulating trypanomastigotes
  • Non-specific symptoms in 1% (malaise, fever, anorexia, LAD) or asymptomatic
  • Chagomas: swelling at site of inoculation
  • Romaña’s sign: conjunctival inoculation (25-30%)
  • Severe acute disease (< 1%)
    • Acute myocarditis, pericardial effusion, and/or meningoencephalitis; high mortality
    • More common with oral inoculation (food contamination) than vector
Clinical Disease

- Congenital
  - Usually asymptomatic
  - If symptoms: low birthweight, anemia, meningoencephalitis, HSM, respiratory disease
  - High mortality
  - Same lifetime risk as other infected individuals for GI and cardiac morbidity (20-30%)

- If mother is positive, test all of her children
Clinical Disease

• Indeterminate Phase (up to 40 years)
  • Between acute and chronic phases
  • May have ECG or MRI findings, but usually asymptomatic

• Chronic Phase (30%)
  • 8-12 weeks to 40 years after infection
  • Parasite present but at low levels, undetectable by microscopy
  • Still able to transmit to vector or other humans (organ, blood, congenital)
  • Many factors: host response, initial damage, immune competence
  • Can have reactivation in IC patients
Clinical Disease

- Cardiac Disease*
  - Dilated cardiomyopathy
  - Thromboembolism
  - Apical aneurysm
  - Arrhythmia
  - Sudden death (55-65%)
Clinical Disease

- GI Disease
  - Destruction of ganglion cell in the autonomic plexus
  - Megaesophagus
    - Reflux, dysphagia, microaspiration
  - Megacolon
    - Constipation, volvulus

- Cardiac and GI: vary by region
Diagnosis

- History of exposure (residence or transfusion)
- Talk to CDC
- Acute Chagas
  - Thin/thick smear or **buffy coat** (90 days), tissue, or other sterile fluid (LN)
  - Anti-T. cruzi IgM **not useful**
  - PCR: sn of 45-100% (most ~ 90%)
- Chronic Chagas
  - IgG serology (ELISA/IFA) not great: recommend 2 assays for 2 dif Ags
  - PCR not useful
- Congenital
  - Microscopy 50% sn, PCR much better, IgG > 9 months
Treatment

• Treat early: acute, congenital, early chronic, children, lab, no pregnancy

• Nifurtimox (Lampit)
  • Parasitologic cure in 70% cases
  • Reduces duration, severity and mortality
  • SE: GI and neurologic symptoms

• Benznidazole (Rochagan)
  • SE: neuropathy, rash, granulocytopenia (CBC q 2 weeks); less overall; no alcohol

• CDC Drug Service: 404-639-3670
## Dosing

<table>
<thead>
<tr>
<th>Drug</th>
<th>Age group</th>
<th>Dosage and duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benznidazole</td>
<td>&lt; 12 years</td>
<td>5-7.5 mg/kg per day orally in 2 divided doses for 60 days</td>
</tr>
<tr>
<td></td>
<td>12 years or older</td>
<td>5-7 mg/kg per day orally in 2 divided doses for 60 days</td>
</tr>
<tr>
<td>Nifurtimox</td>
<td>≤ 10 years</td>
<td>15-20 mg/kg per day orally in 3 or 4 divided doses for 90 days</td>
</tr>
<tr>
<td></td>
<td>11-16 years</td>
<td>12.5-15 mg/kg per day orally in 3 or 4 divided doses for 90 days</td>
</tr>
<tr>
<td></td>
<td>17 years or older</td>
<td>8-10 mg/kg per day orally in 3 or 4 divided doses for 90 days</td>
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</tbody>
</table>
Prevention

• WHO and PAHO
  • Vector control
  • Screening of blood donors (gentian violet tx)
  • Detect and treat congenital infections
  • Treat all children with acute disease

• Vaccines difficult: host response to natural infection is inadequate
• Travelers: rare, use bednets and insecticide if in endemic setting
Take Home Points

• Trypanosoma cruzi
• Disease of rural + low SES, but changing
• Still common (300,000 cases in the US)
• Domestic animal reservoirs
• Reduviid/triatomine “kissing” bug
• Clinical Disease
  • Chagomas, Romana’s sign
  • Acute
  • Chronic: Cardiac and GI disease
• Treatment limited, but helpful if early
African Trypanosomiasis
(Sleeping Sickness)
Epidemiology

• **Glossina** (Tsetse) Fly
• Very focal: may be #1 cause of mortality
• **T. b. rhodesiense**: humans not as important
  • Rapid dz: hard to sustain endemic infxn (Ebola > HIV)

<table>
<thead>
<tr>
<th></th>
<th><em>T. brucei gambiense</em></th>
<th><em>T. brucei rhodesiense</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Geographic distribution</strong></td>
<td>West, Central Africa</td>
<td>East Africa</td>
</tr>
<tr>
<td><strong>Fly species</strong></td>
<td><em>Glossina palpalis</em></td>
<td><em>Glossina morsitans</em></td>
</tr>
<tr>
<td><strong>Fly habitat</strong></td>
<td>Humid, rivers</td>
<td>Dry savannah/woodland</td>
</tr>
<tr>
<td><strong>Primary host</strong></td>
<td>Humans</td>
<td>Animals</td>
</tr>
<tr>
<td><strong>Nature of disease</strong></td>
<td>Chronic</td>
<td>Acute, Epidemic</td>
</tr>
</tbody>
</table>
Pathogenesis

Human stages:

• Chancre: day 10

• Waves every 1-8 days
  • Variant surface gp (VSG)
  • Antigenic Variation: change predominant Ag with each wave
  • 1000 VSG types

• Broad Ab response

• Direct tissue invasion
Epidemiology

- 1999: 45,000 cases of HAT reported (WHO); likely 10x as many
  - Estimated 100,000 deaths/year
- 2010: 7000 cases of HAT reported
  - 50 cases/year outside Africa
Clinical Disease

• *T. b. rhodesiense* -> rapid progression (months), overlapping stages
• Early Infection (Stage 1)
  • Constitutional, HSM, LAD, facial swelling, rash; amenorrhea, impotence (3 years)
  • Chancre: 10 days-4 weeks; painful, can ulcerate; *T. b. gambiense* > *rhodesiense*
  • LAD (56%): soft: *T. b. gambiense* > *rhodesiense*
Clinical Disease

- Late Infection (Stage II): progressive, diffuse meningoencephalitis
  - Poor concentration, personality, anxiety, tremor, HA (79%), ataxia, psychosis
  - Altered circadian rhythm -> daytime somnolence (74%)
  - Seizures common in children
  - Progressive coma -> malnutrition, other infection
  - *T. b. rhodesiense*: weeks to months
    - May include pancarditis

- 100% mortality if untreated

- > 5 WBC/uL in CSF
Diagnosis

• Definitive: ID in blood, LN aspirate, chancre aspirate, or CSF
  • Thin/thick smears, concentrate: early is better, may need to repeat

• Need LP for staging disease (affects treatment)
  • CSF: Usually < 200 lymphocytes/μL, may have elevated protein
  • Mott cells: large eosinophilic plasma cells, contain unsecreted IgM

• Screening: may use serologic testing but need confirmation
  • Card agglutination test for T.b.g. trypanosomes (CATT)
  • Sensitivity: 94-98%
  • If + -> blood smear/LN aspirate +/- CSF

• PCR tests in development
Treatment

• Depends on stage: obtain CSF even if no CNS symptoms (and call CDC)
• Can be very toxic and expensive: 3-5% mortality from tx if late stage!

• Early disease (hemolympathic) options
  • Suramin (1922): *T. b. rhodesiense* preferred, IV for 5 doses over 21 days
    • SE: N/V, LOC, seizure, hepatitis, pruritis, renal, anaphylaxis (1/20,000 – give test dose)
    • IV on days 1, 3, 7, 14, 21
  • Pentamidin (1938): *T. b. gambiense* preferred, doesn’t cross BBB
    • IM x 10 days
    • SE: immediate hypotensive rxn, nausea/vomiting, Herxheimer-type reaction
Treatment

• Late (CNS) disease options
  • Melarsoprol (1949): *T.b. rhodesiense*
    • Previous 1st line: 86% cure rate at 2 years f/u, though failure rate of 30% in some areas
    • GI, rash, hepatotoxicity, peripheral neuropathy, paraplegia, arrhythmias, albuminuria
    • Arsenic encephalopathy: common and fatal, reduced with steroids
  • Eflornithine (1990) +/- nifurtimox: *T.b. gambiense*
    • 94-96% cure in late disease
    • Works well for relapse
    • Contraindicated in pregnancy
    • SE (40%): GI, dizziness, hearing loss, seizure, rash, alopecia, and bone marrow toxicity

• Check CSF every 6 months for 2 years
# Treatment Dosing

<table>
<thead>
<tr>
<th></th>
<th>Trypanosoma brucei gambiense</th>
<th>Trypanosoma brucei rhodesiense</th>
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<tbody>
<tr>
<td><strong>Early infection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Preferred</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pentamidine</td>
<td>4 mg/kg/day IM or IV (over two hours) for 7 days</td>
<td>Suramin</td>
</tr>
<tr>
<td><strong>Alternative</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suramin</td>
<td>100 to 200 mg (test dose) IV, then 20 mg/kg (max 1 g) IV on days 1, 3, 7, 14, and 21</td>
<td>None</td>
</tr>
<tr>
<td><strong>Late infection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Preferred</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eflornithine PLUS Nifurtimox</td>
<td>200 mg/kg every 12 hours IV (over one hour) for 7 days PLUS 5 mg/kg orally every 8 hours for 10 days</td>
<td>Melarsoprol*</td>
</tr>
<tr>
<td>Eflornithine</td>
<td>100 mg/kg IV every 6 hours for 14 days</td>
<td></td>
</tr>
<tr>
<td><strong>Alternative</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melarsoprol*</td>
<td>2.2 mg/kg/day IV for 10 days</td>
<td>Melarsoprol*</td>
</tr>
</tbody>
</table>
Prevention

- Endemic areas are rural, poor, and politically unstable
- Vaccines: difficult given antigenic variation, but possible
- Vector control: also difficult
- Chemoprophylaxis is very difficult and toxic (suramin IV q 2-3 mos) but it is effective (currently not recommended)
- Screening for *T.b. gambiense* should occur 2x/year, but occurs < 10%
  - *T.b. rhodiense* asymptomatic infection is rare
Take Home Points

- *T. brucei gambiense*
  - Slow, endemic, human hosts
- *T. brucei rhodesiense*
  - Rapid, epidemic, animal hosts

- Disease
  - Early: chancre, Winterbottom’s sign
  - Late: CNS symptoms, malnutrition

- Diagnosis
  - Visualize parasite -> get CSF!
  - Screening (CATT Card) measures Ab

- Treatment and prevention: bad options
Leishmaniasis
Epidemiology

- Female sandfly bite -> mammalian host
  - Humans are incidental host
- 23 species of Leishmania
- 12 million people infected = 400,000 cases/year
- 90% of VL in Bangladesh, Brazil, India, Nepal and Sudan
- 90% of ML in Bolivia, Brazil and Peru
- 90% of CL in Afghan., Brazil, Iran, Peru, Saudi Arabia and Syria
- US
  - 2000 cases in military personnel (Iraq, Afghanistan)
  - Autochthonous transmission in TX, OK, ND
  - Top 10 cause of skin disease in returning traveler (Bolivia, Peru, Brazil)
New World

Old World

LEISHMANIASIS

12 million people infected
350 million people at risk

- Visceral
- Cutaneous / Mucocutaneous
- Visceral + Cutaneous / Mucocutaneous
Epidemiology

• Environment Factors
  • Climate change
  • Urbanization/deforestation
  • Increasing rodent populations
  • Decreasing insecticide use
  • Building of dams

• Other SES Factors
  • Extreme poverty
  • Malnutrition
  • Poor housing

• Adventure travel
• Mass population displacement/migration
• New irrigation schemes and urbanization
• Immunosuppression

• Illiteracy
• Gender discrimination
• War
Clinical Disease

- Incubation: days-weeks usually
- Asymptomatic infection common: 10-95%
  - Nutrition, host genetics, virulence
- Cutaneous
  - Exposed skin
  - Papule -> nodule -> plaque
  - Spread along lymphatics -> LAD
  - Resolves over months-years
  - Chiclero’s ulcer (L. L. mexicana, NW)
- Diffuse cutaneous LM
- Mucosal LM (“espundia”)
  - Mucosal destruction
  - Significant morbidity
Clinical Disease

- Viceral Leishmaniasis ("kala-azar," black fever)
  - Incubation: weeks-months (4-6 months usually)
  - Slow progression of malaise, fever, weight loss, splenomegaly
  - Anemia, liver failure: ascites, bleeding
  - Darkening of skin (S Asia): uncommon
  - Renal impairment common (up to 45%)

- Mortality 10% if treated, 100% if not
- Risk Factors for mortality
  - Jaundice
  - Wasting
  - Severe anemia
  - HIV or TB co-infection
Diagnosis

• Need to be from an endemic area - ask the family
• Important to ID species - affects treatment
• Good history and exam: skin, mucosal surfaces, etc.
• Definitive dx:
  • ID organism in tissue (skin, spleen, BM) by histo, culture, or PCR
  • PCR: 95-99% sn and 67-91% sp for CL
• Ab (VL only): direct agglutination test
• Montenegro skin test: intradermal killed promastigotes
  • 82 – 89% sn for localized CL
  • Used in S America
Treatment

• Cutaneous
  • Not always necessary (small, healing, no ML)

• Why treat?
  • Promotes accelerated healing of skin lesions
  • Diminished severity of skin scarring
  • Reduced likelihood of recurrence
  • Reduced risk for metastatic infection
  • Reduce reservoir of transmission (public health benefit)

• Regimen varies a lot based on local resistance
• Biopsy the lesion and PCR if available, especially if in S America (ML)
Treatment

• Cutaneous
  • 105 returned travelers to France
  • 62% tx without systemic therapy
  • Cure rates: 92% for wound care, 79% local tx

• Options
  • Local: miltefosine, cryotherapy, thermotherapy
  • Systemic:
    • Azoles (4-6 weeks): ? efficacy, less toxic
    • Amphotericin (20-30 days): effective but toxic
    • Pentamidine
  • Pentavalent antimonials: local (q3-7 days until healed) or systemic (10-20 days), or paromycin
    • Not available in US (IND), but work!
### Drug Regimens for Treatment of Cutaneous Leishmaniasis in Adults[1-3]

<table>
<thead>
<tr>
<th>Local Therapy</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentavalent antimonials</td>
<td>Sodium stibogluconate&lt;sup&gt;+&lt;/sup&gt;</td>
<td>0.5 to 2 mL of 100 mg/mL pentavalent antimony (Sb&lt;sup&gt;5+&lt;/sup&gt;) intraleosonally every three to seven days until healed</td>
</tr>
<tr>
<td></td>
<td>Meglumine antimoniate&lt;sup&gt;↑&lt;/sup&gt;</td>
<td>0.5 to 2 mL of 85 mg/mL pentavalent antimony (Sb&lt;sup&gt;5+&lt;/sup&gt;) intraleosonally every three to seven days until healed</td>
</tr>
<tr>
<td>Paromomycin</td>
<td>Paromomycin ointment&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Apply topically to lesions twice daily for 10 to 20 days</td>
</tr>
<tr>
<td></td>
<td>WR 279396 cream&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Apply topically to lesions once daily for 20 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oral Systemic Therapy</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azoled</td>
<td>Fluconazole</td>
<td>200 to 600 mg orally once daily for six weeks</td>
</tr>
<tr>
<td></td>
<td>Ketoconazole</td>
<td>600 mg orally once daily for 28 days</td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>100 to 200 mg orally twice daily for 28 days</td>
</tr>
<tr>
<td>Miltfosine</td>
<td>Miltfosine&lt;sup&gt;5&lt;/sup&gt;</td>
<td>2.5 mg/kg (maximum 150 mg) orally once daily for 28 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parenteral Systemic Therapy</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentavalent antimonials</td>
<td>Sodium stibogluconate</td>
<td>20 mg/kg/day intravenously or intramuscularly for 10 to 20 days&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Meglumine antimoniate</td>
<td>20 mg/kg/day intravenously or intramuscularly for 10 to 20 days&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Amphotericin</td>
<td>Amphotericin B deoxycholate</td>
<td>0.5 to 1 mg/kg intravenously every other day for 20 to 30 days</td>
</tr>
<tr>
<td></td>
<td>Liposomal amphotericin B (AmBisome)</td>
<td>3 mg/kg intravenously daily for five to seven doses; if immunocompromised host then give 4 mg/kg for ten or more doses</td>
</tr>
<tr>
<td>Pentamidine</td>
<td>Pentamidine leithionate</td>
<td>2 to 4 mg/kg intravenously or intramuscularly every other day for four to seven doses or until healed</td>
</tr>
</tbody>
</table>

Agents listed, dose regimens, and combinations are effective only against certain *Leishmania* species/strains and only in certain areas of the world. The therapeutic approach to cutaneous leishmaniasis is discussed in the topic "Treatment of cutaneous leishmaniasis." Pediatric dosing is summarized separately<sup>[3]</sup>.

<sup>*</sup> In the United States, may be obtained from the Centers for Drug Control and Prevention Drug Services telephone 404-639-3670 or 404-639-2889 (nights, weekends).

<sup>↑</sup> Effective dose for weight >75 kg may require higher dose off label (with attendant gastrointestinal effects), aiming for >2.5 mg/kg dose.

<sup>→</sup> Compounding instructions and additional information is summarized separately<sup>[5]</sup>.

<sup>↑</sup> For treatment of CL among military healthcare beneficiaries in the United States, may be obtained from US Army Medical Material Development Activity.

<sup>2</sup> Although FDA approved, miltfosine is not yet commercially available. Drug can be obtained by contacting the FDA at 301-796-4145 (Division of Antiviral Products) and requesting an emergency IND. Miltfosine should not be used in women of childbearing age unless a validated contraceptive method is used during treatment and for at least six months following treatment.

<sup>4</sup> Doses are expressed as mg of pentavalent antimony (Sb<sup>5+</sup>) content. Duration of 10 days is appropriate for treatment of relatively mild disease with evidence of clinical response by day 10; otherwise, the duration should be extended. Duration of 20 days is appropriate for treatment of CL due to species known to cause mucosal disease. Meglumine antimoniate has 81 mg Sb<sub>v</sub>/mL, while sodium stibogluconate (SSG) contains 100 mg Sb<sub>v</sub>/mL. Intravenous treatment is usually diluted at least tenfold with 5 percent dextrose in water and SSG is filtered.
Treatment

• ML or VL

• Complicated CL -> systemic therapy
  • Infection with ML species (Bolivia, Peru, and Brazil)
  • > 4 lesions
  • Single lesion ≥5 cm
  • Subcutaneous nodules
  • Lesions on face, fingers, or toes
  • Immunosuppressed host
  • Clinical failure of local therapy after 2-3 months

• Duration 4-12 weeks

• Amphotericin or Miltefosine: approved for use in US for VL
Treatment of visceral leishmaniasis in adults

<table>
<thead>
<tr>
<th>Preferred therapy and duration</th>
<th>Alternative therapy</th>
<th>Other options/issues</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VL in previously immunocompetent patient</strong></td>
<td>Amphotericin B &amp; deoxycholate 0.75 to 1.0 mg/kg IV every other day for 30 days; or Sodium stibogluconate 20 mg/kg IV or IM daily for 28 days</td>
<td>Nutritional support, treatment of hemorrhagic or infectious complications Mitelofosine 2.5 mg/kg/day PO x 28 days</td>
</tr>
<tr>
<td>Liposomal amphotericin B 3 mg/kg IV on days 1, 5, 14, and 21; or 3 mg/kg/day x 7 to 10 days; or 10 mg/kg/day x 2 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV-VL coinfection</td>
<td>Amphotericin B &amp; deoxycholate 0.5 to 1.0 mg/kg IV QO for total dose of 1.5 to 2.0 grams; or Sodium stibogluconate 20 mg/kg IV or IM daily for 28 days</td>
<td>ART should be initiated or optimized Alternative regimen for treatment failure: Mitelofosine 2.5 mg/kg/day PO x 28 days</td>
</tr>
<tr>
<td>Liposomal amphotericin B 2 to 4 mg/kg IV daily x 10 days; or Interrupted schedule (eg, 4 mg/kg on days 1 to 5, 10, 17, 24, 31, 38) to achieve total dose of 20 to 60 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary prophylaxis: Liposomal amphotericin B 4 mg/kg every two to four weeks</td>
<td>Secondary prophylaxis: Sodium stibogluconate 20 mg/kg IV or IM every four weeks</td>
<td></td>
</tr>
<tr>
<td>Post kala-azar dermal leishmaniasis</td>
<td>Amphotericin B &amp; deoxycholate 1 mg/kg/day x 60 days (20-day courses with 20-day rest periods)</td>
<td>Mitelofosine 2.5 mg/kg/day PO x 12 weeks</td>
</tr>
<tr>
<td>Sodium stibogluconate 20 mg/kg/day IV or IM x 60 to 120 days (usually given in 20-day courses with 10-day rest periods)</td>
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</tbody>
</table>

VL: visceral leishmaniasis; IV: intravenous; IM: intramuscular; PO: by mouth; ART: antiretroviral therapy.

* Available from the Centers for Disease Control and Prevention (CDC) Division of Parasitic Diseases (contact 404-718-4745; email parasites@cdc.gov). CDC Drug Service (404-639-3670), or for emergencies outside of business hours, CDC Emergency Operations Center (770-488-7100).

Drugs regimens for treatment of mucosal leishmaniasis in adults[^1-3]

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<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentavalent antimonials[^*]</td>
<td>Sodium stibogluconate[^†]</td>
<td>20 mg SBV/kg[^Δ] intravenously or intramuscularly per day for 28 days</td>
</tr>
<tr>
<td></td>
<td>Meglumine antimoniate[^§]</td>
<td>20 mg SBV/kg[^Δ] intravenously or intramuscularly per day for 30 days</td>
</tr>
<tr>
<td>Amphotericin</td>
<td>Amphotericin B deoxycholate</td>
<td>1 mg/kg intravenously per day or every other day, up to total cumulative dose of 2.5 to 3 g</td>
</tr>
<tr>
<td></td>
<td>Liposomal amphotericin B (Ambisome)</td>
<td>3 to 5 mg/kg intravenously once daily (no more than 200 mg daily) up to total cumulative dose of 40 mg/kg</td>
</tr>
<tr>
<td>Miltefosine[^*]</td>
<td>Miltefosine[^‡]</td>
<td>2.5 mg/kg orally (maximum 150 mg) once daily for 28 days</td>
</tr>
<tr>
<td>Pentamidine[^*]</td>
<td>Pentamidine isethionate</td>
<td>4 mg/kg intravenously or intramuscularly per day or every other day, until healed or up to total dose of 2 g</td>
</tr>
</tbody>
</table>

Agents listed, dose regimens, and combinations are effective only against certain *Leishmania* species/strains and only in certain areas of the world. The therapeutic approach to mucosal leishmaniasis is discussed in the topic ‘Treatment of cutaneous leishmaniasis.’ Pediatric dosing is summarized separately[^1].

[^1-3]: Authors of reference with additional data from:
Take Home Points

• Top 10 cause of skin disease in returning traveler (Bolivia, Peru, Brazil)
• Type (CL, ML, VL) and species (tx) depends on geography
• Consequence of human encroachment on sandfly habitat (and animal reservoirs)
• CL: chronic, usually self resolves, treat if complicated or ML species
  • Azoles, Pent. Antimonial (top, IV); Ampho, Pentamidine, Paromycin (top)
• ML: occurs in SA forms, need a good exam
• VL: 100% mortality, splenomegaly, cachexia; tx w/ systemic drugs
• Biopsy the lesion, send PCR if possible; use local epi data (CDC)
Back to the Case...

• 2 y/o girl with facial lesion
• Patient is from Kabul, Afghanistan!
• DDx: Chagoma, *T.b. gambiense* (stage I), CL
• Leishmaniasis PCR of tissue bx: *L. tropica*
• Mild CL but on the face, family members treated w/ antimonial injection
• Tx: 6 months of PO fluconazole -> improved
  • Stopped tx -> ulcerated after 6 weeks
  • Restarted treatment -> improved
References

References


• Marfurt J, Niederwieser I, Makia ND, Beck HP, Felger I. Diagnostic genotyping of Old and New World Leishmania species by PCR-RFLP. Diagn Microbiol Infect Dis. 2003;46(2):115


• World Health Organization

• Centers for Disease Control

• Up-to-Date
Questions?

• CDC Parasite hotline: 404-718-4745 (parasites@cdc.gov)
• CDC: http://www.cdc.gov/globalhealth/ntd/
• WHO: http://www.who.int/neglected_diseases/en/
• PAHO: http://www.paho.org
• IDSA Pediatric Red Book

• Daniel.Olson@ucdenver.edu