Bacterial Diseases
1. Peptic Ulcers (H. pylori)
2. Tuberculosis (M. tuberculosis)
3. Gonorrhea (N. gonorrhoeae)
4. Necrotizing Fasciitis (S. pyogenes)

1. *Helicobacter pylori*

What is *Helicobacter pylori*?

*H. pylori* is a microaerophilic bacterial species, meaning that it needs a little bit of oxygen to survive, which explains why its optimal environment is the stomach lining. It also has the following characteristics:

- Gram-Negative helical rod
- Flagella aid in motility and adhesion
- Contains urease which neutralizes gastric acid
- Have proteins on surface for adhesion
Mode of Transmission

- Water Contamination
- Person to Person (physical contact)
  - Oral to Oral (kissing)
  - Fecal to Oral (contaminated food)

Mechanism of Disease

- *H. pylori* secretes two cytotoxic factors VagA and CagA
  - Disrupt differentiation and signal transduction in epithelial cells.
  - Protease and lipase disrupt gastric mucus phospholipid layer.
  - Begins colonization.

Cag A vs. Vag A

- Cag A: Cytotoxic protein shown to impact disease. Inhibits B-Cell apoptosis which leads to MALT Lymphoma.
- Antagonistic to each other.
Signs and Symptoms

- Abdominal pain or burning (specially when on empty stomach)
- Nausea
- Loss of appetite
- Sudden weight loss
- Bloody or black stool
- Bloody vomit
- Difficulty swallowing
- Bloating

Diagnosis

Methods include:

- Physical exam
- Breath test (carbon isotope urea test)
- Blood test for antibodies to H. pylori
- Stool test for H. pylori antigens
- Biopsy of stomach to look for H. pylori (most reliable)

Breath test

- Carbon isotope urea test:
  - Based on ability of H. pylori to break down urea
  
  **PROCEDURE:**
  - Patient swallows capsule that contains $^{13}$C labeled urea
  - Sample of exhaled breath is collected & measured for isotopic carbon

  **RESULT:**
  - Urea is broken down and turned into carbon dioxide if H. pylori is present.
  - Carbon dioxide crosses stomach lining, travels to blood, to lungs where it is exhaled.

  WHEN $^{13}$C IS DETECTED
  
  H. pylori IS PRESENT
**Treatment**

- Since *H. pylori* is gram-negative, antibiotics to disrupt its lipopolysaccharide outer layer are prescribed.
- Combination of 2 antibiotics is prescribed for 7 to 14 day period
  - Most often used Amoxicillin and Metronidazole
- **REASONS FOR TREATMENT FAILURE:**
  - Antibiotic resistance
  - Patient Noncompliance

**Prevention**

- Wash hands after using the restroom and before cooking
- Sanitize vegetables before consuming
- Cook meats thoroughly
- Avoid contact with someone who may have *H. pylori* infection that has not been treated (touch, kiss, allowing them to cook your meals)
- There is no large scale vaccine produced that is affective for *H. pylori* to date.

**2. Tuberculosis**

*Mycobacterium tuberculosis*
**Mycobacterium tuberculosis**

TB is caused by infection with Mycobacterium tuberculosis bacteria.

**General Characteristics**
- **Family**: Mycobacteria
- **Gram**: positive aerobic rod-shaped bacilli
- **"Acid fast"** bacteria
- **No capsule or flagellum** (non-motile)
- **Generation time of 18-24 hours** but requires 3-4 weeks for visual colonies (very slow)
- Requires very few bacteria (1-10) to establish infection
- Waxy, thick, complex cellular envelope with mycolic acids

**Pathological Features**
- Intracellular pathogen (alveolar macrophages)
- Produces tubercles, localized lesions of M. tuberculosis

**Effects of Mycobacterial Cellular Envelope**

**Resistance to Drying and Other Environmental Factors**
- Thick, waxy nature of cellular envelope protects M. tuberculosis from drying, alkali conditions, and chemical disinfectants
- Hinders entrance of antimicrobial agents

**Entry into Host Cells**
- Lipoarabinomannan (LAM) binds to mannose receptors on alveolar macrophages leading to entry into the cell

**Interference with Host Immune Response**
- Glycolipids and sulfolipids decrease the effects of oxidative cytotoxic mechanisms
- Inhibition of phagosome and lysosome fusion inside macrophage
- Waxy cellular envelope prevents acidification of the bacteria inside the phagosome

**How Are TB Germs Spread?**

- TB germs are passed through the air when a person who is sick with TB disease coughs, sings, sneezes, or laughs
- To become infected with TB germs, a person usually needs to share air space with someone sick with TB disease (e.g., live, work, or play together)
- The amount of time, the environment, and how sick the person is all contribute to whether or not you get infected
- In most cases, your body is able to fight off the germs
TB Infection vs. TB Disease

- TB Infection: M. tuberculosis cells stay in your lungs, but they do not multiply or make you sick
  - You cannot pass TB germs to others
- TB Disease: M. tuberculosis stays in your lungs or moves to other parts of your body, multiplies, and makes you sick
  - You can pass the TB germs to other people

Common Symptoms of Tuberculosis

- Cough (2-3 weeks or more)
- Coughing up blood
- Chest pains
- Fever
- Night sweats
- Feeling weak and tired
- Losing weight without trying
- Decreased or no appetite
- If you have TB outside the lungs, you may have other symptoms

Diagnosis of Latent & Active TB

Tools for Diagnosing TB Infection

- Mantoux skin test (PPD)
- Chest x-ray
- Sputum cultures
Treatment for Tuberculosis

**Antibacterial chemotherapy:**
- Combination of *first and second line* drugs for the first 2 months which could include:
  - Isoniazid
  - Rifampicin
  - Pyrazinamide
  - Streptomycin or Ethambutol
- Next 4 months, combination of:
  - Isoniazid
  - Rifampicin

- TB disease can be cured if the medicine is taken as prescribed

Drug Resistance and Tuberculosis

- *M. tuberculosis* is naturally resistant to certain antibiotics due to presence of:
  - Drug-modifying enzymes
  - Drug-efflux systems
  - Hydrophobic cell wall
- Mycobacteria undergo natural mutations which can lead to the development of additional drug resistance.
- Administration of **combination chemotherapy** (simultaneous use of multiple drugs) decreases probability of developing drug resistance.
- Development of increasingly resistant strains is mainly due to patient non-compliance (not taking medication as prescribed)

PREVENTION: Protect your family and friends

If you have active TB, follow these tips to help keep your friends and family from getting sick:

- **Stay home.** Don’t go to work or school or sleep in a room with other people during the first few weeks of treatment for active tuberculosis.
- **Ventilate the room.** Tuberculosis germs spread more easily in small closed spaces where air doesn’t move. If it’s not too cold outdoors, open the windows and use a fan to blow indoor air outside.
- **Cover your mouth.** Use a tissue to cover your mouth anytime you laugh, sneeze or cough. Put the dirty tissue in a bag, wash it, and throw it away.
- **Wear a mask.** Wearing a surgical mask when you’re around other people during the first three weeks of treatment may help lessen the risk of transmission.
3. Gonorrhea
*Neisseria gonorrhoeae*

**Description of *N. gonorrhoeae***

- Gram-negative Diplococcus
- Several pili for attachment and motility
- Optimal temperature is 37 degrees Celsius
- Thrive in CO₂ environment and only in humans

**Mode of transmission**

- Sexually transmitted with the exception of a new born babies.
Mechanism of Disease

1. Cytokine release causing leukocyte infiltration, inflammation
2. Epithelial cells destroyed
3. Inflammation of Tendon Sheaths and Septic Arthritis
4. Disseminated Gonococcal Infection (DGI)
5. Formation of Vacuoles for replication
6. Antigen Variation (pilE, pilT, pilS) delays immune responses
7. IgA protease cleaves IgA antibodies to avoid opsonization, neutralization, etc.

Signs and Symptoms

• Inflammation of the clitoris and fallopian tubes in the female causing extreme discomfort and may lead to Pelvic Inflammatory Disease
• Burning sensation upon urination (both males and females)

Signs And Symptoms

• Newborn babies have a yellowish crust around the eyes. If left untreated for too long, this can cause problems in vision, even blindness
• Discharge from both males and females – foul smelling yellowish, cloudy liquid that comes out of penis or uterus
Diagnosis

- Swabbing the persons infected areas and observing Gram stain under microscope to look for diplococci
- Can be cultured to characterize further
- PCR

Antibiotic Treatment

- Ceftriaxone (Rocephin)
- Azithromycin (Zmax, Zithromax)
- Cefixime (Supraz)
- Doxycycline (Vibramycin, Doxy)
- Erythromycin ophthalmic

Prevention

- Only real way to prevent this is to not have sex with anyone that has this infection
- If you can't wait, use protection but not 100% avoidable
4. Necrotizing Fasciitis

Meet "Necro"

Main Cause
Group A Streptococcus pyogenes; Gram positive, aerobic, non-motile

Arrangement & Morphology:
Strepto (chains), Cocci (sphere)

Other Causes:
Clostridium perfringens, Staphylococcus aureus, Escherichia coli

The worst dinner guest!!

- Disease bacteria enter the body through opening in the skin (cut, burn, break on the skin)
- Rarely passed from person to person
- Immunocompromised people are more susceptible (e.g., those with cancer, diabetes, kidney disease)
**Hungry Hungry “Necro”**

Bacteria causing necrotizing fasciitis digest muscle fascia, connective tissues and fat tissue with an array of enzymes and toxins:

- Deoxyribonucleases (break down DNA)
- Streptokinases (dissolves blood clots)
- Hyaluronidase (breaks down hyaluronic acid)
- Exotoxin A (toxemia)
- Streptolysin (kills many human cells)

Tricky symptoms, Bad signs

- Red or purplish skin swelling
- Possible ulcers, blisters, or black spots on the skin
- Fever, Pain, chills, fatigue, nausea, low BP

Diagnosis

- Pain > appearance of injury
- Laboratory tests (score 6-8)
- Imaging studies (CT or MRI)
- Finger test and biopsy
- Gram stain

### Laboratory Risk Indicator for Necrotizing Fasciitis Score (LRINEC)

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<tr>
<th>Factor</th>
<th>Value</th>
<th>Score</th>
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<td>Hemoglobin, g/dl</td>
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<td>&lt;15</td>
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Now What?!

Your Options:
- IV broad spectrum antibiotics (penicillin and clindamycin)
- Cutting away infected tissue, amputation

Your chances:
- Destroys tissues SEVERAL CENTIMETERS OF TISSUE PER HOUR leading to organ failure and a 50% mortality rate.
- Clindamycin + Penicillin = 83% chance
- Survivors average time from admission to operation is ~25 hrs!!

Prevention and vaccination
- Good personal hygiene is best prevention
- Proper wound care
- Be mindful of wound to pain ratio
  ❖ No current vaccine but....

Eukaryotic Diseases

1. Blastomycosis (*B. dermatitidis*)
2. Sleeping Sickness (*T. brucei*)
What is Blastomycosis?

- infectious disease caused by the fungus *Blastomyces dermatitidis*
- found in moist soil, construction, lakes
- occurs primarily in Africa, India, Canada, SE U.S.A.

Pathogen: *Blastomyces*

- Lives in environment as a mold
- Converts to unicellular large budding yeast at 37°C (body temperature)
- Phagocytosis by neutrophils, macrophages is essential to rid body of pathogen before it converts to yeast which is more difficult to destroy
How is the Pathogen Transmitted From One Host to Another?

**Step 1**
Breathe in Spores ➡ Lungs

**Step 2**
Body Temp = Spores to Yeast

**Step 3**
Weak immunity = spread in bloodstream to CNS, skin, bones, organs

How does the pathogen cause damage????

Once converted to yeast it has a thick cell wall and is more resistant to phagocytosis and killing

SIGNS AND SYMPTOMS

**Flu-like Symptoms**
- Chest pain
- Cough
- Fatigue
- Fever/Night Sweats
- Muscle Pain
- Weight loss

**Skin Symptoms**
- Nodules that look like warts or ulcers
- Variation of colors
- Bleed easily
- Cause severe scarring and loss of pigment

Infection areas such as lymph nodes, spleen, breast, etc. - 3%

Chronic Pneumonia
- Respiratory Failure 8%
- Chronic Meningitis 1%
- Skin Lesions 20%

Scarring of Lung Tissue

Infection in Bones 5%

Infection in CNS: Meningitis 1%

Infection in Skin: Lesions 20%

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How is the disease identified?

- Blood or Urine Antigen Test
- Chest X-rays or CT scan of lungs
- Tissue biopsy
- Smear of fluid from Respiratory tract

Treatment

- Antifungal Medication
  - Moderate: Itraconazole
  - Severe: Amphotericin B
- 6 months-1 year
- NO antibacterial drugs
- Non-Steroidal anti-inflammatory drugs for pain and inflammation

Prognosis

Good
- Minimal Skin lesions
- Treated early
- Lungs not affected moderately or severely
- Complete Recovery

Bad
- Self-destructive cell death immunity
- Lack of T-cells
- Mortality rate of 60% in 2 years+
- Advanced bone disease
- Brain affected means no complete recovery
- Permanent lung damage
- Death
- Weak Immunity, lack of T-cells
Avoid travel to areas where infection is known to occur.

PREVENTION

2. Trypanosoma brucei

What is Trypanosoma brucei?

- Trypanosoma brucei is a parasite that causes Trypanosomiasis or also known as “African sleeping sickness”
- African sleeping sickness is a 2 stage illness that is spread by the bite of a Tsetse fly where if left untreated infection of the central nervous system will occur and death will follow.
Description of the Pathogen

Trypanosoma brucei is a Parasitic Protozoan hemoflagellate that belongs to the Genus Trypanosoma.

- Unicellular eukaryotic cell that features a nucleus, cytoplasm, basal body, flagellum, and a kinetoplast which is circular DNA located in the mitochondrion.

The Mode of Transmission

The parasites causing trypanosomiasis, T. b. gambiense and T. b. rhodesiense are primarily transmitted from the blood sucking tsetse fly to humans.

- There are two stages during the transmission of Trypanosomiasis. The “infective” stage when the parasite is within the tsetse fly and the “diagnostic” stage when the parasite is within a mammalian host.
The Mechanism of Disease

- When infection of Trypanosomiasis occurs there are two stages of infection. The first stage is called the hemolymphatic stage and the second stage is called the neurological stage.
- During the hemolymphatic stage the parasite is within the peripheral blood and lymph where it will multiply.
- When the parasite passes through the blood-brain barrier to infect the Central Nervous System it will enter the neurological stage.
- Once the parasite has invaded the CNS this will lead to the development of meningoencephalitis and an irreversible demyelinating process which is deadly without treatment.

Symptoms

- General symptoms of the disease include itchiness, headaches, muscle and joint aches, swollen lymph nodes, and general weakness.
- Symptoms shown during the neurological stage include changes in behavior, sleep disorder, confusion, seizures, partial paralysis, and coma.

Diagnosis

- *T. b. rhodesiense* has a high parasite load and can be easily found in blood or lymph.
- Serologic testing for *T. b. gambiense* is possible, as it is difficult to detect in blood, but is used only for screening and is not readily available.
- Definitive diagnosis of either parasite causing trypanosomiasis is dependant of finding the parasite in the blood.
- Patients diagnosed must have cerebrospinal fluid examined to determine the stage of the infection and the course of treatment.
**Treatment**

- Treatment is dependent on the type of infecting parasite and the stage the disease has progressed to.
- Pentamidine and suramin are used in first stage T. b. gambiense and T. b. rhodesiense respectively.
- Treatment for the second stage of the disease has an 8% mortality rate.
- Eflornithine is used in second stage T. b. gambiense.
- Melarsoprol is the only treatment currently available for late stage T. b. rhodesiense.
- Relapse is also possible.
- Without treatment:
  - T. b. rhodesiense can be deadly within months
  - T. b. gambiense is usually deadly within 3 years

**Epidemiology**

**Prevention**

Preventative measures include:
- Wearing long sleeved shirts and pants that are neutral in color. Tsetse flies are attracted to bright and dark colors and can bite through lightweight clothing.
- Check vehicles before entering. Tsetse flies are attracted to movement.
- Avoid disturbing flies during the day when they aren’t active.

There is no vaccine for prophylactic drug against African trypanosomiasis. So the controlling of the disease is dependant on reducing the reservoirs of disease, by treating infected, and controlling the vector, the tsetse fly.