Cholera

Mechanism of toxicity:
- Cholera toxin indirectly activates CFTR ion channel
- Cl− ions flow out of cells, and water follows
- What would this cause?

Robert Koch, 1843-1910

- Studied anthrax, which led him to:
  - Establish Koch’s postulates in 1882
  - Discover spores
- Isolated the tuberculosis bacterium in 1882
- Isolated the cholera bacterium in 1883

Koch’s Postulates

Establishing the connection between a microbe and a disease:
- 1st: The microbe should be found in diseased tissue, but not in healthy tissue
- 2nd: The microbe should be isolated from diseased tissue, and grown in a pure culture in the lab
- 3rd: That culture should cause the disease in a human or animal
- 4th: The microbe should be re-isolated from that human or animal
Possible 5th postulate

- 5th: Discover a treatment that removes the bacteria and removes the disease

Cholera

Mechanism of toxicity:
- Cholera toxin indirectly activates CFTR ion channel
- Cl− ions flow out of cells, and water follows
- This causes fatal dehydration, due to water loss via the intestinal tract

How do we currently treat cholera?

- Rehydration with water, sugar, and salt is life-saving
- Antibiotics (doxycycline) will shorten the time of illness

How else could we treat cholera?
- e.g. By killing the bacteria?
- e.g. By stopping it from making us sick?
Possible treatment: Phage are viruses that kill bacteria

- Each virus infects a specific host (e.g. birds, humans, etc)
- "Phage" are viruses that infect bacteria

A bacterial toxin is a harmful protein produced by a pathogenic bacterium

- Example of the cholera toxin
- What does it do and why is it toxic?
- What advantage does cholera gain by producing this toxin?

Possible treatment: Antibodies recognizing a toxin ("anti-toxins") could be an injectable treatment for a bacterial disease

A prevention: A vaccine leads to antibodies being produced in the body

Note: This is a rare way to treat bacterial infections!

Note: Why would we not inject the toxin protein for the vaccine?
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Spores & the anthrax scare

- Spores are special dormant cells that are resistant to heat, radiation, dessication, starvation, etc
- The 2001 bioterrorist acts in the US (22 cases) utilized anthrax spores

The pathogen:
Bacillus anthracis bacteria

Reservoir:
Sheep, goats, cattle

Anthrax

Famous case/outbreak:
- Spores are resistant to heat, radiation, dry conditions etc
- The 2001 bioterrorist acts in the US (22 cases) used anthrax spores
- Severity depends on form of exposure (inhalation, broken skin, digestion of contaminated meat)
Anthrax

**Symptoms:**
- If through broken skin, painless black vesicles
- If through digestion, vomiting and diarrhea
- Bleeding into the space surrounding the heart
- Circulatory failure due to very low blood pressure
- Respiratory failure due to leakiness of lungs, causing them to fill with water

**Mechanism of toxicity:**
- Anthrax toxins “EF” and “LF” first impact white blood cells, alter their migration and behavior, and induce their cell death
- They then directly impact vascular endothelial cells, decreasing their integrity (by increasing permeability), and triggering cell death

**What is a main strategy for treatment?**

**Current treatments:**
- Antibiotics for 60 days after exposure (ciprofloxacin, doxycycline)

What might some other strategies be: for treatment? for prevention?

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**Koch’s Postulates**

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Issues with Koch’s postulates, using TB as an example

1\textsuperscript{st} (associated with diseased tissue)
- Carriers
- Staining

2\textsuperscript{nd} (isolate)
- Culturing
- Slow growth

3\textsuperscript{rd} (introduced into new host)
- Ethics
- Animals as models
- Health, age, immune system, and resistance

4\textsuperscript{th} (re-isolate)
- Mutations