Prof. Schauer

- > Toxins and diagnostic microbiology
- ➤ Brock 21.10-21.12 and Chapter 24
- Toxin
 - The latin root applies to a bow (like a bow and arrow) the idea is that it kills like an arrow
 - o Endotoxin lipopolysaccharide
 - o Exotoxins
 - Proteins
 - Mostly enzymes
 - Three broad types:
 - Cytolysins
 - A-B toxins
 - Superantigens
- Cytolysins
 - o Example: streptococcus pyrogenes
 - This is what gives you strep throat
 - Hemolysin produces a toxin that lyses the cells around it
 - You can see this happening to cells if you plate this bacteria on agar
 - This used to be used to diagnose strep throat, before a quicker test was developed
 - Why does this toxin exist? It doesn't lyse red blood cells in your blood stream. It's there to fight the neutrophils that your body sends to kill the streptococcus
 - If you stay sick with strep throat for very long, it can cause an autoimmune disorder where your own immune system attacks and damages the endothelial lining of your heart valve
- A-B Toxin
 - o Example: Corynebacterium diptheriae
 - Diptheria used to be a major public health concern
 - Antitoxin you develop a toxoid (antigenic, but not toxic)
 - If you immunize people with this toxoid, you develop an antitoxin (antibody that will neutralize the toxin)
 - Emil Adolf von Behring
 - In Boston there's a statue of the husky dog that brought the precious load of antitoxin on a sled across Alaska when there was a big outbreak of diphtheria

- It's not clear if it gains benefit from killing the epithelial cells in the throat, or if its some innate response...
- Some of these bacteria have the phage and make the toxin, but others don't.
 - The ones that don't produce the toxin cause a more minor sore throat
- We're vaccinated against the toxin DPT
- o Example: Clostridium toxins
 - Tetanus toxin
 - Used to be used as a bioweapon fear that it could be used that way again
 - Neural toxin
 - Causes muscle contraction
 - Spastic paralysis
 - Theres an inhibition of the inhibitory muscle contractors, so that people are unable to relax their muscles – they just continue to clench and clench, sometimes so severely that their bones break
 - Causes lockjaw
 - Important to stay immunized against this with regular boosters
 - Botulism toxin
 - Causes flaccid paralysis
 - It works in the same way on a different neural group, so that instead it inhibits muscle contraction
 - Muscles can't contract
 - Used consmetically because it inhibits the contraction of the muscles under your face
 - Also used to treat lazy eye, by injecting it into the muscles of the eye.
 - Infant botulism caused by honey contaminated with botulism spores. The honey won't hurt us, because the biota in our gut can take care of it, but infants can't fight it off, and they can die.

Enterotoxin

- o Example: Cholera
 - Causes rice water diarrhea
 - Normally our body prevents constipation and diarrhea by regulating the secretion of ions to maintain the right amount of moisture
 - Nonstop chlorine secretion and all of the moisture leaves your system
 - People actually die of cardiovascular collapse due to dehydration
 - In a modern hospital, you treat this with liquids provided through IV

- In the third world, where cholera is a big problem, this often isn't possible.
 - There, they use ORT Oral rehydration therapy
 - They carefully control the addition of glucose and sodium in water (called "WHO juice")
 - You have to carefully match the volume of water that comes out (diarrhea) with the volume of water that you feed them to replenish it
 - With this method, people can usually survive for the necessary 7-10 days to fight off the disease

Superantigen

- o Example: Staphylococcus aureus
 - Enterotoxin
 - Common cause of food poisoning
 - Severe vomiting, cramping, sometimes diarrhea
 - SEB (Staph enterotoxin B) the best studied
 - Activates a huge proportion of your T cells
 - Causes production of cytokines
 - These act as a hormone and cause you to throw up
 - Most food poisoning, the kind that is rapid and caused by a toxin, are caused by this bacteria.
 - This could be used as a bioweapon in a military setting
 - Rarely fatal you throw it up so fast that you don't absorb enough to get really sick

Culture and isolation

- o Achieving a pure culture an isolate
 - Used to confirm somebody's diagnosis
 - Used to test the strain for antibiotic resistance
 - Used to compare whether an infection is part of the same outbreak as somebody else's infection
- o Chocolate agar, blood agar
- Competition from other microorganisms occurs, so you need to use selective media
- o Differential medium
- o The most reliable way to distinguish pathogenic microbes is through their biochemical activities
- There's a big market for automated ways to detect what type of bacteria might be growing in the bloodstream, because the consequences of blood infections can be very severe
- Antibody production
 - You inject an animal (usually a rabbit or mouse) with bacteria to isolate an antibody for it
 - This method is sometimes imperfect we might not quite isolate a specific antibody

- The only way to get more antibody is to inject another rabbit
- To make a monoclonal antibody, you can actually kill the animal (usually a mouse) and create a cell line that you can culture, that will still continue to produce the antibody
 - To use these antibodies in people, you have to use recombinant DNA technology, so that it's a humanized antibody instead of a mouse one, thus preventing an immune rejection response
 - This kind of technology is also used in transplants today
- o Serological tests
 - Blood tests figure out your blood type
 - You simply mix the antiserum with the blood and see if it agglutinates
 - Natural antibodies