Topic 7: Antibiotics

- Antibiotics second greatest invention in medical history
    - Up until the 1950s the main causes of death were infectious diseases (ex: Plagues)
- Back in the day they did not have effective cures/treatments, this is because they did not understand how people became sick
    - Thought it was caused by bad smells/unclean conditions (miasma theory)
    - Or God
    - Spontaneous generation
- WWI & WWII more death due to infection than to combat
- In 1844 Agostino Bassi proved germ theory of disease
    - The idea that microscopic animals were causing disease
    - Once it was figured out how you become sick you can protect yourself from it
- In 1854 John Snow disproved miasma theory
    - Mapped out where cholera infections occurred
    - Discovered that a water pump was the cause of the outbreak
    - Found out there was a sece pit (sewage pit) under where the water was and that was causing the outbreak
- In 1864 Louis Pasteur develops pasteurization
    - Discovered that milk as it comes out of the cow has bacteria
    - By pasteurizing the shelf life is extended and the milk is safer
    - Heat the milk to a certain temp or a certain period of time
    - Kills bacteria in milk
- IN 1884 HC Gram stains bacteria
    - Gram +/- depends whether it turns red/blue during the test
- In 1907 Paul Erlich
    - Magic bullet: tells the drug where to go and what bacteria to kill
    - Dye reacts with certain bacteria and only colours them
    - Used to concept to develop a drug that finds the bacteria and kills them instead of changing the colour
    - Developed Salvarsan 606, the first true antibiotic
        - Was great to cure syphilis (which killed thousand of people a year)
        - Not very drug like, how to inject many times and in large doses
        - Was not water soluble, so had to be administered very slowly
            - Injected on a weekly basis over a couple months
        - If you administer improperly (push it in too fast) you would develop necrosis in the arm and would have to be amputated
- 1932 the first commercially successful antibiotic, Prontosil, discovered by Gerhard Domagk
    - Discovered that a dye his company developed could also kill bacteria
    - Only works in a living body
    - Turned peoples skin red
- In 1932 Sulfanilamide was discovered
    - Similar to Prontosil, but did not turn the skin red
    - Inhibits bacterial growth
    - Mimics natural substrates

        - Drug jams itself into the enzyme producing infected cells, stopping more from being produces
- Fleming was growing bacteria in a dish, left and found when he came back that a mold has developed in the dish
    - Fleming realized the mold was secreting a substance that was killing the bacteria
    - However it effected one species
    - Thought he had found a chemical substance that could be used to attack a certain bacteria, or to purify bacteria samples, not as a miracle drug (Penicillin)
- Florey & Chain in 1941
    - Found flemings results in a journal
    - Got a sample of the mold
    - And isolated the chemical substance that was killing the bacteria
    - Took 1000 kg to get 1 g of penicillin
    - Experimented with mice
        - Infected mice
        - Half were given penicillin, half were not
        - The ones with penicillin survived
    - Than experimented on a human
        - A policeman who had a cut on his face that became infected and his head swollen, and went into a comma
        - After being given penicillin he recovered with in 24 hrs
        - However did not have enough to successfully kill his infection, and he eventually died from it
- During the war britain was not the best place to conduct research, so they contacted the US to get funding for their research
    - First thing they did was to try and find a better way to produce the mold
    - Pharmaceutical companies discovered that corn steep liquor could be used as a better source than milk to grow the mold, also that it could be produced more efficiently in tanks (like those used to brew beer)
    - Also used better extraction technology
    - US made penicillin a war priority
        - Because more soldiers died from infection than combat
        - Penicillin was stock piled for D Day
        - At first is was reserved for military personnel only
- Penicillin became available in 1944 to civilians
- Fleming, Florey and Chain won the Nobel Prize in ????
- How penicillin kills bacteria:
    - Each cell is a bag of chemicals
    - Human cells are just a bag with ingredients inside
    - Bacteria cells have an outer cell wall, makes the cell into a pressure bottle
    - Human cells have to be very large because we have so much stuff inside to minimize pressure wer need big cells
    - The pressure is higher in the bacteria because their cell wall is stronger
    - When bacteria divide an important part is the reconstruction of the cell wall
    - Penicillin during cell division prevents the cell form repairing the cell wall

- Beta lactam can chemically react with the enzyme that produces the cell wall and makes a permanent bond between the penicillin and the enzyme
- Natural penicillin is not drug like
    - Unstable
    - Must be injected
    - Only works against some bacteria
- So most penicillin we have today is semi synthesized
    - Only downfall is that it is possible to have an allergic reaction
        - The penicillin will react chemically with enzymes in your body
- After penicillin everyone was looking for another miracle drug (golden age of antibiotics)
    - Cephalosporin found in italian sewer
    - Streptomycin in chicken throat
- Antibiotic resistances
    - The bacteria inside you becomes immune to the antibiotic
    - Over prescription is caused by this
        - Sometimes antibiotics are given for viral diseases as a placebo to get a patient to believe the drug will help them
    - Prophylactic use in animals
        - Putting antibiotics into the animal's food as a precursor to prevent the animals to getting sick and gives us safer meat
    - Patient compliance
        - People do not follow the instructions properly when taking antibiotics
        - A certain level of antibiotics must be in our blood for them to take, so if you forget and take the pill too late you give the bacteria an opportunity to mutate and become immune to the antibiotic
- No new antibiotics have been created in year
    - This is because they are super cheap to make and do not profit
        - This is because none of them are pattentied anymore so anyone can make them and sell them cheap
    - Research to discover a new one is too expensive and not worth the cost
    - Major cost is regulatory
        - Clinical trials are also expensive and time consuming
    - Doctors are reluctant to use new antibiotics
        - Need to keep the new ones in reserve in case the bacteria become resistant to the old stuff
- Antibiotics have huge impact on human life
    - Longer life span
    - Improved quality of life
    - Very safe drugs
    - Very effective drugs