Lecture 2 of BPS1101

Reasoning to identify cures :

- Make it up
- Search for "proof afterward"
- Healing often connected with superstition, magic, religion
    - This method was not successful

Hippocrates develops doctrine of humors :

- Universe is made of 4 elements
    - Earth
    - Air
    - Fire
    - Water
- The idea behind the doctrine of humors is that if the earth is made up of 4 elements then humans must be made up of 4 humors
    - Blood
    - Phlegm
    - Yellow bile
    - Black bile
- The idea behind this is that the 4 humors must be in balance
    - Too much or not enough of a humor causes disease
- Cure by re-balancing the humors
    - They would diagnose by assigning different properties to humors, and when someone was sick they would the symptoms of the person to guide you to the different humors that is in problem. You would then go out in the wrold to find the element that would cure it
- Fever associated with hot and dry
    - Cure using cold and wet
- **Too much thinking !!**
    - Properties of the 4 elements
        - Earth - dry
        - Air - cold
        - Fire - hot
        - Water - wet
    - Properties of 4 humors
        - Blood - cold
        - Phlegm - wet
        - Yellow bile - hot
        - Black bile - dry
            - Ex : If someone had an issue with their blood, they would take some out. They would find creative ways of taking out the blood or different areas to take out the blood depending on what the disease is.
                - This is called bloodletting. This is dangerous because we need blood to live, and by doing this they were taking out important nutrients, and these cuts could also get infected.
                - Bloodletting killed george washington. He had a throat infection and when he was diagnosed with it, his doctor

prescribed a removal of certain amount of blood and that didn't work so they actually removed a little bit more. As a consequence of removing the blood, this caused a secondary infection by the cuts that actually killed him

- Doctrines of humors was stupid
    - Based on the incorrect idea that the universe is not made of 4 elements
    - Humans are not made of 4 humours
    - Treatments developed using it were harmful and painful
        - Bloodletting
        - Purges
        - Fasting
        - Special foods

Doctrine of signatures :

- It is associated with Jakob Bohme, shoemaker and philosopher (1575-1624)
    - God left clues to tell us how to use things. If we could decode the things that god left us, we could cure the disease
    - Disease and cure were linked
        - Ex : If you het a disease from a forest, the cure will be in the forest.
    - This approach is or was used by almost all cultures
        - Ex : Walnut looks like brains, so eating walnuts is good for brain health. (this is false).
            - Another ex : Sharks don't get cancer. Sharks have cartilage whereas we have bones. Shark cartilage used as cancer treatment. (There is nothing in shark cartilage that will help treat cancer)
            - Another ex : Breath mints have chlorophyll and they believe that the chlorophyll is what gives fresh breath
                - This idea comes from parsley and fresh breath. People used to chew parsley to freshen breath, and parsley is green, and that it has chlorophyll and thats why chlorophyll gives fresh breath.
                    - What actually freshens your breath is the artificial flavours.
            - Another mandrake root : It looked like a person and was used for a lot of medicinal and magical purposes. Primary use was a cure for demonic possession. They thought once the mandrake root would scream when pulled out of the rook, so they used dogs to protect against the screaming and ensure the magic is preserved
            - Another ex : Powdered rhino horn was used for aphrodisiac (sexual desire) because their horn was in the middle of their head
- The doctrine of signatures is limited to your imaginations. It varies from person to person from what the ycan see
- Doctrine of signatures is crap ! Most remedies developed this way were harmful
    - At best they were harmless. They denied the patient proper treatments
    - Lack of rationality or evidence
        - Based on appearance or location

        - Required imagination to see connections

Some problems require surgery

- Most surgeries were very limited. Most were amputation but there were no anesthetic. It had to be done quickly to try to minimize blood loss and suffering of the patient
    - Amputation was learned by trial and error
- This all changed when Sir Humphry Davy discovered nitrous oxide, the first anesthetic (this is used today as laughing gas)
    - It can also be used as a propellant. People use it to get high
- In 1846, William Morton discovered that Ether was a more effective anesthetic than nitrous oxide. This marked the beginning of early surgery.
    - When surgery was done, the doctors were dressed in their normal clothes cause the cause of disease was unknown.
- **Anesthetics** make modern surgery possible today
    - Even though surgery was possible, the impact on human life was negligible. The reason was because surgery back then was painful, you could die during surgery. Some surgeries were also harmful.
    - Less than 30% survived surgical treatment. The main cause of this was because they would get infected. They didnt take special precautions to protect the patient during surgery because they didnt know how disease was transmitted
- This changed in 1867 when Joseph Lister used phenol as antiseptic
    - During the surgery, he believed that if you could get rid of the bacteria by poisining them, this would increase the survival rate.
    - The antiseptic is used to keep the patient clean
        - Phenol was used to clean the sewers, and he believed if it could keep the sewers clean it could also clean the patients.
    - Carbolic acid sprayer : Sprayer used for phenol used in surgery and over the patient to clean them
        - By spraying the mist, ti would kill the bacteria and the survivability went up alot.
            - Toxic effects of phenol on doctors !
                - The patient only experiences a little dose and is exposed for a short amount of time, this is why it doesnt affect the patient.
                    - However the doctors were exposed to it for longer periods of time and a result of this is they started feeling the toxic effects.
                    - They had to come up with other ways to ensure no infection after surgery ; they used **washing hands and glove use was safer**
- The idea of antisepsis (keeping things clean during surgery) was brought to canada by Tomas Roddick in 1877
    - Dramatic increase of survivability
- Listerine becomes household product (its main ingredient was phenol)
    - It exists today but no longer contains phenol. They substituted it with thymol. Their functions are the same and have the same base structure, but thymol has extra branches which allows it to be less toxic

Drug industry :

- Started in 1856 with william perkin. He discovered the first artificial dye (mauvine)
    - It was used to dye things purple
    - This was made from coal. He would extract the chemicals from the coal and carry out chemical reactions and discpvered ways to make pruply dye
    - This allowed basically anybody to have coloured clothes because coal is a cheap substance and they also discvered that they can carry this reactions for many different colour
    - This started the dye industry in 1856
- It turns out that these dye companies turned out to be the first dye companies because the chemical structures that came from coal can be modified to make drugs
    - The first artificial drug was Aspirin and was discovered in 1897
        - Chemical substance that does not occur naturally
    - This is important because most modern drugs are artificial
        - They are designed for optimal activity, safety
        - Provide convenience
        - Manufactured in large quantities to get them at a lower cost
    - The first genetically engineered drugs since 1982
        - These form a large section pharmaceuticals
        - Safe, cheapest source of human proteins and hormones
            - Ex : Insulin

Rules are important :

- Regulation of drugs, medical devices and procedures
- Key aspect of the modern pharmaceutical industry

Before 1907, there were no rules

- Anybody could make and sell drugs
    - No proof that anything worked
    - No safety testing
    - No testing of any kind
- Most drugs were made-up
    - Put some leaves in a bottle with water or alcool and start selling it

Rise of patient medicine late 1800's :

- Included the word "patented" on the label
    - Patent means legal document that will prevent people from stealing your idea
    - Public thinks patented = quality
- You could sell anything
- Normally, these patented medication had no curing value
    - So, companies would add additives to give the elusion that is was curing you
        - Common additives was opium : This is because opium makes you feel good, and this gives you the illusion that youre recovering from the illness
        - Kickapoo company had alcohol, which would also give the illusion of being cured because it makes you feel good (being drunk)
        - Some of the most common additives were feel good drugs : Alcohol, opium, cocaine
            - Ex of rly harmful stuff that were sold at the time :
                - When radioactivity was discovered, the general public didnt know how harmful it was so companies started to

sell radioactive products (like bottled water that was radioactive)
- William Bailey made Radithor : Water that contained some radioactive materials. He would sell it to make people smarter.
- Eben byers was a believer in the products that William bailey sold. He drank it everyday and after 2 years of consuming it, he had damage to his face and had to get surgery to remove his lower jaw and part of his face. The radiation ruined it. They removed his teeth as part of the radiation.

- Because of this episode, the public put a lot of pressure on the regulators.
- Board of food and drug inspection formed in 1907
    - First government regulations for medicines
    - **Labeling only**
    - No regulation of therapeutic claims
    - No safety testing

Massengill company and drug safety :

- Contained cannabis and morphine but also contains chlorofoam.
- They started selling the first antibiotic (sulfanilamide) as a powder
    - Taking this drug was unpleasant cause it tasted very bad
    - The salesman wanted to come up with a new formulation to make the taste more pleasant to allow kids to take it
    - One of the chemist in the company discovered that they can mix this with **ethylene glycol** and **water** to get this in liquid form. The ethylene glycol gives it a sweet taste and this was created as a product to sell to parents to use on their kids. It was sold under **sulfanilamide elixir.**
        - Unfortunately when this was made, they didnt bother to do any safety testing and they found that this was causing a lot of problems.
            - 3 days after this was put on the market, the chemist sent a message to the AMA to "please wire collect by western union suggestion for an antidote for ethylene glycol poisoning"
            - However it was too late. Lots of kids died from their kidneys shutting down.
            - Legally, they were not doing anything. It was taken off the market for wrong labeling
                - Legal definition of elixir is a substance dissolved in ethanol
            - Government inspectors tack down drug :
                - Recovered 234 of 240 gallons that were sold
                - 107 dead and 260 permanentaly disabled

Food and drug administration (FDA) created :

- Food, drug and cosmetic act 1938
- Ensure the safety of drugs
- Animal testing was now required (safety only)
- Clinical trials were done to follow safety in humans
- Directions for proper use were required on the label

The next disaster :

- Thalidomide was developped as a sedative in 1957
    - Very few side effects : "clean" drug
    - Because it was such a clean drug, this was getting prescribed to a lot of pregnant woman. Thalidomide however caused their babies to be born with birth defects.
- By 1962, thalidomide recognized as a teratogen
    - Teratogen : something that causes birth defects
    - Phocomelia
        - Short limbs or none at all
    - Attenuated limbs

Teratogen causes birth defects :

- From Greek work "teratos" for "monster"
- Thalidomide was tested in rats
    - Rats do not often give birth to deformed pups
    - In humans, problems with a fetus result in miscarriage, stillbirth or birth defects

Modern safety standards :

- Safety testing done in at least 2 species
- At least one must be a primate
- Must show that the drug is bioavailable
    - Gets into body
    - Need to prove that the drug reaches the animals blood stream
- Must use relevant doses

Industry regulation is important :

- Ensures safe products
- Ensures products work
- Ensures good manufacturing quality
- Regulation increases costs

Modern drugs work :

- Each starts with a scientific idea
- Each is optimized using scientific methods
- Each is tested scientifically
- Manufacturing is standardized
- Drug industry is tightly regulated
    - Must provide scientfic proof