

- Life expectancy
 - Canada: 81
 - World Average: 66.5
- Life span is an educated guess
- * only "important" people make it into historical record, life expectancy is mostly "ordinary" people
- There was a sudden increase in life expectancy 150 years ago
- Scientific principles were designed towards health care
- 1900
 - life expectancy: 44
 - Main causes of death
 - Pneumonia
 - Acute respiratory illness secondary to infection and inflammation of lung parenchyma
 - Infection of lower respiratory tract by microbes, inhalation of airborne pathogens
 - Parasites were most common due to unsafe drinking water
 - Tuberculosis
 - Respiratory infection, chronic cough
 - Influenza
 - Disease of birds and mammals caused by RNA virus, transmitted through air
 - (this lasted until 1950's)
- 2004
 - life expectancy: 82
 - Main causes of death
 - Heart disease
 - Cancer
 - Stroke
 - Disturbance of blood supply to brain
 - Lower respiratory infection
 - Traffic accidents
 - Diabetes
 - Metabolic disease, pancreas doesn't produce enough insulin and does not reduce high blood sugar
- In the present it is unusual to get sick



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- Before, worms chronic infections and malnutrition were big concepts for death
- **Improved sanitation**
 - Out houses were common
 - Chamber pots were dumped out of the window and carried to cesspits
 - Very unusual to see dead bodies and dying now will be in hospitals and will be touched by loved ones
- **Safe water supply**
 - Before water was drank from streams and rivers and how diseases came
 - Before science, organisms weren't known to be in water
 - Upstream vs downstream
 - Can be easily contaminated
- **Guinea Worm**
 - Flea gets into digestive system and migrated to muscles
 - Gets out back into water by bursting from skin and secreting chemical that causes intense heat
 - Therefore getting back to water to cool off and eggs to be laid
- Major improvement was **chlorination**
 - Kill microscopic organisms
 - Chlorine also acts as a **preservative** that stops reinfection of water
 - Chlorinated water must travel through pipes and when exposed and is used as a secondary protection for safe water
- **Food Spoilage**
 - Usually rotten food because there was now way of preserving food
 - Before used to use ice house in underground with ice blocks
- Greatest achievement in Medicine
 - **Immunization (vaccination)**
 - Very successful for viral diseases
 - **Eradicated diseases**
 - Best to avoid and cure
 - E.g. **smallpox was eliminated in 1977**
- **Polio eradicated in north America in 1991**
 - Less than 100 cases worldwide



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- 10 or 11 countries
- Major eradication barrier is politics
- Antibiotics for bacterial infections
 - Certain diseases with antibiotics
 - Penicillin
 - Reduces maternal mortality, giving birth was prone to infection
- North American Drug Market
 - Prescription drugs, 300 billion
 - Over the counter drugs, 25 billion
- World drug market
 - Canada 3.8%
 - All others 10.3%
 - USA constitutes half of the market for drugs
 - The drug industry is programmed around FDA
- Types of medical Treatment
 - Surgical
 - Removal of affected body parts
 - Modification of affected body part (modern with drugs)
 - Medicinal
 - Use of chemical compounds to treat disease
- Plants as sources of drugs
 - Older drugs came from plants
 - Description of plants in scripts and books
- Why plants?
 - Plants are major sources of poisons
 - Plants are stationary and therefore use chemical defences
 - Drugs are poisons
- Early drugs were poisons
 - Drugs
 - Produced desired (beneficial biological effects)
 - Poisons
 - Produce undesired (harmful) biological effects
- Dose is the main difference
- Pharmacokinetics: used to denote drug and poison based on dose



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- Sola dosis facit venenum
 - Poison-kill
 - Potion-cure
 - Only dose makes the poison
- Dosages
 - Normally we assume low dosages are beneficial and high doses produce harmful effects
 - Sometimes low doses produce harmful effects and higher doses produce beneficial effects
- Water poisoning
 - Disturbance of brain function, when balance of electrolytes in the body is pushed outside safe limits by over hydration
- How were drugs discovered
 - Observations and experiments
 - People observed the effect of the drug
 - Strong poisons given in low doses
 - Philosophy
 - Cure arrived at by reasoning
 - Based on belief
 - Healing often connected with superstition and religion
 - Only as good as info is based on
 - Reasoning by beliefs
- Drugs from observation and experiment
 - Strong poisons
 - Drugs from observation and experiment
 - Low dose makes it into a drug
 - Weak poisons
 - Large quantity for effect
- Papyrus Ebers
 - Egyptian Medical papyrus
 - 1500 BC
 - 3000 years old
 - 20 meters long
 - Plants descriptions, potions, oxy narcotics
- Hippocrates 460-370 BC



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- Father of medicine
 - Promoted experimental methods
 - Rejected superstition and religion from healing
 - Based cures on reality of world around him
 - Observing how the world works
 - Poppy juice to stop babies from crying
 - Ox liver for night blindness Vitamin A
 - Doctrine of Humors
- Discorides 40-90 AD
 - De Materia Medica
 - Book of herbal medicine
 - 2000 years old of experimental methods that led to some cures
- Identification of opium for pain
 - Opium
 - Extract from poppy seeds
 - Narcotic pain killer
 - Sedative
 - Toxic in high doses but a drug in low doses
 - Outlawed in 1917
- Identification of cocaine as a stimulant
 - Observation
 - Extracted form cocoa leaves
 - Topical pain killer
 - Stimulant
- Quinine as a malaria treatment
 - Flower with a bitter taste, has antimalarial properties
 - Was what created tonic water and gin to be consumed more often
 - Peruvian bark was more valuable than gold but also had antimalarial properties
- Problems with observations
 - Human brain searches for patters
 - Even when they are not there
 - Anecdotal evidence unreliable
 - Drug and effect may be coincidence
 - Prescriptions subject to placebo effects



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- **People lie**
- Once “evidence” is available, hard to contradict
 - Many harmful remedies retained
- Human brain is not suited to look for truth around the world but only looks for patterns and convinces the patterns are real
- **Apophenia**
 - Seeing patterns or connection in random or meaningless data
 - Even when they are not there
 - Can incorrectly apply statistics when there is no pattern
- **Pareidolia**
 - Perceiving sounds or images as something else
- **Anecdotal evidence relies on chance**
 - Medication and cure may not be connected
 - Poison and harm may not be connected
 - Look for random outliers
- Tomatoes
 - Were one thought to be poisonous
 - Fear of contradiction and became a superstition
- Eating bugs
 - Normal part of our diet
 - Enzymes were engineered to digest bugs
- Only experimental evidence is reliable
 - Make a measurement
 - Measure properly
 - Measure accurately
 - Cant rely on word of mouth
 - Clinical trials are sometimes incomplete
- Statistical Significance
 - Collect data form large number of experiments
 - Look for averages and trends
- Problems with herbal remedies
 - **Poor control over dose**
 - Plants produce variable amounts of active ingredients
 - Never consistent with dosage
 - **Variations in preparation and administration**



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- Chemical reactions
- Passing on instructions are different as it is passed from one to another
 - No instructions
 - Information was passed verbally
 - Imprecise
 - Poor reproducibility
 - People were illiterate
- Philosophy to identify cures
 - Cure arrived by reasoning
 - Method requires good information
 - Healing often connected with superstition, magic, religion
 - Strong materials made strong poisons
 - Starting with good information was important for best results rather than starting with bad information
- Hippocrates developed doctrine of humors
 - The universe was made of 4 elements earth air fire and water but was not true
 - He promoted the idea of observation through philosophical methods and concluded the universe was made of 4 elements
 - Since the universe was made of 4 elements the body must be made of 4 humors
 - Blood, Phlegm, Yellow bile, black bile
 - Connection between the 4 elements being dry, wet, hot and cold
 - 4 humors are usually in balance
 - Too much of one or more can cause disease and is cured by rebalancing
 - Solve properties of elements to humors
- Bloodletting and doctrine of humors
 - Too much of a humor needs to be let out of the body
 - Shape, cut, and place are important and is based of astrological signs
 - Increased in mortality due to infections from bloodletting
- Rebalance with emetics and purges



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- Emetics is something that makes you throw up and get it out of the body
- Purges is to empty lower bowels
- Doctrine of humors was crap
 - Based on incorrect idea
 - Made up
 - Treatments were developed using it were harmful or painful
 - Bloodletting
 - Purges
 - Fasting
 - Special foods
 - Bloodletting reduced to a therapeutic as time passed
- Doctrine of signatures
 - Jakob Bohme, shoemaker and Philosopher
 - Thinks god left clues to tell us how to use things
 - Diseases and cure were linked somehow
 - Approach was accepted by almost all cultures
 - E.g. walnuts look like brains and was good to eat for the brain
 - E.g. Boneset stems that grow through the leaves are good for the bones and spine
 - E.g. Sharks get cancer, there cartilage doesn't protect against cancer or cure cancer
 - Mandrake roots look like people
 - Used for medicinal and magical purposes
 - Primary use was to cure demonic possession
 - Looks like a person
 - Legend was that it screams when its pulled out and can turn people to stone
 - Ginseng
- Breath mints have chlorophyll
 - To make breath smell better because is the green pigment in mint and parsley
 - Fresh breath~parsley~green~chlorophyll~fresh breath
- Rhino horn is phallic symbol
 - Powdered rhino horn was used in Chinese medicine as a aphrodisiac



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- Mercury was drunk as a purgative to push toxins out of the body
- Doctrine of signatures was crap
 - Most remedies developed this way were harmful
 - At best remedies were harmless
 - Lack of rationality or evidence
 - Based on appearance or location
 - Required imagination to see connections
 - Could end up harming ones self
- Life expectancy through history
 - Range becomes more appropriate
 - Using philosophy is unlikely to work but plays with the mind to increase life expectancy
- Some problems require surgery
 - Been around for 10000's of years
- Amputation without anaesthetic
 - People holding down patients without anaesthetics
 - Done quickly before bleeding out
 - Has high mortality rate
- Sir Humphrey Davy
 - Nitrous oxide vapour
 - Awake but wont remember what happened
- William T.G. Morton
 - Ether 1846
 - First effective anesthetic
 - Induce unconsciousness
 - Makes modern surgery possible
- Less than 30% of patients survive surgical treatment
 - High infection rate
- Joseph Lister
 - Phenol as antiseptic
 - Believed the work or nitrous oxide but wanted to reduce infections
 - Phenol is used in sewage cleaning
 - Invented carbolic acid sprayer
 - Vaporized chemical to atomize though heat
- Toxic effects of phenol on doctors



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- Small dosage was fine for patients but doctors perform surgery often and undergoes toxic effects due to higher dosages
- Operating rooms eventually evolved to all white and cleanliness
- Antisepsis brought to Canada by Thomas Roddick 1877
 - A student of Listers
- There was opportunity to make useless thing and make a profit
 - Carbolic smoke ball to somewhat clean a house from bacteria
- Listerine becomes a household product
 - Used as a household product
 - Was also used for dandruff
 - Currently no longer contains phenol because of its toxicity and was replaced
- Problems with drugs in the 1800's
 - No regulations
 - Caused big markets
 - Lots of opportunity for fraud
 - Problems existed but there was dramatic increase in the 19 century
- Science is fraud
 - Emergence of science made people trust claims
 - Scientifically proven
 - Patented (legal documents that stops someone else from profiting)
 - Doesn't prove it has been tested
 - Emergence of science made it easier to identify fraud
 - 1862~ first analysis of sugar/alcohol manipulation of wine
 - 1873~ first analysis of morphine content in opium
 - 1874~ first experiments on effects of pesticides on humans
- Experiment on humans
 - Common until WWII
 - Experimented on prisoners and twins
 - Rise of laws to protect people
- Rise of patent medicine late 1800's
 - Patents meant nothing to its effects or if it works
 - Opium was once used to soothe diseases and cure them but only made people feel better



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- Oil cures were in alcohol that made people feel more at ease like alcohol
- Radioactive elements were once used and were also big poisons
- **William J.A. Bailey**
 - **Radithor**
 - Cancer dies when radiation is present so drinking radiation can make morons become geniuses
- **Board of food and Drug inspection**
 - Formed in **1907**
 - **Labelling only**
 - **No regulations on therapeutic claims**
 - **No safety testing**
- Some patent medicine is still sold today
 - Buckley's
- **Sulphanilamide** was an antibiotic powder
 - Sprinkle topically or ingest
 - Targeted children but was a horrible flavour so was chemically became a drink and was known today as **antifreeze**
 - Too late to save children, and company wouldn't take it off shelves because there as no law that they can sell poison
 - Flaw was the use of "**elixir**" that is defined as dissolved in ethanol instead of phenol
 - Government recovered 234/240 gallons
 - 107 dead, 260 disabled
 - History repeats in future
 - **Caused Modern safety standards**
- **Food and Drug Administration FDA**
 - **Ensure the safety of drugs**
 - **Animal testing required**
 - **Clinical trials**
 - **Directions for proper use required on labels**
- **Thalidomide**
 - Developed **sedative 1957**
 - **Very few side effects**
 - **1962 thalidomide was a teratogen**



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- Phocomelia (Latin for seal) birth defects
- Babies born with small or no hands or feet
- Never marketed since it was discovered before FDA approval
- When tested on rats teratogen doesn't work since rats can digest the fetus
- But humans can have miscarriage and still birth or birth defects
- Modern safety standards
 - Safety tests at least on 2 species
 - One must be primate
 - * The drug must be bioavailable
 - Gets into the body
 - Must also use a relevant dose either the same or more for a human
 - Testing done can be altered for false positives and aid in positive results to pass
- Genetic engineering
 - Replaces animals from experiments
 - Facilitates drug discovery
 - When a drug interacts with a molecule or protein
 - Attach to a single spot and cant affect other areas
- Drug Discovery today
 - A new drug costs 80 million to develop
 - Takes 8 years from idea to market
 - High risk but high profit
- Sources of drugs today
 - Biologic 14%
 - Vaccine 4%
 - Natural product 5%
 - Semi synthetic 23%
 - Synthetic 54%
- Drugs designed by computer
 - Interactions with body molecules and drugs
- Dugs found by random screening
 - Looking fro best version of drug
- High Failure rate of new drugs
 - Less than 1 in 10 drugs survive clinical trials and reach market



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- More than 10000 compounds are tested to find each a new drug
- Process is 8-12 years
- Each new drug costs 800 million to bring to market

- Two types of drug market, prescription drugs and over the counter drugs and differ by price
- Prescription drugs 300 billion year US
- 10X more on prescription drugs
- **Over the Counter Drugs (OTC Drugs)**
 - Cheaper than prescription
 - Use OTC much more
 - 25 billion US
- Important things to consider:
 - Safety
 - Indications
 - Counter indications
- **Safety**
 - Dose makes the drug (recommended dose = good; too much = bad)
 - All drugs have side effects
 - Find out what effect is and how often it happens (need both to evaluate risk)
- **Indications:**
 - What is drug used for?
 - What does it cure?
 - How common is it
- **Counter Indications:**
 - When should you NOT use drug? (I.e. conditions -> don't take drug with heart condition, pregnancy)
 - Drug combinations (drugs react with each other)
 - Foods
 - Natural remedies
- Pain Relievers
 - 2.7 billion per a year
 - 50 billion tablets
 - Aspirin most popular – comes from Salix/Willow tree
 - Hippocrates used willow bark for child birth



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- Knowledge of herbs was lost in the dark ages when church dictated all medications that were allowed or a witch was presumed to be present
- Reverend Edward stone
 - Bark had a similar taste to quinine and was thought to be a link but wasn't the discoverer of aspirin
- Doctrine of signatures
 - Association between diseases and cures
 - Concluded that willow bark will cure fever
- Willow bark first used to cure fever/Salicylic acid was extracted from willow powder
- Need 1.5kg of willow bark to get 30g of salicylic acid (doesn't provide enough)
- Salicylic acid can be broken down into salicylic acid
 - Kolbe Schmitt Reaction
 - Henri Leroux
- Salicylic acid could be taken from coal tar (coal tar also used as cloth dye Bayer, waste product)
- Properties
 - Analgesic-pain
 - Antipyretic-fever
 - Anti-inflammatory-swelling
- Natural:
 - Take drugs from stuff in nature
- Synthetic:
 - Not found in the environment naturally
 - Product made from petroleum or oil
- Salicylic Acid
 - Rafaella Pira
 - Analgesic (for pain)
 - Antiseptic (for cleaning)
 - Anti-inflammatory (for swelling)
 - Less Bitter taste} better
 - Stomach pain} bad
 - Ulcers, stomach acid, buffers



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- - Changed drug into A.S.A. (Acetosalicylic Acid) to get rid of bitter taste and stomach pain and later renamed aspirin A.S.A.
- Biological Assay
 - Experiments to make a better drug on animals
 - Used gills to test aspirin that would be as sensitive as a stomach
- (Acetosalicylic Acid)/Aspirin ASA
 - William Perkin
 - Benefits
 - - Pain
 - - Fever
 - - Inflammation
 - - Good for muscle pain (not visceral (organs))
 - Reduce heart attacks
 - Side effects
 - - Death (more than 60 tablets at once)
 - - Ringing in ear (more than 10 tablets) tinnitus
 - - Stomach irritation
 - - Reye syndrome (maybe)
 - More than 10 tablets, salicylism aspirin poisoning
 - Blood clotting
 - Trademarked and sold with heroin
 - Powders became tablets
 - A.S.A. stops the production of prostaglandins (what cause pain)
 - Stops cyclooxygenase (enzyme that produces prostaglandins)
 - Without prostaglandins there is no mucus to protect your stomach from the acid it produces -> stomach irritation
 - Long term use can cause stomach ulcers
 - Reye Syndrome -> swelling of brain (not directly linked with aspirin but associated with) no child aspirin in North America
 - Bufferin cures stomach pain, it's a base to negate stomach acid
 - Anacin combines aspirin and caffeine (be careful -> makes some headaches better but some worse)
 - Can also be extracted and made into bombs
 - Drink water to expand your stomach so aspirin doesn't get caught there



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- Generic brand is the same substance as name brand (only difference = price)
- Bioavailability, must show equivalent amount gets into body as name brand vs. generic brand
- Phenacetin
 - Sold in APC tablet (Aspirin, Phenacetin & Caffeine)
 - In metabolism Phenacetin
- Acetaminophen/Tylenol
 - Raised pain threshold, good for visceral and muscle pain
 - Doesn't help with swelling and inhibits prostaglandin
 - No risk of rye syndrome and low stomach irritation
 - Can poison liver (don't take Tylenol with hangover/drank -> alcohol activates liver -> becomes toxic)
 - Don't take more than 60 tablets, #1 suicide drug in England
 - - Tylenol PM only helps you go to sleep since its anti-allergy medication -> makes you drowsy histamine
 - - Caffeine + Tylenol = effective for migraine headaches
 - - Some crazy guy took apart Tylenol capsules and put cyanide into the capsules and then returned them to stores to be sold, causing multiple deaths -> now Tylenol is in caplet form and has a safety seal so this can't happen again
- Ibuprofen/Advil
 - - Inhibits cyclooxygenase, stops production of prostaglandin
 - - Reduces blood clotting, fights stomach irritation
 - - Sold as Advil and Motrin
- Naproxen/Aleve
 - - Good for inflammation
- Top Pain Relievers
 - Tylenol 43% Acetaminophen
 - Aspirin 28% A.S.A.
 - Advil 26% Ibuprofen
 - Aleve 3% Naproxen
- COX = cyclooxygenase
- COX-1 (bad to inhibit)



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- - Stomach -> mucus production decreases (acid from stomach causes irritation)
- Chance of ulcer
- COX-2 (good to inhibit)
 - - Inhibition -> pain reliever, inflammation reduction, fever reliever
- VIOXX
 - - Prevented gastro intestinal bleeding caused by COX-1
 - - Caused heart attacks and was sued a lot but without it, it causes more death so doctors still wanted to use it but VIOXX took their drug off the market since they were getting sued so much
 - Heart attack had a higher chance than death should have been put back on shelves

• Effect	• A.S.A.	• Acetaminophen	• Ibuprofen	• Naproxen
• Pain	• Yes	• Yes	• Yes	• Yes
• Fever	• Yes	• Yes	• Yes	• Yes
• Inflammation	• Yes	• No	• Yes	• Yes
• Prevent heart attack	• Yes	• No	• No	• No
• Reduced blood clotting	• Yes	• No	• Yes	• Yes
• Stomach irritation	• Yes	• No	• Yes	• Yes
• Rye syndrome	• Maybe	• No	• No	• No



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• Liver toxicity	• No	• Yes	• No	• No
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Headache

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- Cephalalgia = headache
- Surgical cures for headaches
 - Trepanation
 - Drill holes
- Pain is related to the tissue surrounding the skull
- Headaches
 - 12 types
 - 60 subtypes
 - 2 classes
 - Muscular
 - Vascular
- Muscular Headache
 - Contraction of muscles in brain
 - Muscle band around skull
 - Squish the tissue and causes sensations of pain all over
 - Can be caused by stress
 - Treatment
 - ASA, Tylenol, ibuprofen, naproxen
- Vascular Headaches
 - Blood circulation
 - 3 major types
 - Toxic
 - Migraine
 - Cluster
 - Toxic
 - Caused by poison
 - Pain caused by vasodilation: diameter of blood vessel gets larger and squishes surrounding tissue
 - Alcohol and hangover
 - Ethyl alcohol ~ acetaldehyde ~ acetic acid
 - Uses enzymes alcohol dehydrogenase and acetaldehyde dehydrogenase
 - Asians have small amounts of acetaldehyde dehydrogenase and therefore are light weights
 - Aged alcohol increases
 - Alcohol increases liver function



- Acetaminophen will pair with Cytochrome P 450 and become a toxic metabolite
- Cause liver damage
 - Treatment
 - ASA, Ibuprofen, Naproxen
 - MSG
 - Monosodium glutamate
 - In seaweed
 - Flavor enhancer
 - Does not cause headaches
 - Can be disguised as hydrolyzed vegetable protein
 - Normal human metabolite, roughly 5% of our protein composition
 - Caffeine gives rebound to vasodilation
 - Vasoconstrictor
 - If body is condition to have a lot of caffeine
 - Can help to reduce pain
 - Anacin
 - Brain freeze
 - Pallet is cooled down and is sense to response and expand size of blood vessels
 - Migraine
 - Not common in men
 - More in women 18%
 - Men is 6%
 - Starts with serotonin
 - Low levels
 - Amount triggers migraine in aura stage
 - Phases
 - Phase 1
 - Vasoconstriction
 - No pain but vessels get smaller
 - Phase 2
 - Vasodilation
 - Dilates and causes pain



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- Trigger
 - Tension, menstruation, sleep, foods, smells, drugs, pregnancy, relaxation
- Progression once migraine starts
- Prodrome phase
 - Warning
 - 30-40% of sufferers
 - mood swings
 - 1-2 days before headache
- Aura
 - 20-30%
 - 1-2 hours before pain phase
 - auditory, visual, vertigo, reduced sensation, hypersensitivity
 - take medication at this point
 - serotonin levels drop dramatically
 - can be reversed to replace serotonin with drug to stop the migraine
- Pain
 - 1-72 hours
 - Nausea
 - GI disturbance
 - Only half of the head
 - Sensitivity to light, sound and smell
- Postdrome
 - Hung over almost
 - Exhaustion
 - Depression
 - Feel better afterwards
- Pain med to ride it out
 - all of the above
- Triptans
 - Can abort migraines
 - **Sumatriptan** selectively targets migraines
 - **Sumatriptan**



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- Similar to serotonin
- Agonist: mimic action of naturally occurring substance
- Antagonists: attach and stop agonists from taking effect but do not provoke biological response

• Ergot

- Fungus
- Poison and drug
- Poison seen as demonic possession
- Cause vasoconstriction
- Can also induce labor
- Strong hallucinogen
- Ergot extract 1862
- Arthur Stoll isolates ergotamine in 1918 without hallucinogen

• Ergotamine

- Isolated by Arthur Stoll in 1918
- Not drug like
- Prevents and stops migraines
- Gangrene when tissue is dying/ **St. Anthony's fire**
- Death, controlled dose

• LSD

- Albert Hoffman
- Accident
- Bicycle day
- Isolated from ergot

- Most common infection
- 25 to 1 that outnumber all others
- Influenza is only when your old that it should be more important
- Viruses destroy tissue and immune system makes the symptoms that over react
- No cure for common cold
- Average cold lasts a week
- Sneezing does not spread colds
- Common Cold research unit Salisbury England
- Which Island? Were spread of colds studied
 - Tristan de Cunha
- Sneeze collector
- Being cold does not cause colds nor does wet hair
- Cold viruses are in nasal secretions
 - Nasal secretions spread easily
 - Transferred through touching
 - Washing hands may reduce colds
 - Hand sanitizer may reduce colds
 - A mask will not protect u
 - Masks only protect other from the wearer
- Ages is a factor to being infected
 - Illness
 - Illness to response slow and weak
 - Makes antibodies
 - Later exposure to same virus does not make you sick
- Cold remedy ingredients
 - Antipyretics
 - Decongestant
 - Antihistamine
 - Antitussive
 - Expectorant
- Acetaminophen is for pain relief and fever
- No such thing as sinus cold
- Retsyn is blue spots
- Menthol is a weak topical analgesic



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- Cooling sensation that does nothing
- **Cepacol** contains topical anesthetic
 - **Benzocaine**
 - Reduce pain and will kill pain
- **Decongestants** dry a runny nose
 - **Pseudoephedrine: Works**
 - **Amphetamine**
 - **Phenylephrine: does not**
- Snot
 - Mostly **water and little mucin(protein)**
 - Will turn into a thick viscous substance
 - Water gets into the snot through vasodilation
 - Cells separate and become leaky for water to be released
 - Decongestants are vasoconstrictors to stop water from binding with mucin and create mucus
- **Amphetamine**
 - Original **decongestant** that dries up runny noses replaced with pseudoephedrine
 - Advertised as **Benzedrine**
 - **Side effect: appetite suppression**
 - Over use of diet pills: **Amphetamine psychosis** (hallucinations)
 - Over use of diet pills **caused stroke**
- Phenylpropanolamine
 - PPA
- **Sudafed**
 - Contains pseudoephedrine
 - Pseudoephedrine used to make methamphetamine
 - Get rid of OH group
- **Sudafed Pe**
 - Contains Phenylephrine
 - **Cannot be converted into meth**



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- Phenylephrine is **metabolized too quickly** before it can start to work
- Meds contain stabilizers
 - Atmosphere is corrosive as oxygen makes the drug go bad
- Antihistamines
 - **Chlorpheniramine**: drowsiness
 - New allergy meds act differently and don't reach the brain to induce drowsiness
 - Also reduce nausea
 - **Gravol**
 - Diphenhydramine (antihistamine)
 - 8-Chlorotheophylline (stimulant)
- **Dry cough**
 - **Doesn't go away**
- **Productive cough**
 - **Loosens mucus that is trapped**
 - Need more liquids (**expectorants**)
 - Difficult to remove
 - **Guaifenesin makes mucus watery (effectiveness is unknown)**
- Best cough medicine is heroin
- Dextromethorphan is used instead now, almost like heroin almost mirror images
- Multi-symptom medications
 - pseudoephedrine will fight against antihistamines to keep people awake
- Cold meds not for children under 6
- Vitamin C is a myth
- Cold FX is made of a starch
- Ginseng roots resemble a human body
- **15% of colds are due to flu virus**
- **influenza causes seasonal colds 5-15%**
 - **25000-500000 deaths**
- new virus every year



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- Virus proteins
 - Hemagglutinin (viral entry into cell)
 - Neuraminidase (viral exit from cell)
- Spanish Flu 1918
- 2007 Avian flu had 60% mortality rate
- Swine flu Mexico April 2009 with pandemic warning from WHO
- Average flu season is 5-15% infection 4000 deaths
- Severe flu season is up to 30% infection 8000 deaths
- H1N1 had only 401 deaths
- Pain and fever
 - Acetaminophen or ibuprofen
- Decongestant for nose relief
 - Pseudoephedrine
 - Not phenylephrine
- Antihistamine
 - Chlorpheniramine
- Antitussive (prevent/relief cough)
 - Dextromethorphan
- Expectorant helps secretion of sputum
 - Guaifenesin
 - Unknown effectiveness
 -

- Uncontrolled growth
- Hyper-proliferative lesion **benign**
 - Can stop by themselves
 - Benign lesions can be fatal in developing countries
- Hyper proliferative lesion **Malignant**
 - Aggressive, fast, random can be melanoma
- Cancer and Heart Diseases are about **45% of the causes of death** in North America
- **Cancer alone is almost a quarter of deaths in the US**
- Cancer is dependent on age most of the time
- Men often get cancer more often because we are stupid, too lazy to get checked
- Cancer in children is extremely rare
- Cancer treatment is proportional to the disease
- The younger to have treatment the better because there is a higher survival rate
- Incidence of cancer has gone up
- Stabilization of death rates due to changes in classification and coding of causes of death
- **Lung cancer is the most because of self infliction**
- Normal cells become cancerous
 - Rate at which they grow
 - Tumors take all resources
 - Cells change uncontrollably
- **Normal cell growth**
 - Cells divide on command
 - Usually max. 50 cell divisions
 - Cells must touch similar cells
 - Most common reason to divide is to replace dead cells
 - Telomere is a cellular clock about how old the cell is and when time is up to die for the cell
- Cancer cell growth
 - Divide continuously
 - More than 50 cell divisions (**Immortal**)
 - Cells are mobile (**Metastasis**)
- Henrietta Lacks 1951



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- Cervical cancer that found out about immortal cells
- HeLa Cell line source
- Malignant cells are often mobile and move to different places in the body
- Cancer requires 20 years to develop
 - 8-10 mutations in the same cell
- Every single cancer is different
 - Every tissue can spawn more than 100 forms
 - Each tumor is unique
- Cell Division
 - Regulated in 2 ways
 - Stimulation (accelerator)
 - Repression (brakes)
 - Can do both at the same time
 - Fail safe but there can still be something that goes wrong
- Cancer involves loss of function
 - Impossible to repair the function with small molecules
 - Easier to break something than to fix it
 - Cannot repair damage with today's technology
 - Genetic repair is too expensive and difficult or unreliable
- Off switches for cell growth
 - P53 is an important braking protein that regulates apoptosis
 - Apoptosis is required for embryo development, wound healing, protect from infection
 - Important suicide protein
- Apoptosis
 - Programmed cell death
 - Embryo
 - Wound healing
 - Protects body from viruses and cancer
- Chromosome tips look like shoelaces
- Chromosomes fray with age
 - Immortal cells can regenerate tips
- Tumor formation
 - In the same cell



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- Mutations happen continuously
- Damaged cells are eliminated from the body
- Mutations in the same cell are rare
- Accumulation of enough mutations for cancer requires more than 20 years on average
- Tumors form special blood vessels for nutrients
- Codon
 - Codon 3 letter sets
 - Each codon specifies an amino acid
 - Sequence of amino acid determines the protein structure
- Genetic susceptibility
 - Some individuals are more susceptible to cancer than others
 - ONCOGENES
 - Instructions are easier to change
 - Phenotype (light skin= easily damaged= skin cancer)
 - 23,000 genes in a normal cell
- Most cancer death is caused by controllable factors
 - Most common
 - Tobacco
 - 400 toxic chemicals
 - 40 carcinogens
 - harmful at low doses
 - Diet and obesity
 - Viruses
 - Everything else
 - Alcohol
 - Lack of exercise
 - UV radiation
 - Environmental exposure
 - Genetics
 - Medical procedures
 - Radiation
- Nicotine is an addictive substance, not harmful
- Carcinogens
 - Polonium 210



- As a poison
- Radioactive
- Concentrated phosphate deposits (fossilized bird droppings from birds that ate fish where polonium 210 was common) can be fertilizer
- Heat from burning vaporizes polonium
- Polonium antistatic brushes
- Polonium spintharoscope in KIX cereal
- Alpha emitters are normally safe can be blocked with paper but can still cause cancer
- Radio active spark plugs
- Tobacco combustion
 - Incomplete combustion
 - Benzopyrenes
 - Carcinogenicity
 - Produced in any smoke
 - Nitrosamines
 - Ethylene Oxide
- Diet
 - Strong correlation of cancer with diet and obesity
 - Meat spoils quickly and must be cooked, cooking generates flavor and nasty materials
 - Food prep creates carcinogens
 -
 - Beneficial foods protects up
 - Fruits and vegetables
 - Fiber promotes passage of waste
 - Obesity
 - 1980s dramatic increase
 - increase risk
- Viruses
 - 15% of cancer death
 - viruses target p53
 - Gardasil for HPV induces cervical cancer
 - Excess alcohol



- Acetaldehyde
- Other risk factors
 - Leisure time
 - Exposure to UV
 - Environmental conditions man made
 - Pesticide
- Chemotherapy
 - Very difficult to target selectively
 - Drugs can block protein function, cannot restore protein function
 - Cancer cells are human cells and can look the same to the drug
 - Only difference is the rate at which they divide
 - Kill faster cells before killing the patient
 - Side effects: death, cancer, extreme nausea, vomiting, hair loss, immune suppression, sterility
- Mustine
 - Nitrogen mustards (mustard gas)
 - Blistering agent
 - Major tissue destruction
 - Low white blood cell count, indication of leukemia
 - Caused DNA damage, Cell death
 - Changed chemical to make less damage
 - Changed sulfur to nitrogen
 - Normal cell- slow growth, has the ability to repair
 - Tumor cell- grows quickly, wont have time to destroy cancer cell
 - Therefore can cause death in treatment
- Cisplatin
 - Study on effects of E.coli in electric fields
 - Bacteria stopped dividing and realized it was due to a platinum electrode
 - Platinum (oxygen and chloride ions) generates peyrones salt
 - Damages DNA in fast growing cells like bacteria
 - More selectivity on cancer cells
 - Long road for Cisplatin
 - First synthesized in 1845 and used in 1978



- Used in 40-80% of cancer patients
- Cancer cells have less amounts of chloride ions in their cells
 - Cancer cells take up cisplatin and within the cell it is converted to its active form to damage DNA
- Taxol
 - From yew trees
 - Used as poison
 - From Macbeth and hamlet
 - King of eburones killed himself with yew extract
 - Alternate name was Taxus brevifolia (taxus form taxon in greek is toxin)
 - 1964, yew extract in the US form yew bark was cytotoxic
 - Taxol (isolated compound that is toxic) is a first line treatment for breast cancer
 - Taxol is a complicated molecule
 - 360 000 trees ~ 5 year supply
 - European yew was Taxus baccata that had a chemical in its needles
 - Robert Holton devised a semi synthesis to create taxol from the needles
 - Taxol is not manufactured in cell culture
 -

- Stanazolol
 - Filed by John Mason
- Creatine
 - Does nothing as a stimulant
 - No rule for what he took
- Olympics in ancient Greece
 - Athletes encourages to take drugs
 - Wanted to see the best in athletes
 - Used potions and herbs but wasn't spoken of since they thought they were cheating
- Dop
 - A Zulu drink
 - Mild hallucinations, increase courage, aggression
 - Alcoholic
 - Was called doop
- Doping race horses
 - Increase outcomes
 - Doped to fix races, such as the horse with the lowest odds and the best horses were poisoned
 - First doping test
- Cycling
 - Known for doping
- Endurance was enhanced with dope
 - Caffeine
 - Cocaine
 - Alcohol will not help but will make people feel better
 - Nitroglycerine
 - Strychnine (rat poison that acts as a stimulant)
- Olympic marathon
 - High temperature, 100% humidity, dirt roads, shoes were leather, drinking water was perceived as bad
- Runners
 - First administered Strychnine stimulant and was popularized to dope
- Adrenaline
 - Present in body



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- Not ideal for sports because of only **short durations** and required an **IV injection**
- **Was first used in boxing matches**
- **Amphetamine**
 - Adrenaline was altered into amphetamine to mimic natural properties
 - The discoverer injected himself
 - A great **decongestant**
 - First side effect was having **sleepless nights**
 - Due to patent problems army's in North America were forced to test amphetamines instead for the same effect
 - Used by the 8th Air Force
 - Tarawa invasion
 - Allied armies
 - **Can push the body beyond its limits where there is no brake**
 - **Removed the fail safe to brake**
- **Methamphetamine**
 - Blitzkrieg
 - Rapid movement that encircles, stays awake and concentrated in war
 - **Pervitin- derivative of amphetamine for endurance**
 - Captured German soldiers and found Pervitin
- First sport amphetamine was in 1952
- First study of athletes using amphetamines was in 1959
- Rome Olympics, 4 members on a team only 3 need to cross the finish line, one died after using too many amphetamines that over exhausted the body
- Nervous system
 - Several sub-systems
 - **Voluntary and involuntary**
 - **Involuntary subcategorizes into sympathetic and parasympathetic that both use organs**
 - **Sympathetic is fight or flight**
 - **Parasympathetic is maintenance**
 - **Involuntary nerves use different signals**



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- Replaces neurotransmitters with adrenaline and norepinephrine and increases flight or fight response
 - Amphetamines, remove the fail safe system and can last for hours
- Olympics restrict drugs in 1967
 - First testing done in Grenoble 1968
 - Amphetamines
 - Strychnine
 - Heroin
 - Cocaine
 - Antidepressants
 - Tranquilizers
 - Were not banned because of unfair advantages
 - Sport drug abuse is harmful to athletes
 - First person to cheat was because of alcohol intake where testing labs charged more for doing more unnecessary tests
 - East Germany established the doping lab in Kreischa
 - Gained access to testing protocols
 - Developed masking techniques
 - GC/MS
 - Two instruments linked together
 - Usually look in urine
 - Gas Chromatograph, Mass Spectrometer
 - GC
 - Sorts molecules
 - Passes through a tube containing sticky substances
 - Some molecules are slippery and other are sticky
 - Peaks come at specific times and can correspond with a chemical then it's a drug
 - MS
 - Throws molecules
 - Based on weight
 - As force is constant
 - Magnetic field
 - Falls into fragments



- The largest mass on the print out is the molecular weight

- Steroids
 - Fritz Pregl and Oskar Zoth 1896
 - Injected themselves with bull testicular extract
 - Measured muscle strength using middle finger
 - Macerated dog testicles
 - Brown Sequard applied Similia similibus (doctrine of signatures)
 - Treating an organ with itself
 - Testes to treat impotence
 - Transplant testicle tissue from donor to mad that had lost his testicles testing on prisoners
 - Transplanted testicles from executed prisoners into convicts to restore sexual function
 - 1926, isolation of testosterone using slaughter house
 - 40 kg of bull testicles= 20mg of testosterone
 - Semi-synthesis of testosterone in 1935
 - Started with cholesterol
 - 4 ring architecture similarity
 - Testosterone inmate rehabilitation was for rebuilding muscles when they are skin and bones, and malnourished
 - First athletes to use testosterone were race horses
 - Soviets experiment with steroids, weightlifters
 - Side effects, training methods, training cycles
 - Dr. John Ziegler brought testosterone back to North America wanted to improve the drug instead of acting as a hormone
 - Effects of extra testosterone
 - Anabolic
 - Muscle mass
 - Strength
 - Bone growth
 - Androgenic
 - Body and facial hair
 - Deep voice
 - Heavy brow



- Acne
- Increased sex drive
- Testicle shrinkage
- Clitoral enlargement
- Designing a steroid for sports only, is to only keep the anabolic effects
- 1958 Dianabol
- 1961 Stanozolol
- Anabolic steroids were used for wasting conditions such as cancer, coma, muscles when there is decrease in mass
- Steroids banned in Olympics in 1977
 - Abuse was unethical
- Modern semi-synthesis of steroids
 - Progesterone can make any steroid, From Diosgenin
 - Diosgenin is from Mexican yams that look like taro
- Steroids do not build muscles
- Testosterone helps build muscles
 - Permits to exercise longer and more often
 - Tears fibers in muscles, and repairs faster
 - Cycle is important
- Tetrahydrogestrinone
 - The clear
 - Undetectable before 2012
 - Fingerprint was unknown
- Anadarine
 - Failed FDA approval
 - But is still on sale
 - Even though we don't know if it works
- Steroid testing
 - Testosterone to Estrogen ration
 - Normally 1:1
 - Can be as high as 4:1
 - Extra testosterone can be masked by injecting epitestosterone



- Diuretics mask steroid amount by drinking more water and peeing out excess metabolites
- Can add materials to interfere with testing such as alcohol and detergents
 - Chemical clean outs before processing pee into GC/MS
- Steroids originally came from animals and are hard to distinguish
- Atoms have isotopes and an isotopic signature as each isotope has a different mass
 - Carbon 12 is 98.9%
 - Carbon 13 is 1.1%
 - Ratio between the two carbons tells the source
 - Plants and animals have different amounts of C13
- Health risks
 - Liver damage
 - Heart damage
 - Reproductive effects
 - Frequencies are important and are actually rare side effects
 - Anabolic steroids speed recovery, training
 - Effects are difficult to measure
 - Athletes vary doses
 - Mix steroids
 - Keep methods secret
 - Tend to abuse
 - BALCO made designer steroids
 - Designed to avoid detection
 - There was no proof
 - Made their own steroid to have a unique steroid and still can't be found
- Desire
 - To win makes drugs dangerous
 - Used properly are safe
 - Desire to win makes athletes push the limits
- Red blood cells
 - Carry oxygen



- Made in bone marrow
- No nucleus
- Last about 40 days
- 3 million RBC every second
- controlled by erythropoietin EPO
- Hormone
- Endurance athletes benefit from increased oxygen capacity
- Training at high altitudes increases RBC production
- Blood doping
 - Remove blood from athlete, concentrate RBC and store, wait 3 months and reinjection, but is time sensitive
 - Was used to increase performance,
 - Loophole: bring relative of same blood type to give blood
 - Transfusion in a Ramada inn, but viruses were still not educated with people
 - Banned blood doping in 1985
 - IOC banned blood doping in 1986
- Anemia is a serious condition
 - Treat with iron supplements
 - Or transfusions
 - EPO could be a perfect anemia drug
 - But EPO is a protein made of amino acids
 - Chemical synthesis is impractical
 - Animals aren't ideal protein sources since supply is limited and extraction is difficult, aren't human proteins and don't work as well or are immune to humans
 - Humans and animal proteins have the same shape but different sequence
 - Human cadavers are a poor source
 - Solution could be recombinant protein
 - Using bacteria or yeast
 - Easy to grow
 - Easy to isolate protein
 - Product is safe



- Insert human gene into a plasmid
- Recombinant protein is easier to purify
- EPO is one of the best drugs in the last 30yrs
- EPO was abused since day one
- Overdose of EPO thickens blood and causes a heart attack
- EPO banned in 1990
- Testing was impossible because everyone make a different amount of RBC to Plasma ratio (Hematocrit)
- Tested using antibodies and compare values to normal human levels
- ON model detects recent use
 - Hemoglobin, EPO, Soluble transferrin receptor
 - Only good if within one week of testing
- OFF model detects longer term use
 - 2-3 weeks
 - French law (guilty until proven innocent)
- Bubble boy syndrome
 - No immune system
 - Replaced gene but then started cancer
- Drugs are banned from sports for safety reasons

Plague was common throughout history

Cures and treatments failed

- Thought it was bad smells

Cause of disease was thought to be from god and killed them

Post natal infections were 30% death rate

Maternal mortality rates declined in 1930 because of penicillin

Surgery survival rate was less than 30%

WWI and WWII

- More deaths due to infection than combat
- Sexual transmitted diseases
- John Snow
 - Disproved miasma theory 1854 bad air that caused disease
 - Cholera infections were identified at a pump
 - Epidemiology
 - Water pump is a historical landmark
- Agostino Bassi
 - Showed microbes cause disease
 - Soap worms
- Athara-Veda
 - Ancient text
 - Hindu
 - Living animals cause disease
- Louis Pasteur
 - Pasteurization in 1864
 - Food spoilage
 - Safe milk
- Lister
 - Develops antiseptics
- Hans Christian Gram
 - Gram positive and negative staining
 - Selectively now which is a bacteria
- Paul Erlich
 - Magic bullet
 - Chemical difference
 - Consuming a chemical will go throughout the body and would be selective



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- Trypan red
 - Selectively colors trypanosomes
 - Cause sleeping sickness
 - Could be colored purple
 - Used arsenic as the poison
 - Was in the same family as nitrogen to take over
- Salvarsan 606
 - Arsenic antibiotic discovered
 - Treat syphilis
 - Not drug like
 - Wasn't super commercial
 - Not convenient for the patient
- Noble prize in Medicine 1908
- Gerhard Domagala and IG Farben
 - 1932, first successful antibiotic
 - Prontosil
 - Worked in vivo and only living animals
 - Kills certain bacteria
 - Was metabolized into sulfanilamide, made skin red
 - Pro-drug (doesn't have biological activity, easy to get into body and then be converted)
 - Nobel Prize in 1939
- Sulfanilamide is first drug in 1932
 - Successful antibiotic on market
 - Save lives in WWII
 - Inhibit bacterial growth, stop infection and let immune system take over
 - Sulfa drugs stick to enzyme to make coenzyme F
 - Mimic natural substrate
- Alexander Fleming
 - Contaminates culture in 1928
 - Contaminated a culture with mold that was penicillin
 - Interested in purifying bacteria
 - Mold prevented bacterial growth
 - Published crappy results



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- Closer the bacteria is to penicillin the harder it is to grow
- Didn't do the key experiment in proving it would cure infected mice
- **Howard Florey and Ernst Chain**
 - **Isolate penicillin in 1941**
 - **1000kg~1g**
 - **milk bottles, anerobic**
- Britain was not a good place to research
 - **Moved to America**
 - **Used corn steep liquor** (by product of corn syrup)
 - Made larger quantities
 - Peoria Illinois becomes penicillin capitol
 - Merck isolation method of penicillin
 - Production became war priority
 - **Stock piled for D-Day**
- Fleming, Florey, Chain share noble prize in 1945
- **Bacterial cells**
 - **Have outer cell walls**
 - **Highly selective**
 - **Small to resist pressure**
 - **Penicillin prevents cell wall synthesis and bacterial cells explode**
 - **Beta lactam ring is what builds cell walls**
 - Penicillin destroys the beta lactam ring (enzyme)
 - Antibiotics only work on bacteria
- **Artificial antibiotics**
 - **Natural penicillin is not drug like**
 - **Unstable**
 - **Must be injected**
 - **Only works against some bacteria**
 - **Artificial**
 - **Stored longer**
 - **Taken orally**
 - **Work against most bacteria**
 - **95% artificial**
 - better antibiotics though semi-synthesis
 - Penicillin~6 APA~ Amoxycilin



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- Major side effect is allergy
 - Only can get allergy second time
 - OH group changes into a normal protein as an allergy effect
- Cephalosporin
 - Italian sewers
 - Fungus
 - Similar to penicillin
- Streptomycin
 - Chicken throats
 - Inhibits protein synthesis
- Tetracycline
 - Inhibits protein synthesis
 - Semi synthetic
 - Natural form is too toxic, OH group
 - Can create photosensitivity that can last for months
 - Interferes with calcium metabolism
- Antibiotic resistance
 - Too much use of an antibiotic
 - Resistant to strain
 - Prophylactic use may promote resistance
 - Patient compliance
 - Instruction on time and amount is important to keep above a certain threshold
 - Missing a dose creates a resistant bacteria
- Most dangerous bacteria are in hospitals
 - Nosocomial infection
 - Necrotizing fasciitis, flesh eating disease
 - Staphylococcus aureus, 2000000 to 3000000 infections a year
 - 1500 become dangerous
 - Debridement
 - Barrier around bacteria, bacteria scooped out with puss and apply an antibiotic cream under the skin
 - Clostridium difficile
 - 1000000 per a year
 - Methicillin resistant Staph



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- MRSA, 130000 a year, skin infection
-

- Most dangerous substance in the world
- Kills 42000 a year in NA
- Columbus discovers tobacco in 1492
- Natives drank smoke from tobaggos
- Fresh shipments to Spain from Tobago, sources of tobacco unknown
- Jean Nicot introduced tobacco to France
 - Source of nicotine
- Used to be used to revive drowning victims
- Used to be smoked in clubs
 - On special occasions
 - Acid smoke would hurt
 - Stem cooled to precipitate the acid
- Water pipes
 - Remove acid from smoke but not safer
- Snuff became popular with aristocracy
- Chewing tobacco was popular with masses
- Were originally rolled by hand
- Then machines made it cheaper
- Bonsack machine
- Flue-curing reduced harshness of smoke
 - Oven to cure
 - Accelerate the curing of tobacco
 - Less acid in the smoke
- Cigarettes became dangerous
 - Anyone could afford it
 - Smoke was brought deeper into the lungs
 - Became addictive
 - Risk= toxicity X exposure
 - Average smoker is 10000 cigarettes a year
- Cigarette consumption
 - Late 1800
 - 80 a year
 - did not inhale
 - now
 - 10000 a year
 - inhale deeply



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- hold smoke in lungs
- Nicotine
 - Addictive substance
 - 2mg per a cigarette to become an addict
 - acts on **ACh receptors**
 - messenger goes to a receptor to a secondary messenger inside the cell and the receptor changes shape
 - **agonist in low concentrations, mimic natural occurring compounds**
 - antagonist in high doses, doesn't changes shape of receptor on the inside of the cell, block chemical messages
 - **stimulates dopamine release**
 - dopamine system
 - release dopamine
 - part of the learning system
 - **Used as a pesticide lethal dose is 60mg**
 - Kill elephants
 - Stimulates heart muscles and can lead to a heart attack
- Smoking cues add to addiction
 - Religious hobbies when smoking
- Toxic substance in tobacco smoke
 - **Carbon monoxide**
 - Reduces the carrying capacity of oxygen because of the greater attraction to iron
 - **Polonium 210**
 - Fossilized phosphate deposits
 - Benzopyrenes
 - Carcinogenic
 - C450
 - Nitrodamines
 - Aldehydes
 - Epoxides
 - Aza-arenes
 - Trace metals
- Alton Ochsner
 - Linked cancer to smoking 1919



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- 1919 only 400 cases of lung cancer
- 2004 190000 cases of lung cancer
- Women started smoking to stay slim
 - Doesn't help
 - Will gain weight as a craving
- Wrinkles
 - Carbon monoxide destroys collagen that keeps elasticity in the skin
- Emphysema
 - Destroying a protection system in the trachea
- Smoking during pregnancy
 - Linked to low birth rate
- Cigarette
 - Engineered paper with additives to increase chemical effects and cut costs
 - Paper
 - Recon
 - Made from the whole tobacco plant
 - Cheaper
 - Blend tobacco
 - Introduce flavor and additives to effect the burn rate
 - Titanium oxide will keep the paper lit
 - Burn rings
 - When inhaling it burns faster where it is thinner
 - Not inhaling the burning is affecting the thicker areas that will take longer to burn
 - Filter
 - decoration
 - light cigarettes ones have holes to pass tests to prove they have less tobacco, but actually only increase the amount of air to not draw as much tobacco and chemicals
 - not safer or lighter
 - engineered to deliver nicotine
 - liquid to gas
 - combustion makes acids that react with added bases



- liquid to solid and burns since it can't be turned into a gas
- ammonia reacts with acids that destroy nicotine and increases the effectiveness of nicotine dose
- Tobacco companies suppress information
 - CBS was owned by a tobacco company to keep all of its information
- Tobacco companies will have enough money to extend a trial until the patient dies
- Less cancerous cigarette
 - Eclipse charcoal at the end
 - Accord, battery powered to heat
- Tobacco wasn't an addictive
 - Because they added in intoxication to the scientific definition of an addictive
 - Dependence, Withdrawal, Tolerance
- Warning labels
- Nicotine gum 2mg, inhaler, Chantix (partial nicotine agonist, reduce addiction)
- Chantix
 - Cytisine
 - Nicotine agonist
 - From orchid family
 - Difficult to make synthetically but is similar to morphine
 - Made Varenicline
- Cold turkey is the most effective

- Develop immunity after illness
- Minor illness creates damage
 - Damage over time
 - Better not to get sick
- Immune system uses weapons
 - Poisons
 - Defenses
 - Complement
 - Antibodies
 - Immobilize invaders
 - Selectively destroy invader
 - Macrophages
 - Specialized cells to eat foreign cell
 - Specialized cells to kill infected cells
- Innate immune system
 - Immediate response
 - Nonspecific reaction
 - All cells are targeted
 - Maximum response
 - Cold symptoms
 - Responds to damage
 - Releases Cytokines
 - Inflammation gives easier access for immune cells
 - Leukocytes destroy invading microbes
- Adaptive immune system
 - Selective
 - Lag time between exposure and maximum response of 2-3 days
 - Response is selective, only invading cells
 - Immune system retains a memory of the infection
 - Next time same microbe invades to response is immediate
- Antibodies
 - Key recognition devices
 - Y shaped with sticky surfaces
 - Stick to epitopes that are 30 atoms wide
 - Many different antibodies stored, each one goes with a specific epitope



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- Production is random
- Cannot store large amounts of antibodies, small amounts of many different types
- Manufacture large quantities only when needed
- **B cells**
 - Carry antibodies
 - Memory cells
 - Only one type of antibodies per a B cell
 - **Have IgD and IgM**
 - Reach B cell recognizes 1 epitope
 - Immune response triggers replication of specific B cell
 - Amplified B cells target the invaders
 - **After infection some B cells become memory cells**
 - Each infection generates memory cells
 - **<5% of B cells in newborn are memory cells**
 - **>50% of B cells in adults are memory cells**
 - viruses live inside cells and escape B cells
- T cells
 - Body makes **T cells to destroy viruses** in human cells that invaded
 - Infected cells display viral protein fragments that come from cells
 - Infected cells have MHC receptors that contain viral protein fragments
 - **CD8 antibodies Killer T cells recognize MHC receptors** with viral protein fragments
 - **CD4 antibodies Helper T cells send the signal to kill the infected cell**
 - The helper T cell is a fail safe and only signals the killer T cell to kill when it is told that the cell is infected
 - Viral infections trigger replication of specific T cells
 - Some T cells become memory cells
 -
- **Memory cells give immunity**
 - **There will be an immediate and specific immune response**
 - Microbes are killed quickly before infection develops
 - Natural infection: bacteria~severe disease with immune response~immunity



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- Immunity: Bacteria ~ rapid immune response
- Manufacture T and B cells
- **Smallpox**
 - Variola
 - Pustules
 - 20-40% mortality rate
 - 70-80% disfigured
 - Variolation
 - Use puss from pustules and inject into children with live virus
 - High mortality rate
 - Brought to England by lady Montagu
 - **Edward Jenner**
 - Mild way of getting small pox
 - Milk maids had cowpox and couldn't contract smallpox
 - Cattle was source of cowpox
 - **Vaccination was safer than variolation**
 - 1900 smallpox levels became very low
 - eradicated in industrialized countries by 1950
 - Global eradication targeted in 1966
 - CDC
 - Last case of natural small pox in 1977 Somalia
 - **Biological weapons with soviets**
 - Vaccination scar born before 1972
 - Special needle
 - Smallpox: Virus ~ severe disease ~ death or immunity
 - Cowpox: Virus ~ mild disease ~ immunity
 - Body makes memory cells for immunity for rapid response
 - Cowpox was a mild disease, similar molecular structure to smallpox virus
 - Unique situation- smallpox only
- **Anthrax**
 - No squalene
 - **Loss of herd animals**
 - Pasteur
 - Attenuates anthrax bacteria by heating



- Weakened bacteria and cause mild infection
- Used a second shot as a booster
- To make enough memory cells
- Need a certain number of memory cells for immunity as a threshold
- Small risk of severe infection
- Polio
 - 1% paralytic
 - can include lungs and used the iron lung machine
 - President Roosevelt was a survivor
 - Salk vaccine
 - 1955
 - dead virus
 - required injection and booster
 - vaccine was extremely safe and effective
 - Cutter laboratories
 - One defective batch
 - Live viruses
 - 170 cases of paralytic polio
 - 11 deaths
 - Sabin vaccine
 - Small risk of polio, live virus
 - No booster
 - Competitor
- Clinical trials
 - 77 million vaccinated
 - effective
 - 1/1000000 risk of polio
 - sabin vaccines adopted by most countries
- fewer than 300 cases of polio world wide by 2003
- 1600 cases world wide in 2009
 - major barrier to eradication is politics
 - active politics against vaccinations
- Influenza
 - Seasonal colds



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- 5-15% infection
 - new version every year
 - most forms aren't dangerous
 - except very old and very young
 - infected usually once every 3 years
 - occasional severe influenza pandemics
 - 1918~ 20000000 deaths
 - 1957~ 1000000
 - 1968~ 700000
- use dead virus
 - excellent safety record
 - dead virus doesn't cause disease
 - 21 days for full immunity
 - mutates at a high rate
 - main side effect is egg allergy, made in eggs
- number of adverse events exceed number of illnesses
 - most are minor
 - at or around time of vaccine
- anti-vaccine propaganda is effective and dangerous
- most focused on autism
- vaccinations around age 2 and autism appears around age 2
 - wake field study was made up
 - isn't true
 - stripped of medical license in 2011
- measles

Year	% of children vaccinated	Cases of measles (England)
1940	0 %	400, 000
1998	92 %	56
2008	Less than 80 %	1348

- Preservatives



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- H1N1
- Contains mercury
- Less mercury than a piece of fish
- **Thimerosal** doesn't cause autism
- Vaccines don't cause autism
- Adjuvant worries
- **Adjuvants reduce the need for booster shots**
- Alum was used to reduce the need for booster shots
- Lipid adjuvants
 - **Squalene** blamed for gulf war syndrome
 - No squalene in military vaccines
 - Body makes squalene
 - Normal human metabolite
 - Used to make steroids
 - Sold as a nutritional supplement
 - Sharks have squalene
- Vaccines
 - Occasionally cause adverse effects
 - Most are minor such as swelling, redness, soreness, fever, dizziness (psychological)
 - Allergic reactions (rare)
 - Disease (extremely rare)
 - Only with live or attenuated organisms
 - 69 cases of polio between 1978 and 1983
 - 51 associated with vaccine
- **Unvaccinated people keep disease alive**
- Herd immunity is important while a disease exists on the planet
- Reduced vaccination rates are dangerous
- Not vaccinating is dangerous
 - Child has to endure through virus and pain
- **Cervical cancer**
 - Kills 250000 women each year world wide
 - Viral disease
 - Married women and are sexual active
 - Caused by nervous irritability 1842



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- Anal genital warts
- HPV
 - Human papillomaviruses
 - Cause warts
 - More than 200 types
 - Each to a specific tissue and place
 - Only a few types cause cancer
 - Cervical tumors
 - Certain HPV genes are oncogenes
 - Destroy p53
- Immune response can be from an empty virus capsid
 - Outer protein coat
 - Small fragment can cause immunity
 - Capsid protein is immunogenic
 - Just need a small part
 - Gardasil
 - Made from virus protein
 - Recombinant yeast
 - Effective against 6,11,16,18
 - Only works if previously uninfected
 - Administer at age 9-13 and max of 26
 - Available for both sexes
 - Has no effect on sexual activity

• Different disease	• Live attenuated • *small risk of infection	• Dead organism	• Recombinant
• 18 th century			
• smallpox	•	•	•
• 19 th century			
•	• Anthrax (booster), rabies	• Typhoid, cholera, plague	•
• 20 th century			
•	• Polio Sabin no	• Polio Salk	• Hep B



	booster	Booster	
•	• Measles, mumps, rubella, influenza	• Rabies, influenza, Hep A	• lyme
• 21 st century			
•	•	•	• HPV Gardasil

- HIV discovered in 1984 from AIDS
 - Spread rapidly
 - Unsafe sexual practice
 - IV drug use
 - **Anal sex**, responsible for early homosexuals, primary rout in NA
 - **Bareback sex**, blocked with condoms
 - **Dry sex**, in Africa
 - Politics and bullshit
 - Leaders refused to acknowledge the aids existed in their country
 - Africa resistant to condom distribution and promoted abstinence
 - **Thabo Mbeki refused AIDS in south Africa**
 - Claimed HIV didn't cause AIDS
 - 30000 deaths
 - **AIDS now the worlds most deadly disease**
 - Malaria was #1 untill late 1990s
 - **AIDS is 4th of world leading cause of death**
 - **1% of all adults have HIV**
 - >15000 new infections each day
 - 2.7 million new infections in 2008
 - 2 million deaths in 2008
 - 33 million infection
 - 35 dead since 1981
 - **AIDS then and now**
 - Life expectancy after infection in NA
 - 10 years in 1981
 - 20 year in 2010
 - triple combination of chemo
 - Prognosis after infection



- 100% in 1981 and 2010
- treatment
 - unpleasant
 - 16 or more pills a day
 - complex regimens
 - side effects
 - high cost
- only one person cured by radiation to kill all blood cells and transplanted blood from resistant donor
- Vaccine for HIV
 - Difficult to find volunteers
 - AIDS targets helper T cells
- Phases
 - Acute
 - 6-10 weeks
 - flu like symptoms
 - viral load
 - ends when immune system reduces viral numbers to low levels
 - normal infection would be cleared
 - HIV lives in cells that try to destroy it
 - Chronic
 - Asymptomatic
 - Fully infectious
 - 8-12 years
 - immune system destroys most viral particles
 - few virus particles escape to continue infection
 - CD4 cells actively seek out viruses Helper T cells
 - AIDS destroy CD4 cells
 - Phase ends when immune system runs out of CD4 cells
 - AIDS
 - 2-4 years
 - fully infectious
 - viral replication high
 - immune system destroyed



- secondary infections cannot be cleared by immune system
- person dies of secondary infection
- All attempts at vaccine have failed
 - Virus replicates in large numbers
 - Immune system is highly efficient in removing virus
 - Small leakage prevents body from clearing the virus
 - Companies no longer pursue vaccines
 - Combining vaccines delayed infection
 - Effective HIV vaccine is unlikely
 - Infection is permanent
 - 100% fatal
 - expensive and unpleasant
 - virus cant live outside human body
 - use condoms
 - avoid anal sex

- \$1.4 billion spent on antacids
- \$20 billion spent on prescription stomach meds
- Stomach is a storage device
 - Breaks down carbohydrates into glucose with the enzyme amylase
 - Protein is broken down into amino acids with the enzyme pepsin
 - Enzymes work best in an acidic environment
 - HCl
- Small intestine
 - Digests fats, enzyme is lipases
 - Stomach acid is neutralized in the intestine
- Stomach problems
 - Caused by excess acid
 - Eat too much
 - Eat too fast
 - Spicy food
 - Smoking
- Chronic use of NSAID
 - Lead to problem for chronic users
- Antacid
 - Neutralizes excess acid
 - To make salt, water, carbon dioxide
 - Sodium bicarbonate, nahcolite mineral
 - Produces gas CO₂
 - Advantages
 - Cheap
 - Fast
 - Disadvantages
 - Acid rebound, not enough acid and makes more that is too much
 - Short duration
 - Sodium
 - Systemic alkalosis
 - Gas
 - Alka seltzer
 - NaHCO₃
 - Citric acid



- Placebo effect
- A.S.A
- Fizz is for show and makes sodium citrate
- Alka Seltzer Gold
 - Doesn't contain A.S.A
 - Costs more
 - Inhibit prostaglandin production
- 1 tablespoon of baking soda is equal to 1 tablet of alka seltzer
- Calcium carbonate
 - Most common
 - Basically flavored chalk
 - Calcium for osteoporosis
 - In NA
 - Vitamin D is included as instructions for the body to intake calcium
 - Vitamin D is present when light affects the blood under the skin
 - Natural source of calcium
 - Oyster shells
 - Composite material
 - Has protein
 - But hangs onto CaCO_3 and doesn't let go
 - Advantages
 - Cheap long lasting
 - Source of calcium
 - Disadvantages
 - Acid rebound
 - Kidney stones
 - Tetracycline toxicity
 - Gas
- Metal hydroxides
 - Do not produce gas
 - MgOH_2 , Milk of Magnesia
 - Fast acting
 - Long lasting



- No gas only a metal chloride
- Laxative
- AlOH₃
 - In Gaviscon
 - Constipation
- Combined metal hydroxides
 - Laxative effects offset constipation
- Maalox plus, simethicone that treats gas
 - AlOH₃ and MgOH₂
 - Basically silica gel that is ground down
 - Getting us to burp instead of fart
- Advantage
 - Cheap long lasting
 - No gas production
- Disadvantages
 - Acid rebound
 - Constipation with Al
 - Diarrhea with Mg
 - Kidney disease
- Peptobismol
 - Not an antacid
 - Antibacterial
- Gastric ulcers
 - Caused by acid
 - Can cause internal bleeding
 - Common in older people
 - Duodenal ulcers
 - In young people
- Gastro Esophageal Reflux Disorder
 - GERD
 - Acid can tough esophagus
 - Partly genetic
 - Valve at the top of the stomach becomes defective and leaky
- Antacids
 - Only treat symptoms



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- Metals can cause problems
- Our bodies are made to get rid of organic materials
- Regulating acid production is safer for chronic treatment
 - Stomach is controlled in 3 ways
 - Histamines
 - Ach
 - Gastrin
 - That all use a proton pump to make acid
 - Histamine is the best choice
 - Histamine antagonists work selectively in the stomach
 - Tagamet
 - First 1 billion in sales in one year (Block buster drug)
 - Other drugs became available later after being off patent
 - It was safe enough to be OTC
 - Proton pump is an enzyme that pumps HCl into the stomach
- First proton pump inhibitor
 - Company Nexium
 - Omeprazole
 - 2000-6.2 billion in sales
 - Prilosec
 - After getting off patent it lost market share
 - Usually protected for 20 years but only has a window of 8-10 years to sell
 - Esomeprazole
 - Mirror image
- Enantiomers
 - Non superposable mirror images
 - Special property
 - Cant be overlaid
 - Mirror images can be very different
- Biological molecules
 - "handed"
 - chiral – the ability to exist as a non superposable mirror images
- Thalidomide
 - Chiral



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- Was manufactured as a 50:50 mixture
 - Racemic mixture
- Very difficult to manufacture as a single enantiomer form
- Teratogen in inactive forms in most adults or a sedative
- Nexium
 - Made a race mixture to sell both that were safe
 - Once off patent, patent extension of only one hand
 - Single hand chiral drugs
 - Hard to make racemic mixtures
 - Enantiomer acts differently in the body
 - Efficacy-desired result
 - Side effects
 - metabolism
- FDA
 - Allows racemic mixtures if the mixture is proven safe
- 3TC
 - race mixture drug
 - both block AIDS virus replication
 - natural on the left side
 - un-natural on the right
 - natural is highly toxic
 - unnatural has a lox toxicity
 - Uottawa prof, Montreal
- Nexium
 - Both Omeprazole and Esomeprazole is converted into the same molecule
 - Esomeprazole is metabolized slower
- Chiral Switch patent strategy
 - Patent and manufactured as a chiral drug in a racemic mixture
 - Just before expires, use a single enantiomer form of the drug
 - Can get up to an extra 15 years if there is a proven advantage to the FDA
- Peptic ulcer
 - Most ulcers
 - Psychosomatic disorder



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- Doctors believed that it was caused by stress
- John Lykoudis
 - Used antibiotics to treat ulcers and was convicted of malpractice
- Robin Warren
 - Finds bacteria in gastric biopsy
 - Marshall helps
 - Helicobacter pylori
 - H.pylori
 - Extremophile
 - Uses ammonia for protection
 - There is an isotopic signature to urea and burp up CO₂ and test it
 - Infects 20% of population
 - 90% of duodenal ulcers
 - 70% of stomach ulcers
 - Paper was destroyed by lancet publications
 - Bacteria hide in slime
 - Don't live in acid but in the mucus layer
 - Make their own chemical to protect them
 - Marshall infected himself in 1984
 - Zantac
 - 81% of ulcers re-occurred
 - Zantac and antibiotics
 - Less than 2% re-occurred
 - After Tagamet patent expires, doctors start to use antibiotics

- Allergy requires prior exposure
 - Immune system responds
 - Epitopes of molecules from pathogens
 - Immune system “remembers” material
 - Memory cells
 - Subsequent exposure produces reaction
 - Protection from pathogens
 - Allergy to harmless material
- Hay fever is a reaction to pollen
- Different types of pollen from each plant
- Geographic tongue
 - Coded tongue
 - Swelling of tissue like a map
- Atopic dermatitis
 - Surface exposure
 - Skin, rash
 - Contact dermatitis from irritants
 - Non allergy form
 - Hand washing makes it worse
 - Common with industrial powders
 - Irritate skin
 - Can be from washing hands too much
 - Contact dermatitis from immune reaction
 - Immune reaction at the site of contact
 - Can cause blistering
 - Urushiol
 - In poison ivy and poison oak
 - Latex from rubber tree sap
 - Nickel
 - Makes metal stronger
 - Henna tattoos made from plant juice
 -
- Exposure, dose, amount
- Quantity, dose, exposure
- Dust



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- Dust mites live in dust that is made of skin cells that are protein rich
- Gets into mattresses droppings
- Pets
 - Animals lick fur and saliva is on fur
- Mold and fungi
 - Produce nasty chemicals
- Food
 - Allergy 4% of adults
 - Immune system reacts to the food
 - Intolerance 30% of adults
 - Substances in food produce adverse reaction
 -
 - Lactose intolerance
 - Lactase needed to break down lactose into glucose a sugar
- Signs of food allergy
 - Bags under the eyes
 - Dark under eyes
- Peanut allergy is common in NA and rare outside of NA
- Spider and insect bites
- Rare allergies
 - Sunlight, allergic to chemical that is light activated
 - Marigolds make a toxic chemical that is light sensitive
 - Aquagenic allergy
 - Allergy to water
 - 20th century allergy to man made substances
 - total allergy syndrome
 - psychological condition
 - can appear after a traumatic event
 - and won't acknowledge a problem
- Allergy is a disease that has doubled since 1980
- Hay fever was a rare condition in 1900
- Peanut free schools within the last 30 years
- Industrial pollution is more common in the developing world and is exposed more than us, we are too clean



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- Most allergies involve natural substances, most of which are not man made chemicals
- Hygiene hypothesis
 - We are too clean
 - Exposed to less substances
 - Immune system has evolved and doesn't defend as much anymore
- Immunization and antibiotics reduce infection rates
- Children in day are less likely to be allergic
- Younger children in a large family
- East berlin of the communist side had poor health care and pollution
- There were more allergies in west berlin
- Allergy requires prior exposure
 - Involves immune system memory
 - Hypersensitivity on the 1st exposure
 - Unknown previous exposure
- Mast cells
 - Display IgE antibodies
 - Allergen contacts IgE and change shape of the antibody
 - Degranulation releases histamine
 - Once the allergen is attached it is a controlled explosion and releases histamines that starts symptoms
 - Histamine produces allergy symptoms and is blocked with antihistamines
- Managing allergy
 - Avoidance
 - Antihistamines
 - Decongestants
 - Immune modulators
 - Immunotherapy
- Allergy tests
 - Injection test
- Track down food allergy with a log book
- Antihistamines
 - 2 types
 - first generation being sedating, can enter brain



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- second and third generation is non sedating
- Antagonists that block histamines from getting to a receptor
- **Diphenhydramine**
 - Bendadryl
 - Frist generation
- **Chlorpheniramine**
 - Chlor-Tripolon
 - Drowsiness
 - First generation
 - Usually in cold medicines
- **Second generation**
 - **Loratadine**
 - Claritin
 - Cant get into the brain
 - Circulates in blood and trapped in blood vessels
 - **Pro drug that is converted into Desloratidine**
 - Desloratidine is also a prodrug that is in Aeries
 - Seldane
 - Contains terfenadine
 - First non drowsy antihistamine
- Drug-drug interaction with Ketoconazole
 - Toxicity by mixing drugs that react with each other
 - Terfenadine is activated in the body
 - A toxic prodrug that is metabolized into an active non toxic drug (Fexofenadine)
 - Allegra contains fexofenadine (3rd generation)
- Reactine
 - Contains cetirizine
 - 3rd generation
- **First generation** (drowsiness)
 - Diphenhydramine (1940's, Benadryl, generic available)
 - Chlorpheniramine (1940's, Chlor-Tripolon, generic available)
- **Second generation** (non-drowsy)
 - Loratadine (1989, Claritin, generic available)
 - Desloratidine (2002, Aeries, generic available)



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- **Third generation** (non-drowsy)
 - Fexofenadine (1996, Allegra, generic available)
 - Cetirizine (1996, Reactine, generic available)
- Pseudoephedrine
 - Decongestion
 - Sudafed
- Steroid decongested
 - Nasal sprays
 - **Rhinocort spray**
 - **Pulmicort**
 - **Anti-inflammatory steroid**
- **Anaphylaxis**
 - Extreme swelling and hospital because of life threatening
 - **Epi-Pen** for string allergic reaction
- Asthma
 - **50% of allergies progress to asthma**
 - first versions targeted nerve signals
 - Salbutamol targets nerves to the bronchi for the sympathetic system
 - Salbutamol is a selective adrenaline agonist
 - Adrenaline agonists open airway in the lungs
 - Extreme doses will stimulate the heart and an overdose can cause a heart attack
 - **Flovent inhalers delivers a measured dose**
 - **Leukotriene's**
 - Messenger molecule
 - **Singulair is a leukotriene antagonist**
 - fully Canadian
 - no heart attack
 - ingest pill on daily basis
-

- Drugs pass through many barriers and barriers remove some drug
- Most drugs pass through the digestive system
 - First barrier
 - Stomach
 - Drug must survive acid
 - Must dissolve in water
 - Sometimes the properties don't work together
 - Second barrier
 - Small intestine
 - Dissolve in water
 - Survive digestive enzymes
 - Where most drugs get absorbed
 - Pass through intestinal cells
 - Lipophilicity
 - Passive diffusion
 - To get to blood
- Molecules pass through membranes
 - Membranes are like oil and water
 - Must be able to dissolve in fats and water
- Liver
 - Removes poisons from food
 - Changes the chemical structure to help body eliminate it
 - Largest % of the drug that gets through the liver gets to the rest of the body
- Membranes
 - Stomach
 - Intestine
 - Membrane
 - Liver
 - Each successive barrier=loss in % of the drug
 - Target dose is always smaller than the dose of the pill
 - Work backwards from the dose target and towards the pill dose
- Drug
 - Interacts with biological molecules
 - There is a need for enough of the drug at the site of location



- All molecules share, physical contact with a biological molecule for an effect to happen
- Molecules only stick in high concentration where dose makes the drug
- There is a threshold of drug needed to make contact with biological molecules
- Total amount given, ensures an effect
 - An ability to cross barriers
 - Binding to target receptors
 - Works backwards of attrition to estimate the initial dosage
- Drug + desired target = desired effect
- Side effects are undesired effects
 - Drug goes everywhere in the body
 - Side effect: undesired effects
 - Harmful
 - Beneficial
 - Balance risk and benefit
- Reflex response
 - Produces an undesired effect
 - Unintended way
- Drugs working correctly in the wrong place
 - In a separate location will cause a side effect
- Drugs interact with wrong biological molecule
 - Undesired response
- Capsaicin
 - Topical pain relief
 - Found in chili peppers
 - Binds to heat sensing neurons
 - Temperature depends on dose
 - Measured in scoville units
 - Not dissolvable in water
 - Dissolvable in high fat concentrations
 - High dosage, emesis (vomiting)
 - Ring of fire when excreting urinary waste
- Drug safety testing



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- Panlabs in the Philippines
 - Biochemical tests through vitro, (glass or plastic) robots
 - Small animals
 - Primates
 - 60 000 000 animals a year
 - half are rodents
 - 200 000 dogs
 - 50 000 primates
 - Sulfanilamide (no testing), Thalidomide (limited testing)
 - Complexity of living animals cant be simulated
 - No animal testing ~ no drugs ~ no surgical procedures
 - Pro-Test movement
 - Animal testing subject to ethical review if there is a need and a benefit for purpose
- Pills
 - Excipients
 - Fillers
 - Non active drugs
 - Stabilizers, preservatives, binders, flavors, colors
 - Food additive
 - Fillers are important for safety
 - Measurement is easier in larger quantities with limited active drugs
 - Stabilizers
 - Protect drugs from oxidizing or degrading
 - Preservatives
 - Protect drugs from microbes
 - Color
 - Makes drugs distinct from each other
- Clinical trials
 - 90% failure rate
 - 30/300 drugs tested a year world wide is approved
 - testing for safety and efficacy in humans
 - Phases
 - Phase 1



- safety
 - 100 volunteers
 - TGN1412
 - Anaphylactic reaction
 - Phase 2
 - dosing
 - 100-300 patients
 - efficacy- does the drug work
 - Phase 3
 - 1000 of patients
 - rare side effects
 - double blind study
 - neither patient or doctors know which has the active drug
 - Nuremberg code
 - Research on humans
 - Informed consent
 - Prior animal studies
 - Benefits outweigh the risks
 - Qualified scientists
 - No suffering
 - Nazis crossed the line of ethical practice
- Drug development
 - 8-10 years
 - patents last 20 years
 - large profits
 - brand and generic
 - generic substitutes
 - D.A.W (dispense as written)
 - Incorrect prescriptions kill 10000 a year
 - Companies
 - Spend more on marketing, 16% R&D, 23% marketing
 - 60% marketing towards doctors
 - 50 000 per a doctor spent
 - Ethical brand name pharmaceutical companies



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- 1 billion on research for every drug
- patent protection is important to ensure the supply of new drugs
- Generic pharmaceutical companies
 - Once patents expire they can make it
 - Same substance, dose, biological activity
 - Generic drugs are cheaper
 -

- Gladiators wounds provided the first glimpse of function
- William Harvey
 - First one to make details of the heart, functions, visual
- Blood circulation
 - Lungs before heart
 - Arteries get smaller and veins get larger the closer to the heart
- Ibn Al-Nafis
 - Arabic
 - Scholar noted the same functions 500 years before Harvey
- Heart pumps 2.6 billion times during your life
 - 5-6 litres each minute
 - 100 000 Km of blood vessels
 - 60 times a minute
 - only organ to take that much force
- Coronary vessels
 - Feed the heart
 - Key weakness
- Many deaths from heart problems are avoidable
- Smoking kills by poisoning the heart
 - Hemoglobin carries O₂
 - CO stick better to Hemoglobin than O₂
 - Lack of O₂ damages heart and blood vessels
- Obesity kills by overworking the heart
- Diet high in fruits and vegetables
- Variation is key to minimize exposure to particular substances
- Men are at 10X a higher risk
- Heart attacks in young women are often misdiagnosed
- Heart attack risks equalize after menopause
- Estrogen replacement has no effect
- Stress dramatically increases you risk of heart attack
- Exercise improves coronary blood vessels
- Be aware of family history of heart disease
- Microbes links to heart disease
 - Herpes
 - Cytomegalovirus
 - Chlamydia



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- Prophyromonas
- Gum infections can lead to a heart attack
- Homocysteine
 - Levels linked to heart problems
 - Metabolized from methionine
 - Recycled using B vitamins back into methionine
 - Vitamin B supplements have no benefit
- Problems arising with heart
 - Improper functioning of valves
 - Impaired neural activity
 - High BP
 - Failure to pump enough blood
 - Reduced flow through coronary arteries
- Valve function corrected with surgery
 - Artificial valves or natural valves from pigs
- Heart's neural system
 - Stimulated with sympathetic nerves
 - Noreadrenaline antagonist
 - Blocks sympathetic neurotransmitters
 - Beta blockers keep heart rate under control
 - First antagonist drug
 - Propranolol
- Slow the heart with a pacemaker
- High blood pressure is a silent killer
- Blood pressure
 - 120/80
 - Systolic
 - Pressure when heart squeezes
 - 40-50 higher than diastolic
 - Diastolic
 - Pressure when heart rests
 - <90 OK
 - 90-104 mild hypertension
 - 105-115 moderate hypertension and start medications
 - >115 severe hypertension



- each 5mm increase in diastolic pressure increases heart attack risk by 25%
- Hypertension affect 20% of adults
 - Essential
 - High sodium
 - Irreversible
 - Secondary
 - Controlled by an enzyme system
 - Regulate diameter of blood vessels
 - Treatable with drugs
 - Regulate BP
- Pit viper venom lowers BP
 - Bothrops jararaca
 - Vasodilator
- Snake venom isn't drug like
 - Expensive
 - Hard to control dose
 - Severe side effects
 - IV injection
 - Blocks formation of Angiotensin II
 - Blocks ACE
- For a chemical to be drug-like
 - Simple chemical structure
 - Cheap
 - Low dose
 - Fewer side effects
 - Convenient dosing
 - Patentable
- Captopril
 - Anti blood pressure drug
 - Using venom as inspiration
 - First ace inhibitor
 - Side effect
 - Cough
 - Coppery taste



- Enalapril
 - Improved side effects
 - 100X more potent, smaller dose required
 - no coppery taste
- Ang II antagonists for hypertension are the best ones with fewer side effects
- Congestive heart failure
- Dropsy- change in appearance, inflation of the lower half of the body because heart isn't pumping efficiently and fast enough to support the body
 - Gravity draw liquid pools in the body
 - Adema-excess fluid
- Many causes
 - Coronary heart disease
 - High BP
 - Heart valve problems
 - Abnormal rhythms
 - Thyroid problems
- William Withering
 - Discovers heart drug
 - Stimulate heart, speed up circulation
 - Foxglove plant
 - Witches bell
 - Cardiac glycosides
 - Digitalis is the compound that is impossible to make synthetically
- Digoxin/ Digitalis
 - Narrow therapeutic window
 - Gap between effective dose and dangerous dose
 - Will dictate is a med is OTC or prescription
 - At a hospital for sick children but one person wanted a lawyer and was the only suspect
 - Charles Cullen kills over 40 people
 - Serial killer nurse for 13 years
- Coenzyme Q10



- Antioxidant
- Nothing to do with heart failure
- Angina
 - Caused by impaired blood flow to heart
 - Blockage in coronary artery
 - Intense chest pain
 - Nitroglycerine was used to treat angina as a vasodilator
 - Nitroglycerine patch detonated having an exploding patient
 - Before Viagra was nitro
- Arginine
 - Nitroglycerine and arginine make NO in the body
 - No benefit
- Arterial blockages involve cholesterol
 - Cholesterol found in all animal cells
 - High blood cholesterol is associated with heart failure
 - Half of heart attack patients have normal cholesterol levels
 - Cholesterol comes from
 - Animal foods
 - Saturated fats
 - Made in the liver
 - Body doesn't like to absorb cholesterol
 - Omega three eggs have acids from fish that reduce irregular heart beat but chickens fed with fish meal have a fishy smell
 - Omega three from flax seed does not work the same way
 - Last carbon in the chain is called omega
 - Double carbon start 3 carbon lengths from the omega carbon
 - Eicosapentaenoic acid
 - Docosahexanaeic acid
 - Comes from fish oil
 - Cholesterol made in liver from saturated fat
 - 28 chemical reactions
 - Excess cholesterol stored in arterial walls
 - Cholesterol in the plaque becomes oxidized
 - Cholestenone dangerous since its been oxidized



- Antioxidants are useless
- Cholesterol builds up inside arterial lining
- Oxidized cholesterol attracts macrophages that vacuum up cholesterol
 - Become foam cells
 - Produce corrosive materials and destroys arterial walls
- Inflammation causes plaques to burst
- Blood clot forms over the burst plaque
- C reactive protein
 - Signals an increased risk
 - Causes inflammation
 - High levels is heart attack
- High levels of CRP from bacterial infection
 - Not strongly affected by viral/fungal infection
- Body uses lipoprotein to transport cholesterol
 - Doesn't dissolve in water
 - LDL
 - Low density lipoprotein
 - Bad cholesterol
 - Deposit cholesterol at LDL receptors
 - Excess is stored
 - <3.4 normal
 - 3.4-4.1 borderline
 - >4.1 high
 - HDL
 - High density lipoprotein
 - Good cholesterol
 - Excess is collected and disposed in the liver
 - <1.0 not good
 - >1.56 good
 - LDL/HDL
 - <3 low risk
 - >5 high risk
 - Total blood cholesterol is important
 - Not enough is dangerous



- To much is dangerous
- <5.2 normal (mmol/l)
- 5.2-6.2 borderline
- >6.2 high
- Lipids
 - Contain long carbon chains
 - Saturated
 - Mono unsaturated fatty acid esters
 - Esters
 - solids
 - Unsaturated
 - Poly unsaturated fatty esters
 - Cis and trans
 - Liquids
 - Double bonding
 - Hydrogenation
 - Oils to fats
 - Get rid of double bonds
 - Best texture
 - Lose too many double bonds and it gets solid
- Trans fats
 - More than 100 years
 - Right mouth feel for processed foods
 - No nutrition
 - Alter LDL/HDL ratio
 - Body makes too much LDL
 - Not enough HDL being made
- Statins
 - High cholesterol drug
 - Interfere with mechanisms of saturated fat into cholesterol
 - Blocks cholesterol biosynthesis
 - 27 chemical reactions
 - inhibits one of the first reactions
- Lovostatin from *Aspergillus terreus*
 - First statin drug



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- Safe but poor selling
- Afraid to prescribe them
- Four S study of Simvastatin
 - Scandinavian simvastatin survival study
 - 35% reduction in cholesterol
 - 42% less likely to die from heart attack
- Lipitor
 - Bruce Roth
 - No better than lovastatin in animals
 - Roger Newton sang to the tune of Al Jolson's you made me love you
 - Clinical trials
 - 24 company employees
 - 38% drop in cholesterol at 10mg, better at 10mg at half the dose
 - significant advantages in curves trial
- Pfizer gambles with dose
 - Most statins at 20mg
 - Lipitor at 10mg
 - safe at 80mg
 - molecular weight matters more than dose
 - convinces FDA for fast track approval
 - Considered an orphan drug
 - Familial hypercholesterolemia
 - Preparing medications for rare diseases
 - So much cholesterol you can see it on the skin
 - Though Mona Lisa had it
 - Lipitor became the #1 drug in the world
 - Lowers heart attack risk
 - Crestor study 100% reduction in heart attacks
 - Statin
 - 83 heart attacks in 8901
 - Placebo group
 - 157 heart attacks in 8901
 - 100 percent reduction
 - But



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- Must give drug to 120 people to prevent 1 heart attack
- \$290 000
- 1.5 million heart attacks a year
 - 25% die immediately
 - 25% are unaware

- all religions use mind altering substances for different purposes
- **Incense acetate**
 - From frankincense
 - Hallucinogenic incense
- Drug are illegal because they are dangerous
 - Adverse effects on health
 - Employability
 - Destruction of relationships
 - Health costs
 - Economic impacts on companies and families
 - Fines up to 200 and up
 - Up to life in prison
 - Criminal record
 - Buyer beware
 - Don't know what it contains
 - Not pure substances
 - Can contain anything
 - Secondary crime
 - **75% of property crime is drug related**
 - violent crime
- Solvent abuse in elementary school
 - getting high off dry erase markers, paint thinner, liquid paper
 - nitrous oxide in whipped cream
- **Marijuana**
 - Easy to grow
 - **Buds are high in THC**
 - Easily vaporized
 - Resin on the plant surface is ingested
- **New Orleans**
 - **Casually smoke it as a recreational drug**
 - Over reaction to drug, from thought of drug use
 - **Marijuana tax act, only to buy and sell if you had a stamp but no stamps were issued**
- 1960s resurfaced drugs
- **THC**
 - **Anandamide agonist**



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- Neurotransmitter
- Receptor for THC for chemical reaction
- Euphoric effect
- Impairs memory
- Slows reaction time
- Can be manufactured synthetically
- Used for AIDS related anorexia MARINOL
- Sativex, for MS
- Anti nausea properties
- Questionable medical sense
- Mandatory minimums for trafficking
- 1.5 million users in Canada
- Fake pot in herbal incense
 - Soak plants
 - Grind them up
 - Analgesics
- Leaves spiked with synthetic cannabinoids
 - Synthetic forms of THC
- JWH-018 more potent than THC
- Cocaine
 - Stimulant
 - Cocoa leaves
 - Before was in coke
 - In patent medicines
 - Harrison Tax Act 1914
- Stephan chemical in New Jersey
 - Import cocoa leaves
 - Sold leaves to make flavors
 - Side batch was for cocaine
- Topical anesthetics designed from cocaine
 - Benzocaine
 - Dental anesthetics inspired by cocaine
 - Novocaine
 - Rapid metabolism
- Snorting cocaine hydrochloride



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- Contacts nose and into blood stream
- Addiction
 - Strong
 - No tolerance
 - No physical withdrawal
 - Most unsatisfying drug
 - Never satisfied and will always want more
- Freebased cocaine
 - Form cracks
 - Crack cocaine
 - Add baking soda to cocaine hydrochloride and it will turn back into crack cocaine
 - Crack required a lower dose
 - Usually smoked
 - Prevents dopamine reuptake
 - Side effects
 - Seizures
 - Psychiatric disturbances
 - Coke bugs
 - Stroke
 - Cardiac arrhythmia
 - Death
 - Addictiveness
- Amphetamines
 - Used in WWII
 - Abuse in military prison
 - Low doses stimulate flight or flight response
 - High doses induce euphoria
 - Benzedrine
 - Inhaler
 - 250mg
 - folded paper to distribute doses
 - amphetamine extracted using coca cola
 - dissolve the drug in water and it can be a greater dose
 - used to treat depression



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- prescribed to rich and famous
- Max Jacobson Dr. Feelgood
- Amphetamine psychosis
 - Led to decline use
 - Extreme aggression
 - Auditory and visual hallucinations
 - Similar to schizophrenia
 - Paranoid psychosis
 - Accumulate weapons
- Methamphetamines came back in the 1990s
- Used pseudofed to make Methamphetamine
- Smerfing provided raw material
- Pseudofed becomes restricted
- Methamphetamines are potent vasoconstrictors
 - Can cut off blood supply to face and teeth
 - Meth face
- Dependence is very strong
- Opiates
 - Poppy latex
 - Poisonous
 - Was consumed in ancient china
- Hypodermic syringe invented in 1856
- Morphine became common after civil war
- Heroin was sold as a non addictive cough suppressant
 - Stronger dependent response
- Harrison Narcotic Act 1914
- Heroin
 - Usually injected
 - Created linear bruises
 - Damage to artery or vein contracts blood vessels
 - Necrosis downstream of killing one vein at a time
 - Build up scarring
 - Codeine
 - Tylenol 3
 - Prescription for pain



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- Oxycodone
 - Thebaine to oxycodone
 - Opium contains 40% Thebaine as a byproduct
 - Thebaine has no medicinal value
 - Hillbilly heroin
 - Oxycotin is stolen from pharmacies
 - Opiates
 - Depress CNS
 - Analgesia
 - Drowsiness
 - Apath
 - Lethargy
 - Unconsciousness
 - Depress bodily functions
 - Cough reflex
 - Respiration
 - Peristalsis
 - Endocrine secretion
 - Overdose makes them stop breathing
- Strong physical addiction
- Tolerance dependence withdrawal
- Retail market of heroin is 12 billion
 - DEA estimates 75% of property crime is drug related
- Opiates are important pain killers
- Doctors are reluctant to use opiates on terminal patients
- Many hallucinogens mimic serotonin
 - usually central brain
- Magic mushrooms
 - Psilocybin
- Cane toads
 - Bufotenine
 - Milky poison secretion
- PCP
 - Angel dust
 - Trigger schizophrenia episode



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- Serotonin and dopamine
- Ergotamine
 - Ergot
 - Demonic depression
 - Muscle movement
 - Feelings of flying
 - Witchcraft
 - Can be converted into LSD lysergic acid
 - Albert Hoffman
 - Worked at sandos
 - Bicycle day
 - Used by CIA at McGill in 1950s mind control experiments
 - MK ultra project
 - Hallucinations have religious significance
- Timothy Leary at Harvard
 - Believed in hallucinations
 - Tune in turn on and drop out
- The end on 10 000 mikes
 - 10 000 micrograms
 - Jim Morison
 - Killing himself and raping his mother
- Atropine
 - Deadly night shade
 - Beauty aid
 - Dilates pupils
 - Large pupils are attractive
 - Ach antagonist
 - Ach transmits nerve signals in brain
 - Can paralyze organs
 - Used in surgery
- Hyoscine
 - Scopolamine
 - Henbane plant
 - Truth serum
 - Not effective



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- Atropine and Hyoscine used in witchcraft
 - Flying potion
 - Not water soluble
 - Best trans dermal absorption is through mucus membranes
 - Stick and masturbate with it
- Original narcotic laws were very specific
 - To be convicted they would need to have it on them
 - Designer drugs provided a way around the law
 - Existing drugs were a starting point
 - Original practitioners were chemists
- Fentanyl
 - Industrial strength pain killer
 - Methyلفentanyl was initially legal
 - 200g of methyلفentanyl was worth 1 billion
 - addicts often died from over dose
 - called china white
 - chemical warfare agent
 - Kolokol-1
 - Used in crowd control
 - Killed hostages
- Ecstasy MDMA
 - Gordon Alles also discovered amphetamines
 - SKF-5 used for psychotic depression because they didn't know how to market the drug
 - Tested by military
 - Ravers use MDMA
 - Illegal in 1988
 - Euphoria, empathy, inhibition, feel close to everyone, auditory hallucinations, sexuality, hyperthermia, loss of appetite, overheat, dehydration, depression, lack of judgment
 - Made in underground labs
 - Safrol -> mercury reaction
 - MDMA tabs were usually not pure
 - Additives were dangerous
 - Neurotoxic



- Ketamine
 - Vet anesthetic similar to PCP
- GHB
 - Date rape drug
- Methamphetamine
- Rohypnol
- Many didn't contain ecstasy tabs don't contain MDMA
- Khat
 - Cathinone
 - Stimulant
 - Consumed in Somalia and Africa
 - Spawns designer drugs
 - Dopamine release
 - High doses increase aggression
 - Synthetic versions tested as appetite suppressants
 - Methcathinone
 - Mephedrone
 - Highly addictive
 - Massive weight loss
 - Hallucinations
 - Psychosis
 - Extreme dehydration
 - Was legal until recently
 - Crystals are large and salt like
 - Bath salts
 - Began in 2002
 - Highdoses cause violent psychosis
 - Blamed for violent killings
 - Ronald poppo lost his face
 - Didn't know what was in him
- New versions of drugs are always produced constantly
- Bath salts banned in Canada
- DEA bans chemicals used in bath salts
- Demerol
 - Systemic painkiller



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- MJ's
- Euphoria
- MPPP is the legal toxic designer version of the real drug Demerol that is illegal
- Frozen addicts, destroyed a part of the brain
- Byproduct in synthesis HCL as acid make MPTP that will paralyze instead of MPPP by its self being toxic
- MPTP
 - Destroys brain tissue
 - Gave themselves Parkinson's disease
 - L-DOPA was given for limited movement
- Salt has iodine
 - Thyroid
- Some drugs improve cognitive function
 - Minimal and small effects
- Drugs for narcolepsy keep you awake
- Amphetamines improve concentration
 - Dexedrine
 - Adderall
 - Good for repetitive tasks
- Ephedra was widely used
 - Euphoric feeling in high doses
- Ritalin improves ADHD
- Feeling good doesn't mean feeling better
- The threshold of max for a certain task can decrease
- Small effects as stimulants
- Each person responds differently
- Cognitive functions have different drug sensitivities
 - Affects more than one ability
- All drugs have side effects
- Counterfeit drugs are 75 billion market
- Drugs are illegal because they affect health, personal life, society
- Illegal
 - Fines, jail time, criminal record, buyer beware
 -

- Herbal remedies migration 40% of the population
 - 20 billion business
 - mass produced
 - only a few rules
- Organic products became popular
- There were no regulations over the use of "natural" any thing can be stated at natural
- Modern drugs are standardized
 - Purified substances
 - Consistent dosing
- Omega-3 fish oil
 - Eicosapentaenoic acid
 - Docosahexaenoic acid
- Testing
 - Limited or nonexistent
 - Adverse event reporting isn't required
 - Efficacy is based on previous reports
 - Doctrine of signatures
 - Doctrine of humors
 - Anecdotal evidence
 - Quality of science is highly variable
 - No placebo
 - Small group of subjects
 - Easy way to get positive results
 - High attrition rates
 - Publication biases
 - Positive results, increased quality
 - Honor system for adverse event reporting
- Echinacea
 - Most popular herbal today
 - From flowers
 - Wards off colds
 - Sold for over 200 years
 - Snake oil
 - Arthritis doctrine of signatures
 - Native recipe



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- No effects on colds
- Cold-fX
 - Clinical studies were low quality
 - Ginseng root resembles a human body
 - Claims are non-specific
- Ginko
 - Ginko biloba
 - Ginkolides
 - Anticoagulants
 - Increase blood circulation in the brain
 - Circulation doesn't translate to improved brain function
- Saw palmento
 - Benign prostate hyperplasia
- Remedies
 - Labels are carefully written
 - Regulated as foods
 - No efficacy testing is required
- Garlic was used to improve strength for Egyptians
 - Adolphus Hohensee in garlic cleansing
- People like visible effects
- Allicin
 - Thought to affect cholesterol
 - Garlic uses allicin for protection
 - Uses allinase the enzyme
 - Unstable
 - After human digestive enzymes, turns into allyl mercaptan and allyl methyl sulfide that enters the blood and exits the lungs
 - Garlic doesn't reduce cholesterol
- St.Johns Wort
 - Popular supplement
 - Against depression
 - Ineffective
 - Induces liver enzymes to get rid of more pharmaceutical medications
 - Affects 50% of all medications



- Cytochrome P450 3A4 Enzyme

- Supplements

- Do not contain active ingredients
- Purity of natural supplements is questionable
 - Pesticide residue
 - Heavy metals
 - Undeclared pharmaceuticals
 - Added to produce effects
 - Cheap

- Many products contain the wrong plant

- Incorrect product label
- Substitution
- Contaminants
- Fillers
- No sequence
- Could be a dangerous plant
- Natural materials can interact with pharmaceuticals
 - Most patients don't inform their doctor
 - Because they don't think supplements are medications

- Liver

- Protects against foreign substances
- Grapefruit inhibits liver function
 - Can be a drug overdose

- Kava Kava

- Antidepressant
- South Pacific
- Village virgins that chew it and bottle it
- Kavalactones can damage the liver
- Still available under the counter

- Weight loss medications

- Act as appetite suppressants
- Flight or fight response in the sympathetic division
- Repressive effects on parasympathetic division

- Ephedra

- Amphetamine



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- Heart attacks
- Strokes
- Seizures
- Deaths
- Amphetamine psychosis
- Banned in the US in 2003 still available under the counter
- Bitter orange
 - Amphetamine like compounds
- Glucosamine doesn't improve joint function
- Placebo
 - 35% effective to have a therapeutic effect
 - bitter pills work better than sweet
 - color is important
 - capsules work better than tablets
 - IV is better than pills
 - Only work if patient is aware of treatment
 - Drugs work better than placebos
 - Side effects are stronger with drugs
 - Some drugs can be effective enough that placebos aren't needed
 - Conditions that consistently report placebo effects
 - Pain
 - Depression
 - We should get what we pay for
 - Plausibility is important
 - Supplement should contain substance with biological activity
 - Consumer safety is important
 - Cyanide was used to kill cancer cells
- Science VS magic
 - Science
 - Collects facts
 - Draw conclusions based on facts
 - Test conclusions in several ways
 - Magic superstition
 - Draw the conclusions that we want



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- Find facts that fit conclusions
- Life expectancy improves because of science
 - 44 to 82
- Pauling and mega dose vitamin C
 - 90 mg
 - 18 000 mg
 - clinical studies show no benefit
 - FDA banned vitamin regulation in 1975
 - FDA attempted to regulate supplement industry 1990
 - Dietary supplement health and education act 1994
 - Listed retailers get customers to congress leaders and senators to stop messing with supplements and prevent FDA from testing at all
- Government approval gives false impressions
 - Limited or no efficacy testing
 - Standards are flexible
 - Limited or no safety testing
 - Past experience
 - No enforcement
 - No inspections
- Top 10 health frauds compiled by FDA
 - 1) Arthritis products
 - 2) Cancer treatments
 - 3) AIDS cures
 - 4) Weight Loss
 - 5) Sexual Aids
 - 6) Baldness cures and Bust enlargers
 - 7) Chelation therapy
 - 8) False nutritional schemes
 - 9) Muscle stimulators
 - 10) Candidiasis
- Natural pharmaceuticals
 - Taxol
 - Penicillin
 - Erythromycin



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- Digoxin
- Bleomycin
- Colchicine
- Ergotamine
- Morphine
- Capsaicin
- Natural or artificial the source is irrelevant
- Samuel Hahnemann
 - Opposed bloodletting
 - Applied doctrine of signatures
 - Thought remedies dot stronger when diluted
 - Developed serial dilutions
 - Succussions was thought to be important
 - Only shake and not stir
 - Final treatment contains only water
 - Taste is a biological response
 -
- Homeopathy is the ultimate placebo
 - Emphasis upon relationship
- Appearance of the patient is important
-

- We are chemical machines
- Formation and maintenance of relationships
 - Attraction
 - Romantic love
 - Attachment
 - Love
 - Pleasure
 - Sex
 - Addiction
- Pheromones
 - Substance produced by an organism that elicits and unlearned response in another member of the same species
 - Messenger molecules
 - Used for pest control
 - Relatively non-toxic fragrance
 - Species specific
 - Tiny amounts required
 - Integrated pest management works better
 -
 - Female silkworm secretes bombykol
 - Periplanone is the most potent pheromone
 - 75000 virgin cockroaches to obtain 20 mew grams
 - detection is less than a millionth of a mew gram
 - was used by the CIA for tracking
 - Chiloglottis trapeziformis
 - Uses wasp pheromones
 - Orchid uses pheromones that resemble wasps
 - Ophrys exaltata
 - Bee pheromones
 - Mixture of chemicals
 - Z-7-hexacosene
 - Z-7-pentacosene
 - Z-7-tricosene
 - Overlapping pheromones
 - Autographa californica
 - Elephant and butterfly



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- Female dogs in heat secrete methylparaben
 - Common preservative
- Truffles and boars produce androstenone
 - Used in boar spray
 - Present in human sweat
 - Andron-first perfume with androstenone
 - Found in many perfumes
 - Axe
- Skatole
 - Produced by intestinal bacteria
 - Called civetole in perfumes
 - Small amounts is good and will make perfumes last longer
 - Civet oil from civet cat that is endangered
 - Skatole is naturally present in flowers
 - An artificial flavor
 - Ice cream
 - Icing
 - Cigarettes
 - In large amounts smells like shit
- Musk
 - Synthetic Musk ketone replaces Muscone from the deer
 - Axe contains Musk ketone
- Human pheromones don't exist because we are missing a vomeronasal organ
- Human attraction is mostly visual
- Phenethylamine
 - Released during romantic love increases dopamine levels
 - Similar to cocaine and tobacco and amphetamine responses
 - Found in chocolate but can actually enter the brain
 - Increased dopamine during early stages of love causes serotonin to decrease
- Serotonin controls mood
 - High levels causes anxiety
 - Normal levels are balanced
 - Low levels are depression, and compulsive behavior



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- Long term attachment and bonding
 - Vasipressin in males
 - Oxytocin in females
 - Released during labor
 - Increase mother and child relationship
 - Released during lactation
 - Both released during sex
- Prairie voles produce oxytocin and are monogamous
 - Oxytocin antagonist leads to promiscuity
 - Block the function of oxytocin
- Mountain voles do not produce lots of oxytocin
 - Injecting oxytocin doesn't produce monogamy in mountain voles but mountain voles lack the receptors
- Molecules dissociate at low concentration
- Molecules associate at high concentrations
- Mountain voles didn't have enough receptors
- Recombinant mountain voles are social but not monogamous
- Aphrodisiacs
 - From doctrine of signatures
 - Materials that increase sexual ability
 - Rhino horn
 - Phallic symbol
 - Aggressive animals have macho signature
 - Stinkhorn
 - Mushroom
 - Oysters resemble female genitalia
 - Horny goat weed, just the name
 - Chocolate can enter the brain
 - Testosterone increases sex drive in men and women
 - Cocaine may promote hyper sexuality
 - Ecstasy reduces inhibitions
 - Spanish fly
 - Beetle
 - Chemical is a strong irritant is bull breeding
 - Empties bladder and ends with an erection



- Catharidin, vesicant (blisters)
- Internet versions are capsaicin
- Alcohol is the primary aphrodisiac
 - Too much impairs performance
- Yohimbine from yohimbe is not an aphrodisiac but is used as one
 - Prescription bark for erectile dysfunction
 - Non prescription is dangers and can cause priapism (long lasting erection that can cause necrosis)
 - Drugs for erectile dysfunction are not aphrodisiac
 - Corrects physical problem not psychological and doesn't increase desire
- Erectile dysfunction was called impotence and considered psychological
- Vasodilation produces an erection
- Nerve impulses block vasodilation, stimulate sympathetic and suppress parasympathetic
- Giles Brindley 1982
 - American Urological association
 - Block nerve signal to get an erection
 - Proved no penile prosthesis (semi-rigid rode)
 - Or inflatable changers
 - Or surgical implant
- First drug
 - Alprostadil
 - Effective but poor insales
 - Had to be administered via syringe
- Viagra was a drug in search of disease
 - Safe
 - Rapidly entered body
 - Inhibited known enzyme
 - 1) failed an blood pressure drug
 - 2) failed for angina (heart blood vessel contraction)
 - during clinical trials some men got erection
 - before investing money the company needed to verify the results
 - what is the biochemical basis
 - is there a market



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- how to confirm the effect
- drugs that produce NO produce erections
 - nitroglycerine
- NO
 - Molecular messenger
 - Signal molecule to start erection
 - PDE is the braking molecule that converts it back to a storage molecule
 - Healthy men get enough NO to get erections
- Viagra
 - Blocks messenger recycling signal molecule PDE
 - Pilot study
 - 83% improvement with one dose
 - market analysis only 2% of men reported impotence
 - Diaries were used to keep a record of the clinical trial
 - Nobody returned the unused pills and there was a zero drop out rate
 - Patients were begging to be kept on the drug
 - Compassionate use: loop hole
 - Considered a serious condition
 - Bob Dole
 - Republican senator conservative (religious belt)
 - War hero
 - Lost right arm in WWII
 - Presidential candidate in 1996
 - Spokesperson for Viagra
 -

- - Radithor = a patent drink that contained radioactive water, used to make you smarter

Cold and Flu

- - Aspirin = acetylsalicylic acid (ASA)
- - Bufferin = contains MgSO₄, an antacid that helps to reduce stomach pains from aspirin
- - Ibuprofen = found in Advil and Motrin
- - Acetaminophen = found in Tylenol
- - Anacin = contains ASA + caffeine
- - APC tablet = contains ASA + phenacetin (older version of acetaminophen) + caffeine
- - Tylenol migraine = contains acetaminophen + caffeine + ASA (ASA is not included in Canada)
- - Tylenol PM = contains acetaminophen + diphenhydramine (1st generation anti-histamine for drowsiness)
- - Naproxen = found in Aleve

Headache

- - Cafergot = an older form of isolated ergotamine still available today to relieve migraine
- - Sumatriptan = from the class of Triptans, which can stop migraines before they occur. Acts as an agonist to mimic serotonin

Cold and Flu

- - Amphetamine/Benzedrine = decongestant
- - Phenylpropanolamine (PPA) = decongestant that for a while was being used for appetite suppression – now off the market due to stroke
- - Pseudoephedrine = found in Sudafed/Sinutab/Benlylin, a decongestant that can be used to make methamphetamine
- - Phenylephrine = a decongestant found in Sudafed PE, does not work



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- - Chlorpheniramine = 1st generation anti-histamine, makes you sleepy
- - dexamethorphan = anti-tussive for coughing
- - guanifesin = expectorant expel sputum

Cancer

- - Mustine = inspired by mustard gas, a chemotherapeutic that causes DNA damage, low red blood cell count (leukemia)
- - Cisplatin = chemotherapeutic which enters the cell and jams into DNA, platinum electrodes, peyrone salts can become a DNA altering agent
- - Taxol = chemotherapeutic derived from Yew needles and is now through cultures
- - Benzopyrenes/PAH = converted into a substance by the kidney that can react with DNA and cause cancer (carcinogenic). Found in anything that's burnt (tobacco, steak)

Sport Drugs

- - Stanozolol = steroid used by Ben Johnson in the Olympics, created by John Manson (all Canadian!)
- - strychnine = acts as a stimulant in low doses, used in 1904 St Louis Marathon by Thomas Hicks
- - Pervitin = methamphetamine tablets given to German soldiers
- - Dianabol = steroid created by Dr Ziegler of the York Barbell Club, one of the first synthetic steroids used
- - Diosgenin = derived from Mexican yams, used to make steroids
- - tetrahydrogestrinone = "The Clear", undetectable steroid until 2002

Antibiotics

- - Salvarson 606 = 1st antibiotic developed by Ehrlich, from Trypan Red (trypanosomes) arsenic



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- - Prontosil = created by Domagk, antibiotic that is converted to sulfanilamide, which blocks folic acid production in bacteria to produce coenzyme F
- - cephalosporin = antibiotic discovered in Italian sewer. Blocks cell wall synthesis
- - streptomycin = antibiotic that was discovered in chicken throats. Blocks protein synthesis in bacteria
- - Tetracycline = antibiotic that also blocks protein synthesis in bacteria.

Tobacco

- Chantix = partial nicotine agonist (patch) from plant which contains cytisine (similar to morphine). Morphine is used to make varenline

Vaccine

- - Thiomersal = preservative with mercury for vaccines. Shown not to cause autism
- - Squalene = lipid adjuvant which was thought to have caused Gulf War Syndrome, wasn't in vaccines. Used as a something to avoid booster.

Stomach

- - Alka Seltzer = sodium bicarbonate (antacid) + ASA + citric acid (makes fizz)
- - $Mg(OH)_2$ = antacid, in milk of magnesia. Problem is that it is a laxative
- - $Al(OH)_3$ = antacid, found in Gaviscon. Problem is that it causes constipation
- - Maalox = magnesium hydroxide + aluminum hydroxide (therefore both effects cancel each other out). Also contain simethicone (from silica gel) to prevent gas
- - Pepto Bismol = poisons bacteria in the stomach, antibacterial
- - Tagamet = stomach anti-histamine to reduce stomach acid, also causes gynecomastia (man boobs) as a side effect, blockbuster drug



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- - Omeprazole = in Prilosec, it is a proton pump inhibitor, enantiomer
- - Esomeprazole = found in Nexium, also a proton pump inhibitor (the S-form of the previous chemical) slower metabolism, chiral

Allergy

- - diphenhydramine = 1st generation anti-histamine found in Benadryl. Makes you drowsy
- - Loratadine = 2nd generation anti-histamine, used against allergies, found in Claritin. Converted in the body to Desloratidine (which is found in Alerius). No drowsiness
- - Fexofenadine = 3rd generation anti-histamine, used against allergies, found in Allegra. The metabolite of terfenadine, which was shown to react with ketoconazole. No drowsiness
- - Cetirizine = 3rd generation anti-histamine, used against allergies, found in Reactine
- - Rhinocort spray = steroid decongestant for allergy
- - Pulmocort spray = same as above
- - Salbutamol = inhaler that allows for bronchodilator (asthma), selective adrenaline agonist
- - Singulair = blocks leukotriene synthesis involved in asthma, leukotriene antagonist

Heart

- - Captopril = developed from snake venom, it is used to decrease blood pressure by inhibiting ACE (which produces angiotensin II). Produces a copper taste, therefore they created enalapril which reduces side effects and is more potent
- - Digitalis = from foxglove plant, a drug that increases heart function. Used for treatment of congestive heart failure
- - Nitroglycerin = vasodilator, used to treat angina



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- - Statins = drugs that are able to decrease cholesterol production by inhibiting the enzyme in the liver that produces them (HMG CoA reductase). Ex: Lovostatin (4 "S" study)
- - Lipitor = Statin from Pfizer

Street

- - THC = chemical found in marijuana. Buds are used for smoking, resin is used as hashish. Is an anandamide antagonist. Used for treatment of AIDS-linked anorexia and in Satovex for multiple sclerosis
- - Novocaine/benzocaine = 1st is dental anaesthetic, the other is a topical anaesthetic. Inspired by cocaine
- - Psilocybin = hallucinogen in magic mushrooms
- - Bufotenine = hallucinogen in cane toads
- - PCP = hallucinogen found in Angel Dust
- - Atropine = from deadly nightshade, called "belladonna" to dilate pupils. Used in witchcraft. ACh antagonist
- - Scopolamine/Hyoscine = similar to atropine. Used in truth serums
- - oxycodone = Hillbilly Heroin
- - Urushiol = chemical found in poison ivy
- - Methylfentanyl = derivative of fentanyl, which is an industrial strength painkiller. Used for chemical warfare and is sold on the black market as China White (similar to heroin), Kokolol-1
- - MPPP = derivative of Demerol (systemic painkiller) though toxic – creates "frozen addicts", used for Parkinson's research. (MPTP)

Nutraceuticals

- - Ginko biloba = contains ginkgolides, which increase circulation to the brain (though does not improve brain function). However, it reduces blood clotting therefore dangerous when combined with anticoagulants
- - Kevalactones = found in Kava Kava, which can cause liver damage
- -Allicin=garlic, allinase, cholesterol, ineffective, enters blood and out of lungs



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Aphrodisiacs

- - bombykol = pheromone produced by female silkworms. The males have specialized antennae for this
- - periplanone = pheromone used by cockroaches
- - androstenone = produced by truffles, pigs, and found in human sweat. Also used in Axe and Andron
- - methyl paraben = pheromone produced by female dogs, and is used as a preservative
- - Skatole = produced by intestinal and oral bacteria (high concentration), but also found in flavourings and flowers (low concentration). Called civetole in perfume, to mirror Civet Oil (from the glands of Civet Cat)
- - Muscone = musk from the musk deer. No longer in use and now musk ketone is used (also found in Axe)
- - Phenylethylamine = released during romantic love, which increases dopamine levels and decreases serotonin
- - Cantharidin = used for bull breeding (irritant), vesicant blistering
- - vasopressin(males)/oxytocin(females) = hormones in humans that are released during sex and other activities which allow for attachment
- Autograph californica=butterfly and elephant
- Alprostadil-IV, impotence
- Viagra-1)failed as BP drug, 2)failed as angina drug, antagonist of PDE to stop the conversion and cease the decrease in NO that causes erections

- We are more scared of unfamiliar risks
- Dread
 - Uncontrollable risks
- Feel about risk
 - How well do we know the risk
 - Being familiar, we are less worried
 - Uncertainty creates risk
- Health risk
 - Probability of something happening to health
 - Hazard, Dose Exposure
- Worth ~ stuff happens ~ worth after
- Intervention always happens to avoid the loss of worth
- Feeling being at risk
 - Uncertainty
 - Risk is not equal to the value sometimes
 - Brain or feelings
- Hazard vs risk
 - Hazard: possibility of something causing harm
 - Risk: probability of harm
 - Hazard ~ Action/Exposure ~ Risk
- Risk
 - Measure loss of worth
 - A specified loss occurring probability