COLD

Cold are the most common infection

- Outnumber all others by 25 to 1

More than 200 viruses cause colds

- Influenza virus it's very hard to know whether you have a cold or flu

Virus destroys tissue, immune system makes symptoms

- The immune system responses by enacting symptoms

No cure for the common cold

- Average cold lasts a week
- Some cold medications relieve symptoms
- Many remedies do nothing
    - Doing something makes you feel better
- No medication will prevent colds
- No matter what you do you can't cure a cold or prevent a cold
- Can have medications to treat the symptoms but it's not curing the underlying sickness in the body

Common Cold research Unit Salisbury England

Free vacation for research

- In exchange to allow them to test them

Test subjects in extreme comfort

The vacation was not exactly free

Sneezing does not spread colds well

Sneeze collector

Artificial sneeze

Being cold does not cause colds

Wet hair does not cause colds

Direct exposure to virus does not always cause cold

Cold virus in nasal secretions

Nasal secretions spread easily *(Confirmed by the **Mythbusters**)*

Cold viruses are transferred by touching

Colds are more common in crowds

School season is cold season

Tristan ca Cunha in the middle of nowhere

- Isolated island

Incidence of colds and contact with outside

- Black mark represents a person with a cold and the gaps are represent no colds

Cold viruses spread through crowds
Washing hands may reduce colds
Hand sanitizer may reduce colds
Don't overdo it avoid skin damage

- You can wipe off the protect oil that protects the skin from drying

Incidence of colds decrease with age

- You get more sick when you're younger and once you come in contact with a certain bacteria, you will never come in contact it with it again

Young children more social
As you age you acquire immunity by being infected

- Exposure to virus causes illness
    - Immune response is too slow and weak to prevent
- Body makes large amounts of antibodies only during infection
- After each infection you build up "memory" cells
- Later exposure to the same virus does not make you sick
    - Rapid and strong immune response

4.1 Billion on colds each year (North America)
Read the back not the front
Cold remedy ingredients

- Pain reliever or fever reducer
- Decongestant
- Antihistamine
- Antitussive
- Expectorant

Acetaminophen for pain relief and fever
Ibuprofen becoming a common replacement
No such thing as a sinus cold
Menthol for sore throat

- You get the cooling effect (sensation)
- Menthol was designed to give the sensation of cool to counteract the heat

Menthol is a weak topical analgesic

- Menthol 22 mg
- Has a questionable effect

Menthol cough drops for sore throat

- Menthol 2.5 mg
- Has less menthol
- Gives a short term relief

Cepacol contains topical anesthetic

- Benzocaine 15 mg
- Don't want to use it every time

Decongestants dry a runny nose

- Pseudoephedrine
- Phenylephrine
- Most affect (pseudoephedrine)
- Avoid the phenylephrine doesn't have a good effect

Snot is mostly water with a little mucin

- 95% is water

Water is supplied by the blood

Decongestants are vasoconstrictors

Amphetamine for cold symptoms

- One of the best for decognitions

Problems with phenylpropanolamine (PPA)

- Side effect is appetite suppression
- Amphetamine is used as a recreational drugs so we limit the use
- So we create different products similar to amphetamine
- Side effects don't have to be bad and it's more like an unintended results
- Could be used as a diet

Diet pills used phenylpropanolamine (PPA)

- Side effect was decongestion

Overuse of diet pills cause hallucinations

- Amphetamine psychosis
- Tends to take more pills and overdose

Overuse of diet pills cause strokes

- Some causes strokes because it raised their blood pressure

Sudafed contains Pseudoephedrine

- Can't get this product in canada
- Because they were able to convert cold medicine to crystal meth

Pseudoephedrine to make methamphetamine

Drug dealer used to buy direct

- Up to 50 % of pseudoephedrine used to make methamphetamine
- DEA restrict this by having certain licenses

Dealers turned to "smerfing"

Pseudoephedrine only by prescription

- Still available OTC but is always bundled with pain reliever
- They add pain relief in it to make it harder for drug dealer from converting it to meth

Sudafed PE contains Phenylephrine

Phenylephrine is not effective

Pseudoephedrine is still widely available

Generic versions are available for all cold meds

- Pseudoephedrine is the active ingredient

Nasal sprays contain decongestants

- Both work in the same way

Antihistamines for sneezing, runny nose, watery eyes

- Useful for a cough

Antihistamine side effect is drowsiness

Antihistamines reduce nausea

- Dimenhydrinate
- This is a combination of
- Diphenhydramine (antihistamine) 8-chlorotheophylline (stimulant)
- this stimulants counteract the sleepiness side effect

Chlorpheniramine is most common antihistamine for colds

- Side effect is drowsiness
- Makes it easier to sleep

Diphenhydramine is most common antihistamine for allergies

- Side effect is drowsiness
- Can use this as anti nausea

Dayquil does not contain antihistamines

Dry cough and productive cough

- Intent to target to types of coughs
- Two types are dry or productive cough
- PC has mucus

Cough syrup is a marketing trick

The best cough medicine money can buy

- Heroin

Dextromethorphan used today

- Suppresses the coughing reflex

Dextromethorphan and heroin

- very similar

Expectorant for productive cough

Thick mucus is difficult to remove

- If the mucus is relatively thick it’s hard to dislodge it

Watery mucus is easily coughed up
Guaifenesin makes mucus watery
Drink liquids with expectorants
Guaifenesin proven to work
Drink liquids with expectorants
Beware multi-symptom medication

- Are a bit of a rip off
- We want all the symptoms to go away
- Designed to fight against each other
- Decognation (included in the night version) keeps you up

No cold meds for children under 6

- Giving a child medicines that worlds against each other

Some take vitamin C to prevent colds
Vitamin C will not prevent or cure a cold

- Doesn't do anything

#1 seller in Canada
Cold-fX ingredients
Ginseng is used for everything
Ginseng root resembles a human body

- resembles a human body then it's assume it will help the human body

Cold-fX claims highly questionable
Clinical studies are low quality and do not show benefit

- Didn't have a double blind procedure
- Excluded certain people after the results were taken
- Still found no good benefits

Buyer beware

- before address nausea but rebranded as a way to treat colds

Very weak antiviral effect (no animal data)

- Killed 80% of viruses and 300 ug/ml was the concentration

What's in the box?

- 200 mg willow bark (15% salicin)
    - 30 mg salicin
- 20 mg ginger (25% gingerols)
    - 5 mg gingerols
- Minimum effective dose of salicin is more than 300 mg
- In a perfect world, minimum dose is 1500 mg
    - Based on 300 μg/mL and assuming 100% of the gingerols reach the bloodstream
    - This dose gives 80 % viral reduction in the lab
- 300 mg (for a small person)

- It's about 10x too small
- Almost 70x too low to have the diesire effects

15 % of colds due to flu virus

Influenza causes seasonal colds

- Normally infects 5 to 15 % of population
- New virus formed every year
- Most forms not dangerous
    - Very young and very old are at risk
- You general can't tell the difference between cold and flus

Occasional severe influenza pandemics

- Very virulent strain occasionally arises
    - 1918 ~20,000,000 deaths
    - 1957 ~1,000,000 deaths
    - 1968 ~700,000 deaths

Virus contains an outer envelope

- Hemagglutinin (viral entry into cell)
- Neuraminidase (viral exit from cell)

Flu virus classified using envelope proteins

- Hemagglutinin (H)
    - 16 types
    - Human flu H1 through H5
- Neuraminidase (N)
    - 9 types
    - Human flu N1 or N2

Disease and virus type

Antibody response	virus
H1N1	Spanish flu (1918)
H2N2	Asian flu (1957)
H3N2	Hong Kong (1968)
H1N2, H3N2, H1N1	"normal" flu (seasonal)
H5N1	Avian flu (2007)
H1N1	Swine flu (2009)

Name brands vs generic

- They use the exact same ingredients

Name brands vs Name brand

They all use same ingredients and same doses

- Pain and fever
    - Acetaminophen 500 mg
    - Ibuprofen 200 mg
- Decongestant
    - Pseudoephedrine 30 mg
    - Phenylephrine 10 mg
- Antihistamine
    - Chlorpheniramine 2 mg
- Antitussive
    - Dextromethorphan 15 mg
- Expectorant
    - Guaifenesin 200 mg

Price per 100 tablets

Medications for colds and flu

- You will get colds
- Nothing will cure it
- Primarily spread on surfaces
- Some medications may reduce symptoms
    - You cannot treat all symptoms
    - Choose which symptoms you want to treat
- **Read the back not the front**
    - Choose the right medication
- **Avoid multi-symptom products**
- **Compare before you buy**
- Touching your face is not a good thing

CANCER

Cancer is uncontrolled growth

Hyper-proliferative lesion-benign

Benign lesions can be fatal in developing countries

Hyper-proliferative lesion-malignant

- Eats you from the inside and out

Cancer is a disease of the Aged

- Over 75% of all cases occur after age 55
- Causes 570,000 deaths per year in North America (1500 per day)
- More common in males than females

Cancer death rate by age
Cancer in children is extremely rare
Cancer treatments are unpleasant
Change in the US death rates* by cause, 1950 & 2001
Cancer death rates*, US

- Gotta get it young and detect it early
- When you're younger you can survive the treatment and when you know about it earlier than the treatment won't be as heavy

US Cancer death rates*, men
US Cancer death rates*, women
Normal cells become cancerous

- Your cells can become cancerous cells

"Make-your-own" parasite

- One of your cells become cancerous and begin to divide uncontrollable

Normal cell growth is closely regulated

- Cells divide only "on command"
- Maximum of 50 cell divisions
- Cells must be touching similar cells (tissue)
- We have a tight control over cell division
- Each cell has a lifespan
- Some cells divides more than others
- After 50 cell division they become useless and die
- They must be touching similar cells

Cancer cell growth is uncontrolled

- Cells divide continuously
- More than 50 cell division (immortal)
- Cells are mobile (metastasis)

Many cancer cells are immortal
HeLa cells from Henrietta Lacks 1951

- She died but her doctor collected the cancerous cells
- The cancerous cells will live longer than you do

Cancer requires 20 years to develop

- Requires 8 to 10 mutations in same cell
- Every tissue can spawn
    - More than 100 forms
    - Each tumor is unique
- Basic processes are similar
    - Loss of control over cell division
-

- It's a family disease

Cancer mutations involve loss of function

- Proteins STOP working properly
    - Random mutations destroy function
- Cannot repair the damage with today's technology
    - Genetic repair expensive, difficult and unreliable
- Only way to treat it is to kill the cancer
- Get cancer through random mutations

Biological regulation is complex

- Gives an idea on how communications happens

Cell division is regulated in 2 ways

- Stimulation (accelerator)
- Repression (brakes)

"Ogg" switch for cell division is broken

- Cell division gets switched on
- Cannot switch off
- "gas pedal" stuck to the floor

Ras is the cell's off switch

- Non-functional in 30 % of tumors
- Gets "stuck" in the ON position and cannot switch OFF

"Brakes" for cell division are broken

- "Brake pedal" does not work

p53 is an important braking protein

- Non functional in more than 50 % of tumors
- Represents significant weakness where if it loses function, can have cancer in different areas

Apoptosis–programmed cell death

Programmed cell death in embryo development

Programmed cell death in wound healing

- Before you can repair you need to kill the damages cells to allow healing to occur

Programmed cell death protects the body from viruses and cancer

- Cells receives instructions to die to protect the body
- Does the same thing for viruses (kills cells that carry the virus)
- Both happen in control way

p53 is an important suicide protein

- Non functional in more than 50% of tumors
- You're in big terrible because you're stuck on the break and can't kill themselves

Normal cells count cell divisions

- There's a counting device found on the tips of the chromosomes

Chromosomes tips are like shoe laces

- Each time it divides it chops off the tip of the chromosome and eventually after 50x the chromosome with unwind and die

Chromosomes become "frayed" with age

Cancer cells are immortal

Tumor formation requires 8 to 10 mutations

- **<u>In the same cell</u>**
- Mutations happen continuously
- Damaged cells are eliminated from the body
- Several mutations within the same cell are rare
- Accumulation of enough mutations for cancer requires more than 20 years on average

Gene is a set of instructions to make protein

- Genes are just a list on how to make individual proteins
- Instead of 26 letters only 4

Gene uses 3 letter words called codons

- Creates words called **codons**

Each codon specifies an amino acid in a protein

Sequence of amino acids determines protein structure

- The gene has no info it's just a list
- 3-d shape determines the function

Sequence of amino acids determines protein structure

- If you change one letter it changes the corresponding protein word
- You have change the shape it doesn't function like it's suppose to
- It's a defect or no longer functions

Mutation is a "typo" in the gene

Genetic basis for cancer

- Proto-oncogenes
    - Genes involved in control of cell division
- Mutations change proto-oncogenes into oncogenes
    - Form found in cancer
- Determines whether cell divides and when it divides

Genetic susceptibility

- Some individuals are more susceptible to cancer
    - Have pre-existing genetic changes in proto-oncogenes
    - Proto-oncogenes are easier to damage
- Some individuals are more susceptible to some cancer types than other

Most cancer death is caused by controllable factors

- **Tobacco**
- **Diet and Obesity Viruses**

    - Everything else (in order of prevalence)
    - **alcohol**
    - **lack of exercise**
    - UV radiation
    - environmental exposure (2 - 4 %) genetics
    - medical procedures
    - (X-rays and chemotherapy)
- cancer is a pretty avoidable disease
- bold is in our control and black is out of our control
- tobacco is 60%
- controllable factors 70%

Tobacco smoke contains over 4800 chemicals

- 400 toxic (harmful at low doses)
    - 40 carcinogenic

Nicotine is the addictive substance

Carcinogens in tobacco-Polonium 210

***α* emitters are normally safe**

Polonium anti static brushes

- Used in labs when you weighing materials

Radioactive spark plugs

Polonium spinthariscope in KIX cereal

Cereal is just not cool anymore

Polonium 210 as a poison

- Alexander Litvinenko

Heat from burning vaporizes polonium

Tobacco smoke combustion products

Benzopyrene carcinogenicity

- Gets process in the liver

Tobacco use in the US

Tobacco companies recruit women

Mommy, it's good for you

US Cigarette smoking prevalence*

Strong correlation of cancer with diet and obesity

- 1/3 is due to smoking
- 1/3 is due to dieting

Cooking for safety and flavor

- Meat is tend to be associate to cancer
- We cook food for flavour and safety reasons
- Meat can spoil quickly and the bacteria can negatively affect us

- Anytime you cook you increase your chances

Meat spoils quickly and must be cooked

Cooking generates flavor and some nasty materials

- Don't overcook the food

Food preparation creates carcinogens

Beneficial foods protect us

- Fruits and vegetables

Fruits and vegetables protect us

Fiber promotes the passage of waste

- Fruits and vegetables contain fibers
- Promotes passage of waste
- Removes some of the carigones so they aren't absorbed in the blood

Consumption of five or more vegetable and fruit servings for cancer prevention

Obesity* (%), by gender, adults aged 20 to 74

Obesity increases your risk for EVERYTHING

Changes in eating habits

- Increase pre-prepare foods
- Add MSG, fat and sugar to increase flavouring (population eats more fats/sugar after the 1980s)

Changes in portion size

- it's turns bigs because of the psychology factor
- The bigger the better
- Advertise based on the size not a health wise

Viruses responsible for about 15 % of cancer death

- Contain oncogenes

High risk viruses target p53

- Contains materials that deal with p53

Gardasil for HPV induced cervical cancer

- Lead to a vaccine for cervical cancer (sexual transmitted diease that can lead to gential warts)

Excess alcohol increases your risk

Alcohol as a carcinogen

Leisure-time physical activity

- Internal organs are able to function better when you exercise
- Reduces risk

Exposure to UV light induces skin cancer

- In canada skin cancer is the most common cancer and it's rare for someone to die from cancer
- Since it's outside the skin it's easier to treat

Environmental exposure–man made

- Most people are worried about
- 2-4% is what they're responsible of

Environmental exposure – natural sources

- Most potent are the naturally derived one

Strongest carcinogens occur naturally

- happens from a fungus
- not a big deal bc it's in small amounts

Phorbol is used to induce cancer

- rubbing or brushing this plant can cause skin cancer & it can cause an immediate reaction

Medical procedures X-rays and chemo

5 Year Survival Rates

1974-1976 50 %

1983-1985 52 %

1992-1999 60 %

Cancer very difficult to target selectively

- Abnormal human proteins (junk protein)
    - Non-functional enzymes
    - Non-functional protein
- Poor drug targets
    - Drugs can block protein function
    - Cannot restore protein function

Cancer cells are human cells

- Normal cells have 23,000 genes
- Only 8 or 10 are changed in a cancer cell
    - Changes very small (typo)
    - Drug has to "know" which cell to target
- Major difference is cell division
    - Cancer drugs are strong poisons
    - Cancer drugs target cell division
    - Fast growing cells killed first
- We focus on the differents on cell division
- Chemo kills fast growing cells (hair loss and nausea is why it happens)

Strategy for cancer chemotherapy

- Kill the cancer faster than you kill the patient
- Side effects are guaranteed – 100 %
- Side effects are severe
    - Death
    - Cancer

    - Extreme nausea, vomiting
    - Hair loss, immune suppression, sterility
- The younger you are the more likely you'll survive

Nitrogen mustards in World War I

- The first ever cancer drug was developed from a weapon of war

Nitrogen mustards destroy tissue

Nitrogen mustards in World War II

- All armies had chemical weapons available

Air raid on Bari, Italy

- The ship released and the material was on the surface of the water
- Where anyone in the water would be affected

Survivor had fewer white blood cells

- Connections was made between leukemia and white blood cells loss from the drug

Mustine was the first cancer drug

Fast growing cells are more susceptible

- Not selectively killing the tumor but all fast growing cells

Cancer drugs cause death and cancer

- Potent drug and very dangerous

Rapid cell growth provides selectivity

Serendipitous discovery with E. coli

- Effects of electric fields on bacteria
- Generated chemicals that stopped bacterial growth
- Discovered by accident

Current and oxygen corroded the electrode

- Damage DNA in fast growing cells (bacteria)
- Tests with tumors in rats proved successful

Long road for Cisplatin

- First synthesized 1845
- inhibition of cell division discovered 1965
- Anticancer activity discovered 1969
- Approved for human use 1978
- Cure rate for testicular cancer approx 90 %
- Today used in 40–80% of all cancer patients

Cisplatin moves in and out of normal cells

Cisplatin activated and trapped in cancer cells

USDA searches for new poisons–1950's

- Poisons can be medications

Yew bark extract found to be cytotoxic-1964

Taxol identified as toxic substance-1971

Taxol effective against breast cancer 1989

- 30%

Taxol is a complex molecule

- Impossible to make a synthetic version

Taxol manufacture from yew trees

- 13,000 Kg of bark gave 1 Kg of Taxol
- 38,000 trees gave 25 Kg of Taxol
- Total demand in North America
    - More than 360,000 trees per year

Clear-cutting the ENTIRE Pacific NorthWest

- A 5 year supply

People or trees

Taxus baccata is the European yew

Semi synthesis of Taxol

Robert Holton - Florida State University

- Between 1993 and 2007 FSU made $350,000,000
    - 40 % to Holton
    - 30 % to Chemistry Department
    - 30 % to University

Taxol now manufactured using cell culture

- Plant cells suspended in growth medium
- Genetically modified to maximize production

Cancer drugs are unpleasant

- Kill the cancer faster than you kill the patient
- Side effects are common – 100 %
- Side effects are severe
    - Death
    - Cancer
    - Extreme nausea
    - Hair loss, immune suppression

SPORTS

Sports drug scandals on the rise

Ben Johnson wins and loses gold

- The world knew who Ben was and was pretty famous at that time
- But a few days later, they found out he was doping with steroid and they stripped gold medal

Johnson's drug invented by John Manson

- Drug was invented by a Canadian

Stanozolol patent

Johnson Used a Canadian drug

Barry Bonds hits 762 home runs

- Contract was never renewed and no team wanted him
- This is because he was associated with a company that was known for doping

Marion Jones surrenders her gold medal

- Her husband was associated to the same company
- But later changed her story and said she did use some forms
- Spend some jail time because she purged herself when she spoke at congress

Olympics in ancient Greece

Ancient Olympic athletes used a potions and herbs

- Athletes were encouraged to do because people wanted to see the best athletes
- Didn't talk about with people because they didn't want to reveal their secrets and lose their competitive advantage

Zulu warriors prepare for battle

Dop is a Zulu drink

- It's an alcoholic beverage that would pump up there courage
- In English we say dope and in their tribe they would say doop

Doping racehorses

- You don't dope the same as a human would
- They want horses to run slower unlike humans who want to be faster

Horses were doped to fix races

- Bet money on horses who are long shots
- It's easier for a horse to run slower by making them sick instead of making them faster

First doping test— on horses!

- Collect saliva and test whether a horse was doped

Cycling was notorious for doping

- Best endurance wins

Endurance was enhanced with "dope"

- Caffeine
- Cocaine
- Alcohol
- Nitroglycerine
- Strychnine

Olympic marathon St. Louis, August 1904

Conditions were perfect!

- Temperatures above 40 ºC

- 100 % humidity
- Dirt roads
- Didn't drink water because it was believed it would slow you down

Thomas Hicks in the 1904 Marathon

- Poured a mixture of whites, alcohol and strychnine (stimulate)
- He collapse more than 3 times and everytime gave him the mixture
- Eventually won the olympic marathon
- The drug use was celebrated

Thomas Hicks wins the 1904 Marathon

Adrenaline used as a drug in 1901

- Became popular

Adrenaline was not ideal for sports

- Short duration of action (minutes)
- Required i.v. injection
- Common in boxing
- Not user friendly
    - Designed for a short term use (you would have to inject multiple times)
    - More convenient if you can take it as a pill

Gordon Alles discovers amphetamine 1929

Gordon Alles notebook

- Took them awhile to figure out how to properly use it
- Drys up nasal secretion

Amphetamine was a great decongestant

Amphetamines for cold symptoms

Amphetamine's first side effect

Methamphetamine in total war

- German army
- Wide spread use of machinery
- The germans created this to destroy their enemy from all sides by circling them pretty fast

Blitzkrieg required endurance

- WWII was an example of every resource used to fund the war
- Pervitin was used to help soldiers to stay awake and is what crystal meth is today

Pervitin use discovered by the Allies

R.H. Winfield experiments with Stirling aircrews

- They all have the same effectiveness to keep people awake
- Amp and meth has negative side effects but it improves confidences and aggression

Amphetamine use by the 8th Air Force

- The chose the amp drug because it improve the aggression

Amphetamines in the Tarawa invasion

- Also used in this case

Amphetamine use by Allied armies

- Triggered the pharmaceutical complaints to produce a new product
    - Made tablet forms

Soldiers are athletes

- Essential athletes and some were athletes before soldiers

First sports amphetamine use 1952 Olympics

- Discovered later that the Norwegians were using it

First studies of athletes use of amphetamines 1959

Knud Enemark Jensen at the Rome Olympics

- Started to generate problems in the 1960s
- This was a team event (all must cross the finish line)
- They still believed the water was bad for you to use in an event
- He collapse and got up after
- Collapse again and caused a pile up and got a skull fracture and later died
- Toxic reports showed he has large amounts of amphetamines in his blood
- But the skull caused his death

Tom Simpson in the Tour de France

Mont-Ventoux is a Moon-scape

- His race temperature was 45 C
- 8 degrees higher than the body temp
- Still weren't allowed to drink water
- He collapse and his second collapse he died

Tom Simpson's last few meters

Attempts to revive Simpson failed

Tom Simpson monument on Mont Ventoux

- Heat exhaustion was the cause of the death
- But also had large amounts of amphetamines
- But the drugs set up a situation that would lead to this

Nervous system has several sub-systems

- Sympathetic
    - Does things that you need when your life is endanger
- Some of these things are stuff athletes would benefit from

Amphetamines can push the body beyond it's limits

- Large dose can keep you from feeling fatigue and keep working till essentially death

Olympics restrict drug use in 1967

- First testing done in Grenoble, 1968

    - Sympathomimetic a
      mines
        - Amphetamines
    - Central nervous system stimulants
        - Strychnine
    - Narcotics
        - Heroin
        - Cocaine
    - Antidepressants
    - Tranquilizers
- Amphetamines were number 1 on the list

Drugs were not banned because of unfair advantages

- Not ban for unfair advantages

Sports drug abuse is harmful to athletes

Hans-Gunnar Liljenwall wins and loses bronze

- Tested positive for drugs and strip of medal
- He ate food with a beer
- Then he was tested after his won

People associate steroids with sports

- Steroids are artificial version of testosterone

Fritz Pregl and Oskar Zoth 1896

- Injected themselves with bull testicle extract
- Measured muscle strength using middle fingers
- This is made up and will not improve muscle strength

Oskar Zoth 1896

- "The training of athletes offers an an opportunity for further research in this area…"

Charles Éduard Brown-Séquard 1889

- Injected himself with macerated dog testicles
- "internal secretions" as physiological regulators
- He reported beneficial effects but it wouldn't work the way he reported it

Brown-Séquard applied Similia similibus

- Treating an organ with itself
    - Heart for courage
    - Brain for idiocy
    - Bile
    - Blood
    - Bone
    - Feces
    - Intestine

    - Placenta
    - Teeth

Àyurveda of Suśruta 1000 B.C.

- Testes to treat impotence

Victor D. Lespinasse 1913

- Transplanted testicle tissue from donor to man who had lost his testicles
- The effects are probably not linked today

Leo L. Stanley, physician at San Quentin

- Transplanted testicles from executed prisoners into convicts to restore sexual function
- Common to experiment on prisoners

Fred C. Koch and Lemuel McGee 1926

- these guys in Chicago's
- Chicago was home to the largest slaughterhouse

First isolation of the male sex hormone

Testosterone was hard to get

- 40 Kg of bull testicles = 20 mg of testosterone
- didn't have a large quantity

Semi-synthesis of testosterone 1935

Testosterone for inmate rehabilitation

- The nazi would starve them to death
- To help restore testosterone you can help them recover body mass

First athletes using testosterone

- Horses

Soviet athletes use testosterone 1950's

Soviets discover fundamentals of testosterone use

- Side effects
- Training methods
- Training cycles

Dr. John Ziegler – York Barbell Club

- Had lunch with an Russian he explained everything about the effects of testosterone
- Went back to the us and decided to do this but one step further

Effects of extra testosterone

- **Anabolic**
    - Muscle mass
    - Strength
    - Bone growth
- **Androgenic**
    - Body and facial hair
    - Enlarged vocal chords

    - Heavy brow
    - Acne
    - Increased sex drive
    - Testicle shrinkage
    - Clitoral enlargement
- Decided to make an artificial version
- Have the anabolic but limit androgenic

Design a steroid for sports only

- Use testosterone as a drug can cause issues when you use it at high levels

Dianabol in 1958 and Stanozolol in 1961

Anabolic steroids reduce side effects

- Doesn't necessarily work the way you expected it to

Anabolic steroids for wasting conditions

- Have legit medical uses and are still used today
- Didn't use it for sports
- Pretty safe if you use them in a proper way

***Arnold Schwarzenegger* (Mr. Olympia 6 consecutive years)**

- in those days you didn't have to deal with the black market, you could go to your physician and just say 'listen, I want to gain some weight and I want to take something'. *Then the physician would say 'do it six weeks before competition, then it will be safe'"*
- Can improve physique

Dr. Manfred Höppner

- Director of sports medicine, East german Swim team
- Decided to administer steroids to all olympic athletes committing
- East German was a small country
- They end up winning everything
- The women swim team had body hair and facial hair
- The media noted it

East Germany wins 11 of 13 gold medals at 1976 Olympics

East German swimmers forced to take steroids

- Force young talent children in taking drugs
- No choice and cant say no

Steroids banned by Olympics in 1977

- Ethical issue so the olympic banned steroids

East Germany established doping lab in Kreischa

- Accredited by IOC for Olympic testing
    - Volunteered to set up a accredited IOC olympic testing
- East Germany gained access to testing protocols
- Developed masking techniques

- Half of the building was dedicated for olympic test and the other half was a secret lab to find ways they can beat the test

Steroid testing GC/MS

- Two instruments that are combined together

Finding a drug in urine

- You can use blood or urine to find drug
- Looking for one chemical among the thousands

Molecules isolated from athletes as mixtures

Gas chromatograph sorts molecules

- first want to separate it by physical characteristics

Mixture is passed through a tube containing a sticky substance

- **(GC)** use a long tube where the inside has a sticky coat
- Whether the molecule is sticky will stick to the coating but if it's slippery probably won't stick to it
- Blown through fast (slippery goes through the tube pretty fast, sticky tends to go through slower)

Gas chromatograph sorts molecules using speed

Gas chromatograph sorts with times

Gas chromatograph measures amounts

- Peak represents piles

Mass spectrometer weighs molecules

- Identify the molecules by how much they weigh

Mass spectrometer throws molecules

- Depending on how much the molecule weighs determine how far I can throw it

Mass spectrometer throws molecules in a magnetic field

- Magnetic field replaces the gravity

Mass spectrometer weighs molecules

Molecules fall apart in mass spectrometer

- Causes them to break into pieces and then you can measure the pieces

Mass spectrometer obtains a fingerprint

Fingerprint used to identify compounds

- Compare and contrast with known

Steroid testing measures T to E ratio

- Normally 1 : 1
- Can be as high as 4 : 1
- Produces epit as a by-product
- The steroid modifies the way the body produces testosterone
- Where there is more testosterone than epitestosterone

Masking agent for steroid testing

- "Mask" the presence of extra testosterone by injecting epitestosterone
- They would inject a couple days before the competition

Diuretics mask total steroid amounts

- Diuretics makes you pee where it essential flushes out all drugs out of the body

Add materials to interfere with testing

- Add alcohol to urine

Urine switching in extreme cases

- Empty athlete's bladder
- Fill bladder with "clean" urine using catheter

Floyd Landis claims his 11 : 1 ratio was natural

Original synthesis of steroids

- raw sources of testosterone was chelsotrol mainly from animals

Modern semi-synthesis of steroids

Diosgenin from Mexican yams

- Produces lots of natural testosterone

Atomic structure and isotopes

Carbon has two isotopes

- 98.9 % of carbon atoms have mass of 12
- 12C
- 1.1 % of carbon atoms have mass of 13
- 13C
- The ratio of 13C to 12C tells you the source

Plants and animals have different amounts of C^{13}

Floyd Landis is a plant!

- His body is not manufacturing it

Steroids do not build muscle

- Work harder to get a physique like this when you're on steroids

Testosterone HELPS build muscle

- Microscopic damage to this fiber and body fixes it
- The body realize you can damage it again so they mix it stronger than before

Building muscle requires exercise

- Have to exercise harder and more intense to gain the muscles/benefits

Health risks of steroids

- Liver damage
- Heart damage
- Reproductive effects
- Pretty safe drugs as long as you do it safely

Anabolic steroids speed recovery

- Give steroids can give you a faster recovery time

Anabolic steroids speed training

- You have to be at your best during a specific time
- Steroids can speed up the training

Long term health risks are unknown

- Because they're illegal it's hard to do accurate clinical test and find long term health risk

Effects are difficult to measure

- Athletes vary doses
- Athletes mix steroids
- Athletes take large doses
- Athletes keep their methods secret
- Have to go underground
- Hard to correlate because you don't know what they take

BALCO made "designer"steroids

- Designed to avoid detection
- No testing done

Drug testing based on molecular fingerprints

- If there is no fingerprint in their database you don't know the source or who it belongs to

Tetrahydrogestrinone – "The Clear"

- Was undetectable before 2002
- "fingerprint" was not known

Temptation to abuse is too great

- If you follow the instructions by the doctor there is no problem and it's pretty safe
- But the urge to win shadows it

Desire to win makes drugs dangerous

- Used properly, they are safe
    - Medical supervision
    - Limited dosing
- But…….
- Desire to win makes athletes push the limits
    - Overuse of drugs
    - Mixing drugs
    - Improper use of drugs
    - Designer drugs

Red blood cells only carry oxygen

- Bags of chemical where they transport oxygen place to place

Red blood cells made in bone marrow
Body makes 3 million RBC's every SECOND
RBC production controlled by erythropoietin (EPO)
Endurance athletes benefit from increased O2 capacity
Training at high altitudes increases RBC production

- The amount of oxygen is lower at high altitudes than at cities at sea level

U.S. Olympic training center

- Gives benefit in increase production of RBCs

"Instant" altitude training

- Blood doping where you use your own blood
- Remove the liquid and store it for 3 month
- Athletes natural; replenishes it
- Add the blood back into the body; increases amount of RBCs in the body

Blood doping

- Remove blood from athlete
- Concentrate RBC's and store them
- Wait 3 months
- Athlete's body replaces missing RBC's
- Just before competition put stored RBC's back into athlete
- Athlete now has improved O2 capacity

1984 Olympics in Los Angeles
Ed Burke proposes blood doping to USCF in 1983

- Proposed it to the USCF

Danny van Haute used blood doping during 1984 Olympic trials

- Wasn't expected to make it
- But qualifies
- Used blood doping on it's own
- Didn't have the 3 month lead time so they did a transfusion

Transfusions in a Ramada Inn

- Ethical lie crossed
- Use different people blood

U.S. Cycling Federation banned blood doping January 1985

- Sanctioned 3 officials involved in Olympics

IOC outlawed blood doping in 1986
Fresh blood
Blood after overnight storage

- Freezing blood and using your own is not a 0 risk because you are damaging it

Blood after frozen storage

Blood transfusions important in medicine

- Risk of infection
- Risk of rejection
- Serious decision

Use EPO instead of a transfusion

- Helps patient make their own blood

EPO is a protein

- Linear chain molecule made by connecting amino acids together
- Cause it to fold into the 3d shape
- That 3d shape determine the amino acid function

Chemical synthesis of protein is impractical

- Very expensive
- Limited quantities
- Produces large amounts of waste

Some proteins are available from animals

Animals are not an ideal protein drug source

- Supply is limited
- Not human proteins
    - Animal proteins don't work as well in people
    - Possibility of rejection
- Small risk of contamination

Cadavers not ideal source for human proteins

Human cadavers make a poor drug source

- Very limited supply
- Very expensive to produce
- Possibility of infection (very rare)

A solution is recombinant protein

- recombine dna from different species

Make human protein in a bacteria or yeast

- Human protein is a good drug
    - Normal human protein works well
    - No immune reaction
- Problem is making large quantities
- Use a single cell organism to make protein
    - Easy to grow
    - Protein easy to extract
    - Product is safe (no risk of infection)
- Use genetic info from a human

Insert the human gene into a bacteria

- Bacteria will use the gene to make human protein
- Protein is easy to make in large amounts
- Make a living factory

DNA is an information storage device

- Stores info in a physical construct

Cells use DNA as a template to make protein

- Organisms on this planet use the same genetic code

Remove human gene from chromosome

- Identify human gene then remove it

Insert the gene into a plasmid

- An artificial chromosome then gets inserted into the bacteria

Insert the plasmid into a bacteria

- Bacteria will now make the protein

Genetic engineering to make human protein

- Copy the gene describing a human protein
- Put this gene into a bacteria or yeast
- Make it a safe way and not worry about contamination

Bacteria and yeast are easy to grow

- Take juice and attract the protein which then becomes the drug

Recombinant human proteins are better drugs than animal proteins

- Protein is human
    - No immune reaction
    - Human protein works better
- Source is safe
    - No risk of infection
    - No problems with allergy
- Can make large quantities
    - Bacteria or yeast easy to grow
- Unlimited quantities

Recombinant EPO is one of the best drugs in last 30 years

- Any disease requiring blood transfusion
- May use EPO instead
- Don’t need to work about infection

Recombinant EPO abused from day 1

- Clinical trials 1987 to 1989
- 18 pro cyclists die from heart attacks
    - 5 Dutch in 1987
    - 1 Belgian and 2 Dutch 1988

    - 5 Dutch in 1989

Clinical trials are used to establish doses

- Can only be done using humans
- Use by athletes before proper dosing was known resulted in overdosing
- Overdose of EPO "thickens" blood causing heart attack
- They didn't know the safe doses
- The Blood became too thick for the blood to push

IOC banned EPO in 1990

- Before the drug went on the market
- Was a precaution

Testing for EPO was impossible

- Hematocrit
- Know the same regular amount

EPO and rhEPO have same amino acid sequences

- Can't test it because it's the same as the human body

Today can detect EPO using antibodies

- Urine test for total EPO
- Confirm using blood tests
- Compare values to normal human levels

***ON* model detects recent use**

- Hemoglobin
- EPO
- Soluble transferrin receptor

***OFF* model detects longer term use (2-3 weeks)**

- Hemoglobin
- Reticulocytes
- EPO

EPO use is easy to hide

- Difficult to detect
- He was tested on a regular basis

Only evidence against Armstrong

- Only evidence was his confession was on Oprah
- You're guilty until innocence
- They did this on monthly basis
- He didn't show up to a meeting then they strip his titles

The future – gene doping?

- Insert the gene for EPO into a person
- Requires genetically modified virus

Repoxygen on the internet

- Never marked cause it wasn't safe

Ripoffxygen

Bubble boy syndrome and gene therapy

- Born with non functional immune system
- Grew up in a bubble to protect themselves
- Used gene therapy but after almost half of them got cancer

Desire to win makes drugs dangerous

- Used properly, they are safe
    - Medical supervision
    - Limited dosing
- But…….

Temptation to abuse is too great

- Ends justified the means

Desire to win makes drugs dangerous

- Athletes push the limits
    - Overuse of drugs
    - Mixing drugs
    - Improper use of drugs
    - Designer drugs

Drugs are banned from sports for safety reasons

ANTIBIOTIC

Life expectancy then and now

1900

- ***44 years***
- Main causes of death
    - Pneumonia
    - Tuberculosis
    - Influenza
- (this lasted until 1950's)
- Infection use to be the leading cause of death

2004

- ***82 years***
- Main causes of death
    - Heart disease
    - Cancer
    - Stroke

Plagues were common throughout history

- Large portion of the population would die from this infection

Cures and treatments failed

- Useless because they had no idea what causes it
- They believed the flower or spice scent would protect the doctor
- The stick use to be the main diagnostic because they didn't want to touch them

Causes of disease was unknown

- Curse from God
- Spontaneous generation
- Bad smell or unclean conditions (miasma)
- They would make it up

WWI and WWII – more deaths due to infection than combat

Agostino Bassi proved germ theory of disease 1844

- He was the first to propose this idea

John Snow disproved miasma theory 1854

Map of cholera infections identified the sources

- Investigate the cause of disease by creating a map
- The black boxes represent the cases of cholera

Water pump is a historical landmark

- The water pump caused the cholera infection so they removed the handle since the water people were drinking were getting mixed with fecal matter
- The city policy marker didn't believe it so they got the handle back but then a widespread of cholera infection happened again; finally realized the pump is the cause
- Preserved as a historical landmark

Louis Pasteur develops pasteurization 1864

- He developed effective ways to present disease from infecting humans
- Purified milk

Lister developed antisepsis 1867

- Killed bacteria during surgery

H.C. gram stains bacteria in 1884

- Certain bacteria could be coloured differently (for chemical difference)

Paul Ehrlich and the magic bullet 1907

- Discovered through the observation of colour

Trypan red selectively colors trypanosomes

- There was a chemical where it would get taken up by some cells but not others

Erlich knew As was similar to N but more poisonous

- Elements in certain columns have similar properties and characteristics
- Able to kill bacteria and leave the body cells untouch

Salvarsan 606

- It worked

Salvarsan 606 for syphilis- the great pox

- 140,000 deaths per year
- Could be fatal

Salvarsan 606 not very "drug-like"

- Treatment required several months
- Many injections
- Large injection volumes
- Drug was highly toxic
- Not a commercial success
- Not user friendly
- About 600ml injected in the body over a period of time

Erlich wins Nobel in Medicine 1908

- Was a scientific breakthrough
- Did what it was supposed to do

Gerhard Domagk at IG Farben 1932

- Based on a dye substance
- Found it worked in the lab setting
- Gave the chemical to his daughter when she was suffering from a bad throat infection and she recovered

Prontosil only worked in vivo

- Administer drug on the petri dish it doesn't work

Why was prontosil only effective in vivo?

- It got converted to sulfanilamide
- Prontosil was a pro drug (was inactive until it gets converted to sulfanilamide)

Sulfanilamide becomes first sulfa drug 1932

- First drug for a family of drugs

Sulfa drugs save lives in WWII

- Issued for combat kits to treat infections

Sulfa drugs inhibit bacterial growth

- The enzyme grabs onto one component and to another
- Brings them together to form a substance

Sulfa drugs mimic natural substrate

- Does this so it can grab the right chemicals
- Once it's jammed it can't grab the components so therefore it can't work

Gerhardt Domagk wins Nobel in medicine 1939

Alexander Fleming contaminated culture in 1928

- Father of antibodies was him
- Most drugs are based on penicillin
- Petri dish became contamination and then penicillin was discovered

- It was by accident

Mold prevented bacterial growth

- Found the area near the mole is where no bacteria would grow

Fleming publishes his results in 1929

- Wrote in a style that was difficult to understand and publishes in a journal that nobody would read

Fleming used an extract to purify bacteria

- The juice from the model is letting one bacteria to grow and the others to die

Fleming was a bacterial artist

- He was interested in this type of stuff

Fleming did not do the key experiment

- He didn't go a step further in testing an infected rat with his theory simply because he didn't understand the significance

Howard Florey & Ernst Chain isolate penicillin in 1941

- They rediscovered it 10 years later and took another 2 years to recreate it

Penicillin first produced in milk bottles

- 1000 kg mold gave 1g penicillin

Florey and Chain publish their discovery

- Showed that the substance could be used as a drug cure
- They gave pincilin to a guy who was in a coma and he recovered but later die
- Because there wasn't enough penicillin to completely cure it

Britain not best place for research

- It was happening during the ww2 and was worried that they're researched would get bombed

Scale-up of penicillin production

- Mold requires oxygen to grow
- Initially grown on thin layers of milk
- Industrial quantities by forced injection of oxygen into tanks
- So gave it to the USA

Peoria, Illinois becomes penicillin capitol

- Because it was the beer growing capital

Drug companies develop better extraction technology

- Drug companies took over the purification process
- So they could grow large quantities

Penicillin production became war priority

- Funded by the us army

Penicillin stockpiled for D-day

Penicillin used by U.S forces in the Pacific

- After d day was used in the pacific

Penicillin available to the public in 1945

- After ww2 available to the public

Fleming, Florey and Chain share Nobel in 1945

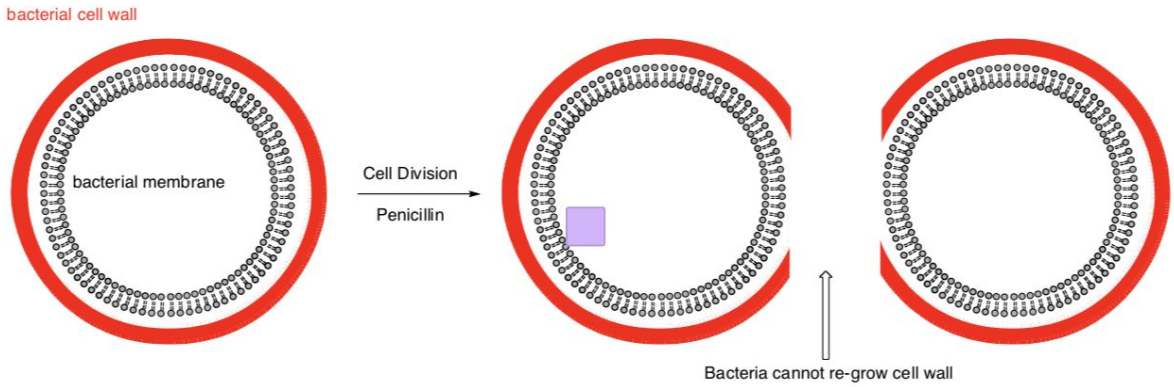
Bacterial cells are different from human cells

- Extremely safe drug
- Cell wall prevents liquid from escaping

Cell walls rebuilt during cell division

- When they become two you must reconstruct the cell wall very quickly (enzyme does this)

Penicillin prevents cell wall synthesis



No wall to hold internal pressure cells explode

Secret to activity is the β-lactam ring

Penicillin destroys enzyme that makes cell walls

- Can't regrow the cell wall
- No where the cell can react

Antibiotic only work on bacteria

- We don't have cell wall so it can affect us

Most antibiotics today are artificial

- Natural penicillin not drug-like
  - Unstable
  - Must be injected
  - Only works against some bacteria
- Artificial penicillin drugs are drug-like
  - Can be stored for long times
  - Can be taken orally
  - Work against most bacteria

Design better antibiotic drugs by semi-synthesis
Major penicillin side effect is allergy
Cephalosporin found in Italian sewer
Streptomycin found in chicken throats
Golden age of antibiotics – 1940s and 1950s

- Most antibiotic families discovered in 1940's and 1950's
- No new antibiotic families since 1997
- Vast majority of antibiotics found around 40-50s
- After then we found out only 5 more

Antibiotic resistance is a growing problem

- Resistant bacteria are not killed by the antibiotic
- The bacteria is resistance not the person
- The bacteria has evolved to become resistance

Over-prescription contributes to resistance

- not major reason

Prophylactic use may promote resistance

- Some animals are given antibiotics to allow the animals not to get sick and not have infected meat

Biggest problem is patient compliance

- The user is the primary problem
- The patient doesn't follow the instructions properly

The reason for the instruction
Missing doses creates resistant bacteria

- Forces the body to develop bacteria that becomes resistance

Only the tough survive

- Everytime they get through the survival process the bacteria becomes stronger and stronger eventually becoming strong enough to the antibiotic

Important to kill all the bacteria

- Survivors are less susceptible
- After several generations can become resistant
- Will not be killed by antibiotics
- They work every quickly

Most dangerous bacteria are found in hospitals

- Nosocomial infection

Necrotizing fasciitis
Staphylococcus aureus

- Very common bacteria
    - 15% of population permanently infected
- 20,000,000 to 30,000,000 infections each year

- Small number – 1500 – become dangerous

Kill the bacteria by debridement

- You have to undergo a procedure
- The treatment doesn't guarantee the bacteria will all be killed

Lucien Buchard 1994

- He lost his leg to this disease
- The treatment was not enough to save his leg

Clostridium difficile in hospitals

- 1,000,000 per year (North America)
- Affects our intestine and is very difficult to get out

Methicillin resistant Staphylococcus aureus

- MRSA
- 130,000 cases per year
- Only a few drugs that can treat it

Timeline of Discovery for antibiotic classes

- Economic reason why we don't have new drug invention on 2000s

Antibiotics are commodity chemicals

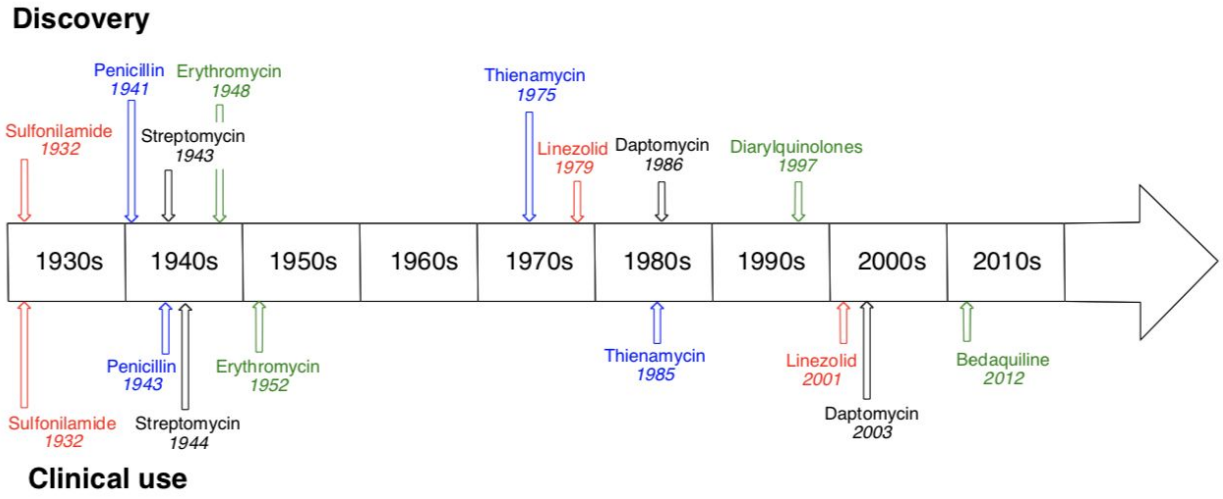
- There's no profits for antibiotics because you won't make any money
- Costs a lot

Developing new antibiotic is not cost effective

- No chance to make up your investment

Sales will not recover research costs

Discovery times then and now



Major costs today are regulatory

- Takes a long time for it to be approved

Doctors are reluctant to use new antibiotics

- Profit margin is small and doctors will mostly not use it

- Going to need a crisis to happen for a new drug to be invented

Antibiotic have huge impact on human life

- Longer life span
- Improved quality of life
- Very safe drugs
- Very effective drugs

Tobacco

Tobacco is the most dangerous substance in the world

- Kills more people than
    - DDT
    - PCB's
    - Industrial chemicals
    - Pesticides
    - Cocaine
    - Alcohol
    - Homicide
    - Suicide
- COMBINED

Tobacco kills 420,000 per year (North American)

- The number is 20x higher

Columbus discovers tobacco 1492

- He just notice that other people were consuming it
- Notice the population in caribbean were drinking smoke

Natives drank smoke from tobago's

Tobacco used to revive drowning victims

- At one point it was used a medicinal product

Tobacco smoking in clubs

- Smoking infrequent
    - Harsh taste (acid)
    - Expensive
- Back then they consume tobacco differently
- People smoke in clubhouses
- It was very expensive
- The burn releases acids that can irritate the throat
- The long tubes allows the smoke to cool down and remove some of the acid

Water pipes popular in eastern countries

- Bubbling it with water removes the acid
- Don't consume the same amount of tobacco
- The doses are generally low

Cigarettes originally rolled by hands

- Luxury for rich people

Bonsack machine reduced production cost

- Changed in the 1800s
- Automated way to roll the cigarettes
- Drop the price down and more people could smoke

Flue-curing reduced harshness of smoke

- Use a stove to dry the leaves faster
- Different chemical reactions happen where the acid amount found in smoke is lower and not as harsh

Cigarettes became dangerous

1) Machine manufacturing reduced cost
    - Could afford to smoke a lot
2) Flue curing reduced irritants in smoke
    - Smoke brought deep into lungs

- **Cigarettes now addictive**
- These two factors increase exposure to toxic substances
- Risk = toxicity X exposure
- Both factors allow cigarettes to be addictive

Average smoker smokes 10,000 cigarettes each year

Cigarette consumption then and now

- ***Late 1800's***
    - 80 cigarettes per year
    - Did not inhale because the acid hurt the throat so they didn't smoke it in
- ***Today***
    - 10,000 cigarettes per year
    - Inhale deeply
        - Allows the smoke to go deeper since the acid is a big deal anymore
    - Hold smoke in lungs
    - Risk = toxicity X exposure

Nicotine is the addictive substance

- 2 mg per cigarette required to addict smokers

Cigarette delivers 2 mg nicotine to addict

- 2mg is the standard dose

Nicotine acts on acetylcholine receptors

- it interacts with the receptors and the Ach
- As the signal hit thes terminal, the neurotransmitters are released
- When they come in contact the receptors they allow the info to be continuous

Receptor molecules transmit information

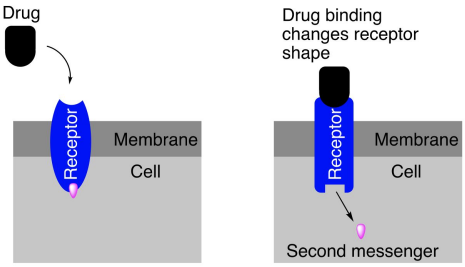
- Messenger molecule sticks to a complimentary pocket on the receptor
- Messenger binding causes the receptor to change shape
- New receptor shape triggers other events inside the cell (message)
- Changes shape in the inside of the cell as well

Nicotine is an agonist at low doses- stimulant

- Sends signals without normal messenger
- Amplify normal signals

Agonist sends messages without the normal messenger

- Agonist molecule sticks to "active" pocket on the receptor
- Agonist binding causes the receptor to change shape "normally"
- New receptor shape triggers other events inside the cell

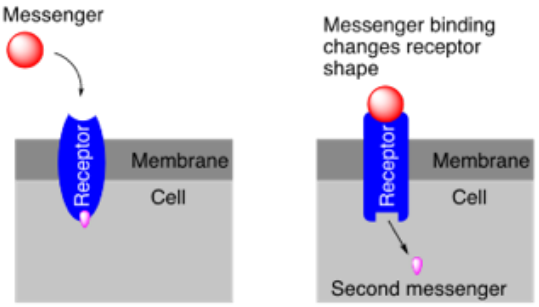


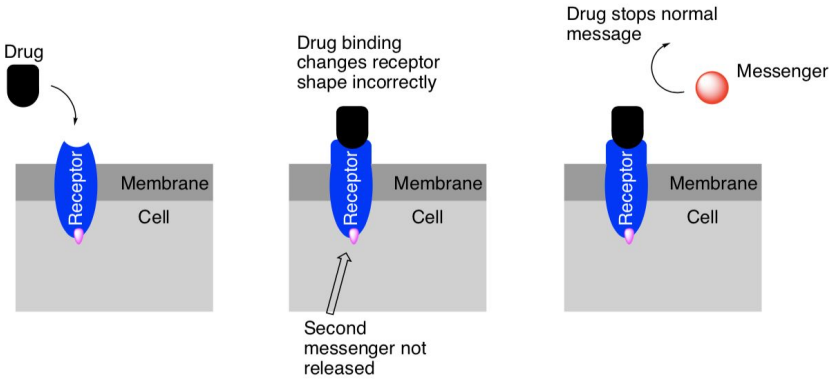
Nicotine is an antagonist at high doses - relaxing

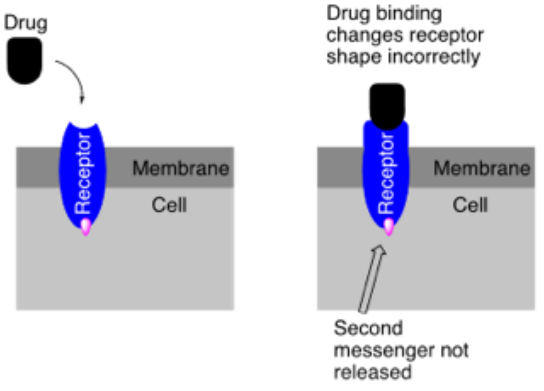
- Increase nicotine doses changes how they interact with acH
- Doesn't change the shape in the normal way
- It changes messaging system

Antagonist block chemical messages

- Blocks signals
- Attenuate normal signals







Smokers learn to regulate the dose

- Buff and gives them a lower dose of nicotine

- If you want to relax, they will draw the smoke deeper and then changing the way it interacts with acH

Nicotine stimulates dopamine release

- Dopamine is the “reward” chemical
- Important for learning
- **All addictive drugs affect this neurotransmitter**

Smoking cues add to the addiction

- Psychological addiction also known as ***cues***
- Develop habits or rituals

Lethal dose of nicotine is 60 mg (adult)

Common form poisoning in children

- Lethal dose is 60 mg (adult)
- Lethal dose of cyanide is 70 mg

Nicotine to kill large animals

Toxic substances in tobacco smoke—carbon monoxide

- Carbon monoxide kills heart tissue
- Heart attacks kill more smokers than cancer does

Carbon monoxide (CO) reduces oxygen capacity of blood

- Carbon monoxide sticks tightly to hemoglobin
- Requires several hours to remove
- Prevents oxygen transport
- Damages heart and blood vessels

Nicotine stimulates the heart muscle

- Increases heart rate
- Heart attack
    - Approx 5 % of smoker heart attacks
- Lead to heart attack risk but its relatively small compared to co2

Polonium in tobacco smoke-cancer

Combustion by-products in tobacco smoke

- Strong carcinogens
    - Benzopyrenes (PAH’s)
    - Nitrosamines
    - Aldehydes
    - Epoxides
    - Aza-arenes
    - Trace metals
- Don't need to know the names

Combustion by-product carcinogenicity

- React chemically with DNA

    - Damage and mutations
- Electrophiles
- Changes the chemical structure of dna

Normal lung and smokers lung

- Smoker's lung is black and has tar

Lung cancer then and now

- 1919 only 400 cases in North America
    - Chimney sweeps
- 2004 190,000 cases in North America
    - Smokers
- All smoke is the same
- Only different is the cigarette is a direct exposure while wood burning is indirect

Tobacco use and lung cancer in the US

- male is red (higher jump than the women
- women blue

Tobacco advertising emphasizing glamour

Tobacco companies paid stars to smoke in movies

Cigarettes were provided free to soldiers

Tobacco advertising targeted women in 1950s

Women start smoking to stay slim

- It's often seen when you stop smoking you will gain some weight
- It's because nicotine gives you dopamine and when you stop you don't get it anymore but when your full you get that same effect

Smoking created wrinkles

- Skin is not tight anymore as you age
- You start to develop wrinkles at a young age

Second hand smoke is harmful

- It determines how much the dose is

Cigarettes are highly engineered drug delivery device

Use of reconstituted tobacco

- Recon
    - Paper made from tobacco
    - Cut into small strips
- Can use the whole tobacco plant
    - Cheaper
- Can blend tobacco
    - Cut costs by mixing small amount of high quality tobacco with cheap tobacco
- Easy to introduce additives
    - Flavor, burn rate

- Control nicotine content

Paper is specially designed

- Many chemical additives to control burning
    - Even burn rate
    - TiO2 keeps the paper lit
- Burn rings regulate combustion
    - Thin areas burn quickly when smoker draws
    - Thick areas burn slowly between puffs

The filter is a decoration

- added in the 1950s

Charcoal filters don't work any better

Cigarettes are engineered to deliver nicotine

- To deliver the appropriate amount of nicotine
- The engineer the amount of ammonia so you can get the 2 mg of nicotine

Light cigarettes just as dangerous as regular

- Use it to get less tar or nicotine
- They are almost identical
- Designed to fool the government policies

Laboratory testing of cigarettes

Smoking machine collects fixed amounts of smoke

- As the cigarette burns the smoke is vacuum and collect to see the amount of stuff in it

Light cigarettes designed for laboratory testing

- They have holes inside where the machine don't really suck the smoke just mostly air

Vent holes placed at top of filter

Holes placed outside machine connection

- Holes are accurately placed
- Generates you suck in air not smoke

Light cigarettes are not safer or lighter

- To get 2 mg dose of nicotine
    - People draw more deeply on light cigarettes
    - People smoke more light cigarettes
    - People cover the holes with fingers or lips
- They alter their behavior to get more nicotine

Tobacco companies suppress information

- The number 1 risk of heart attacks was cigarettes

60 minutes muzzled first and only time

The insider tells the story

- Rose cipollone vs Philip Morris 1988

Florida sues big tobacco in 1998

- The person eventually outlived their strategies and ended up winning

Companies always claimed tobacco not addictive

- Dependence
- Withdrawal
- Tolerance
- ***Intoxication***
    - They modified the legal definition of addiction by adding the word intoxication

Nicotine substitutes to stop smoking

- To get passes the psychological addiction
- Once that happens they are able to address the chemical aspects

Safe delivery of nicotine

e-Cigarettes use is controversial

- Smoking sensation

About as effective as other methods of quitting

- Same effectiveness and helps the person quit

Vaping bars in NYC

- Rent an e cigarettes and buy the liquid
- The idea the people are going to take up vaping not smoking

Concerns over youth use

Is it a safe alternative to smoking?

Health Canada is very conservative

- Not a lot of data about vaping
- So the government goes with the answer no

Specialized heater and e Fluid or E-juice

- Heater generates an aerosol
    - Droplets suspended in vapor
    - Simulates the texture of smoke
- In lungs, nicotine is absorbed
- Remaining aerosol is expelled

eFluid is a flavoured vapor source

- Solvent
    - Propylene glycol
    - Glycerol (glycerin)
    - Polyethylene glycol (PEG)
- Nicotine (0 to 20 mg)
- Flavour
    - Artificial food flavour

Is it safe? NO

- Solvent
    - Propylene glycol
    - Glycerol (glycerin)
    - Polyethylene glycol (PEG)
- Nicotine (up to 20 mg)
    - Heart attack risk
- Flavour
    - Carbonyl compounds
- When they are heated some small amount is converted to acrolein (cancer associated)
- The flavouring can have nasty effects

Is it safer than cigarettes? YES

- Cigarettes
    - Carbon monoxide
    - Polonium
    - Combustion by products
    - Particulates
    - Nicotine
- E-Cigarette
    - Nicotine
    - Carbonyl compounds
    - Glycols
- Nicotine is the less dangerous on cigarettes
- Nicotine is the most dangerous to e cigs

How much safer? Current best estimate

- 95 % harm reduction with respect to cigarettes
- Not enough data to answer this question

Concerns about use by non-smokers

Nicotine consumption in England

- Small recent increase in amount of nicotine consumed

E-Cigarettes worth switching to?

- Are they safer than cigarettes? ***Yes***
- How much safer? ***95 % (current best estimate)***

Cannabis is now legal in Canada

- So far only to buy plant-derived version

Active ingredient

- Tetrahydrocannabinol
    - This one gives you the high and impairs you

Prescription THC for cancer and severe infections

- Side effect of THC is increased appetite
- Used to treat anorexia

Sativex for multiple sclerosis

- Gives them more control

Other medical benefits are questionable

THC impairs memory

THC slows reaction times

- Effect is stronger for occasional users
- Daily users can be impaired 30 days after cessation

Cannabis impaired driving

- Driving under the influence
    - 2 ng/mL THC in blood within 2 hours of driving
    - Maximum $1000 fine
- Drug impaired driving
    - 5 ng/mL or more THC in blood within 2 hours of driving
    - Minimum $1000 fine
    - Maximum 10 years in jail

THC has a long residence time

- Dissolves in body fat
- Can be detected in blood 30 days after use
- Avoid driving
    - 4 hours after smoking
    - 6 hours after oral ingestion

The source of smoke doesn't matter

- Carbon monoxide (heart attack)
- Carcinogens (cancer)
    - Polonium
    - Combustion by-products
- Toxins
    - Cyanide

DOSE MAKES THE POISON!!