



CHEM 183 Midterm 1

Chemistry of drug (Mcgill University)

CHEM 183
WORLD OF CHEM: DRUGS
MIDTERM #1 (30%)

Drug History

FDA (Food and Drug Administration) has strict rules and guidelines about drugs.

- Many countries (i.e. Canada) follow FDA regulations because they don't have the time/money to redo all testing.
- Only 27 new drugs from January to August 2018

Martin Shrekli: 31-year-old who became CEO of a drug company

- Raised price of antiparasitic *Daraprim* from 13.50\$-750.00\$ a pill (5,555% increase)
- Got 7 years in prison and payed millions in fines (most hated man in America)

The media gives some misconceptions about how good it was in the old days when food wasn't as processed, and people lived longer

- Radio show in 1989: "Way back when there weren't that many problems with health"
 - False. Life expectancy in 1950 was only about 50 years old.

In late 1700s, King Charles' doctor led 14 physicians in bloodletting and other medical practices to rid the king of disrupted humors.

- He had convulsions, and was bled and given the stone from a goat's stomach... He died

A **uroscopy flask** was the doctor's symbol. A **uroscopy wheel** had different colours that urine in the flask could be and the diagnosis for each colour.

- Urine was the only window into what was wrong with people. Pulse and temperature (later)
- 147 different compounds are found in urine. Not that far off from what we can do today.
- Grey is infection, brown is liver problems, red is food/blood, yellow is vitamin B2 (riboflavin)

At the end of the last century, life expectancy was only about 47 years. Maternal mortality rate was 50/10,000 births until the discovery of penicillin in WWII.

- Today, it's approx. 80 years.
 - Japan has the highest life expectancy.
 - It's about 2 years more for women.
 - Higher in developed countries.
 - Canada is between 9th and 18th country with best life expectancy. The US is 31st.
 - Sierra Leone is the worst.
 - In Russia, men is 65 and women 76 due to men's extreme drinking.

Kane Tanake (Japanese) is the oldest woman alive today.

- In Canada, the record is 117 years old.
- World record is 122 (Jeanne Calment, French woman)
 - Smoked until she was 100 and ate chocolate frequently.
 - Old enough to have met Van Gogh as a teenager.

At 20 years old today, there's a 91% chance you have a living grandmother.

- 100 years ago, 83% chance to have a living mother.

In 2020, 16% (1/6) of the USA population will be over 65.

- In Japan, it'll be 28%
- The world average will be 9%

Influenza pandemic (the grip) in 1918 killed 30-40M people worldwide. Most deaths in US history.

- First was found in a US army base in Kansas.
 - Screens called sneeze screens were used to try to stop germs from spreading between patients.
 - People on the outside wore masks to prevent transmission, mostly in cities

Diary from a 1911 pandemic: Harpp's dad's

- Kemp's Balsam is an extract of various plants that was thought to give relief to a sick person
- Laying out: term for putting a body in a cold part of the house until he can be buried
- 5 people died in a short span in a very small community

A reconstruction of the Spanish influenza virus from a person found in permafrost

- Bacterial pneumonia was the cause of most deaths from the influenza
 - Normal nose and throat bacteria invaded lungs by a path created by the virus destroying bronchial cells
- Blood samples from 32 survivors (between 91-100 years old) reacted to the virus, which means they still had antibodies. (A good path for future outbreaks)

The 2017-2018 flu vaccine is only 36% effective.

- 600,000 deaths worldwide due to the flu virus per year.
- 10% of the deaths 100 years ago.

Several diseases have been eradicated. The WHO (World Health Organization) says that vaccines have saved 40 million people in 20 years.

- Small pox virus was eradicated by vaccine. Queen Mary II had it.
- Polio(myelitis) has no cases in the Americas since 1991, and only 31 reported worldwide in 2016
- Leprosy has been eradicated by multi-drug therapy. It's a bacterial infection called Hansen's disease. In 1980, there were 12M cases worldwide, and now only about 200,000.
- Guinea worm disease is a parasitic nematode larva carried by fleas, that can be contracted through drinking water in western India and western Africa. Also called dracunculiasis.
 - The life cycle of a guinea worm: in drinking water, migrates to lower limbs, grows and causes blisters and exists body to put more larvae in water.
 - Can be treated simply by filtering the water.
 - Animals in North America can also get it.
 - Jimmy Carter set up a center for it.
 - Bill and Melinda Gates foundation also gave a grant for it (for filters and education)
 - From 148 cases in 2013 to only 5 in 2017, worldwide.
- Chagas disease is caused by a parasite on a bug called the kissing bug
 - Symptoms appear 10-20 years later.
 - Charles Darwin described it sucking blood.
 - Insecticides are effective against it but are now regulated.
 - Drug developers are starting to take aim at it
 - ⇒ *Trypanosoma cruzi* (parasite) can be controlled by a molecule that suppresses cysteine protease, crucial for parasite
 - ⇒ Reduced Chagas to 8M cases worldwide

- Many diseases that most people in North America have never heard of are rampant in other countries.
 - Coming further north due to global warming: Chagas and ticks (lyme disease)
 - ⇒ Chagas now found in Northern US (called assassin bugs)

Many diseases aren't very well known

- A fungus grew in the oesophagus of a person who had had radiation treatment, at couldn't eat properly. This caused oesophageal shrinkage.
 - Antifungal treatment first
 - Expansion of the oesophagus by **balloon angioplasty**. This is putting an empty balloon in the funnel and blowing it up (very quick and only requires some sedatives)

A drug is a chemical agent that affects living matter

- Any preparation which, in a person's mind, had a beneficial effect on his/her well-being.

Prescription drugs are a 450 billion \$ industry in North America.

- Worldwide it's about 1 trillion \$ (in 2018)
 - This is only about 2 times what North America consumes. Huge consumers.

Over-the-counter (OTC) drugs are a 45 billion \$ industry (6B in Canada)

- Canada takes more OTC drugs than prescription drugs.

The Sumerians (2,200BC) had 16 beer recipes.

- A Sumerian tablet shows a person holding a poppy, which is where opium (morphine) comes from)
 - Morphine was isolated and purified for the first time in the 19th century

There was a focus on plant and animal materials to relieve pain.

- Hippocrates tried to exclude superstition. He did believe in these remedies.
 - The fat of a snake/lion/hippopotamus was thought to be a cure for baldness.
 - ⇒ Clearly false considering Hippocrates was always depicted as bald.
 - Ox liver was a cure for night blindness.
 - ⇒ Possible because it's a precursor for vitamin A
 - Poppy juice and excrements of flies were cures for crying babies
 - ⇒ Poppy juice because of opium, but how do you collect fly excrements?
- The Hippocratic oath is what doctors take: DO NO HARM.
- The profit motive is incompatible with devotion to the practice.
 - Doctors must learn to despise money.
- Galen thought that wounds are windows into the body (when gladiators were hurt)

The gold standard for a clinical study is double-blind. Neither the patient nor the physician knows what they're being administered (only a few people know)

- In the bible, a clinical study is explained where some men eat meat and others eat nuts.
- However, these studies weren't repeated for many years.

Discorides wrote a book: *De materia medica*. It showed medical plants.

- The drawings haven't been altered when republishing.
 - Wormwood: plant used in absinthe
 - Arum discorides: plant with expectorant properties
 - Saffron: with passum (sweet drink from wine) has diuretic properties

The Greek word for drug is pharmakon/pharmakeutes

Distilling was used to purify substances.

- Maimonides prescribed chicken soup for colds (broth of the fowl)
- We shouldn't be afraid to not know things. A friend will explain, an enemy will laugh.

Arabic and Persian worlds held on to logical methods of medicine.

- They were lost in Europe until 700AD when Moors brought it back to Spain.
- Doctrine of humors: blood (air), phlegm (water), black bile (earth) and yellow bile (fire)
- Paracelsus change life at the time by challenging nonsensical doctor's treatments (bleeding etc.)
 - He thought that some chemicals were more therapeutic than things from a goat stomach.
 - He opposed polypharmacy, the taking of excessive numbers of herbs instead of working out what is actually efficient
 - Only the dose makes the poison (poison and potion are interchangeable)
 - He was the first logical medical person in western history.

Poison dart frogs: very small animals that are highly coloured.

- Have a potent neurotoxin under their skin
 - Painkiller 200 times more potent than morphine
- Used on poison darts in South America
 - Roast them on fire and coat dart with the toxin that seeps out
 - Animals can be brought down with dart

Religion started to play a role in pharmaceuticals when monks started making potions, not only alcohol.

Mandrake root looks like little people and caused a lot of superstition.

- To get it out and not touch it, people would starve a dog and tie it to the root, and then offer it meat so the root would be pulled out.
- Like in Harry Potter

Blood transfusions were attempted but very rarely successful

- We weren't aware of blood types and infections

Smelling salts were used to wake people up from a faint. A modern equivalent is simple cures.

- Contains ammonia, which when smelled feels like needles running through the nose.

Bohme, a shoemaker, influenced a lot of philosophers with his ideas like Hegel.

- The doctrine of signatures: god has marked everything he created with a signature to indicate its purpose.
 - Walnuts good for the brain (look like a brain)
 - Hepatica acutiloba good for the liver (leaves look like liver)
 - Eupatorium perfoliatum (boneset) good for healing broken bones (stems grow through leaves)
 - Carrots good for vision (look like eyes)
- Bezoar stones were gall stones from a goat dressed up with a gold amulet
 - Used as a cure for the black plague
- Nails were added to wine.
 - The acidity of the wine dissolved some iron, so it was actually good for people

Pharmacists used plant remedies a lot

- Ipecac induces vomiting: if someone ingests something harsh (NaOH), it can save their lives
 - Makes you throw up instantaneously
- Aconite: the poison used by Romeo

Foxglove was discovered by William Withering from a beautiful flowery plant. It was used by gypsies.

- Good for heart conditions
 - Dropsy is congestive heart failure (because people would build up too many fluids and fall to the ground in weakness)
 - Doctors would bleed patients to get rid of fluids
- Book: *Account of Foxglove and its Medical Uses*. This was the first scientific article.
- Charles Darwin's dad wanted credit for Foxglove discovery (science is competitive)
 - Now called Digoxin (Lanoxin) medication for congestive heart failure
 - ⇒ Problematic for people with atrial fibrillation (A fib). 20% of people on this medication die earlier.
- Withering also wrote book accounting all the vegetables in Great Britain.

The first scientific journal came out in the late 18th century: *Medical repository*

- Account of the Plague of Athens (400BC) that is a medical mystery.
 - Very similar to the Ebola virus: vomiting, skin blisters, ulcers and diarrhea, then death.
- Text about manures because land was overused and needed to be fertilized

William Osler was an important doctor at McGill and Johns Hopkins (helped found schools of medicine)

- “Medicine is an art and not a trade. It is a calling and not a business.”
- You must think equally with your heart as with your head as a doctor.
- Listen carefully to patients, they will tell you the diagnosis
- Medicine classrooms were very vertical auditoriums to see the instructor well (in Redpath Library)
- The desire to take medicine is what distinguishes man from animals
 - This is false. Chimps and orang-utans find leaves with medicinal properties when they appear sick. Helen Morrogh-Bernard studied this in Borneo for over 20,000 hours.
 - They chew the plant and then rub it into fur: topical analgesic

Malaria is a parasitic disease that affects mostly Africa (50% of those affected are children)

- 60 out of 380 different types of mosquitoes are carriers
- Causes changes in the brain that makes people very lethargic
- It is considered to slow the economic growth of Africa by 1% a year (3-4% a year is a normal economic growth... so it's a lot)
- 1-2 million deaths a year, 120 million cases.
- An early cure was quinine (discovered by locals)
 - The wife of the viceroy of Peru was treated with this after contracting malaria, and it was named after her (Anna del Chinchon)
 - It comes from alkaloids in tree bark, in a tree that had 6% alkaloids
 - ⇒ Alkaloids are very active molecules, but there's much less in tree bark (abt 1%)
 - Soldiers took quinine for no malaria in the war. It had a bitter taste and was mixed with fizzy water.

- ⇒ This became known as Tonic Water: very small amounts of quinine. Need 0.5-1g per day for protection.
- It was first synthesized in WWII. Can be prepared in lab but it's much more effective to extract it because it's a complicated molecule.
- Artemisinin is another cure for Malaria. It's from a plant.
 - In an organic structure, if you change only one molecule the properties change.
- DDT can kill mosquitoes. It was synthesized in late 19th century and found to be an insecticide in mid 20th century.
 - It's so effective that Muller, who discovered it, won a noble prize in medicine.
 - It's toxic to insects but not to humans. Can be sprayed in solution.
 - However, it bioaccumulated in birds that ate insects.
 - ⇒ The shells of their eggs were too thin for parents to sit on.
 - ⇒ A book called *Silent Spring* was written about this
 - ⇒ It was banned by Western countries
 - By 1966, 500 million lives were saved by DDT
 - When DDT was banned, there was a peak in deaths in South Africa
- Insecticide treated nests work very well
 - However, people often live in open spaces with still water which is a breeding ground for mosquitoes
- Parasite-resistant mosquitoes can be engineered by genetic modification or by cross-breeding species
 - There's currently a lot of work concerning this.

- Dr. Lister in Scotland found that 1/3 of women would die in childbirth in the 1800s (very bad odds)
- Doctors didn't use gloves at the time
 - Using a phenol, a disinfectant usually used for floors, as a spray in the room, the death tolls went down.
 - People trusted phenol so much that it was often burnt, and its smoke inhaled (harmful)
 - He eventually found that the spray was unnecessary, and that washing hands and wearing gloves was far more effective.
 - Sepsis, also called SIRS (systemic inflammatory response syndrome) is the body's response to infection and can lead to general inflammation and blood clotting, which can cause organ failure and gangrene (damaged tissues)
 - Thomas Roddick worked with Lister and brought antiseptic technique back to Canada (Roddick gates)
 - Lister's name was associated with the product *Listerine* that contained phenol at the time.
 - It was used for bad breath and dandruff control
 - Thymol (menthol) is like phenol but safe
 - Propofol also resembles it very much. This is the painkiller that Michael Jackson OD'd on.
 - **Small differences in molecules change the physiological response.

The patent medicine era is from the 1850s to 1906.

- Pharmacies could deliver anything they wanted to the public.
- False claims were made about medications that were actually only extracts of plants, heroin, cocaine, chloroform, turpentine and other harmful substances that could be passed on to the public.
 - **Scrofula** is another name for tuberculosis.
- Collier's magazine (like McLean's) started a campaign to get rid of all of these hazardous materials from drugs.

The FDA changes regulations for what/how drugs could be sold in pharmacies.

- Before, Pinkham's vegetable compound claimed to heal everything.
- After 1906 regulations, claimed hardly anything.

Salversan 606 was a medicine to treat syphilis, that was named so because it was the 606th compound the scientist had tested, and it worked the best (early 1900s)

- There were no ethic boards. Often, people in prison were used in clinical trials.

Aspirin (acetylsalicylic acid) was also developed during this era.

- Some think that's it's good to take it for the heart (blood thinner)
- It causes stomach bleeding
- Close to the extract from a willow tree that native people used before (salicylic acid)
- There were advertisements for the Bayer pharmaceutical company on trucks: aspirin but also heroin until it was realized that this wasn't a good medication.
- Aspirin had a huge impact during the late 1800s and early 1900s

In 1938, there was a revision of the 1906 FDA regulations that required proof of safety, and the regulation of cosmetics and food. There were no regulations for opioids.

Thalidomide was a medication for pregnant women with morning sickness taken in the US and Canada.

- It is a **teratogen**, meaning it causes birth defects.
- People who are now in their 50s were born with limbs affected.
 - Guy with short arms that is a baritone opera singer
 - Guy with no arms that plays guitar with his feet
- Dr. Frances Kelsey (McGill graduate) was in charge of the FDA research of thalidomide.
 - She didn't feel the testing had gone far enough on animals, so she blocked it from the market
 - Teratogen qualities were found shortly after and she was given an award by Kennedy
- It's still being considered for other diseases: myeloma (blood cancer), multiple sclerosis (MS), UBD/Crohn's, other cancers, Sarcoma, canker sores, leprosy etc.
 - It probably won't be used/approved due to the baggage this drug carries.

In 1951, drugs were divided into two categories of sale: over-the-counter (OTC) and prescriptions

- Before, prescriptions were only for narcotics and cocaine

New drugs take 10-15 years to develop and cost 2-3 billion \$

- Drugs can be fast-tracked if they're for a very important disease
- The steps are: identifying target, finding leads, developing leads, picking candidates, making drugs, formulation, toxicology, clinical trials and approval.
 - Most costly as of making the drugs
- Good research stops toxic drugs from getting on the market

Only about 30-35 new drugs are approved each year

- The costs of developing these has gone up massively
- Target 10-12 years to make it to the marker

Kaplan-Meier plot: looks at drug effects compared to placebo effects

- We expect a 30% reduction in risks with the placebo
- The drug needs to be at least 50-60% effective to hit the marker
- The drug should show a straight line (not dipping down into risks)
- The placebo should dip down a lot further than the drug

New drugs can originate from many different places:

- Frogs (pain medication) toxins can be modified to be less toxic and be therapeutic.
- Periwinkle plant gives vincristine, a powerful cancer drug
- Shaman and native tribes have ways to treat in which we can sometimes find real therapeutic compounds

Molecular modeling now allows us to know the 3D structure of a drug (make it fit to binding site)

- The drug acts like a key in a lock (receptor) and can cause the body to stop producing something and have it function better.
- With molecular modeling, we can find active sites and then carve out the right shape for a drug to interact properly with it.
 - Interleukins 1 are a family of 11 cytokines that are small proteins that have a role in inflammation and cell signaling
 - When there's an interaction, we can modify one or the other of the units to disrupt the activity at the binding site

Fragment based lead discovery is based on the fact that simple atoms bind to biological targets for multiple purposes, and are sometimes known to be important

- If we get a drug to bind to several different sites, it'll be more effective at a lower dose

Drugs with most prescriptions in the US per year (similar to Canada)

- (1) Synthroid → Thyroid conditions
- (2) Crestor → Cholesterol
- (3) Ventolin HFA → Asthma
- (4) Nexium → Acid reflux

Drugs that make most money in the US per year (similar to Canada)

- (1) Humira → Arthritis
- (2) Abilify → Anti-psychotic
- (3) Solvadi → Hepatitis C
- (4) Crestor → Cholesterol

Drugs that make most money in the World per year

- (1) Humira → Arthritis
- (2) Eyelea → AntiVEGF (eye tissue)
- (3) Revlimid → Multiple myeloma (cancer)
- (4) Rituxan → Cancer
- (5) Enbrel → Arthritis

There are fewer and fewer pharmaceutical companies because the bigger ones are buying them up

- (1) Johnson & Johnson (378B\$)
- (2) Roche (224B\$)
- (3) Pfizer (204B\$)
- (4) Novartis (223B\$)

(5) Merck (178B\$)

- The top 4 together equate to Apple.

The US is the 3rd most populous country but accounts for ½ of all of global medication sales

- Canada is 3.8% of global drug sales. Our population is about ½ of the UK, but we take as many drugs.

To know the number of years it takes to double prescription sales = $70 / \% \text{ increase per year}$

Sometimes, drugs for something are then found to have another purpose.

- *Minoxidil* was initially researched for high blood pressure but found useful for hair growth

Drugs are cataloged and coordinated based on many different factors (i.e. formulation, derivative, combination etc.)

Excipients are the materials in pills that aren't medicinal. They can be separated into 40 categories.

- Expiry dates on medicine isn't always useful.
 - Part of aspirin will hydrolyse to acetic acid (5% maybe), but it'll just smell like vinegar.
 - Don't throw out medication past the date so they don't get concentrated in nature.
- Excipients are a 4B\$ market worldwide to stabilize drugs and make them last longer.

Side effects for all drugs are very similar.

- If more than 1-2% of people experience effects, they must be listed

The placebo effect (or response) can still happen even if people know they're taking a placebo.

- Makes people feel better 1/3rd of the time
- Amir Raz (McGill) is studying this as a medical feature

Key risks aren't always diseases.

- Obesity is massively going up.
- Cigarettes used to be much more prevalent, even on airplanes.
 - Smoker and non-smoker sections. Culture around this has changed a lot.

Julian Adams was an undergraduate in the prof's lab. He ended up becoming the primary developer of *Velcade* for multiple myeloma (bone marrow cancer).

- This drug generated 2.7B\$
- He saved his wife's friend's life and also Matt Damon's father's life.

Toxicology

Toxicology is the study of the effects of chemicals on living organisms

- This encompasses everything we do: food, cosmetics etc.
- Toxicologists are most concerned with humans
- It's very confusing due to the internet and misinformation. We are in the era of fake facts.
 - Eat fish because of Omega-3 fats that are beneficial to health, reduce the risk of arrhythmia, and when eaten during pregnancy, kids have higher IQs. However, limit intake because fish are contaminated with mercury and PCBs.

North-American diet (meat based): meat is contaminated with dioxins from incinerators that get into rain and then grass, and the cows eat grass.

Grain-based diet: Anything baked with wheat contains acrylamide (toxic).

Alcohol: ethanol is a known carcinogen

- New research finds that NO alcohol is safe, and it is a risk factor in disease even as of one drink a day.
 - This study was criticized based on an overall graph that combined data for all diseases and showed little to no difference at one drink a day.
 - However, the details are important! Sometimes risks go up with alcohol and sometimes they go down. The overall graph was an average that considered all conditions studied.
⇒ Breast cancer risk increased a lot with 1 drink a day.
 - The criticism was misleading because with specific conditions, there is an increased risk as of one drink.

Tap water: chlorinated to kill microbes, but this can lead to the formation of trihalomethanes (by-products of water chlorination), that are known carcinogens.

Big bottles of water: made with polycarbonate plastic called bisphenol A (BPA) that is a known endocrine disrupter.

Small bottles of water: made out of polyester with a catalyst that's an antimony compound, that stays behind and leeches into the water. Antimony is in the same family as arsenic.

Antiperspirants: preserved with parabens.

- One study connected parabens to breast cancer since they're endocrine-like compounds.
- It's based on flimsy evidence: by blocking sweat glands in armpits, toxic compounds accumulate in lymph nodes near breasts and cause cancer.
 - Sweat glands don't release anything into the blood stream. Carcinogens are removed by the kidneys and the liver.

Shower curtains release 108 chemicals when we take showers.

- Testimonial to the talent of analytical chemists that can find substances down to parts per trillion.
- This doesn't mean the chemicals are actually doing anything.

Nail polish: to conform to the nail, dibutylphtalate is added as a plasticizer, but this is another endocrine-like substance.

- In high doses administered to pregnant rodents, the male offspring have a smaller distance between rectum and testicles.... This is very uncertain.

Pillow: made of polyurethane that releases isocyanates into the air.

Balloons/condoms: expose you to nitrosamines, known carcinogens.

*Science is ALL about numbers. We always have to know how much.

- Ex. In polyester bottles, the catalyst shows up at 3 parts per billion (1 ppb is 1 second in 32 years). The ADI is 6 ppb.
- **Acceptable daily intake (ADI)** is the amount that you can consume every day of your life without any issues.
 - This already has a huge safety factor in it.
 - No testing on humans (unethical) so tests are on animals.
 - You give the animal increasing doses until you see effects. Then you cut back until there's no effect whatsoever to find the **NOAEL (no observed adverse effect level)**
 - NOAEL/100 is the ADI

Hazards and risks are not equivalent terms.

- A **risk** is something you can try to minimize (you can do something about)
- A **hazard** is the innate property of a substance/process to do harm
 - Risk is a function of hazard. $\text{Risk} = \text{hazard} * \text{exposure} * \text{vulnerability}$
⇒ Children and people with medical conditions are at greater risk (vulnerable)

Chemicals aren't to be feared or to be worshiped. They're to be understood.

- 134 million known chemicals make up the world (99% are naturally occurring)
- It's remarkable that people are healthy when so many things can go wrong.
 - There are 3000 chemicals in urine.

A cup of coffee contains 1000 different chemicals, some of which are known carcinogens.

- Caffeic acid, benzene, styrene, formaldehyde, furfural are all carcinogens
- However, coffee isn't a carcinogen
- This could be due to small amounts of the chemicals, or interactions between them that get rid of carcinogenic properties.

In California, carcinogens that are known must be revealed to the public by warning signs.

- This is counterproductive because they're everywhere, so they become invisible

Natural substances aren't necessarily safe; nature isn't benign.

- The juice of the hemlock plant (coniine) was used for executions in Ancient Greece
- The castor bean plant contains ricin, a chemical weapon (powder in an envelope)
- Poison dart frogs have poison in mg quantities.
- Bacteria and viruses can be very pathogenic

Synthetic substances aren't necessarily dangerous.

- Aspirin (acetylsalicylic acid) is a better alternative to salicylic acid from willow bark, that's very irritating to the stomach.

The only way to know the toxicology of a substance is by studying it.

- Publishing in peer-review literature is the best way. However, this isn't fool proof.
 - Papers are sent to referees, who can ask you to rewrite part of it
 - However, they can't redo entire experiment, that's often the work of several years
 - ⇒ They have to assume that what is said was done was actually done
 - Ex. The paper linking autism to vaccination was published in a prime medical journal
 - ⇒ 15 years later, no one else was able to correlate these things experimentally.
 - ⇒ It was found that this study was published to defraud vaccination companies
- A new study shows that aspirin should be taken daily only if recommended by a physician
 - Not useful to reduce risk of heart disease and stroke if no pre-existing condition, because it causes gastrointestinal bleeding

In the late 1500s in the amazon, monkeys jumping from one tree to another could be hit with arrows. Walter Raleigh discovered this.

- The name and potency of the poison was dependant on how many more trees the monkey could jump to.
 - Ex. 3-tree poison means the monkey jumped 3 trees before paralysis
 - A one tree poison would be much more potent.
- The substance on the darts was called Urari (means he to who it comes, falls)
 - A natural poison extracted from the vine
 - Curare is the English term
 - ⇒ Waterton, an English physician, saw that curare in the right dose caused muscle relaxation (early 19th century)
 - ⇒ Bernard found that curare blocked nerve impulses from the brain to the muscle
 - The active ingredient is tubocurarine.
 - It was used in surgery for muscle relaxation.
 - ⇒ In Montreal, Dr. Harold Friffith was the first to use it at the Queen E medical center.
 - ⇒ It's more effective as a standardized dose called Pavulon (synthetic).
 - ⇒ This same drug was used to carry out executions

Paracelsus (16th century) said "only the dose makes the poison"

- Aspirin in 1-2 tablets makes a headache go away, but the entire bottle will kill you.
- Sulfanilamide predates penicillin and was used as a remedy for strep throat (usually kids)
 - In Europe, it was used as a pill
 - In the US, children were used to taking liquid suspensions.
 - ⇒ Watkins (a scientist) found diethylene glycol as a solvent.
 - ⇒ He tasted it with his finger to make sure it was safe.
 - ⇒ 107 people died from this, as it was toxic.
 - ⇒ Watkins didn't believe his solvent had killed people, so he drank some of his medicine. He then had to ask for an antidote. He committed suicide.
 - ⇒ Frances Kelsey (for the CDC) worked to recover 234 out of 240 sold gallons.
 - Due to this incident, Roosevelt signed a law for drugs to be thoroughly tested before being put on the market

Although some substances are harmful even in minute amounts, most fall into the category with a safe threshold.

Hormesis is a biological phenomenon in which a beneficial effect results from exposure to low doses of an agent toxic at higher doses.

- A small amount of sunshine allows vitamin D synthesis, but too much exposure to UV light can be a carcinogen
- There's also the possibility that a small dose could be more harmful than a large dose of a same substance.
 - BPA has a greater effect on prostate tumors at a smaller dose than a larger dose

Some foods can also be very dangerous.

- Lima beans contain amygdalin which can release cyanide poison upon digestion
- Cassava is a potato-like tuber that makes up a large part of the diet in Africa. It contains amygdalin which can become cyanide if not properly processed.
- Pufferfish has to be prepared by trained chefs because it contains a very toxic substance that can kill a human in trace amounts.

Clostridium botulinum is an anaerobic bacterium that produces botulinic toxin, which is the most toxic substance we can come across. Its name is Latin for sausage.

- 0.03mg can be fatal. Can be found in anaerobic conditions (unwashed garlic stored in oil)
- Botox can be used to stop tremors, treat anal fissures and headaches, or reduce the appearance of wrinkles

Toxicology is a very difficult science due to many different variables.

- The type of exposure can have a very big impact. Ingested, topical etc.
 - Substances highly toxic when eaten can be fine when inhaled or on skin.
- We are all biochemically individual.
 - Some people may be much more susceptible.
- The effects may vary.
 - Acute effects will be observed after a one-time big dose.
 - Chronic effects arise when a small dose is administered over a long period of time (bioaccumulation)
 - Teratogenic effects only affect the next generation (offspring)
 - ⇒ Ex. DES was a drug for women with a history of miscarriages. There was an increased risk of vaginal cancer among female children (1 in 1000 risk).
 - ⇒ BPA exposure is less than 1/1000th of that dose of medication.
- It's difficult to recognize a toxin because we're exposed to so many different things.
- Humans aren't giant rats and don't have similar physiology, so animal models are not always applicable.
 - Dogs resemble us more, but chocolate is toxic to them.
- We're influenced by psychological factors
 - The nocebo effect can happen if you believe that something will do you harm.
 - ⇒ Fluoride was a rat poison before being used in water. People in the first town to have fluoridation said they experienced symptoms, yet the water fluoridation equipment hadn't arrived yet.

In 1903, Dr. Wiley of the Bureau of Chemistry (precursor of the FDA) was concerned with chemicals added to food.

- Enlisted volunteers in the poison squad (A.K.A. the borax unit)
- Were served very good meals that would be doctored with substances often used as food additives and preservatives (0.5-4g a day). The chemicals were consumed in gelatin capsules.
- All the meals were eaten at the hygienic table.
- Urine and feces were collected from the volunteers.
 - High doses of substances caused nausea, vomiting and stomach aches, but no long-term consequences were noted.

The Pure Food and Drug Act of 1906 was caused by the poison squad findings. This still didn't require proof of safety or effectiveness.

- Today, we have very stringent regulations. We still can't prove if things are ok for everyone in all conditions.
- Overall, the human body deals very well with toxic substances.

Detoxication involves the kidney and the liver.

- Phase I enzymes convert potentially toxic substances to water-soluble compounds to facilitate excretion.
 - Cytochrome P450 family
- Phase II enzymes attach their unit to allow transportation out of the body even more easily.

When you barbecue meat, you form benzopyrene (a by-product of fat combustion) that's insoluble in water.

- In an attempt to make it soluble, phase I enzymes attach an oxygen to it. This forms a carcinogen because the O can now interact with DNA.

Detoxication enzymes can be induced by certain products.

- Green tea, broccoli, broccoli sprouts and garlic: glucuronyl transferase
- St-John's wort is an example of how this can have a negative impact.
 - It stimulates cytochrome enzymes.
 - After a heart transplant, the gentleman was given an immunosuppressant (cyclosporine) to not reject the transplant. The body still tried to reject it.
 - ⇒ St-John's wort stimulated cytochrome P450 which metabolized the cyclosporine more quickly and reduced its levels dramatically.
 - ⇒ It's sold as a natural antidepressant or anti-anxiety medication (nature's Prozac)
 - Many medications are reduced by St-John's wort. Always tell your physician what you're taking.

Xanax is a common anti-anxiety agent that can build up if cytochrome inhibitors like antifungal ketoconazole are taken with it.

- Therapeutic activity also reduced by St-John's wort.

Acetaminophen (Tylenol) should never be taken with alcohol.

- Alcohol induces cytochrome 450 which creates the reactive intermediate instead of the easiest pathway (glucuronyl transferase). This can cause severe liver damage.
- There's a third pathway once the reactive intermediate is created, that stops liver damage. It's induced by glutathione.

- Glutathione is available as a supplement but it's useless taken orally.
- n-Acetylcysteine is the limiting amino acid. It can be taken to alleviate liver damage.
 - ⇒ You need a huge amount through IV to detoxify liver when alcohol-acetaminophen poisoning

In the last few years, liver toxicity has gone up due to supplements.

- Aegeline is a natural plant product in gym supplements has made people need transplants.

Red blood cells carry oxygen through the blood by hemoglobin.

- Heme binds to oxygen, but eventually has to be broken down. It then forms bilirubin.
- Bilirubin is excreted by the liver using glucuronyl transferase.
 - If the liver isn't functioning properly, bilirubin builds up and causes **jaundice**.
 - If it builds up in the brain, there can be severe damage.
 - ⇒ This can happen with premature babies with insufficiently developed liver. Blue light allows bilirubin to become more accessible to transferase and exit the body. (Bili light or bili blanket)

Allergies are very common.

- Seldane was the first non-drowsy allergy medication.
 - It gets converted to its soluble form in the body, which is the actual active metabolite.
 - When taken with antifungal ketoconazole, cytochrome is blocked which causes original material to build up. This triggers heart attacks.
 - The way to deal with this is to market the active metabolite: Allegra.

Felodipine is an anti-hypertensive medication.

- When ingested, it's metabolized by cytochrome p450.
- If cytochrome is inhibited, too much can build up and the blood pressure will become too low.
 - Grapefruit juice inhibits cytochrome p450. MUHC has banned it as a safety precaution.
 - ⇒ Furanocoumarins are the part of grapefruit juice that inhibits cytochrome.
 - ⇒ This is a promising possibility for mixing it in with drugs to need less of the actual drug, which would reduce the side effects.

Monoamineoxidase inhibitors (MAOI) allow higher concentrations of norepinephrine, serotonin and dopamine.

- This lowers depression.
- MAO is the enzyme that metabolizes these neurotransmitters.
- When taking an MAOI, you must avoid certain foods.
 - Tyramine from cheese builds up and causes hypertension and stroke.

Activist groups say that it's a miracle we're alive when so much is toxic around us.

- Quackery is science without corroborating evidence
- Research about plastic ducks that have bacteria and fungi inside.
 - Ducks without holes in them won't have bacteria inside.
 - We don't live in a sterile environment!

What we should actually be wary of:

- Moth balls contain 1,4-dichlorobenzene which can cause severe respiratory problems
- Cosmetics (soaps, perfumes, creams) can contain lylal which is an allergen

LD50 is the amount that'll kill 50% of a population.

- It varies from one species to another.
- TCDD is the most potent carcinogen in animals.

Dioxin is the most toxic man-made chemical.

- It is never made on purpose. It's always a product of a side reaction.
- TCDD is the most toxic of all the dioxins.
- Darwin discovered plant hormones called auxins in 1928.
 - 2,4D and 2,4,5T are chemically similar to auxin and behave like it. They cause plants to grow so fast that they can't get the necessary nutrients and die.
- During the Vietnam war, a mixture of these chemicals was sprayed onto the forest to kill trees, so armies couldn't hide.
 - This was called agent orange due to the orange band on the drums containing chemicals.
 - The barrels got contaminated with TCDD through a side reaction where two 2,4,5Ts react with each other. This is ONLY possible with 2,4,5T because there has to be 3 chlorine atoms to create TCDD.
 - 2,4D can't create TCDD. It'll form a dioxin with two chlorine atoms, which is non-toxic.
 - 2,4,5T hasn't been manufactured for years due to this.

When we burn polyvinylchloride (PVC), TCDD is created.

- Incinerators that capture organic molecules can be used to stop TCDD from getting into the environment.

In Seveso, Italy, manufacturers of chlorohexidine created TCDD in an unfortunate chain reaction.

- Soil from around the plant is still filled in drums.
- Men who were exposed fathered a disproportionate number of girls
- There was an increase in cancer and lower sperm count in children whose mothers were exposed during pregnancy

The former president of Ukraine, Victor Yushenko, was given dioxin in food as an assassination attempt. It didn't kill him.

- He has severe chloracne, a common symptom of TCDD poisoning.
- He had the most dioxin exposure anyone ever had and is still alive
 - 1000 times more than animals in tests.

In Vietnam, there is circumstantial evidence that there were more birth defects after agent orange.

Love Canal was a neighbourhood in NY built on top of a waste disposal site that didn't maintain waste properly. Dioxin soaked into the soil and water systems.

- Residents recalled a disturbing chemical sent
- Nobody wanted to buy their houses, so the government moved anyone who wanted to go.

There are some unreasonable concerns about dioxins, especially that TCDD is formed when heating plastic in the microwave.

- This only happens in incineration of plastic that contains chlorine.
- Still, don't use plastics that aren't microwave safe.

Summary:

- Numbers matter! We need to know how much and in what conditions, otherwise data is meaningless
- Chemicals are the building blocks of life.
- Natural doesn't mean safe, and synthetic doesn't mean dangerous.
- An association doesn't mean it is cause-effect.
- Repetition of a false statement doesn't make it true
 - Dioxins are NEVER formed in microwaves
- Opposing views aren't equal
 - Global warming IS an issue
- You can't always predict outcomes
 - Who could've known that we would find frion from refrigerators destroying the ozone layer
- Nonsense can be made to sound scientific
- The plural of anecdote isn't data
- Certainty is elusive in science. It's a race to a receding finish line.

Toxicology can conjure up images of poison, but we often indulge in alcohol.

- With alcohol abuse comes hangovers. The severity can be due to dehydration, low blood sugar or not sleeping well because of inebriation.
- Some drinks make hangovers worse: tequila and whiskey contain congeners that give taste but cause worse hangovers.
- Sunscreen for alcohol: dihydromyricetin (DHM)
 - From the Japanese raisin tree and other plants.
 - ⇒ Used in traditional Japanese medicine for alcohol poisoning and muscle spasms
 - Was studied in rats in 2012 and was found to counteract acute alcohol withdrawal symptoms and led to rats consuming less alcohol.
 - ⇒ The founder of the company selling a hangover cure used this paper as proof
 - ⇒ Although the experiment had 315 rats in it, some experimental groups had only 2 rats in it.
 - Was tested on humans with 19 men and 8 women.
 - ⇒ There was a 50% decrease in hangover symptoms.
 - ⇒ However, there was no blinding or placebo control
 - ⇒ Methodology: volunteers got drunk and reported feelings next day, then got drunk again with the pill and reported it.
 - ⇒ This is not legitimate.
- The issue is that we still don't fully understand hangovers.
- Abstinence and moderation are the only ways to avoid them.

Allergies

You can be allergic to anything you encounter, even food.

- In a Montreal hospital, a woman threw a tomato sandwich at a man and he immediately went into anaphylactic shock. At least he was in a hospital.
 - He was allergic to salicylates, that are in a lot of plants (fruits and vegetables)
 - The woman was charged with assault with a deadly weapon

An allergy is an adverse reaction to a substance that's usually harmless, where IgE antibodies are involved.

- It's a reaction between allergens and antibodies
- 10-20% (low estimate) of the population has an allergy
- The richer the country, the higher the allergy prevalence
 - More likely to be diagnosed and see a doctor in a rich country
 - Exposure to many more chemicals in cleaning products and everywhere. The more you're in contact with, the higher the risk of a reaction.

Anaphylaxis is a rapidly progressing, life threatening allergic reaction that can cause the circulatory system to collapse and breathing to stop.

- The allergen is what you're reacting to
- Atopy is the genetic tendency to develop allergic diseases and asthma.
 - Atopic dermatitis: when babies develop redness (eczema), they're more likely to develop hay fever
 - ⇒ 50% get asthma
- Hay fever (allergic rhinitis) is an allergy to pollen, pet hair, dust and mold.
 - You can only be allergic to hay if it's contaminated with mold
 - ⇒ Roll in the hay frat party where 20 students were hospitalized due to inhalation of mold spores
 - It's usually a reaction to pollen, the plant equivalent of sperm
 - ⇒ Pollen is small spheres made up of a protein, which is the real allergen
 - Common symptoms include sneezing, red eyes, watery eyes, cold-like symptoms
 - ⇒ Geographic tongue is only discoloration, and no sensation

Allergies to animals are actually to the proteins in animal cells.

- Allergies to dust are often allergies to the proteins in skin cells that are in dust.
 - You can't be allergic to the hair. It's simply a vehicle for the skin cells
 - You're 4 times more likely to be allergic to a black cat due to genetic difference with other cats
 - ⇒ Its cells have a more allergenic protein (why black cats are unlucky?)
- Even if they're not allergic to animals, people with asthma can have their condition triggered by animals

Dust mites are everywhere on your body and in dust. They're microscopic animals.

- An allergy to dust mites is actually an allergy to a protein in their feces.
 - Their feces can get into the air and cause allergies to dust
- Dust mites can be found in mattresses
 - You can get bed covers that lock in the dust mites, or vacuum a lot

Total allergy syndrome, also called 20th century disease, is an allergy to everything having to do with modern living.

- Can cause a reaction to perfumes, cleaning agents, foods, soap, paint
- People who have this pathology need to live in an isolated environment, often with their walls lined with aluminum foil (non-allergenic)
- There's a large psychogenic component to it. Often people who are concerned about modern living, pharmaceutical companies and toxins in the environment.
 - When in isolation chambers, they can be exposed to things they say they're allergic to and not have a reaction.
 - Sometimes, however, this is very legitimate.
 - ⇒ Woman who came to see prof about strong reaction to acetone.
 - ⇒ He hid acetone and she knew right away.

Food allergies are extremely common.

- Fish is a very dangerous/severe allergy that the prof suffers from (easy to avoid fish)
- It's recommended to eat fish twice a week because of fatty acids

You must have prior exposure to an allergen to have a reaction. There's never an allergic reaction on the first encounter.

- At the first encounter, the body generates antibodies
 - It isn't always clear when the first time happened
 - ⇒ Gelatin in marshmallows and then allergic reaction when vaccine
- The next time it attacks the allergen

Royal jelly is secreted by worker bees for larvae. The queen bee has it for longer.

- You can have a reaction even the first time, because you're reacting to pollen

Allergies are increasing. The rates have doubled since 1980

- Asthma is at an all-time high
 - This could be due to population increase (if there are more people, more people will be allergic)
 - We're more likely to be diagnosed in the developed world
 - We have a greater chemical exposure (more scented products in the house)
 - ⇒ The degree of pleasantness of a smell has nothing to do with its capacity to induce allergic response
 - ⇒ Most scents are synthetic substances, and there are more and more of these
 - Psychological factor: a group of asthmatics were exposed to a rose scent. Roses are not known to be an irritant.
 - ⇒ Half of them were told the scent would make their asthma better. It did.
 - ⇒ Half of them were told the scent would make their asthma worse. It did, actually causing increased airway inflammation.

There are a lot of connections between allergies and other substances that might've induced them.

- We always need to look for several studies that have the same results (consensus).

The hygiene hypothesis stipulates that we're being too clean, and by wanting to live in an antiseptic world, we don't properly prepare our immune system to fight off threats.

- Like a loaded gun, it attacks itself when there are no enemies
 - 2800 school children in Ecuador had less allergies if they'd been infected by a parasitic worm in the past
 - Children in daycare are less likely to become allergic because they're exposed to a lot of bacteria
 - ⇒ Less likely to develop Hodgkin's lymphoma and leukemia, which can be fought off by the immune system
 - Dairy farmers are 5 times less likely to develop lung cancer because they breathe in bacteria which prepares the immune system
 - Cotton factory workers have lower rates of some cancers because cotton has endotoxins that are produced by bacteria as well as cancer, which prepare the body to fight cancer

The microbiome is very important.

- Contact with bacteria early on in life can change its composition.
- Babies born by C-section have a different microbiome to those born through the birth canal (bacteria from the canal)
 - C-section babies are more prone to develop allergies

4% of adults have food allergies, which translates to millions of people

- An allergy MUST involve antibodies and people can react at trace amounts
- 30% of people have food intolerances, which are due to missing enzymes
 - They require a significant amount of material to cause discomfort

Several foods are extremely allergenic: tree nuts, soy beans, fish, peanuts, shellfish, eggs, wheat and dairy

- The proteins are different in each category.

Some symptoms from food allergies wouldn't be automatically linked to them

- Bags under the eyes
- Tongue reactions (lesions, painful)
 - It's difficult to know what you're reacting to since food contains so many compounds

Yellow dye #6/sunset yellow dye is an allergen

- A physician had terrible gastrointestinal pain to the point of needing morphine. He'd had cereal, vitamin pills etc. with yellow dye.
 - The only way to trace down an allergy is by writing a very rigorous food diary.

Allergies to peanuts are caught quickly and can be very serious.

- It takes a remarkably small amount of the allergen to cause a reaction
 - Wrapped candy bar with peanuts can still cause a reaction
 - ⇒ This means that the protein had to go through the wrapper. Protein volatility is minute, so this means it was a very small amount.
 - Girl kissed her boyfriend who'd had a sandwich and dies.
 - ⇒ When you're in anaphylaxis, you often have 4 minutes to live. An ambulance takes 8 minutes to get there.
 - Dental student at McGill ate at Strathcona cafeteria and had a reaction. His best friend forgot the combination to the locker and couldn't get the epipen in time. He died.

- ⇒ Always have your epipen on you
- ⇒ Don't trust attendants behind a cafeteria counter to know what's in the food
- Canoe trip at a camp in the Laurentians. A girl had a reaction but her epipen was in the doctor's office at the camp. She died
 - ⇒ Ongoing legal battle
- Epipen is synthetic adrenaline (epinephrine)
- Benadryl is diphenhydramine

Israel had a very low rate of peanut allergies.

- At 6-8 months, Bamba (snack) is given to children. It has some peanuts in it.
 - There's a window in which you can expose children to allergens to desensitize them.
 - ⇒ You need small and controlled exposure
 - ⇒ Must be very careful because those with atopic dermatitis are very prone to reactions

More allergies to sesame seeds because of sesame seed bagels.

Soy beans are low in methionine (amino acid), but otherwise cheap and easy to grow.

- To be the best feed for animals, methionine is necessary. Not meant to be given to humans.
- The gene for methionine in brazil nuts is put into soy beans, because they're rich in it.
 - This was tested for allergens due to the off-chance humans would eat it.
 - Those with allergies to brazil nuts had an allergy to transgenic soy beans
 - ⇒ So, the research was abandoned. Testing works.

Allergies to insect stings usually cause only skin rashes. Anaphylaxis is rare.

Contact dermatitis is a skin reaction that can happen to anyone. It is a dose-dependent irritation.

- Putting hands in concentrated NaOH

Immune system mediated dermatitis is an allergy, and only affects those who are allergic. It can look like a contact dermatitis.

- Poison Ivy
- Japanese lacquer tree (toilet seats)
- The most widespread contact allergy is to nickel metal.
 - This can be demonstrated with a coin. Snap on a garter belt, purse clasp, cell phone casing...
 - Jean buttons are made with nickel that's covered with copper
 - ⇒ Brooke Shield did Calvin Klein ads that insinuated wearing them without underwear. This caused the copper to wear off and many people had a reaction.
 - Necklaces are often made with a gold-nickel alloy
 - ⇒ You can cover jewelry in a shielding material, like clear nail polish
- You can also have allergies to detergents, glue in shoes, henna, makeup, jewelry cleaner
- Hair dye: try it on arm or neck first. The reaction can affect your entire body.
- A new brown dye used in German money caused people to react through their pockets

Hydrocortisone is the main weapon of a dermatologist against skin conditions.

Benadryl is an antihistamine that you can get as a pill or as cream

You can have allergic reactions to nail polish (gel) or fake nail glue.

The rubber tree is tapped for latex. Gloves and condoms can be allergens.

- Before surgery, you can be asked if you have an allergy to papaya, because it is a similar plant to latex

The surgeon general had a reaction to his underwear waistband

- It was found that a plastic used for this is highly allergenic

A woman had an allergy to coke when her boyfriend consumed it and then they had sex, but not when she consumed it directly

- The coke was somehow transformed in his body in a way that it wasn't in her own

Aquagenic pruritus is an allergy to water. When water touches the skin, it erupts.

- Not internally allergic, so you can still drink water,
- To wash, you must use alcohol or rinse and dry quickly with water.

Photoallergy is an allergy to the sun, that's usually triggered by something else.

- The wife of the chancellor of Germany received penicillin as a treatment for an infection, and her allergy to sunlight was triggered
- She had to live indoors with the blinds shut
- She committed suicide.

Mechanisms of an allergic reaction:

- White blood cells called mast blood cells are central to allergic reactions
 - They harbor histamine
 - When they associate with the allergen, they explode and release the histamine
 - They explode: Superman explosion of Krypton
- Histamine makes you scratch, sneeze and cough. It's your body's effort to get rid of the allergen.
 - It's a key that fits into receptors (key locks). When they meet, there are symptoms.
 - An antihistamine has chemical similarity to the histamine and occupies the receptors while not causing symptoms (key in lock but it's not the right one so it won't turn)
- Allergen (AG) is the bad guy. IgE is the good guy who tries to protect you. They get into a fight and there's an explosion that releases histamine, and triggers symptoms.

Chlortripolon was the first drug even developed with an understanding of molecular structure.

- It was an antihistamine but that made you drowsy, so you couldn't drive.
- It's now used as a sleeping agent.
 - An example of using a side effect as the main purpose.

Avoidance of the allergen can also be used to avoid the reaction.

- For pollen, you can use positive pressure sunglasses, or glass helmet
- Eventually, there might be hypoallergenic milk.

Non-drowsy antihistamines had issues at the beginning with antifungal ketoconazole.

- This was dealt with by synthesizing the active metabolite: Allegra.
- People respond differently to different antihistamines:
 - Reactine and Zyrtec: Cetirizine
 - Claritine: Loratidine
 - Sudafed: Only decongestant (if only symptom is congestion)

- Those based on steroids are extremely effective. They reduce inflammation and are innocuous to health.
 - Beconase, Rhinocort and Flonase
- There are also some natural remedies.
 - Butterbur is a plant with decongestant qualities, sold as petadolex
 - ⇒ Not as efficient as actual medication
 - Stinging nettle leaf extract has mild antihistamine properties

Asthma makes you feel as if you cannot breathe. It can be induced by allergies.

- Leukotrienes are released instead of histamines.
 - They interfere with bronchial tubes
 - Anti-leukotrienes like Singular or Montelukast work
- During an attack, you need immediate dilatation of the bronchial tubes
 - Adrenaline is the fight or flight hormone. It allows you to do things you can't usually do when in high-stress situations. To do so, you need more oxygen, so it dilates bronchial tubes.
 - ⇒ Adrenaline receptor agonists can be used during asthma attacks
 - ⇒ These are rescue inhalers
 - ⇒ Ventolin activates faster than taking actual adrenaline

To prevent an asthma attack, steroids can be taken to reduce the constant inflammation of an asthmatic system, that gets worse when there's exposure to a trigger

- This reduces the chances of having to use a rescue inhaler
 - ADVAIR
 - Pumeicort: powder that coats the bronchial tubes to soothe them
 - Intal: coats mast cells to stop them from exploding and releasing leukotrienes (not used very often). Less used since steroids.

Allergy tests can be done by applying a small amount of the substance to the back or arm of the patient and then measure the extent of the reaction

- This can create false positives because skin contact, inhaling and ingesting isn't the same

Immunotherapy is the injection of a small amount of the allergen to become tolerant.

- Subcutaneous: allergen is taken as an injection into subcutaneous fat. Must be performed by a physician
- Sublingual: receive the allergen in drops or tablets that are dissolved under the tongue. This can be administered daily by the patient himself with instructions. This necessitates less visits to the doctor.
 - This is long term and you have to go regularly. It only lasts a few years.
 - 70% efficacy that's very variable (a bit high)
 - Good for hay fever, but more difficult for peanuts and other foods

IgG antibody: instead of generating IgE, when your body is exposed to small doses of a substance, it generates IgG.

- It prevents the allergen from reacting with IgE.