

MENTAL ILLNESS

- Neurotransmitters – released by neurons, modulate brain function, role in mental illness
 - Ex.: serotonin, dopamine, norepinephrine, GABA
 - Neurotransmitters are synthesized within a nerve cell and stored at tip of axon of transmitting cell in vesicles
- Neuron fires, electrical impulse carried along one cell and is transmitted to next – carrying electrical impulse constitutes the nerve signal
- When impulse reaches end of axon, neurotransmitters released into synapse and react with neurotransmitter receptors, causes propagation of electrical impulse on dendrite of next neuron
- **Dendrites** – involved in receiving a signal – short wavy arms from cell central body
- **Axon Tail** – involved in transmitting signal – long-tail
- **Synapse** – space b/w axon of one cell and dendrite of another
- **Ways to Chemically Interfere with Neurotransmitter Signaling Pathway:**
 1. Lock and Key Method – drug designed to block neurotransmitter-receiving receptors on signal-receiving cell, no electrical impulse transmitter b/w cells
 2. Drugs designed to interfere with synthesis of neurotransmitters
 3. Prevention or Stimulation of Neurotransmitter Release
 - Neurotransmitters are recycled – taken up by transmitting (original) cell following signal firing where it is recycled to produce more neurotransmitter – drugs can interfere with enzymes that modulate biochemical recycling of neurotransmitter
 - Drugs designed to block reuptake, by blocking enzyme involved in reuptake
- **Reserpine** – stops nerve impulses by causes norepinephrine to leak out of vesicles (if neurotransmitter leaks out then impulse cannot be transferred across synapse)
- **Amphetamines** (are stimulants) – squeeze Norepinephrine and Dopamine out of vesicles, causes them to release into synapse
- **Tricyclics** (mood elevators) – prevent reuptake of neurotransmitters, by increasing concentration of neurotransmitters in synapse
- **MAO Inhibitors** – interferes with enzyme responsible for breakdown of neurotransmitters, preventing breakdown of neurotransmitters, which increases concentration in synapse
- **Neuroleptics** (used to treat Schizophrenia) – block receptors on receiving cells specific for dopamine neurotransmitter

Schizophrenia

- Classic mental illness, ‘mad people’, not a split-personality disorder
- Historically (up to 20th c.) treated horrifically
- Mental condition characterized by a loss of contact with reality – visual/auditory hallucinations, delusions of persecution, common belief that people are out to get them
- **Henri Laborit (1952)** – physician, contributed to development of modern treatment of schizophrenia
 - Noticed patients had heart attacks right before a planned surgery, believed it was due to anxiety. Anti-histamines were available at the time to cure anxiety. Laborit thought anxiety could be treated with anti-histamines, b/c histamine was a bad thing to have released in your blood
 - Used **Promethazine (Phenergan)**, an anti-histamine to try and stop anxiety – did not alleviate anxiety, but made patients more prone to sleeping – suggested use of it to psychiatric dept.
 - Scientists analyzed Promethazine, tried to find similar molecules to see if they had parallel effects on patients
 - **Chlorpromazine (Thorazine)** – similar to Promethazine – induces calming effects with patients by reducing dopamine levels through blocking dopamine receptors – psychiatric patients and schizophrenics treated with this – problem was it provoked shaking and paralysis (Parkinson-like symptoms)
- **Nathan Kline (1952)** – psychiatrist, experimenting with drugs for schizophrenia
 - **Reserpine** – snakeroot plant – used for lowering blood pressure, antihypertensive – had tranquilizing and calming effects – used on Schizophrenics, had Parkinson-like symptoms
- Chlorpromazine and Reserpine have different structures, but appeared to have the same effect – possible because there is a difference in the mechanism of action – both drugs deprive a post-synaptic neuron of dopamine
 - **Chlorpromazine** – blocks dopamine receptors – overproduction of dopamine causes schizophrenia, by blocking receptor’s activity on receiving nerve cells dopamine cannot carry out its function
 - **Reserpine** – causes dopamine to leak out of vesicles – less dopamine released upon nerve excitation which reduces level of dopamine in synapse
- Parkinson’s Disease – caused by lack of dopamine – too much dopamine blocked, may causes Parkinson’s-like symptoms

- **Perphenazine** – improved version of Chlorpromazine – molecular structure similar to Chlorpromazine – reduces side effects which is why its a popular drug for treatment of Schizophrenia
- **Haldol (Haloperidol)** – Schizophrenia drug, still has Parkinson's-like side effects – also used on agitated patients esp. in retirement homes and hospitals
- **Other Common Drugs:** Clozapine (Clozaril), Risperidone (Risperdal), Olanzapine (Zyprexa)
- 25% of Schizophrenics achieve remission with approp. medications
- **Best Drug?** just b/c a drug is new does not make it better, new drugs more expensive and efficacy is relatively the same as old drugs

Depression

- Characterized by a feeling of hopelessness, pessimism and uselessness – depressed feel this way for no apparent reason
- Antidepressants used to treat depression, most popular prescription drugs
- Scientology – against the use of drugs to treat mental illness
- **Tricyclics** – first group of antidepressants discovered
 - Called Tricyclics b/c they have 3 rings of carbon atoms in their molecular structure
 - Discovery was the result of a search for a better version of Chlorpromazine
 - **Imipramine (Tofranil)** was a Chlorpromazine derivative – ineffective in treating Schizophrenia, but improved mood – blocks reuptake of serotonin and norepinephrine (neurotransmitters involved in mood), causes an increased concentration of neurotransmitter in synapse leading to constant firing of neuron causing improved mood
 - **Amitriptyline (Deprex)** – discovered by modifying Imipramine – very successful antidepressant
 - **Anafranil**
 - **Side Effects of Tricyclics:**
 - Anticholinergic – dry mouth, blurred vision – Anti-Acetylcholine actions caused by blocking Acetylcholine neurotransmitter receptor
 - Antiadrenergic – irregular heart beat – Anti-Epinephrine actions caused by blocking epinephrine (adrenaline) receptor
 - Also block reuptake of other neurotransmitters which leads to side effects
 - Ideally, antidepressant will minimize cross-reaction with receptors of other neurotransmitters, thereby reducing the severity of side effects caused by drug
- **Selective Serotonin Reuptake Inhibitor (SSRI)** – prevent reuptake of serotonin, no cross-reactivity with acetylcholine or epinephrine – blocks serotonin reuptake, increases concentration of serotonin in synapse, results in increased feelings of happiness
 - **Prozac** – increases levels of serotonin and norepinephrine in synapse without causing side effects of tricyclics – it is the most frequently prescribed antidepressant by psychiatrists
 - Other SSRIs: Sertraline (Zoloft), Fluvoxamine (Luvox), Maprotiline (Ludiomil), Paroxetine (Paxil), Trazodone (Desyrel), Citalopram (Celexa)
 - **Side Effects of SSRIs:**
 - Nausea, Anxiety, Sleep disturbances, Sexual dysfunction
 - A possible side effect is a higher suicide rate – debate over if the drug is causing the higher suicide rate or if it is the depression itself – no scientific proof it is the SSRIs
 - Joseph Wesbecker, Louisville, KY (1989) – went on shooting spree, was taking Prozac for depression – Prozac never shown as cause of rampage
- **MAO (Monoamine Oxidase) Inhibitors**
 - Discovered accidentally in 1950s, prime drug used to treat TB was **Iproniazid**, also caused patients to be happy
 - Nathan Kline tried Iproniazid on depressed patients and found that it worked
 - Some patients developed high blood pressure or suffered strokes – patients that suffered from these side effects had eaten aged cheese or meat
 - Tyramine (found in cheese, red wine, aged meat) is a vasopressor, leads to high blood pressure
 - tyramine is broken down by MAO, blocking MAO with MAO inhibitors stops breakdown of Tyramine, which raises blood pressure
 - Patients on MAO Inhibitors should stay away from foods with tyramine: beer, wine, chocolate, chicken liver, herring, aged cheese, demerol, decongestants
 - **MAO regulates: norepinephrine, dopamine, serotonin**
 - MAO is the enzyme that breaks down these neurotransmitters – to increase amount of neurotransmitters, decrease the action of MAO – MAO inhibitors (ex. Iproniazid) increase the concentration of neurotransmitters and happy moods

Bipolar (Manic-Depressive) Disease

- Depression is sometimes associated with mania
- Characterized by extreme changes in an individual's personality – personality type seen as cyclic
- Behavior predictable based on certain stimulus
- **John Cade** – in a Japanese prison camp during WWII, observed a mental illness that is maybe caused by some toxin that enters the brain and is subsequently excreted in urine – was referring to Bipolar Disease
 - Cade examined urine, injected urine from mentally ill patients into guinea pigs, urine from manic patients killed guinea pigs faster
 - Postulated that **Uric Acid** was killing guinea pigs – wanted to test if Uric acid could kill guinea pigs alone, could not do so because uric acid is not soluble in water – neutralized it with **Lithium Carbonate** (which is a base, so he formed a salt), formed **Lithium Urate** which is soluble in water
 - Found **Lithium Urate** had a calming effect on guinea pigs – began to use it to treat agitated patients and manic-depressive individuals
- **Lithium** – interferes with inositol synthesis (messenger within a cell that responds to neurotransmitter signaling) – side effects: trembling hands, odd tongue movements, nausea
- **Depakote** – used to treat bipolar disorder

Obsessive Compulsive Disorder (OCD)

- 2% of population suffer from OCD
- 20% of first degree relatives of sufferers of OCD also have OCD – suggests a genetic component to the disease
- 20% of OCD patients have ticks, 50% of people with Tourette's have OCD
 - Tourette's is a condition where the person makes sounds or utters obscenities and cannot control it
- Trigotylomania: pulling and twisting of hair to the point of removal (type of OCD)
- Obsession: unwanted, unreasonable and intrusive thought
- Compulsion: rituals performed to gain relief from obsessive thoughts
- Howard Hughes – built Spruce Goose, largest wood-built plane – had OCD
- OCD is not due to some deeply rooted emotional conflict
- Patients with OCD see 3–4 doctors, spent 9 years seeking treatment before correct diagnosis, takes 17 years from onset of OCD to find approp. treatment
- **Causes of OCD**
 - Manifested by a physical change in brain chemistry
 - OCD-suffering individuals have high energy use in the brain – PET scans show the reductions in brain caudate nucleus activity following drug treatment or successful behavior therapy
 - Sometimes physical injury to brain can result in OCD-like symptoms
 - Gourmand Syndrome: OCD that involves obsession of eating, cooking, talking/writing about food
 - has occurred in individuals who had a stroke
 - Streptococci bacteria believed to cause OCD
 - Pediatric Autoimmune Neuropsychiatric Disorders (PANDA) associated with streptococcus infections – thought that antibodies generate to protect against streptococcal bacteria can attack brain and cause OCD, these antibodies can be filtered out to relieve OCD symptoms
- **Treatment for OCD**
 - **Anafranil** – antidepressant – increases serotonin levels
 - Side Effects: dizziness, sedation, dry mouth, weight gain, sexual dysfunction
 - **Prozac and other SSRIs** – best chance of working and best side effect profile
 - Side Effects: anxiety, decreased libido, sexual dysfunction, diarrhea, sedation, headaches, insomnia, dizziness, nausea
 - 40–60% of OCD patients response to SSRIs with an improvement in symptoms in 30%
 - 10–12 weeks to see improvements
 - 90% of patients will relapse if drugs are stopped, no cure for OCD
 - Other Drugs: Fluoxetine (Prozac), Fuvoxamine (Luvox), Sertraline (Zoloft), Paroxetine (Paxil)
 - **St. John's Wort** – mild antidepressant, available OTC
 - **Behavior Therapy** – 10–20 sessions can improve symptoms by 85%, most effective treatment
 - Confrontation or Challenge Therapy – confront their fear while assured they are safe
 - Transcranial Magnetic Stimulation sometimes used

Anti-Anxiety Agents

- **Anxiety**: feeling of apprehension, uncertainty or fear that is out of proportion to a stimulus
- With anxiety you have an excess of activity of neurotransmitters
- **Barbiturates** – introduced in late 1800s as sleeping agents – first drugs used to treat anxiety – effective but addictive
- **Frank Berger** – testing drugs for antibiotic activity, tested **Mephensin** which turned out to have muscle relaxant properties (used in surgeries) and anti-anxiety effects
- **Meproamate (Miltown)** – synthetic, anti-anxiety effects
- **Librium and Valium** (chemical derivative of Librium, better side effect profile) – popular b/c of good side effect profiles
 - Increases quantity of GABA (gamma-amino-butanoic-acid, an inhibitory neurotransmitter), slows down information transmission b/w brain cells, can induce sleep at high doses, often abused
- **Dalmane (Flurazepam)** – anti-anxiety drug, can put you to sleep at high doses
- **Xanax (Alprazolam); Ativan (Lorazepam)**, famous, puts people to sleep
- Note: if it ends in “pam” means it has strong sleep inducing effects
- None of these drugs can be taken with alcohol, should not be mixed
- Barbiturates can cause CNS depression, some people also commit suicide

DRUGS OF ABUSE/STREET DRUGS

Drugs of Abuse:

- Cannabinoids – Marijuana, Hashish
- CNS Stimulants – Cocaine, Amphetamines
- CNS Depressants – Barbiturates, Valium
- Hallucinogens – LSD, PCP, Psilocybin
- Opioids – Heroin, Morphine
- Anticholinergics – Belladonna, Jimson Weed
- Volatiles – Solvents
- Designer Drugs – Fentanyl Analogues
- High school students in US: 12% regularly use marijuana, 12% use cigarettes, 35% use alcohol (2x/week), 35% have never tried a cigarette, 55% have never tried marijuana

Marijuana

- Comes from a plant, can be grown anywhere with the use of lights
- Contains THC (tetrahydrocannabinol)
- **Hemp Rope**: made from stalks for marijuana plants, it is the primary reason these plants were first planted, today the plants used to make it have a low THC content
- Hemp seeds have low THC content, nutritious b/c they are high in Omega 3
- Smoke from marijuana is damaging to lungs, but there is less exposure to smoke b/c people do not smoke as many joints as cigarettes
- To use must dry leaves, cut them, roll in paper and smoke
- Leaves have microscopic oily drops on surface which contain high concentrations of THC – scraping this oil give you Hashish – concentrated THC, highest THC content
- **History:**
 - **Chinese** – Shen Nung dynasty, cannabis seeds used as currency
 - **Ancient Greeks** – throw cannabis seeds into fire and inhale fumes
 - **Middle East** – supposedly Hassan was a hired assassin who lived 1,000 years ago and would offer visions of heaven and bribe and reward people with his drug Hashish
 - **Napoleon** – introduced marijuana to Europe, discovered plant in Africa
 - **Alexandre Dumas** – one of the founders of ‘Club Des Hachichiens’ in Paris
- **New Orleans, 1930s** – port city, crowded, high crime rate, marijuana was an active commodity
 - High crime rate blamed on marijuana, began passing of laws against it
 - **National Law – Marijuana Stamp Act**, almost passed, was realized cannabis seed that was being banned was used for bird seed
- **Effects:**
 - Euphoria
 - Boosts appetite (often to given to anorexics, HIV patients, patients who need to gain weight)
 - Used during sexual activities, but it is not directly an aphrodisiac
- **Tetrahydrocannabinol (THC):**
 - Resembles Anandamide – naturally occurring compound in our bodies that controls mood
 - Effects our reaction time, accidents more likely to happen

- Papers showing it causes: sterility, impotence, chromosome damage, lung damage, brain damage – unsure if this is factual, studies done on animals in high doses
 - Increases heart attack risk
 - Chronic users will suffer from cognitive impairment
 - **Medical Marijuana:** can also be used as a medication – Canada first to legalize use in 2001
 - Strong Anti-Nausea Effect – often used to counter effect of chemo
 - Appetite Stimulant – used to counter wasting diseases – available under prescription as **Marinol** pills
 - Anti-Convulsive – reduces convulsions, used for epilepsy
 - Useful for MS – reduces pain – available as **Sativex spray** containing THC and cannabidiol for treatment of neuropathic pain, patients claim smoking pot works better b/c smoking gets into blood stream faster
 - Glaucoma – reduces eye pressure – first weed prescriptions used on people with glaucoma, grown at U. of Missouri, came up with USDA standard joint with 2.04% THC
 - Marijuana carries a **stigma of abuse** – 1.5M smoke it recreationally in Canada, 600,000 Canadians have a criminal record for possession which costs \$1.3B per year
 - Caught with 15g – \$250 for youth, \$400 for adults
 - Caught with 15–30g – police have discretion for fines or criminal charges
 - Max. Sentence for illegal grow-ops was raised from 7 to 14 years, can get life in prison for trafficking
- Stimulants** – compounds that energize your body, ex. caffeine, cocaine
- **Caffeine:** is a potent stimulant
 - High doses leads to high blood pressure
 - **Strychnine:** used as a rat poison, can stimulate death, small doses can have invigorating effects – extracted from berries from a tree

Cocaine

- Only similarity with marijuana is that it is also produced by a plant (Coca plant, semi-tropical, hard to grow)
- Cocaine effects dopamine by inhibiting reuptake of dopamine
- Chewing leaves does not have a strong effects, since it is insoluble in water
- **Effects:** euphoria (a sense of well being, reduced anxiety, heightened state of alertness)
- Coca Plant – flavoring agent used in Coca Cola, was never any significant amount of cocaine in drink, Stepan Chemical Company in NJ is the only one that can legally import the leaves
- Vin Mariani (French Wine) contained cocaine
- Previously used as a medication – ex. for toothaches, local anesthetic; physicians used it as a stimulant
 - Today is sometimes used as anesthetic for eye/nasal surgery if patient is allergic to others
 - Freud was one of the first to experiment with cocaine, reported its local anesthetic effects
- Not physically addictive (meaning if you take cocaine away from someone they won't have a physical reaction) but it is psychologically addictive
- Withdrawal Symptoms – signs the drug is psychologically addictive
- Addiction can involve the development of a tolerance, whereby more of the drug is needed, BUT this is not true for cocaine more is not needed to get high
- Need to convert leaves into Cocaine Hydrochloride before it can be turned into powder form
 - When leaves are boiled in hydrochloric acid, cocaine from leaves is converted into cocaine hydrochloride which is soluble in water, water is evaporated and then you get the powder, it is not volatile so you need to convert it back to cocaine using a base like ammonia
- **Freebase Cocaine:** take cocaine hydrochloride and treat it with a base like sodium hydroxide/ammonia, this will transform it back into its original form, like the cocaine found in the plant – cannot be snorted because it is not water soluble, but has a lower melting point so can be smoked
 - Makes cracking sound when burned, hence **crack cocaine**
 - Hits bloodstream quickly, can cause effects on first contact with drug, like cardiac arrhythmia, stroke, seizures, psychiatric disturbances

Amphetamines – another class of stimulants, introduced during search for drugs to open bronchial tubes for treatment of asthma, however they did not work

- Resembles ephedrine, found in plants
- Sometimes used to treat for appetite control or to treat attention disorders
- Amphetamines force dopamine out of storage vesicles in nerve cells
- Dopamine is the euphoria-inducing neurotransmitter – high doses can cause schizophrenia, or schizophrenia-like symptoms (sometimes used to treat Parkinson's disease, but there are better drugs)

- **Methamphetamine (Meth):** easily synthesized, contains an additional methyl group (-CH₃)
 - Produced by converting Sudafed (Pseudoephedrine) to amphetamine
 - Ammonia needed, crystal meth manufacturers often steal it from farmers who use it as fertilizer
- **Opioids:** poppy plant, mostly grown in Afghanistan
 - Previously used as a medicine
 - **Opium** – obtained directly from plant, smoked
 - **Morphine** (compound) – purified from Opium (a mixture of compounds)
 - Named after Morpheus (greek god of dreams) – can put you to sleep or if a little to much is taken it will cause death (therapeutic window not wide)
 - Has a ring containing nitrogen
 - Can be synthesized, but extracted from poppy because it is economically feasible
 - Adding an acetyl group makes Heroin (Diacetylmorphine)
 - \$2000 worth of morphine can be transformed into \$1M as heroin
 - **Heroin (Diacetylmorphine):** initially created to curb morphines addictive properties, turned out to be more addictive
 - Used to be used as a cough suppressant, sold by Bayer (makers of Aspirin)
 - Heroin addiction is a fuel for crime
 - Physically addictive, may die if you stop using
 - Injected intravenously, potential lethal contaminants (HIV if needles are shared)

Hallucinogens – caused hallucinations

- **Peyote Cactus** – produces **mescaline**, chemically similar to dopamine – causes visions when smoked
- **Serotonin Psychedelics** – resemble serotonin, happiness molecule
 - Psilocybin is found in magic mushrooms
 - Toad Licking – Bufo Toad produces **bufotenine**, high doses has hallucination-inducing effects
- **Ololiuqui Plant** – hallucinogenic seeds
- **Lysergic Acid** – produced by ergot fungus (grows on rye), can get people high – 1692 Salem witch trials
 - Albert Hoffman, discovered **Lysergic Acid Diethylamide (LSD)** – Isolated lysergic acid from fungus to make a derivative of it – Got some in his mouth, noted weird symptoms (pleasant intoxicated condition, hallucinations)
 - Do not really need a chemical background to make
 - LSD chemically resembles serotonin, fits into serotonin receptors
 - Need a milligram to have an effect, strong – strong hallucinatory effects – after a single use can have another trip later on, molecules of drug are stored
 - Timothy Leary believed all students should take LSD
 - **PCP (Phencyclidine)** – danger of LSD, “Angel Dust” – more dangerous than LSD, can cause stroke or intracranial haemorrhage

Anticholinergics – Ex. **Belladonna Plant:** Atropine is the active ingredient

- Romans believed dilated pupils made a woman beautiful (side effect of atropine), hence the name
- Atropine is an anticholinergic, which blocks action of acetylcholine and can cause hallucinations
- **Angel’s Trumpet** – flower that produces atropine

Volatiles – **Sniffing Solvents** – similar to inhalation of methane – bag often placed over head to maximize inhalation

- Inexpensive hydrocarbon solvents – liquid paper, paint thinner, glue, pen ink

Designer Drugs – Ex. **Fentanyl Analogues**

- Drugs made illegally by people with some chemical knowledge
- Goal is to make a drug that has never existed before, since technically it is not yet illegal
- Primitive equipment is used
- **Fentanyl** - commonly used as an anesthetic in hospitals
 - **Methylfentanyl** (White China) – once sold legally as the new version of heroin, but it is more dangerous – 200g of fentanyl makes 200,000,000 doses of methylfentanyl – \$2,000 of fentanyl leads to \$1B profit of methylfentanyl
 - 20 years ago, 30 cases of patients with permanent Parkinson’s-like symptoms due to use of White China
- **Meperidine (Demerol)** – commonly used as a pain killer – chemist switched oxygen compound for a carbon compound, making it legal for him to sell it – had a euphoric effect – chemist did not purify the compound properly
- Today, certain compounds structures are on a list of illegal substances, any sort of derivative is illegal

- **Ecstasy – Methylenedioxymethamphetamine (MDMA)**

- Made easily, 800,000 users in N. America
- Induces euphoria
- Neurotoxic in animals – can cause hyperthermia, which can be lethal, increases heart rate and blood pressure
- Dose Dependent – high dose can cause confusion, depression, anxiety
- Concern – getting **ketamine**, anesthetic used by vets that is easier to obtain than ecstasy
- **Herbal Ecstasy**: ephedrine, extracted from ephedra plant – once used as an appetite suppressant, higher doses cause euphoria, illegal b/c it causes heart attacks

Homeopathy – Therapeutic system of medicine based on hypothesis that “like cures like”, that a substance that can cause certain symptoms in a healthy person can cure similar symptoms in an unhealthy person in dilute doses.

- Not very trusted in Western countries, more trusted in Brazil and India – more homeopaths than Indian physicians, homeopath more commonly used than traditional medicine
- Chemically and biologically implausible, can be psychologically compelling
- Form of Alternative Medicine: medicine that is not taught in medical schools because there is no evidence to back it up
- **Samuel Hahnemann**, introduced concept of “like cures like” – favored dilution of 30C
 - Malaria – cinchona tree bark extract (Peruvian bark) contained quinine, an active ingredient that worked to reduce fever caused by Malaria – tried some bark and got a fever and then used it to treat Malaria patients and it works (was a coincidence that he got fever)
 - Law of Infinitesimals: more dilute a substance would be, the more powerful it would be when given as a drug
 - Principle of Succession: when he made a house call found his substances worked better, logic was as he rode on stone the vibrations potentiated the remedies
- **Dilution Process** – 1 drop in 99 drops of alcohols, take one drop from that and mix it in another 99 drops of alcohol etc...Each C signifies one dilution, ex. 12C means process was done 12 times
- Sit John Forbes, Queen Victoria’s Physician said homeopathy was an outrage to human reason
- 1988 – Nature (respected scientific paper) published a paper documenting a homeopathic effect by Jacques Benveniste
 - Diluted an antigen to the extent that there were no original molecules left (10^{120}) and showed it could give rise to a biological response when shaken not stirred, b/c shaking it left an imprint on the water
 - Editors of Nature did not believe results, but Benveniste was well respected, asked to duplicate experiment under eyes of committee and results were not duplicated and Nature published an article to clarify
- Benveniste maintained his original results were sound, founded a company (Digibio) to investigate effect further
 - Concluded could transmit homeopathic info. over the internet using electrodes
- Homeopathic journals are packed with papers that demonstrate efficiency of homeopathy – due to randomness it is possible that results seem positive
 - Most experiments use $P=0.5$ to represent the chance that results reported are accurate, meaning that results obtained would be expected 19/20, also meaning same results may have been obtained 1/20
 - Only papers with positive results are published
- **Meta-Analysis** of all homeopathic studies published in The Lancet (2005) showed their results are no better than placebo
- **The Cochrane Collaboration** – findings currently available in Cochrane review studies of homeopathy do not show that its any better than placebo
- Different homeopaths give different treatment for same illness
- **UK House of Commons Science and Technology Committee** – looked into homeopathy, concluded it was a placebo effect and should not be financed by state
- Health Canada gives DIN-HM (drug identification number for homeopathy) – only requires proof of safety
- Every Oct. 23rd (10th month, 23rd day = Avogadro’s number 10^{23}) people protest homeopathy by swallowing many homeopathic pills to prove there is no effect
- **Oscilloccinum** – given for treatment of flu, made from a substance from the duck liver, diluted to 200C
- **How is Homeopathy Still Around?**
 - Placebo effect
 - Regression to the mean – symptoms come and go
 - Standard treatments used in combination
 - Fear of conventional treatment

TOBACCO

- Tobacco kills more people per year than AIDS, Cocaine, Alcohol, Homicide and Suicide combined
 - 400,000 deaths in N. America due to smoking related illnesses
 - Second-hand smoke kills 500 Canadians per year
- If smokers were to quit, avg. lifespan in N. American would increase by 10 years
 - 965 50% of Canadians smoked, today 20% of Canadians smoke, 25% of Quebecers smoke, lowest BC 16%
 - Highest territory Nunavut 61.3%, NW territories 35.7%, Yukon 35.5%
- China – 385M smokers
- Nov. 12, 1492 – Columbus noticed natives in DR smoking
- Tobacco comes from the word Tabbagos meaning rolled leaves (or island of Tobago, which is where first shipment came from to Europe)
- Tobacco placed on bridges in Europe in the form of Tobacco Resuscitator kits, believed blowing into a drowning persons mouth would revive them
- Initially smoked in pipes with a long stem b/c tobacco smoke was harsh – chemicals would deposit on insides of long pipe so they weren't inhaled
- Used to be snuffed – stuffed up nostrils, distinguished – nasal passages have a thin skin membrane causing chemicals to get absorbed quickly
- **American Revolution** – people stopped snuffing tobacco and started chewing it – popular in S. States, Spittoons for people to spit it out (rich would snuff, poor would chew)
 - **World record for spitting is 25 ft. 10 in.**
- **La Cometa by Goya** – first representation of someone smoking
- **Crimean War (1853–1856)** – Britain & France vs. Russia – near Turkey – Europeans began smoking, before this was mostly done in Middle East
 - Early cigarettes came from Turkey, considered to be better – cigarettes rolled by hand, making them expensive and a luxury
 - Never light 3 cigarettes on the same match – 1st opposing soldiers see you, 2nd they aim, 3rd fire
- **1880 – Bonsack Machine** – could roll cigarettes automatically (2000/min)
- **1990s – Flue-Curing Process (or the American Process)** – allowed for less harsh cigarette smoke
 - Prior to this people did not inhale smoke, now people began inhaling which led to lung problems
 - Camel Cigarette first made to use this process in 1913, American Cancer Society also founded in 1913
 - Many cigarettes had Oriental names – thought to be better quality
- Late 1800s average smoker smoked 50 cigs/year; today 10,000 cigs/year
- 4,800 chemicals in cigarette smoke – 400 are toxic, 40 are carcinogenic
- Cigarettes leading cause of accidental poisoning in children, b/c children have pica syndrome (urge of putting things in their mouth)
- Freud addicted to cigars – smoked 20–30/day – died from jaw cancer
- **Theory:** people smoke b/c at a young age they had a lack of oral stimulation – however, studies have shown that children who sucked their thumb have higher odds of smoking
- **Heart disease is the #1 cause of smoking-related deaths** – chemicals in cigarette smoke injure artery walls, increasing blood clotting and deposits of cholesterol, decrease oxygen uptake
 - Men and women equally affected by heart disease
- Asthma, lung cancer, emphysema and other lung problems originate from smoking
- **Alton Ochsner (1919)** – first person to link smoking and lung cancer
 - At this time few developed lung cancer, only chimney sweepers – US saw 400 cases in 1919
 - Today there are 150,000 cases per year
- Incidence of lung cancer has increased recently – cancer death rate per 100,000 men has gone up drastically, women began smoking later than men in history their lung cancer death rate is still going up
 - Breast cancer is the #1 cancer in women, but lung cancer is the #1 cause of death by cancer in women (as of 1987)
- 1930s – Philip Morris organized workshops to teach women how to smoke, b/c they did not smoke as much as men
- Smoking causes wrinkles at a younger age b/c chemicals in smoke clog arteries of your skin making it less irrigated by blood and less healthy; smoking increases amount of MMP-1 (enzyme), which destroys collagen causing gravity to take over
- Since 1999 illegal to smoke in public places in Quebec, since 2006 illegal to smoke in bars/restaurants

Nicotine – addictive substance in cigarettes – alkaloid

- Nicotine named after Jean Nicot, the French man who introduced tobacco to France
- Used to be used as a pesticide, tobacco leaves soaked in water, water used on plants
- **Addictive amount is 2mg; lethal amount is 60mg**
 - Cigar has twice the lethal dose of nicotine, 120mg – will only kill you if eaten
- Nicorette contains 2mg, enough to relieve an addicted individual
- Difficult to quit smoking b/c nicotine has a **duel effecting depending on the dose** – works on acetylcholine receptors
 - **Low Dose** – boost CNS, stimulate you, acting like an amphetamine – activates acetylcholine receptors – stimulated by little puffs
 - **High Dose** – depress CNS, relaxing effect – blocks acetylcholine receptors – relaxed by big puffs
- **Long-Term Effect** on heart b/c nicotine speeds up heart rate and carbon monoxide prevents uptake of oxygen by hemoglobin in RBC
 - Smoker's hemoglobin has about 20% of it tied up by carbon monoxide – people who smoke become short of breath rapidly
- Nicotine allows you to increase your metabolic rate – allows your body to use more calories faster
 - Women smoke today because they are concerned about their appearance – more women smoke than men – when women stop smoking gain some weight
 - Solution is to increase your basic metabolic rate (BMR) through exercise (brings up your BMR so you burn more calories while exercising and resting)
 - Chemicals in cigarette smoke affect taste buds causing food to taste blander

Tobacco Advertising

- \$6B spent per year on advertising by tobacco companies – tobacco companies are always killing their customers, need to find new ones
 - Marlboro man (Wayne McLaran) died in '92 at age 51 from lung cancer, was paid to smoke
 - Pay to place their products in movies (Ex. License to Kill)
- 1998 some states decided to sue tobacco companies for medical expenses, settled for \$204B over 25 years and restricted advertising
- Since 2008 not allowed to display cigs, because previously companies use to pay to have their product displayed (stores could be paid up to \$20,000)
- 1994 executives of tobacco companies brought to court and asked if nicotine was addictive, all said it was not
 - Addiction can be defined as: dependence, intoxication, withdrawal, tolerance
 - Executives claimed it was not addictive because you do not get drunk off nicotine, however nicotine is addictive in all 4 ways

How do you Quit Smoking?

- **Snus**, substance that an individual puts under lip to alleviate cigarette cravings
- Acupuncture, gum, patches (23mg/24h)
- **Zyban** – antidepressant – however has been shown that some die of heart attacks, but the cause of death is uncertain
- **Best way: cold turkey**

DRUG MARKETING

- In Canada there are 5,000 drugs to choose from – 254M prescriptions are written for drugs, approx. 5/person
- Lipitor has the top sales in all of the world

Top 3 Prescriptions in Canada	Top 3 Prescriptions in the World (Sales)
(1) Lipitor – cholesterol lowering – 15M	(1) Lipitor – cholesterol lowering – \$13B
(2) Synthroid – hypothyroidism – 11.5M	(2) Plavix – blood clots – \$6B
(3) Crestor – cholesterol lowering – 7.7M	(3) Nexium – acid reducer – \$6B

- Salicylic Acid – isolated from the Willow tree – used to produce ASA or Aspirin
- Taxol – isolated from the bark of a tree – used in Cancer treatment
- Colchicin – used for treatment of Gout, extracted from a flower
- Vincristine – chemotherapeutic agent isolated from periwinkle flower

- Drug company that has developed product wants to make a brand name that is specific to the product made by that company
 - Ex. of a Tetracycline brand name is Tetrex
 - 5,000 drugs with 15,000 drug names
 - Can lead to confusion, many drugs used for different purposes have similar names (Ex. Celebrex used for arthritis, Cerebyx used for seizures, Celexa used for depression)
 - 10,000 people die per year in the US due to incorrect drug prescriptions
- Ritalin is one of the most prescribed drugs – approx. 3M suffer from ADHD – often wrongly prescribed to hyper children, 38% increase in prescriptions in the last 5 years
- Canada – possible to substitute a drug for another one that is cheaper – can get prescription at pharmacy changed for a generic brand
 - Brand names represent 56% of prescriptions in Canada, but account for 82% of market share in terms of sales
 - Apo-diazeam (Apotex), generic costs \$0.61 vs. Valium (Rocher), brand name costs \$14.45
 - **DAW (Deliver As Written)** on a prescription means prescription cannot be substituted for a cheaper alternative
- **Bioavailability** – drug companies may claim that although their products are the same as the generic brand, there is better delivered to the metabolism, meaning it exhibits better bioavailability
 - If there is a difference it is small – Ex. Naproxen Sodium is an anti-inflammatory, syntex produces it in its brand name and generic form – Naprosyn = \$69.25 vs. Naxen = \$37.30
- Patent for Losec (Omeprazole) was expiring – Omeprazole exists as two optical isomers
 - S-Omeprazole (Esomeprazole) is the newer drug = Nexium
 - No proven clinical benefit of Nexium shown over Losec
- Proscar – used for treatment of benign enlargement of prostate – somewhat effective
- Generic name is finasteride, also effective in oral treatment of Male Pattern Baldness (MPB) – starts at the front and goes towards the back as the man ages
- Off-Label Marketing – marketing drugs directly to doctors for indicators that were not approved – illegal
 - Note: doctor is allowed to prescribe a medication for something that is not approved
 - Ex. Zyprexa (Olanzapine tablets) developed to treat schizophrenia, makers decided to push it to treat dementia, number of serious side-effects were discovered, makers fined \$1.4B and there were \$2.6B in claims – ended up making \$40B in sales
- Patent for Lipitor ended, problem for Pfizer – Pfizer bought company that developed drug, 11 years made \$131B on drug
- Drug companies do not like to produce **Orphan Drugs**: drugs that treat only a small subset of the population b/c there are not enough patients to make the drug profitable
 - Ex. Fabrazyme, drug developed to treat Fabry disease (genetic disorder)
 - **Orphan Drug Act** – American gov. gives money to companies to develop orphan drugs by paying for the purchase of the drug once it is developed
- Much Brand-name drug research used to be done in Quebec, they have all closed

How New Drugs are Introduced to the Market

- Antibiotics discovered following isolation of Penicillin by observing other fungi and organisms and seeing if they could produce substance detrimental to bacteria
 - Ex. Streptomyces Aureofaciens – mold that has some antibacterial activity (myces means from the soil)
- (1) Identification of Organism**
- (2) Isolation of the Compound (the Active Ingredient)** – antibacterial agent is isolated and has a specific chemical structure, if needed can improve structure: engineer it to better fit for a receptor site, can make it more water soluble – if agent is altered it becomes a semi-synthetic drug
 - Name molecule in a simple fashion, chemical name too complicated
 - Ex. Tetracycline – structure has 4 cycles – technical/generic name of substance
- (3) Testing of the Drug** – tested for Acute Toxicity – how much is required to kill the animal
 - Acute Toxicity measured by LD₅₀ (Lethal-Dose 50) – the amount of a substance that will kill half of the test population (i.e. 50%) – the smaller the LD₅₀ the more toxic the substance
 - After Acute Toxicity is tested Long-Term Toxicity is tested – things that occur in the LR are tested on the test subject and offspring
 - Ex. Thalidomide found to cause birth defects – Frances Kelsey – being used to treat Leprosy

- (4) **Effectiveness of the Drug** – weigh benefits vs. risks – usually tested in animals
 - Sheep used to test urinary/hypertensive drugs (similar urinary tracts to humans), rabbits used to test antipyretics (develop fever similar to humans)
 - In N. America 60M animals are sacrificed (30M rodents, 200,000 dogs, 50,000 cats, 50,000 monkeys)
- (5) **Clinical Trials: Phase I** – try drug on 20–100 healthy individuals
- (6) **Clinical Trials: Phase II** – try drug on 100–300 sick patients
- (7) **Clinical Trials: Phase III** – try drug on up to 20,000 sick patients – examine side-effects, sometimes rare side effects only show up in larger populations
 - To minimize placebo effect, drugs tried using the **Cross-Over Double-Blind Study Method**
 - Blind Study – one group given drug, one group given sugar pill
 - Double Blind Study – person administering pills does not know which pill is placebo
 - Cross-Over – change groups receiving pill and placebo halfway through trial for ethical reasons
- Takes 10–15 years to develop a drug, most money spent in clinical trials

Nuremberg Code of Ethics

- Informed consent
- Follow prior animal studies
- Benefits must outweigh risks
- Carried out by qualified scientists
- Must not cause physical/mental suffering

Tuskegee Study – Untreated Syphilis in the Male Negro Study, 1932–1972

- Study aimed to identify how syphilis progresses as a disease
- Participants were told they were being given medications that would help their situations, while scientists purposely withheld medication in order to study them
- At the beginning of the study antibiotics to treat syphilis were not available, however they became available during the study and were withheld
- Many drug studies carried out in third world to save costs
 - Trovan, study by Pfizer, developed for meningitis, participants not given full informed consent
 - **Constant Gardner** – movie about Trovan in Kenya

Patent Act – Allows anyone to mimic the product after a set amount of years

- **Before 1969** – patent registration 14 years
- **Bill 102 in 1969** – no patent on product, instead company that developed drug paid royalties (4%) for the use of their product – Compulsory Licensing
 - As a result, many drug companies had competitors producing same drug under different brand names, brought down price of medication due to competition
- Changed to Bill C22 in 1988 – offered 7–10 years of patent protection – 7 years for drugs produced abroad, 10 for ones produced in Canada
 - Patent began when the product was put on the market
- Changed to Bill C91 in 1993 – offered 20 years patent protection
 - Patent began the moment the drug was patented, since it takes years for a drug to be developed and marketed this does not add 13 years over Bill C22
- Price review board installed to ensure that drug companies would invest in drug development in Canada
 - Medications are well priced in Can compared to US:

Canada	United States
90 tablets Lipitor = \$180	90 tablets Lipitor = \$332
100 tablets Zocor = \$208	100 tablets Zocor = \$440
90 tablets Prevacid = \$197	90 tablets Prevacid = \$451
100 tablets Zoloft = \$182	100 tablets Zoloft = \$274

How does the company get a Dr. to prescribe a specific drug?

- \$23B spent on advertising in US vs. \$3B in Canada
 - US – \$18B spent on advertising to doctors, \$5B to patients
 - Canada – \$2.5B spent on advertising to doctors, \$500M to patients – Canada has a higher proportion of advertising going to doctors
- Advertising less burdensome in Canada b/c of smaller population and different types of advertising
 - Ads can include condition a drug is suppose to treat but not the name OR the name of a drug and not the condition
- US – ads can give name and what it is used for but must list side effects
- More money is spend on advertising (23% of the total cost of the drug) of drugs than on R&D (16% of the total cost of the drug)
 - Pharmaceuticals are more advertised than Beer (10% of total revenue), Cosmetics (10% of total revenue), Other consumer products (4% of total revenue)
- When Pfizer came out with diplovax vaccine awarded prizes to doctors for selling a certain number
 - 100 doses = book; 250 doses = tape recorder; 500 doses = calculator; 1,000 doses = freezer
- Today, organize conferences in vacation spots
- Before Vioxx taken off market spent \$200M on advertising

HORMONES

- Story of Goliath is a story of Hormones – Goliath suffered from Multiple Endocrine Neoplasia which leads to excessive growth and visual problems due to Pituitary insufficiency – Goliath had low blood sugar due to pancreatic problems, his skull was also soft due to parathyroid problems leading to insufficient bone formation
- **John Hunter** – english physician – one of the first to do experiments on hormones
 - Castrated roosters, comb of rooster collapsed following castration – this is a hormonal consequence, but Hunter didn't realize this
 - Testes produce main male sex hormone – testosterone
 - Comb is used to attract chickens, when it is up it is mating time
- **Arnold Berthold (1849)** – castrated roosters, returned testicles into body cavity and noticed the comb became erect again – concluded there was a substance in the testicle released in the blood causing the effect
- **Thomas Addison (1855)** – role in the early understanding of hormones
 - Carried out autopsies on decreased patients
 - Noted people who had atrophied adrenal glands had shown poor appetite, low blood pressure, weakness, nausea, vomiting, anemia, and bronzed skin (hyperpigmentation — excess melatonin production) prior to death – concluded adrenal gland must be releasing something that prevents these symptoms – **Addison's Disease (adrenal insufficiency)**
 - JFK had Addison's Disease
 - Hydrocortisone used for treatment of Addison's – used in other conditions where immune sys. needs to be suppressed
- **Dolanski (1894)** – first to attempt to unravel hormone mystery – work focused on digestive system
 - Food passes from stomach to SI, digestive juices released from pancreas and recruited to perform digestive reactions, juices break down food, food taken up into blood stream
 - Sought to understand how the body knew when to secrete these digestive juices
 - No nerve connection b/w pancreas and SI
 - Postulated a chemical signal modulated this activity – thought some acid produced by stomach when food is eaten does into blood and reaches pancreas – tested this by injecting stomach acid into rectum of dog, no secretion
- **Charles Brown-Sequard (1889)** – looked at role of hormones – injected himself with macerated dog testicles b/c noted that removing testes of rats caused them to age faster and when injected with macerated testes rat would be invigorated
 - Injected himself with monkey gland extract, said he felt rejuvenated, likely a placebo effect
 - First example of hormone therapy
- **Sir Arthur Conan Doyle** – writer of Sherlock Holmes, did not like concept of injecting oneself with substances b/c we did not know enough about it to start doing it – wrote "The Adventure of the Creeping Man", story based on Charles Brown-Sequard
- **John Romulus Brinkley** – got a mail-order surgeon degree (1800s could pay to become a surgeon after doing a stage with a physician and no school was needed)
 - Inspired by Brown-Sequard's work – realized male goats were horny, began goat to man testicular transplants, made an incision in human scrotum and inserted goat testicle – performed over 1,700 with no complications

- **1895** – more serious attempts at hormone therapy were made
 - Adrenal gland extract could be injected to raise blood pressure – done b/c Addison noticed that people who suffered from adrenal insufficiency (Addison's Disease) had low blood pressure – today adrenaline used in EpiPens to treat allergies
- **Ernest Starling (1902)** – intrigued at how pancreas knew when to release digestive juices
 - Suggested some kind of chemical released from intestine upon stimulation with food and then circulated in blood to pancreas
 - Macerated a piece of a dog's duodenum and injected it into another dog's jugular vein – flow of pancreatic juices began – showed that a chemical contained within walls of intestine could trigger release of digestive juices from pancreas – hormone now known as **Secretin**, protein released by lining of duodenum
- Hormone – stir into action
- Endocrine Glands:
 - Hypothalamus, Pituitary, Thyroid and Parathyroids, Stomach, Kidney,
 - Ovary and Testicles release sex hormones
 - Adrenal releases Adrenaline
 - Pancreas releases Insulin
 - Duodenum releases Secretin
- Hormone imbalance can cause physical abnormalities

Pituitary Gland

- Master gland of the endocrine system – secretes chemicals that cause other endocrine glands to secrete hormones
- Size of a pea, located in center of brain underneath hypothalamus
- Secretes 1 millionth of a gram of hormones per day (i.e. 1 microgram) – despite small amount it is required for physiological maintenance – good ex. of a chemical that causes an effect at a very low dose
- Without a functioning pituitary gland the rest of the body cannot function
- **Produces:**
 - Adrenocorticotropic Hormone (ACTH) – tells adrenal gland to secrete its hormone
 - Follicle Stimulating Hormone (FSH) – tells ovaries when an egg is to be released
 - Thyroid Stimulating Hormone (TSH) – tells thyroid gland to release hormones
- **Hormones triggered by gland:**
 - Prolactin – triggers mammary glands to produce milk
 - Somatotropin – growth hormone, needed until we are fully grown
 - Excess causes gigantism, deficiency causes dwarfism
 - Pituitary gland tumors often caused by excess somatotropin
 - General Tom Thumb, famous dwarf b/c body was proportioned
- Sufferers of pituitary problems usually die before 50 of heart problems, heart cannot keep up with demand, skeleton has difficulty supporting weight resulting in fractures
- Sandy Allen, tallest lady, 8 ft., excess somatotropin which caused Acromegaly – condition where bones grow out of proportion, face and chest often deformed
- Tallest man ever was Robert Wadlow (1918–40) died at age 20 due to circulatory problems
- Andre the Giant – 7'4 over 500 lbs. – died of a heart attack at 42
- If someone is short in stature b/c pituitary gland is not producing enough hormones, can be injected with hormones to reach normal height
 - Originally done by taking cadaver pituitary extracts, posed a problem b/c could inject virus
 - Today, use recombinant DNA technology to produce pituitary hormone
 - Medically short stature is adults under 4'10

Human Growth Hormone (HGH) – pituitary gland produced HGH as long as we are growing

- Finish growing, amount of HGH in blood stream lower – dramatic decline in HGH with age
- If HGH is injected into someone with a tumor, it will cause it to grow
- **1990 – Daniel Rudman** – took elderly volunteers and injected them with HGH – results were good, demonstrated physical improvements – 8.8% increase in muscle tissue, 14.4% decrease in fatty tissue, 7.1% increase in skin thickness, 1.6% increase in avg. density of lower back vertebrae
 - However, study stopped after 6 months b/c: blood pressure increased, plasma glucose increased, development of carpal tunnel syndrome (painful neurological condition of hands), breast enlargement in men
 - Rudman showed that there were no measurable improvements in muscle function or physical performance in spite of improved muscle-fat distribution
 - Clinics popped up in Nevada, inject people with HGH

- **HGH is a protein**, must be injected not taken orally b/c it would be broken down like any other protein
- **Secretagogues** – oral supplements to stimulate body's production of growth hormone – as amino acids in our body originate from diet (i.e. b/c protein is broken down into amino acids), they state their product contains the same ratio of specific amino acids as HGH does – ABSURD
- Our protein production gears down with age b/c enzymes required to make these proteins are less active not due to lack of protein in diet
- Growth hormone has benefits – ex. helps with hip fracture recovery
- Growth hormone useful in animals
 - Cows produce Bovine Somatotropin (Bovine Growth Hormone – BGH) (in their pituitary gland) = HGH but in cows
 - Responsible for growth and milk production – allows for 20% higher milk yield
 - Used to be sold by Monsanto under name Pozilac
 - BGH causes mastitis – inflammation of the udder
 - BGH ban in Canada vs. in US farmers push for it b/c they can produce as much milk as they want, in Canada we have a quota sys. so there is no incentive
 - Hormone therapy used in pigs – porcine somatotropin is the pig growth hormone, used to give animal less fat and more meat, rapid growth, better muscle to fat ratio

The Thyroid

- Controls **Metabolism** – the sum total of all the chemical reactions going on in your body at any time
- **Malfunctioning or deficient thyroid (Hypothyroidism) causes:**
 - Sluggishness, slow heart rate, obesity, cold skin
- When thyroid gland is deficient in producing hormone, tries to make itself more efficient by increasing its size
 - Thyroid requires iodine, gland tries to make more out of blood stream which causes it to grow larger – known as **Goiter** – can be fixed by adding iodine into diet
 - Does not happen a lot in N. America
 - **Cabbage Goiter** happens in Poland – natural compound in cabbage prevents thyroid from taking up iodine
 - Deficiency in thyroid hormones from birth results in **Cretinism**, a mental illness, can be aided with iodine salt
- **Hypothyroidism** – thyroid is overly active and produces too much hormone – causes anxiety, nervousness, rapid pulse, fatigue, weight loss, protruding eyes – known as **Grave's Disease**
 - **Treatments:**
 - Drugs that block thyroid hormone formation, ex. Methimazole
 - Radioactive iodine, concentrates in the gland, damages it, renders it less active
 - Most common method used, ends up overcorrecting, Synthroid (synthetic thyroid hormone) needed to correct
 - Surgery to cut out a piece of thyroid to produce less hormone
- **Parathyroid Glands** sit on top of thyroid
 - Parathyroid Glands + Thyroid regulate calcium and phosphorous metabolism, critical to bone formation – bone is dynamic not static
- Everything in our body come from our diet
 - Calcium in intestine must get into blood (in plasma) to be deposited into bone
 - Vitamin D required to calcium to get into plasma
 - Calcium, 2 Functions: physical basis of bone and signals NS
 - Calcitonin, thyroid gland hormone, dictates if calcium will be deposited into bones
 - Insufficient bone formation due to lack of calcitonin, synthetic calcitonin can be taken, will increase bone structure – calcitonin is a protein so it needs to be injected

The Adrenals

- Located on top of the kidneys – activity is stimulated by ACTH (Adrenocorticotropic Hormone, produced by Pituitary Gland)
- Glands are stimulated to produce **Adrenal Cortex Hormones: Aldosterone, Cortisol, Corticosterone**
 - **Adrenal Cortex Hormones** – immunosuppressants, undermine activity of immune sys. (inflammation, redness, swelling, warmth, pain – can reduce inflammatory properties)

- **Gland divided into 2 sections:**

1. **Cortex** – outer gland – produces corticosteroids (protect body from infection, exertion and counter allergic reactions)
 - Corticosteroids can be used to treat asthma, allergies, Rheumatoid Arthritis, Lupus, Crohn's Disease (chronic inflammation of digestive system, can cause pain)
2. **Medulla** – middle gland – secretes adrenaline (fight or flight hormone, adrenaline triggers release of glucose into blood, causes increased circulation and blood pressure, dilates bronchial tubes making breathing easier)

- **Harvey Cushing (1869–1939) – Cushing Syndrome** – caused by excess adrenal gland activity, characterized by a moon face (fat deposits on face), buffalo hump (fat deposits on back), weak bones/muscles, easily bruised skin, peptic ulcer, diabetes, high blood pressure (hypertension)

- Symptoms can occur in people taking corticosteroids over a long period at high doses
- Osteoporosis results from too much corticosteroids

- **Pancreas** – under liver – produces insulin to regulate blood glucose levels and uptake of glucose

- Insulin discovered by **Banting & Best** (Canadian) in 1921, did tests on 92 dogs, extracted pancreatic juices, found these juices contained something that could be used to treat diabetes

- **MacLeod** isolated insulin later – earliest insulin extracted from pigs and dogs

- **Type 1 Diabetes** – no insulin produced in pancreas, insulin needed to live

- **Type 2 Diabetes** – diet and lifestyle related, linked to metabolic syndrome – do not respond to insulin produced by pancreas, they are insulin-resistant

- Glucophage XR – increases insulin production in pancreas

- **Gonads** – determinants of sex (sex organs)

- Both sexes have both hormones – testosterone (hormone) and estrogen (class of hormones)

- Estrogen-Testosterone Balance determines sex of individual

- Testosterone can be used to treat diminished libido, raise change prostate grows cancerous

- Sex drive controlled by testosterone

- Chemical Castration – using drugs that block effect of testosterone or production of it – Ex. Cyproterone Acetate, used in treatment of prostate cancer

- Transsexualism – feeling that one has been born into body of wrong sex

- Estrogen therapy can lead to higher cancer rates

- Prostate hyperplasia (excess growth) caused by dihydrotestosterone, formed from testosterone, Proscar blocks formation and has minimal effects on libido

- **Anabolic (producing/growing) Steroids**

- Body builders use anabolic steroids, stimulate muscles causing more muscle tissue to be produced upon repair

- Russian and East Germans were among the first adopters of steroid use in 1970s

- 1976 Montreal Olympic Games – drug testing was becoming routine

- Ben Johnson (1988) – 100m sprint winner in Seoul, stripped of medal for doping

- **Side Effects:** acne, excess hair growth, aggression, liver disease, depression, reduction of good cholesterol, testicular atrophy (shrinking b/c no longer needed to produce testosterone), breast development (testosterone:estrogen too high, body compensates by producing more estrogen)

- **Menstrual Cycle:**

- Women are born with all the eggs they will have, each cycle an egg is released from ovaries – pituitary gland released FSH (follicle stimulating hormone) needed to release egg

- During ovulation there is a spike in estrogen, if egg gets fertilized and is implanted in uterus levels of progesterone do not decline

- Progesterone is the pregnancy hormone needed to keep egg viable in uterus

- No eggs are released b/c pituitary gland stops producing FSH, hormonal communication – pituitary gland senses pregnancy

- No fertilization progesterone levels decrease

- PMS occurs last 10 days, progesterone is causative hormone – caused by fluctuating hormone levels – idea of using hormones to counter this (ex. progesterone cream, 200mg Magnesium/day, Vitamin B6)

- 70% of all breast cancer is hormone driven – estrogen sensitive – higher amount of estrogen exposure, more likely to get breast cancer (i.e. more menstrual cycles)

- **The Pill:**

- Company made a deal with milk delivery company, collected urine from pregnant women and were able to isolate progesterone
- **Russell Marker** – pioneered extraction of progesterone from urine
 - Sweet Potato (Yam) produced a compound called Diosgenin, that could be converted into something similar to progesterone
- **Problem:** progesterone had to be injected to work
 - Norlutin, different structure but could be taken orally – first version of the pill, tested in rabbits then humans in Puerto Rico
 - Difference b/w today's pill and the first – less active ingredient b/c it was determined that less was needed than originally thought and adding estrogen to pull remedied side effects
- **RU-486, Antiprogestosterone – Morning After Pill** – interferes with action of progesterone and causes an abortion, needs to be taken twice
- **Efficacy of Birth Control:**
 - Oral Pills – safest, not 100% efficient due to human error and deficiencies
 - Condom – 85% efficient
- **Estrogen** – used in hormone therapy – treat menopausal symptoms – can reduce risk of osteoporosis, weakening of bones, shrinking of skeleton
 - Estrogen supplement derived from estrogen hormone, called Premarin (Pregnant Mare's Urine) – can be taken orally or patch
 - Should not use estrogen: migraines, stroke, kidney disease, hypertension, diabetes, liver disease, breast/uterine cancer
 - Estrogen supplements initially claimed to increase breast cancer risks by 30% – in a 10 year period 3–4% of post-menopausal women will develop breast cancer, taking estrogen increases risk to 5% – a post-menopausal woman who takes estrogen reduced her chance of remaining cancer free from 96% to 95%