CHEMISTRY OF THE HEART

- Ancient Egyptians fascinated by heart, believed it was the center of emotions and intellect
- Ancient Romans intrigued by heart
    - Galen, Roman Physician – observed heart in open chest cavities (he took care of gladiators) – believed heart manufactured blood and it pumped this blood through arteries, delivering vital spirit to the body
- **Leonardo Da Vinci** – first real scientist to look at heart – diagrams of the heart very detailed, allowed for development of surgical procedure
    - Francis Wells developed technique to repair mitral valves based on drawings
- **William Harvey (1600s)** – realized heart was a pump and did not manufacture blood
    - Heart had 2 functions:
        1. Pump out blood into the lungs, then oxygenated through pulmonary artery
        2. Pump blood back from lungs (picked up oxygen in lungs) into heart to be circulated through body (comes out of heart through aorta – subdivides to deliver blood and nutrients to body – smallest subdivision called Capillaries, so narrow RBCs pass through individually)
- Heart located at centre of chest cavity, size of human fist, pumps 5–6 L of blood/min through 100,000km of blood vessels, beats 2.6B times in our life

How the Heart Works

- Red – blood vessels carrying oxygenated blood; Blue – blood on way to heart and lungs to pick up oxygen
- Blood returns to heart via Vena Cava (largest vein) – there are 2: one from lower body and legs, one from head and arms – veins enter in Right Atrium, right side of heart collects used blood. Blood pumped down into Right Ventricle, which pumps blood to lungs via Pulmonary Artery. Newly oxygenated blood comes back via Pulmonary Vein into Left Atrium. Blood pumped down to Left Ventricle – needs to be the strongest to give oxygen to heart, fed by coronary arteries. Blood pumped out through Aorta (biggest artery) to rest of body.
- Arteries: carry blood away from the heart
    - All arteries carry oxygenated blood except for **Pulmonary Artery**
- Veins: carry blood to the heart
    - All veins carry deoxygenated blood except **Pulmonary Vein**

What Can Go Wrong? – Heart Diseases

- **Failure to Pump Enough Blood:** cells oxygen starved – heart needs constant supply of oxygen b/c it is a muscle
- **Impairment of Electrical Signal:** cells on heart that act as a pacemaker, heart will not pump regularly when signal is defected
- **Reduced Flow of Blood Through Coronary Arteries:** arteries feed heart constant supply of oxygen (Corona means crown, arteries surround heart like a crown)
- **Improper Functioning of Heart Valves:** hearts pumping efficiency decreased

Risk Factors Predisposing us to Heart Disease

- Downward wrinkle or crease on earlobe – indicates greater susceptibility to heart disease
- Baldness – men who go bald earlier have a higher risk of developing heart disease
- There are all independent risk factors, the more of these risk factors you have the more you should pay attention to them
- **Being Male** – risk factor
    - Men more likely to develop heart disease, after women undergo menopause the amount of heart attacks evens out b/w men and women
    - Prior to menopause risk of heart attacks for men 10x greater – estrogen has nothing to do with it, women in menopause taking estrogen just as likely to get a heart attack as those who are not
    - Heart disease not as prevalent in women, but is a #1 killer – physicians assume problem is something else, heart disease may not manifest itself with classic symptoms
- **Smoking** – huge risk factor, bigger risk factor for heart disease than for lung cancer
- **Obesity** – more weight you have, more blood vessels, harder heart has to work
- **Diabetes**
    - Glucose is a source of energy, cells burn glucose (why we need oxygen) – blood delivers oxygen to burn glucose, which gets converted into CO^2 and water
    - If blood glucose levels are high and all glucose is not used for energy, starts to get converted to fat deposits in fat cells – Glucose gives rise to glycocerated end products, risk factors for heart disease
    - *How do you know if you have higher blood glucose?*
        - **Measure:** Milligrams/Deciliter (mg/dl used in US) or **Millimoles/Liter** (mmol/L in Can, Europe)
            - Conversion Factor: mg/dl = (mmol/L)(18)

- Blood glucose b/w 5.5–7 mmol/L – Pre-Diabetes
- Cutoff Level: blood glucose = 7mmol/L after an overnight fast
- Blood Glucose + 7mmol/L after overnight fast do an **Oral Glucose Tolerance Test:** given a fixed amount of glucose to drink, 30m and 1h later check levels, if result is over 11mmol/L after 1 hour you have diabetes (7.8–11 mmol/L = Pre-Diabetes)
- **Hemoglobin A1C Test** – gives idea of your average blood glucose levels over past 2–3 months, analyze how much hemoglobin in RBCs reacted with breakdown products of glucose, less than 7% = blood glucose of 8.3 mmol/L (diabetes)

- 50% of pre-diabetics develop diabetes in 5 to 10 years unless blood glucose is lowered
- **First Symptoms/Signs:** double vision, excessive thirst, excessive urination

	Fasting/Pre-Meal	1/2hrs. Post-Meal
Ideal	4–6 mmol/L	5–8 mmol/L
Optimal	4–7 mmol/L	5–10 mmol/L
Sub-Optimal	7.1–10 mmol/L	10.1–14 mmol/L
Inadequate	10+ mmol/L	15+ mmol/L

- **Cholesterol** – essential biochemical for life – our body makes it, we do not need to consume it
  - High levels in blood leads to deposits forming in blood vessels, can cause heart attack
  - Saturated fats are the main cause of high cholesterol, they induce the body into making more cholesterol
  - 1/3 of all heart attacks and strokes could be prevented by taking Statins: drugs that reduce cholesterol
    - Statins prevent liver from producing cholesterol by interfering with enzyme that makes cholesterol
    - All Statins have side effects, liver function needs to be constantly examined
    - Lipitor most popular Statin, main side effect is muscle ache; Zocor another example
- **Homocysteine** – chemical that is thought to be a risk factor – higher levels of this naturally occurring compound (formed from amino acid, Methionine) linked to a greater cause of heart disease
  - Metabolized by B vitamins, inadequate B vitamin intake can lead to high levels of homocysteine, which can be toxic to cells lining blood vessels where deposits can then form
- **Inflammation** – swelling, increase in temperature, pain, redness (internal inflammation)
  - When inflammation inside arteries, deposits build and risk increases
  - C-reactive Protein (CRP): inflammatory marker – high levels indicate high risk of heart disease
    - Harvard, 1997 – healthy men with high levels of CRP had highest levels of heart attack risk
- **Chalmydia Penumoniae** – theory that bacteria can cause heart disease (developed after ulcer bacteria)
  - Treatment of heart disease using antibiotics was investigated – not true
- **Hypertension** – elevated blood pressure
  - Measuring blood pressure: **Systolic/Diastolic**
    1. Systolic Blood Pressure: when heart is pumping out blood, during a heartbeat
    2. Diastolic Blood Pressure: while heart is resting inb/w pumping, blood flowing back into heart
  - Normal = 120/80mm Hg (millimeters of mercury); Hypertension 135/90mm Hg
  - White Coat Hypertension: when people stress about their blood pressure being taken and it goes up
    - Blood pressure needs to be measure several times for this reason
  - 2 Types of Hypertension: Mental Stress-Caused and Essential Hypertension (cause unknown)
  - Case Study – bad marriage can raise blood pressure, people in bad marriages have 6mm Hg higher blood pressure
  - *Reducing Blood Pressure:*
    - **Exercise** – 30m/day, 7 days/week
    - **Diet** – DASH (Dietary Approach to Stop Hypertension) – whole grains, fruit, vegetables, low-fat dairy, restricted fat (low in animal fat and red meat) – bananas important b/c contain potassium, which reduces blood pressure – apples high in antioxidants – cut down salt intake (increase blood pressure b/c sodium causes body to retain water, more liquid, more pressure)
  - *Medications to Reduce Blood Pressure:*
    - **Diuretics** – should be first used, best safety profile – make you urinate more, causing more excretion of water and salt, decreases blood pressure by removing water from blood which lowers total amount of liquid – drugs normally end in 'ide' – may cause potassium loss
  - **ACE Inhibitors (Angiotensin Converting Enzyme Inhibitor)** – Ex. Vasotec

- Block formation of Angiotensin II by blocking enzyme that makes it – Angiotensin II required to raise blood pressure when body is exercising , blood pressure drops by blocking formation
- **Beta Blockers** – Ex. Inderal – interfere with activity of Adrenaline by blocking Adrenaline receptor sites, beta blockers reduce blood pressure by throttling back the force and speed of heart – side effects are bad dreams and muscle aches
- **Calcium Channel Blockers** – Ex. Adelate – cause arteries to relax and dilate, lets blood flow through more easily – calcium important for nerve function
- **Angiotensin II Receptor Antagonist Drugs** – Ex. Diovan – work by blocking reception Angiotensin II would normally bind to
  - New class of drugs so not widely used

Angina – Symptom of Heart Disease

- Angina: painful constriction in the chest
- Anginas are mainly exercised induced
- Occurs when heart not getting enough oxygen – Aorta is filled with oxygenated blood as it comes out of L Ventricle of heart, it subdivides, one subdivision is coronary arteries, which deliver oxygenated blood to heart – Problem when coronary arteries are blocked and oxygen supply to heart is slowed (pain due to low supply of oxygen)
- Decrease in cross section of coronary arteries, less blood can flow through – deposits become a part of lining of artery wall causing ballooning of lining – heart put under stress and unable to meet its own oxygen requirements b/c not enough blood flowing through coronary arteries
- Dangerous if a plaque bursts, blood clot forms, plugging arteries completely which causes tissue being fed by artery to die
- Vasospastic Angina: Angina during rest, arteries go into spasm which chokes off flow of blood – if there are large plaques already deposited in arteries, less intense spasm can choke off flow of blood
- **Treatments:** common to be on beta blockers and calcium channel blockers
  - **Nitroglycerine** used to treat Anginas (also used in dynamite, flammable and explosive substance)
    - Dilates blood vessels – taken orally (tablet under tongue or spray under tongue for acute treatment – tissue under tongue thin allowing chemicals to quickly get into bloodstream)
    - Relieves symptoms by dilating arteries, does not treat condition
    - Can also be rubbed on skin, slow-releasing patch form, time releasing tablet
    - *Side Effect:* Headaches
  - **Beta Blockers** – Ex. Propranolol (Inderal) – LT control of angina symptoms to prevent an attack
    - Bets Blockers reduce workload of heart by reducing force of contraction of heart so it does not need as much oxygen – block action of adrenaline
  - **Calcium Antagonists** – Ex. Cardizem
    - Relaxes muscles that constrict arteries, widens blood vessels – influx of calcium into muscle cells can trigger contraction
  - **Natural Products** – Arginine (Amino Acid) may reduce incidence of Angina – promotes formation of Nitric Oxide (neurotransmitter) which widens blood vessels

Congestive Heart Failure (Dropsy)

- Occurs if Angina and High Blood Pressure (Hypertension) not addressed
- Heart is inefficient and in a low oxygenated state – heart unable to fill or empty property or a combination of both
- L. Ventricle is part of heart affected and weakened – most important part of heart, sends blood flowing through Aorta to rest of body
- **Symptoms:** tired all the time, unable to physically exert yourself, bloating due to retention of liquids
  - Bloating – heart unable to pump enough blood to body, liquid in blood cells leaks out and water in bloods leaks out into surrounding tissues causing bloating (Dropsy)
- **Causes:**
  - *Coronary Artery Disease* – buildup of deposits and low oxygenation of heart
  - *High Blood Pressure* – arteries do not expand or contract, heart works harder
  - *Heart Valve Problems* – heart works harder b/c does not empty and fill properly
  - *Abnormal Heart Rhythms* – if chambers of heart are not coordinated the heart has to pump harder
  - *Thyroid Problems* – controls the way the heart beats
- **William Withering** – first treatment for congestive heart failure – foxglove plant
  - Digitalis is the active ingredient, it is a mix of compounds referred to as cardiac glycosides
  - Digoxin was isolated from those compounds and helps heart beat more forcefully
- **Treatment:**
  - *Diuretics* – role in reducing fluid build up

- *Beta Blockers* - improve pumping function
- *ACE Inhibitors* – relax constricted blood vessels
- *Coenzyme Q-10 (CoQ-10) – OTC* – essential coenzymes that work together to synthesize ATP (Adenosine Triphosphate), the body's energy molecule – all our cells contain CoQ-10, increasing it can increase amount of energy that can be made by cardiac muscle cells
- Beta Blockers + Diuretics + ACE Inhibitors often used in combination

Cardiac Arrhythmia
- Heart beats irregularly – detected using stethoscope
- **Treatments:**
  - Sotacor and Amiodarone (most common)
  - Pacemaker – electrical device implanted underneath skin, takes over job of natural pacemaker

Heart Attack (Myocardial Infraction)
- Most severe heart problem – 1.5M heart attacks/year in N. America – 25% die immediately, 25% not aware they suffered one (silent heart attack)
- Symptoms: pain in left arm or chest, sweating, pain in jaw and back
- When no symptoms occur known as Silent Heart Attack
- Main Cause: blockage of coronary artery, generally where there is already plaque – occurs inside artery, blood flow stopped to part of heart and heart attack occurs
  - Where blockage is determines severity of heart attack
- Blood Clot – formed when platelets adhere to site of injury producing chemicals causing protein fibers to form and creating a mesh that traps everything passing by – heart starved of oxygen
- If you survive heart attack, need to get to hospital ASAP – usual treatment **MONA**:
  - Morphine – relieve pain
  - Oxygen – increase oxygen content of blood
  - Nitroglycerine – dilate blood vessels, helps decrease pain
  - Aspirin – prevents more blood clots from forming, starts dissolution of original blood clot
  - Also test blood for presence of Troponin, Creatine Kinase – released for muscular cells that have undergone damage – confirm heart attack
  - If clots are not too severe can use Aspirin, Plavix or Heparin (blood thinner – administered intravenously, prevents further clot formation and dissolves existing clots)
- Ventricular Fibrillation: caused by blockage of one of the coronary arteries – heart fibrillates (flutters) instead of pumping, pumping is inefficient and not enough blood expelled from L. Ventricle
  - CPR can be used, Defibrillator, shots of Adrenaline or Atropine which immediately increase force of contraction of heart
- **To Dissolve Clots:**
  - **Thrombolytics** – Thrombus another name for blood clot
    - TPA (Tissue Plasminogen Activator), used intravenously – Ex. Activase, Streptonkinase – interact with proteins in blood called Plasminogens, which release Plasmins (protein) that dissolves clot
  - **Balloon Angioplasty –** Cath Lab – Physically dissolve clot – insert a **Catheter** in the femoral artery, snake it up to heart, inflate a balloon to open up blockage site
    - Stents can help prevent further damage by holding artery open – stent can injure artery walls by promoting inflammation b/c body perceives it as foreign – Solution was a **Drug Eluding Stent:** released anti-inflammatory drugs but did not prove useful
    - 15–25% of people have a re-narrowing (in-stent restenosis) of arteries – caused by scar tissue
- **Bypass Surgery** – used when condition cannot be solved by diet and exercise (lifestyle) changes
  - Chest cavity opened, heart exposed, arteries taken from the leg and sewn on bypassing the blocked coronary arteries – heart-lung machine used, heart stopped during surgery
    - Single, Double and Triple bypasses
  - 2 groups perform surgery – one opens chest up, one harvest artery from leg
  - After surgery patient needs to take anticoagulants, heart tissue injured and clots could form
  - Increases quality of life, but not necessarily expectancy
- **Valve Surgery** – valves replaced or repaired – replaced using pig valves or artificial valves
- **Artificial Heart** – simple to engineer a pump that will circulate blood, but not one that meets body's needs of speeding up and slowing down, power source difficult to find – could only be used in ST
- Heart Transplants – first one 40 years ago in 1967 by Chris Barnard in S. Africa – used to entail problems of survival rates and rejection, now real problem is lack of hearts for transplants

MENTAL ILLNESS

- Affects 25% of population, stigmas associated with metal illness
- Mental illness is a physical disease
- **Schizophrenia** – not a split-personality disorder, it is a disassociation from reality – have hallucinations (auditory or visual), loss of grasp on reality
- **Depression**
- **Mania** – opposite of depression
- **Anxiety** – anxiety in the absence of provoking stimuli is not normal
- **OCD, Obsessive Compulsive Disorder**
- **What Causes Mental Illness?**
    - Brain malfunctioning – chemical errors can cause illness (when chemical reactions not happening in right way
    - Potential of treating by means of chemical or pharmaceutical treatment
- **Bizarre Treatments:**
    - Trepanation – Amanda Fielding – 1970s, believed trepanation can alleviate mental disorders, Peter Halvorson – American advocate for hold in the head treatment
    - Middle Ages – mentally ill were thought to have fool's stone embedded in their brain – some placed in oven to get rid of evil spirits
    - Ancient Romans – believed moon had an effect on mental stability, hence term *lunatics*
- **Sigmund Freud** – first to start studying mental illness – believed mental illness came from a struggle b/w consciousness and subconscious mind – significant b/c understood mental illness was some sort of chemical imbalance
- **Luigi Galvani (1780)** – understanding of brain chemistry
    - Interested in frog legs, developed machine to generate static electricity
    - Performing procedure on frog, static electricity device turned on, spark traveled from machine to scalpel to frog, frog quivered as if it were living – **Animal Electricity**, believed animal internal electricity released whenever animal touches metal (this was the opposite of what was happening)
- **Alessandro Volta** – cooperated with Galvani – believed electricity within metals caused the twitching to animals
    - Belief let to his invention of battery
    - Frog's legs acted as electrolyte allowing passage of electrical charge across from 2 dissimilar metals
    - Took Copper and Zinc, sandwiched them together with paper drenched in salt water (electrolytic material), found current flowed b/w metals
- **1900s** – apparent human nervous system functioned through electrical impulses
    - Brain collection of trillions of interlinked neurons
    - Nerve cells communicate through electrical impulses
- **Transformation of Electrical Signal into Physical Action: Otto Loewi (1920)**
    - Was known that connecting a battery to certain portions of the heart could make it beat artificially – stimulating heart in different places led to different beat strengths
    - Frog hearts placed side by side – induced though battery stimulation a heart to beat fast and ran water over location of stimulation, collected water and rain it again over different heart with no battery attached and it caused the heart to beat
    - Electrical stimulation causes the release of a specific chemical which causes the heart to beat – this was the **birth of the concept of neurotransmitters**
- **Acetylcholine** – neurotransmitter, causes heart to slow down
- **Epinephrine (Adrenalin)** – neurotransmitter, causes heart to speed up
- More than 50 neurotransmitters: serotonin, dopamine, norepinephrine, gamma aminobutyric acid (GABA)
- **Ways to interfere with the neurotransmitter signaling pathway**
    - Design a drug to block neurotransmitter receptors, no electrical impulse can be transmitted b/w cells, for example Beta Blockers
    - Prevent or stimulate neurotransmitter release – what mental illness is caused by, improving this neurotransmission activity may help people with mental illness
- Electrical impulse reaches end of axon, neurotransmitters released into synapse where they react with neurotransmitter receptors, causes electrical impulse on dendrite of next neuron – neurotransmitters stored at tip of axon of transmitting cell within vesicles
- **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