Physiology II Final Exam Review

Homeostasis:

- From one cell to many (embryo to adult) there is differentiation which means specialization (complexity) in all tissues, organs, and cells...
- Specialization requires communication to maintain whole body function, your body coordinates these functions by:
  - the brain sends commands (hormones (blood), neurotransmitters (nerves))
  - the brain receives info (feedback)
  - through regulation of in/out and is adaptable to changes
- Homeostasis is maintaining a relatively constant internal environment: temperature, blood glucose, blood pressure.
- Sensitivity of the detector (receptor) determines the range of oscillation, some effectors have very specific effects, others more general, local homeostatic mechanisms do not involve the integrating centre, antagonistic effectors improve responsiveness.
- A **Set Point** is the desired physiological value, the hierarchy of importance determines which variables have priority
- The **steady state** is the normal range of values above/below the set point and requires energy to maintain
- An **error signal** is any deviation from the set point
- **Relative Constancy** means that the "set point" is actually a range of acceptable values (dynamic). The set point is adaptive and can be reset. For homeostasis to work your body needs sensors and receptors, effectors and nerve hormones.
- The classic homeostatic regulation mechanisms are negative feedback vs. Positive feedback vs. Feed forward.

Negative Feedback: is the coordination of responses, a signal is detected and a response counteracts the initial stimulus, it returns the body to its original state. Negative feedback is the most common homeostatic regulation mechanism.

Homeostatic Reflex Loop:

1) What is the variable being maintained relatively constant
2) Where are the receptors detecting the changes in the variable
3) Where is the integrating center that collects info and sends out instructions through efferent pathways
4) What are the effectors and how do they impact the variable

Antagonistic Effectors: are 2 systems that are in opposition from each other-

Temperature – sweating, vasodilatation vs. Shivering, vasoconstriction

Heart rate – parasympathetic nerves vs. Sympathetic nerves

Blood Glucose – insulin vs. Glucagon

Positive Feedback: not an attempt to restore homeostasis, it strengthens the stimulus. Transcription factors regulate production of certain genes and are also an example of positive feedback. Responses add to the initial stimulus and strengthen it, do not return the body to its original state, and are not commonly used in your body.

Feed Forward: is anticipatory, occurs in anticipation of an event, and prepares the body for imminent challenges. For example the food in your stomach induces insulin release before you eat, or the body of a runner at the starting line in a race is preparing for the upcoming exercise through thought.

Levels of Regulation: intracellular, intercellular, and tissue are <u>Intrinsic controls</u>, systems and organisms are <u>Extrinsic controls.</u>

Intrinsic controls: are local control mechanisms inherent to an organ

Extrinsic controls: initiated outside an organ, accomplished by nerves and the endocrine system

<u>Respiratory System: Chapter 13 pgs. 471-516</u>

Functions of the respiratory system:

- Brings oxygen - Removes CO2 - Regulates Ph (hydrogen ion concentration)
- Defence against infection - Sound Production

Lung Structure: <u>Conducting zone</u>- determines airflow

Consists of: Trachea, bronchi, bronchioles, and terminal bronchioles

- Conducting zone is a low resistance pathway
- Walls are reinforced with a ring of cartilage
- Warms, humidifies, and filters air
- No gas exchange

<u>Respiratory zone</u>- consists of: respiratory bronchioles, alveolar ducts, and alveolar sacs

- Enables gas exchange
- 300 million alveoli total
- Total surface area is 700 square feet

Cellular composition of lungs:

- All airways are lined with cuboidal epithelial cells, ciliated in the conducting zone, mucous secreting epithelial cells in the conducting zone
- Bronchioles wrapped with smooth muscle cells, bronchiodialation (good) and bronchioconstriction (bad)

- Macrophages in airways and alveoli remove airborne particles and bacteria, called resident immune cells
- Type 1 alveolar cells are flat epithelial cells, and take up the majority of the alveolar wall
- Type 2 alveolar cells are rounded epithelial cells which secrete surfactant which allows alveoli to stay in an open state

Steps of respiration:

Ventilation: exchange by bulk flow

Gas exchange: O_2 and CO_2 exchange by diffusion

Gas Transport: O_2 and CO_2 carried in blood by bulk flow

Gas Exchange: O_2 and CO_2 exchange by diffusion

Cellular Respiration: Use of O_2 production of CO_2

Breathing Mechanics:

Structure: Trachea, Lung, Intrapleural fluid, Parietal pleura, and Visceral pleura

- Air flow requires a pressure gradient: high pressure to low pressure, resistance is determined by the airway diameter.
- F= flow
  Delta P= pressure difference
  R= Resistance

Relevant Pressures:

Atmospheric pressure: the pressure exerted by the weight of the gas in the atmosphere on objects on the Earth`s surface. 760 mmhg

Intra-alveolar pressure: pressure within the alveoli 760 mmhg

Intrapleural pressure: pressure within the pleural sac the pressure exerted outside the lungs within the thoracic cavity.

- Inspiration occurs because the lung pressure is < than atmospheric pressure
- Expiration occurs when atmospheric pressure is < than lung pressure
- Mmhg = millimetres of mercury
- The thorax is a closed chamber that is bounded by muscles (diaphragm on bottom: intercostals on sides). A change in volume causes a change in pressure

The Relation between Volume and Pressure:

- Boyles law: a change in volume results in a change in pressure

- Atmospheric pressure (Patm) –Alveolar pressure (Palv) determines airflow in/ out of lungs.
- Patm is usually constant, so you need to change Palv, this is done by Palv – Intrapleural pressure (Pip)
- Transpulmonary pressure determines lung volume (Ptp = Palv- Pip)
- When it is equilibrated there is no net movement
- Positive Ptp means there is lung expansion
- Negative Ptp means lungs collapse
- Ordinarily Ptp is always positive, so lungs do not collapse, Ptp is more positive or closer to zero
- To fill your lungs with air, airflow requires a pressure gradient, there is lower pressure in your lungs vs. The atmosphere

Stages of Inspiration/Expiration:

1) Atmospheric air pressure (Patm) is equal to alveolar pressure (Palv) and there is no air movement, the pressure is equal no air flow.
2) Increased thoracic volume results in increased alveolar volume and decreased alveolar pressure. Your diaphragm contracts, thorax expands, Pip increases, Ptp increases, lungs expand, and Palv decreases.
3) Atmospheric pressure now is greater than alveolar pressure, and air moves into the lungs. As long as Patm > Palv air will enter the lungs.
4) End of inspiration, no more lung expansion, Palv= Patm, no air movement.
5) Decreased thoracic volume results in decreased alveolar volume and increased alveolar pressure. Your diaphragm relaxes, thorax recoils, Pip increases, Ptp decreases, lung recoils, Palv increases. Generally this is a passive process. Things that are used to assist people with breathing are normally, activate inspiratory muscles, raise Patm (positive pressure ventilators) Change Pip by changing chest pressure (negative pressure ventilator, or iron lung)
6) Alveolar pressure is greater than atmospheric pressure and air moves out of the lungs. As long as Palv>Patm air leaves the lungs.

- It is important to always that a negative Pip Intrapleural pressure, lower than Palv alveolar pressure.
- The increase in lung volume during inspiration is dependent on compliance.

  Compliance = Delta lung volume / Delta (Palv-Pip)

- Compliance is the opposite of stiffness. Compliance is how easy it is to stretch or inflate the lung (restrictive disorders).
- Elasticity is how easy it is to recoil or deflate the lung, predominately due to elastin (obstructive diseases- smoker’s lung emphysema due to loss of elastin).
- Compliance is determined by the structural composition of the lung, the amount and type of connective tissue in the lungs (fibrosis) collagen = stiff= compliant. Also compliance is determined by surface tension, Alveoli have water lining, and try to collapse the air sacs, the greater the surface tension the harder it is to keep the alveoli expanded, greater surface tension

the more work to breathe the same volume of air. Hydrogen bonds are between neighbouring water molecules.

Law of Laplace:

P= 2T/r

- Pressure inside a sphere varies directly with surface tension and inversely with radius. This would result in many empty alveoli and some over-inflated alveoli. Fewer alveoli are ventilated, reduce efficiency in gas exchange. But, our lungs maintain alveoli of small and large volumes so that the great majority of alveoli are ventilated with each breath.
- Collapsing Pressure: must be overcome to inflate the lung as a result more work is required to inflate the lung if alveoli are small.
- Surfactant: is produced by type 2 alveolar cells, is detergent like, reduces alveoli surface tension by disrupting hydrogen bonding between water molecules. Surfactant production starts weeks 25 to 30 of fetal development, lack of surfactant in premature babies cause respiratory distress. Surfactant molecules intersperse between water molecules.
- Surface tension decreases most in the smallest airway, it makes small bronchioles easier to inflate, to get better inflation of the alveoli.

Alveoli Interdependence:

- Alveoli are not closed bubbles or clusters of grapes, walls are shaped with adjacent alveoli. In order to collapse single alveoli, there would be a need to overcome the elastic recoil so all the surrounding alveoli.

Breathing Mechanics:

Flow = Delta P/ R

- R (resistance) is determined primarily by the radius (r) of the conducting passages. Normally resistance is very small.
- Resistance is increased by:
    - Acute Airway Constriction: allergic reactions, asthma (histamine acetylcholine) cause contraction of smooth muscle cells lining the airways
    - Chronic narrowing of airways: (mucous, inflammation, fibrosis)
- Prevention or remedies are anti- histamines, epinephrine, and carbon dioxide.

Mast Cell Activation:

- Preventing mast cell activation from releasing the granules, and prevent the smooth muscle cell from contracting.
- Both the mast cell and smooth muscle cell have Beta2 adrenergic receptors, which try to stabilize the secretion processes. Epinephrine helps with this stabilization or relaxation.
-

Asthma:

- Intermittent periods of airway smooth muscle contraction, increasing airway resistance. Chronic inflammation leading to hyper-responsive smooth muscle and swelling of airway. Can occur when a contracted smooth muscle experiences inflammation, swelling, or mucus.

Gas Exchange- occurs in 2 locations

- Between the alveoli and blood, and from blood to cells throughout the body. Gas exchange is dependent on the pressure gradient, and pressure is dependent on temperature and concentration.

Dalton's Law of Partial Pressures:

- In a mixture of gases, the pressure of each gas is independent of the others. The sum of all individual pressures it the total pressure (P), partial pressure (Pp)
- Partial pressure = Total pressure X Gas exchange.
- Pgas= Patm X Fgas
- Atmospheric air consists of: 79.04 % N2= FN2 0.7904, 20.93% O2=FO2 0.2093 and 0.03% CO2=FCO2 0.0003.
- For example @ sea level Patm= 760 mmhg, therefore PO2= 760 mmhg X 0.2093... = 159 mmhg
- If Patm changes then Pgas changes also.

Gas Exchange:

- Gas exchange occurs by diffusion (movement from high to low pressure), and diffusion between liquid and gas phases.
- Fibrosis Edema Inflammation is caused and affected by diffusion distance. Supplemental oxygen altitude hyper/hyperventilation is caused and affected by the pressure gradient.
- The vertical gradient of blood flow in the lung goes from Low flow and High ventilation to a High flow and High ventilation. Some alveoli do not get to exchange gases because capillaries around them are not prefused with blood.

Henry's Law:

Concentration gas = Pgas X solubility

- At rest your body's oxygen consumption is 250mL of O2 per minute.

Hemoglobin:

- 1 hemoglobin molecule (heme unit) has 4 heme sub units, oxygen binds to Fe, there are 4 O2 binding sites per molecule, and hemoglobin is only found in red blood cells.
- PO2 is determined by dissolved oxygen molecules no on a hemoglobin molecule.

Alveolar – Plasma exchange of Oxygen:

- PO_2 = 105 mmhg
- In the capillary PO_2 = 40mmhg (venous side)
- Continuous gradient- goes from Alveolus to Plasma to RBC... PO_2 = 105mmhg (arterial side)
- There is 200mL of oxygen per litre of blood

Hb – O2 Affinity:

- Anything that changes conformation of hemoglobin may alter its O_2 affinity (allosteric modulation)
- Decreased affinity (when O_2 unloads from Hb) there is a high temperature, high 2.3 bisphosphoglycerate, and a high acidity (i.e. pH < 7.4).
- Increased Affinity (when O_2 stays on Hb) there are traces of CO, a low temperature, and low acidity (i.e. pH >7.4)
- Y globulins do not bind with 2.3 bisphosphoglycerate, so HbF always has a higher affinity for O_2 then HbA.
- HbS is sickle cell anaemia.
- Hb aggregation forms a paracrystalline gel, sickle shape of a red blood cell.

Hypoxia (lack of oxygen)

- Hypoxic Hypoxia is when the atmospheric pressure of oxygen (PatmO2) is LOW.
- Anaemic Hypoxia is when oxygen content is low (there is a decreased number or function of Red Blood Cells)
- Ischemic Hypoxia is when there is an insufficient O_2 delivery (i.e. blood flow is too low, decreased blood pressure or occlusion)
- Histotoxic Hypoxia is when the cell is unable to use O_2 (i.e. mitochondria issue)
- Breathing rate is dependent on internal environment.
- Hyperventilation is when breathing rate increases in excess of metabolism (blood PCO_2 decreases)
- Hyperpnoea is when breathing rate increases at the same level as the metabolism increases (blood PCO_2 remains constant) i.e. in exercise

<u>Cardiovascular Physiology:</u>

The Heart:

- The circulatory system consists of transportation (gases, nutrients, and waste), regulation (hormones and temperature), and protection (clotting and immune).

Blood: Plasma = 55% of whole blood, < 1% platelets and white blood cells, and 45% red blood cells (whole blood, packed cell volume/ hematocrit).

Hematocrit: (Red Blood Cells % in blood)

Normal hematocrit = 45%

Anaemia hematocrit =70%

Polycythanaemia hematocrit= 70%

Dehydration hematocrit = 70%

Red Blood Cell Production: Kidneys detect reduced oxygen carrying capacity of the blood, when less oxygen is delivered to the kidneys they secrete the hormone erythropoietin into blood, erythropoietin stimulates erythropoiesis by the bone marrow, the additional circulating erythrocytes increase the oxygen carrying capacity of blood, the increased oxygen carrying capacity relieves the initial stimulus that triggered erythropoietin secretion.

Cellular Components of Blood:

Platelets = 250 million mL blood

Erythrocyte = 5 billion mL blood

Leukocyte = 7 million mL blood

- Polymorph nuclear granulocytes Neutrophils 60-70%
  Eosinophil 1-4%
  Basophile 0.25-0.5%
- Mononuclear granulocytes monocytes 2-6%
  Lymphocyte 25-33%

The Heart: 4 chambers, 2 atria, 2 ventricles, valves separate atria from ventricles (tricuspid on right, bicuspid on left), valves separate ventricles from aorta/pulmonary artery (semi-lunar).

- Heart valves are: right AV valves, Left AV valve, and the aortic and pulmonary valve.
- Pressure and valves regulate flow through the heart: valves ensure blood flow in one direction through the heart (prevent back flow), when valve is open the flow is determined by pressure and resistance. F= P/R

The Heart Muscle: (spiral layers of muscle)

- Cardiac muscle cell consists of mitochondria, nucleus, contractile proteins, and intercalated discs.
- Intercalated discs consist of: *Desmosome* which is an adhesive junction that keeps adjacent cells close together, and *Gap Junction* which are low resistant to electrical signals and allows waves of depolarization to spread from one cell to another.

Heart Beat Coordination: All cardiac are “excitable” i.e. depolarize and generate action potential. All cardiac cells need to be excited to contract. Cells must be excited in the correct order. Some cells are more excitable then others (*Pacemaker cells* which can spontaneously depolarize).

Electrocardiogram Signal: P = atrial depolarization, QRS = ventricular depolarization, T= Ventricular repolarisation, PR = delay in transmission of signal atria to ventricles, ST segment = duration of ventricular depolarization, TP segment = before a new atrial and ventricular contraction.

Membrane Potential: Resting – intracellular anions, electrogenic Na+ and K+ + ATPase

Action Potential – involves moving ions through channels going from negative to positive, open and closed gates are voltage gated ion channels. Sodium, potassium pump continuously moves Na+ into the cell and K+ out (called *Electrogenic*).

SA Node Action Potential "Pacemaker Cell":

- Self-induced action potential. Slow depolarization (pacemaker potential).
- The pacemaker potential gradually becomes less negative until it reaches the threshold, triggering an action potential. Ion movement during an action and pacemaker potential, state of various ion channels.
- Differences between SA node and ventricular monocytes action potentials are the resting membrane potential, pacemaker current and rapid depolarization.

Cardiac Contraction and Relaxation:

1. Depolarization
2. Open Ca2+ channels, Ca2+ enters
3. Ca2+ diffusion to SR
4. Ca2+ release from SR
5. Ca2+ accumulates in cytoplasm
6. Ca2+ binds to troponin enabling cross-bridge formation between actin and myosin
7. Contraction
8. Ca2+ unbinds from troponin
9. Ca2+ pumped into SR
10. Ca2+ pumped out of the cell
11. Relaxation
    (Ca2+ is essential for contraction)

Cardiac Cycle:

1. Blood flow from high pressure to low pressure
2. Contraction increases pressure in that chamber
3. Relaxation decreases pressure in that chamber

Cardiac Output:

Q = HR X SV

Q (minimum cardiac output)

HR (at rest 70 beats per minute, at maximum exercise 190 b/min)

SV (at rest is 70 mL, at maximum exercise 110mL)

Types of Channels:

If Channels - a type of sodium channel, funny current channel exclusive to pacemaker cells

Ca2+T and Ca2+L channels – T-helper cells reach the threshold potential, L cause depolarization – 40mv

- Self –regulation of stroke volume (intrinsic)

Frank Starling Mechanism: As EDV increases (greater filling), cardiac monocytes become stretched and contract harder pushing out more blood.

Sympathetic Stimulation – Cellular Effects:

- More Ca2+ enters the cell via the plasma malemma Ca2+ channels, more cross bridges are formed, increasing the rate of cross bridge cycling, SR Ca2+ pump is increased (faster relaxation). The Effect of sympathetic stimulation on stroke volume is contractility.
- Ejection fraction = SV/EDV the typical EF is 0.5 to 0.75

Vascular System:

- Cardiac output = mean arterial pressure – right arterial pressure / total peripheral pressure
  Q = MAP / TPR (MAP can be recalculated by altering Q + TPR)

Differences between SA and Ventricular myocytes Action Potential:

- Resting membrane potential: -90mv (steady) vs. -60mv (depolarized)
- Threshold for depolarization: -65mv ventricle vs. -40mv SA node
- Pacemaker current: funny Na+ channels only in pacemaker cells
- Rapid depolarization: only atrial/ventricular myocytes have fast Na+ channels.

Effect of Radius:

- Q= P/R
- Larger diameter tube exerts less resistance; resistance (*a)* 1/radius to the power of 4, resistance is also affected by tube length and viscosity of blood.
- Elastin = compliance
- Weight lifting- high SP increases risk of aortic aneurysm, physical/emotional stress increases SP and causes an aortic aneurysm.

- The arterioles distribute blood to each organ

Arterioles:

- Are located within individual organs, they are the greatest contributors to "total peripheral resistance" and important regulators of MAP.
- They determine blood flow to individual organs, and are comprised of b2 cell types *Endothelium* and *vascular smooth muscle*.

Functions of endothelial cells:

- They line the heart and blood vessels, prevent blood cell and platelet adherence, they regulate exchange of fluid and nutrients.
- Secrete vasodilator (nitric oxide) and vasoconstrictor (endothelin) substances
- Mediate new capillary growth (angiogenesis) and influence smooth muscle cell proliferation (atherosclerosis)

Nitric Oxide: is produced by endothelial cells, released by some nerves, acts on smooth muscle cells, and causes relaxation (vasodilatation and increased blood flow)

Functions of smooth muscle cells:

- Maintain shape of blood vessel (structural support)
- Set blood vessel diameter (vasoconstriction or vasodilatation), they regulate blood flow, and are the main contributor to atherosclerosis/coronary artery disease/hypertension

Local control of blood flow:

- Signals within an organ are responsible for controlling blood flow to that organ, they are not dependant on nerves or circulating hormones
- Local control mechanisms are selfish and ensure that specific organs receive sufficient blood flow, not designed to regulate MAP
- Functional or reactive hyperaemia metabolic factors that increase local blood flow are adenosine (ATP hydrolysis), Potassium, increased Hydrogen due to a decreased pH, and increased carbon dioxide, these are all important in the heart, brain, and skeletal muscle. Flow auto regulation is important in the kidney and brain.

Control of Blood Flow (systemic):

- Neural – sympathetic nervous system
- Hormonal – epinephrine, angiotensin, and vasopressin
- The purpose of these are to regulate MAP

Capillaries:

- The capillary network is a large area with low speed

- Velocity = distance / time
- The capillary morphology is that form fits function
- Exchange across the capillary wall = glucose + O_2 --- CO_2 + H_2O + ATP

Lymphatic System:

- Interstitial fluid collection – the lymph vessels
- Determinants of venous pressure and stroke volume – venous pressure determines venous return
- Detecting mean arterial pressure (MAP): baroreceptors (aortic and carotid bodies) are activated by stretch they send signals to the brain via afferent nerves then are received at the cardiovascular center medulla oblongata and are sent to either the sympathetic or parasympathetic nervous systems
- Examples of baroreceptors responses are: aortic pressure pulse, baroreceptors action potentials, parasympathetic and sympathetic action potentials
- Baroreceptor activity causes increased parasympathetic activity and decreased heart rate, decreased sympathetic activity decreased heart rate and contractility, and decreased vasoconstriction of Q and TPR

Cardiovascular challenge: exercise:

- Metabolic > SNS – causes increased cardiac output with the same blood volume, and large increase in metabolic activity of skeletal muscle

Transition (rest to dynamic exercise):

- MAP = CO X TPR
- The decrease in total peripheral resistance and increase in cardiac output cause changes in heart rate, stroke volume, EDV, and SBP.
- Blood volume alter MAP and can be continuous, the problem is that baroreceptors adapt to a prolonged change in MAP.
- Hormones involved in the long term regulation of blood volume and MAP are angiotensin II and vasopressin which cause vasoconstriction and H_2O reabsorption

Summary

- Erythrocyte production is regulated by erythropoietin a protein hormone secreted by the kidneys. It is secreted by special hormone secretions connective tissue cells in kidney's response to decreased oxygen delivery to the kidneys.
- Doubling the radius of arterioles in an organ would increase by a factor of 16 the blood flow to that organ. Blood flow to an organ is inversely proportional to the resistance offered to the flow.
- Heart-rate would increase when adrenergic receptors on the pacemaker cells are activated. The heart is innervated by both sympathetic and parasympathetic nerve fibres.

- Sympathetic postganglionic fibres release Norpinephrine which acts on beta-adrenergic receptors. HR increases when receptors are activated. SA node is the normal pacemaker for the heart. Pacemaker potential or slow depolarization in SA cells is due to an increase in cation permeability.
- During the cardiac cycle AV valves are opening during ventricular diastole, and blood is passing from the atria to ventricles through the AV valves. Ventricular pressure is less than aortic pressure during isovolumetric contraction. Time between QRS and T waves is when the ventricle is contracting and pushing blood into the aorta, the aortic valve is open.
- Following a haemorrhage there is a loss of blood volume, resulting in a decrease in blood returning to the heart, and therefore a decrease in end-diastolic volume and therefore stroke volume.
- The decrease in stroke volume results in a decrease in arterial pressure, which would be sensed by baroreceptors and cause an increase in heart rate, subsequent to sympathetic activation and increased discharge of the sympathetic nerve fibres to the heart. Also, a decrease in arterial pressure results in decreasing capillary filtration.
- Following a haemorrhage, as a result of blood loss, blood pressure would rapidly decrease, leading to a decrease in the firing rate of baroreceptors in response to less stretch. This signals the medullary cardiovascular areas to increase activity of the sympathetic nerves to the heart arterioles and veins. This would cause heart rate to increase and the peripheral resistance to go up, in effort to bring the stroke volume and cardiac output back to normal arterial pressure.
- During exercise there is a patterned redistribution of blood flow. Blood flow to the heart and exercising muscle increases dramatically (3.5 times in the heart, and 10 times in skeletal muscle), whereas blood flow to kidneys and abdominal organs decreases (30% in the kidneys). Blood flow in brain does not change in skin increases 4.5 times to help heat exchange.
- The formation of plasmin occurs in response to formation of a fibrin in the clot and activation of the fibrinolytic system.
- Arterioles receive a vast supply of post-ganglion sympathetic nerve fibres that release Norpinephrine. Norpinephrine acts on the alpha adrenergic receptors on smooth muscle to cause vasoconstriction, and there is always at least a basal level of firing by their neurons known as sympathetic tone. Dilation of the arterioles can be obtained by decreasing the rate of sympathetic activity below this tonic basal level.
- The normal systolic and diastolic valves within the main arteries are 120 and 80 mmhg. The values for the left ventricle are 120 and 10 mmhg.
- The 2 physiological pumps help increase venous return to the heart are the skeletal muscle pump and thoracic pump.
- The T-type calcium channel is important in the oscillation of spontaneous discharges in pacemaker cells of the SA node, is the T-type calcium channel.
- Cardiac output is the amount of blood delivered by either of the ventricles in one minute. It is defined by heart rate X Stroke volume (the amount of blood ejected by each ventricle per stroke). At resting condition the average HR is about 72 bpm and the average SV is 70mL. This is equivalent to 5 litres of blood.

- Purkinje fibres are the part or the conductive system of the heart that directly delivers the action potential to the ventricular monocytes.

Renal Physiology:

Kidneys:

- The kidneys can only conserve fluid, they cannot restore lost volume. If the volume drops too low the glomercular filtration rate (GFR) stops.

The Nephron:

- Cortical nephrons are in the outer 2/3rd of the cortex
- Juxtamedullary nephrons are in the inner 1/3rd of the cortex, long Henlés loop, produce concentrated urine

The Glomerulus:

- 3 main functions of the nephron are:
  1) Glomerular filtration – non-discriminant filtration of a protein free plasma from the Glomerulus into Bowman's capsule
  2) Tubular reabsorption – selective movement of non-filtered substances from the tubular lumen into the petitubular capillaries.
  3) Tubular secretion – selective movement of non-filtered substances from the petitubular capillaries into the tubular lumen.
- Amount filtered – amount reabsorbed + amount secreted = amount of solute excreted

Plasma Filtration and fluid reabsorption:

1) Plasma volume entering afferent arteriole = 100%
2) 20% of volume filters
3) Less than 19% of fluid is reabsorbed
4) > 99% of plasma entering kidney returns to systematic circulation
5) < 1% of volume is excreted to external environments

- Not all substances are handled equally: for substances filtered and not reabsorbed or secreted like insulin, all of the filtered plasma is cleared of the substance
- For a substance filtered, not secreted and completely reabsorbed such as urea, only a portion of the filtered plasma is cleared of the substance
- For a substance filtered and secreted but not reabsorbed, such as hydrogen ion, all of the filtered plasma is cleared of the substance, and the petitubular plasma from which the substance is secreted is also cleared.

Balance of Pressures:

- Major determinant - favouring filtration Glomerular capillary blood pressure (PGC)
- Opposing filtration – fluid pressure in Bowman's space (PBS), osmotic force due to protein in plasma (pie GC), net Glomerular filtration pressure = PGC – PBS – pie GC
- If increased MAP should see increased pH thus GFR would increase, but flow auto-regulation occurs when increased MAP afferent arteriole constricts to maintain pH
- The process of reabsorption: trans-epithelial transport: to be reabsorbed (more from the filtrate to the plasma) a substance must be traverse 5 distinct barriers
    1) The luminal cell membrane
    2) The cytosol
    3) The basolateral cell membrane
    4) Interstitial fluid
    5) Capillary wall
- Basic concepts of tubular reabsorption:
    1) Sodium absorbed by active transport
    2) Creates an electrochemical gradient that allows anion reabsorption
    3) Ions create an osmotic gradient
    4) Water moves by osmosis, following solute reabsorption
- As water is reabsorbed, remaining solutes become concentrated and some are reabsorbed by diffusion
- Sodium reabsorption:
    1) Na+ enters cell through Na+ channels, down electrochemical gradient
    2) Na+ is pumped into basolateral side of cell by Na+/K+ ATPase
    3) Na+ diffuses into petitubular capillary
- Glucose reabsorption:
    1) Na+ enters cell down electrochemical gradient using the Na+ - glucose transporter. Glucose comes with it against concentration gradient
    2) Glucose diffuses out of the cell using GLUT down concentration gradient
    3) Na+ is pumped to basolateral side of the cell by Na+/ K+ ATPase. Both are reabsorbed by petitubular capillaries

Features of Nephron segments:

- Proximal tubule (very permeable to H2O, Na+, Cl-, and H2O reabsorbed at similar rates)
- Descending loop of Henle is permeable to H2O, no Na+ reabsorption
- Ascending loop of Henle is impermeable to H2O, Na+ reabsorption (controlled by aldosterone)
- Collecting duct (H2O permeability is controlled by vasopressin

Loop of Henle and Collecting duct:

1) Fluid is isosmotic to ECF
2) Active transport of solute creates hyposmotic fluid

3) Urine osmolarity depends on permeability of the collecting duct
4) Urea transport helps keep interstitial osmolarity high

Counter Current Exchange:

- Filtrate entering the descending limb becomes progressively more concentrated as it loses water
- Blood in the vasarecta removes water leaving the loop of Henle
- The ascending limp pumps out Na+, K+, and Cl-, and filtrate becomes hyposmotic

Vasopressin:

- Produced by the hypothalamus
- Acts on collecting duct epithelium
- Stimulates H2O reabsorption water pores are inserted into the membrane to absorb water and transport it across the cell
- Increased reabsorption/decreased excretion
- Plasma volume is conserved

Urinary Excretion:

- Controlled by – modifying Glomerular filtration, modifying Na+ reabsorption (atrial Natriuetic peptide, aldosterone, and angiotensin II)
- Atrial Natriuetic peptide (ANP) is secreted from atria in response to stretch (i.e. excess volume) it causes increased GFR, increased Na+ excretion, and reduces plasma volume and Na+ levels

Regulation of Renin:

- Is critical for the production of angiotensin II
- Rate limiting step of angiotensin II production
- Secretion by juxtaglomerular cells in response to SNS stimulation, intrarenal baroreceptors, and Macula densa paracrine factors
- The regulation of Renin occurs under circumstances of decreased plasma volume (decreased Baroreceptor activity... increased SNS), intrarenal Baroreceptors in JG (sensitive to stretch, less stretch, more Renin produced), and Macula densa detects low Na+ in-tubular filtrate.
- The net effect is reduced Glomerular filtration, production of aldosterone, and plasma volume retention.

Aldosterone (mechanism of action):

1) Aldosterone combines with cytoplasmic receptor
2) Hormone-receptor complex initiates transcription in the nucleus
3) New protein channels and pumps are made
4) Aldosterone-induced proteins modify existing proteins
5) Result in increased Na+ reabsorption and K+ secretion

Hydrogen ion regulation:

- GAIN - generation from CO_2, metabolism of proteins (phosphoric acid, lactic acid), and loss of bicarbonate (diarrhoea and urine)
- LOSS – metabolism of organic anions, loss of hydrogen (vomiting, urine), and hyperventilation

Acidosis: when H^+ exceeds HCO_3, may be buffered by other anions, and may be excreted

Alkalosis: HCO_3 in body exceeds H^+, HCO_3 is excreted in urine

Hydrogen regulation:

- When H^+ balances HCO_3, HCO_3ions are filtered, HCO_3 is reabsorbed by the generation of new HCO_3 in tubule epithelium (no apical transporter for HCO_3), maintains the status quo
- When H^+ exceeds HCO_3, net new bicarbonate reduction allow increased H^+ excretion during acidosis. Net loss of H^+ and pH increases
- Excretion of ammonium occurs when H^+ exceeds HCO_3, net loss of H^+ causes pH to increase

Acidosis and Alkalosis (respiratory and renal systems cooperate):

- Respiratory acidosis/alkalosis imbalance generated by CO_2 transport in lungs can be corrected by the kidney
- Metabolic acidosis/alkalosis (diet/metabolism excess or kidney problem) imbalance of HCO_3 homeostasis can be corrected by changing ventilation