Introduction

Single cell organisms are in direct contact with the environment.
Metabolism happens via the cell membrane which is very important.
Survival of such cells depends entirely on the extracellular space.

In multicellular organisms, individual cells are not in contact with the environment.
Extracellular fluid in such organisms remove waste and provide nutrients.

Nervous and Humoral (hormones) systems helps maintain the normal conditions in the cells.

Lungs: Gas exchange
Kidneys: Urine removal
GI Tract: Providing nutrients

Capillary beds take away waste from individual cells and provide nutrients.
Diffusion is usually used but only work over short distances.

Fluctuations in organisms internal environment should be minimized via homeostatic mechanisms.

Homeostasis - The processes which maintains nearly constant internal conditions.
Looks after body temperature, blood pH, blood sugar level, Na^+, K^+, Ca^{2+}, Cl^- concentration

Nutrients come from: GI tract, Respiratory system, Liver
Removal of waste from: Respiratory system, Kidney, GI tract

Regular ranges of:
Blood pH: 7.38-7.42
Blood glucose level: Less than 6mMol/L
Body temp: Around 37 degrees celsius

Homeostasis uses humoral and neuronal systems

Noradrenaline, Glutamate, Acetylcholine

IPSP neurotransmitters: GABA, Glycine

GABA and glycine cause opening of chloride channels.

Nerst equation is for 1 ion only.
GHK equation for multiple ions.
Na+ equilibrium potential is +60mV
K+ equilibrium potential is -110mV

K+ is the most permeable ion to the lipid due to the many K+ leaky channels.

In depolarisation Na+ channels open
In hyperpolarization Cl- channels open.

After crossing the threshold, very sharp increases in slope due to voltage gated channel. Over threshold, all voltage gated channels channels remain open at the same time leading to sharp, massive influx of Na+. Increases permeability of Na+.

Theoretically maximum voltage is +60mV but practically it is +30mV.

These voltage gated channels can be open or inactive.

In relative refractory period, a higher stimulus could elicit an action potential.

Tetraethyl ammonium (TEA) blocks voltage gated K+ channel.
TTX blocks voltage gated Na+ channels.

Electrotonic Potential is the potential before an action potential.
It is the potential in depolarisation uptil threshold value.
Electrotonic potential is due to ligand gated leaky channels.

Excitatory transmitter - Glutamate.
After binding to post synaptic receptors, excitatory neurotransmitters cause an inflow of Ca2+ ions into the post synaptic neuron.
This causes local and graded depolarisation of the post synaptic membrane

IPSP - Inhibitory Post Synaptic Potential
Inhibitory transmitter - GABA/Glycine
After binding to a post synaptic receptors, inhibitory neurotransmitters cause an inflow of Cl- ions via chloride channels into the post synaptic neuron. They can also cause an outflow of K+ ions.
This causes hyperpolarization in the post synaptic neuron.

Multiple EPSPs and multiple IPSPs can be summed up together.

Spatial Summation:
EPSPs and IPSPs from different dendrites are received at the same time and simultaneously send to the cell body and are summed at the axon hillock.

Temporal Summation:
EPSPs and IPSPs do not appear at the same time. There is some delay and once all gathered together, they are added up at the axon hillock.

Summation allows the threshold to be crossed.

Synaptic Delay value - 1.5 millisecond.

Electrical synapses (gap junctions) have connexions.
Connexons are made from 6 connexions with a hole in between.
Electrical synapses are the pathway for fast transmission.

Chemical synapses
Presynaptic terminus is always a neuron.

Neurotransmitters

Neurotransmitters rarely work alone. They often use co transmitters.

Co transmitters: Peptides released after high frequency stimulations. They prolong the EPSPs and IPSPs

Neurotransmitter - Co Transmitter
Acetylcholine - Vasoactive Intestinal Polypeptide (VIP)
Norepinephrine - Neuropeptide (WPY)
Glutamate - Substance P (SP) / Calcitonin Gene Related Peptide (GRP)

Classification of neurotransmitters:

1) Acetylcholine
2) Amino Acids (GABA, Glycine, Glutamate)
3) Biogenic Amines (Dopamine, Serotonin, Adrenalin)
4) Peptides (Endorphins)
5) Gases (NO, CO)
6) Purines (ADP, ATP, Adenosine)
7) Lipids (prostaglandins)
7 is synthesized from plasma membranes.

Acetylcholine, Amino Acids and Biogenic amines are typical neurotransmitters.

Neurotransmitter receptors can be:
Ionotropic (ligand gated) ion channels
Metabotropic (G protein coupled receptors)

Acetylcholine is the key of the autonomic nervous system.
Ionotropic receptorss: Nicotinic
Metabotropic receptors: Muscarinic

Smooth muscles can be multi units or single units.
Smooth muscles have lower energy requirements for contraction
There is long, sustained contraction with little energy expenditure.
Force generated however is not very high.
This is because in smooth muscles, cross bridge takes longer to form and stay for longer

When skeletal muscles contract, 2 bones are pulled towards each other.

Epimysium surrounds the whole muscle.
Perimysium surrounds the fasicle.
Endomysium surrounds surrounds the muscle fibres.

Skeletal muscles are striated and voluntary.

Myofibrils are surrounded by sarcoplasmic reticulum.
The membrane of the muscle fiber is called sarcolemma.

Myosin head has ATP activity.
Ca2+ comes from sarcoplasmic reticulum.

Action potential activates DHPR.
DHPR are on the transverse tubule membranes .
Rianodine Receptors are activated by DHPR.
Rianodine Receptor allows Ca2+ to flow out of the sarcoplasmic reticulum (via terminal cisternae) into the sarcoplasm.

Troponin has 3 parts.
Troponin I: Inhibition
Troponin T: Acts as a glue for Tropomyosin

Blood Plasma

2 compartments are Intracellular, Extracellular.

Isotonicity:
concentration/osmolarity should be the same in all 3 compartments.
If the concentration or osmolarity is not similar in all 3, then there will be movement of water.

Too much water in a cell leads to swollen cell and ruptured cell membrane .
Extracellular space (Interstitial tissue) can also be swollen.

Edema is due to changes in isotonicity.

Isovolemia:
Have to maintain same proprtion/ratio of things between all 3 compartments.

VIQ:
Total water in human body = 0.6 x body weight
Intracellular fluid = 0.4 x body weight
Extracellular fluid = 0.2 x body weight.

The interstital fluid - 0.75 of extracellular fluid
Intravasal (blood plasma) is 0.25 of extracellular fluid
Transcellular is part of extracellular compartment. Includes eye and inner ear.

VIQ:
To measure volume of fluid compartments:

Amount of indicator/concentration of equilibrium

Indicator gets distributed in the body after administration. It can be measured how much indicator is present after a while.

Intravasal measurement uses albumin because it stays in the intravasal space. Evans Bkue or I131 can be bound to albumin.
For measuring extracellular space: Inulin is used.
Inulin is easy to absorb, not toxic or metabolized and doesn't go into the cell.
To measure total fluid in every compartment: radioactive water is used.

Thrombosis:
Continuity of intravasal space is disturbed. There is no or reduced flow in the blood vessel.

Ahead of the thrombosis there is decreased or no blood flow.
Behind the thrombosis there is congestion, increase in pressure and edema (due to disruption of isotonicity and isovalemia of blood)

Centrifugation is required to separated blood cells and fluid.
Cells (RBC, WBC, Platelets) accummlatae at the bottom of the tube after centrifugation.

45% of total blood volume is RBC
Less than 1% is WBC and platelets
55% is blood plasma. Yellow and top region. Blood plasma made up of electrolytes, proteins, blood glucose.

Blood Sera = Blood plasma without the protein fibrinogen

Hematocrit: Proportion of cells (mostly RBCs) in the blood.
Males: 0.44-0.46
Females: 0.41-0.43
Difference is due to testosterone production

Components of plasma:
1) Inorganic electrolytes (Na, K, Ca, Cl, Mg ions)
2) Organic substances (proteins, glucose, urea, amino acids, lipids)

Proteins of blood plasma are mostly synthesized in liver and gut.
Blood plasma proteins regulate oncotic pressure, transport and act as acid-base buffers.

Albumin. Has a huge and crowded surface.
Attracts/Binds to water
Tranpsorts/binds to drugs
Can donate protons cuz protons are present on their surface.

- Alpha 1 globulins: Bind to hydrophobic specific hormones and vitamins (thyroxine, cortisol, Vitamine D)
- Alpha 2 globulins: bind to copper via the ceruloplasmin.
Importaant cuz free copper is toxic.
- Beta globulins: Includes transferrin (iron binding protein)
- Gamma globulins: Are aantibodies
- Fibrinogen: Works in blood coagulation

Electrophoresis is used to separate proteins according to their sizes and electric properties.

60% of blood plasma proteins are albumin.

Liver Cirrhosis:
Liver cells are dead and replaced by connective tissue.
There is less albumin and increased gamma globulin (antibodies) in the blood plasma.

Nephrosis syndrome: Kideny can no longer keep albumin in circulation and thus albumin is secreated out in urine.

Multiple myeloma: Albumin and gamma globulin are present at the same level.

Transport of hydrophobic substances in blood is with lipoproteins of plasma.
Hydrophobic core is triglycerides and cholesterol.
Hydrophilic periphery has phospholipids and apoliproteins.

Lipoproteins can be chylomicron, VLDL, IDL, LDL, HDL
This is in increasing density and protein content.
Chylo means absorbed from intestines.

HDL is the good cholesterol.
syntheitized in liver.
It picks up cholesterol from the blood vessel walls and protects against atherosclerosis.

Total body water content - 42 litres (60% of human)
Intracellulcar fluid - 25 litres
Extracellular fluid can be:
Blood plasma (3 litres)
Interstital fluid (13 litres)
Transcellular fluid (1 litre)

There is more protein in the blood plasma than in the interstitial fluid.

Blood:
Erythrocytes: Approx 5 million per microlitre
Leukocytes: 4000 - 10,000 per microlitre
Thrombocytes: 150,000 - 300,000 per microlitre.

Blood is made up of plasma and corpuscular elements.

Hematocrit is the:
volume of corpuscular elements/total blood volume.

Since the leukocyte and thrombocyte number is negligible hemttocrit practically measures the erythrocyte quantity only.

Usual hematocrit level: 0.41-0.46

Leukocytes can be granulocytes, monocytes, lymphocytes.
Granuclocytes can be neutrophils, basophils, eosinophils.

GLUT 1 needs no insulin and has high capacity.
Ankyrin is a very important stabilizing protein in the RBC membrane

Glycolysis is the only metabolism inside RBC

Under the membrane is a cytoskeleton (mesh) which provides flexibility.
This mesh is made up of spectrin.

The required iron uptake is 1-2 mg/day.
Fe2+ is better absorbed than Fe3+ and this is why Fe3+ is converted to Fe2+.

Free iron is toxic.
In cells, iron binds to ferritin.
In circulation (plasma), iron binds to transferrin.
Iron is stored in the liver and the spleen inside macrophages. This iron storage complex is called hemosiderin.

Ferroportin causes the release of iron from storage cells.
Ferroportin is inhibited by hepcidin which is produced by the liver.

Iron deficiency causes Microcyter Hypochrom anaemia.
RBCs will be pale as there is less iron and less hemoglobin in the RBC.
MCH and MCV will be low.

Before binding to ferritin, Fe2+ must become Fe3+.

Vitamin B12/Folic Acid is used in the synthesis of DNA.
Vitamin B12 binds to R protein in saliva and then to intrinsic factors in intestine.
Intrinsic factors are protecting proteins for B12. Prevent B12 from bein destroyed by acid.

Erythropoeitin enhances the production of erythrocytes.
Erythropoeitin is made in the kidney.

Vitamin B12 enhances the production of DNA and cell division.
Anaemia - low number of erythrocytes.
Due to vitamin B12 deficiency, RBC precurosrs don't divide and keep on growing. Thus number of erythrocytes is low and there is a certain type of anemia.
Intrinsic factors are made by the stomach wall.
Intrinsic factors are essential for the absorption of vitamin B12.
Lack of intrinsic factor will mean lack of B12 absorption meaning the above mentioned anemia problem.

RBC lifespan is 120 days.
Then it is broken down in the spleen.
1) Hemoglobin is taken up by the macrophage.
In the macrophage, globin is separated from the heme.
2) Biliverdin formed 3) When bilirubin formed.
Jaundice : too much bilirubin, skin becomes yellow.
Bilirubin normal levels - 17micromol/litre
4) In blood plasma: Bilirubin + Albumin ----> Unconjucgated (indirect) bilirubin
5) In liver: albumin leaves and Bilirubin + Glucoronic Acid ----------> Conjugated (direct bilirubin)
Conjgated bilirubin sent to bile and excreted as
urobilinogen (urine) and stercobilinogen (faecese)

Transition of unconjugated bilirubin to conjugated bilirubin is the rate limiting factor.

Fe2+ is needed for hemoglobin production.
Lack of iron causes microcytic hypochromic anaemia.
RBC are small and there isn't enough hemoglobin.

There is 8-27 micromol of iron in blood plasma.
Recommended daily intake of iron: 10-12 mg.

WBCs & Immune system

Normal WBC count: 4000 - 10000 cells per microlitre of blood.
Differential leukocyte count: Determination of the ratio of vatrous WBCs.

Staining of bloodmear (Pappenheim model):
Concentrated May Grunwald solution (3 minutes)
Dilute with equal amount of distilled water (1 minute)
Add freshly diluted Giemsa solution (1:20 ratio with distilled water)
Wash off Giemsa solution after 15 minutes

All blood cells originate in the bone marrow (multipotential hematopoietic stem cells)
Gives rise to either common myeloid progenitor or common lymphoid progenitor.

Granulocytes:
1) Neutrophils
60%-80% of WBC
Segmented nucleus
Have specific granules (phospholipase, lyzosime)
Act as phagocytes, produce cytokines

2) Eosinophils
1%-5% of WBC
Bilobed nuclei
Pro inflammatory cells
Produce cytokines & lipid mediators
Fights against viruses and parasites.

3) Basophils
(0.5% of WBC)
Largest granulocyte
Segmented nucleus
Have large granules with histamine and heparin.
Inflammatory response, inhibition of blood clotting, Allergic reactions, produces pro inflammatory cytokine.s

Natural Killer cells are large T lymphocytes.

Effector T cells: T killer and T helper cells
T regulator and T mediator cells also exist.

T lymphocytes become functional/activate after antigen presentation which is done in a secondary lymphoid organ.

MHC I and MHC II does antigen presentation.
T killer cells have CD 8 marker. MHC I binds to CD 8 marker.
T helper cells have CD 4 marker. MHC II binds to CD 4 marker.

After activation, T cells proliferate.

T killer cells kill pathogens by secreating granzymes and perforins .
Perforins create a hole in the pathogen membrane. Granzymes go through this hole.
NK cells also produce perforins and granzymes.
Capazes induce apoptosis.

T helper cells bind to antigens presented by B lymphocytes.
T helper cells then produce cytokines which activates B lymphocytes to produce antibodies
Cytokines are signal molecules for the immune system (Interleukins)

B lymphocytes produce immunoglobulins (antibodies). Antibodies are gamma globulin
Antibodies can be IgM, IgA, IgE, IgD, IgG
IgM is a pentamer - ABO antibodies
IgA is dimers
IgE, IgG, IgD are monomers.
IgD - Rh antibodies

Antibodies have Y shape with 2 heavy and 2 light chains.
There are disulfide bonds between heavy and light chains.

FAB part on antibody is for antigens
FC part is for NK cells.

Complenet system is a part of the humoral immune system.

Immune system:

	Innate	Adaptive
Cellular	Phagocytes	T, B lymphocytes
Humoral	Complenet System	Antibodies

Complenet system acts as a cascade
Have C1-C9
C1 to C5a are proteolytic enzymes. They hydrolyze next protein in the cascade

Opsonization: marking of the pathogen

C5b - C9 forms the MAC (membrane attack complex) which makes a hole in the membrane of the pathogen.

1st Landsteiner rule is valid for ABO and Rh
2nd Landsteiner rule only valid for ABO

Immunization occurs when Rh+ blood of fetus goes into Rh- blood of mother.
Henolysis occurs (erythroblastolis fetalis) RBC of fetus is destroyed.

Every time Rh- mother is expecting Rh+ baby, Rh profilaxis has to be done

Rh antigens are proteins encoded by genes.
AB antigens are sugar chains.
A antigen produced when someone genotype is AA, AO
B antigen produced when genotype: BB, BO
AB antigen produced when genotype: AB
Neither A or B antigen made when genotype: OO

Rh antibodies are IgG type. Monomoric.

H_2CO_3 ----------> HCO_3^- + H^+

There is bicarbonate-chloride exchange. Is antiport
Chloride (hamburger) shift
H^+ binds to haemoglobin.

oxygen diffuses from alveoli to capillaries due to partial pressure difference.
O_2 binds to the hemoglobin and this binding causes the hemoglobin to releases its H^+.

CO_2 goes from plasma to alveoli due to partial pressure difference.

Respiration has neuronal and chemical control.

Neuronal control center is in medulla and pons.
Dorsal respiratory group (dorsal side of medulla) - is the center of respiration (inspiration)
Ventral respiratory group - rhythm generator of breathing, used during exercise
Pontine respiratory group - Regulates breathing rate

Chemoreceptors are present in the medulla, carotid and aortic bodies. These cells are sensitive to changes in oxygen partial pressure and then changes in pH and CO_2 partial pressures.

CO_2 diffuses into cerebrospinal fluid and binds with water.
HCO_3^- and H^+ produced.
Chemoreceptor cells recognize higher H^+ concentration and activates inspiratory center to remove CO_2 and bring in O_2.

Lung Metabolic Functions - Produce and eliminates local vasoactive substances. Such substances cause vasoconstriction and vasodilatoin
Lungs can eliminate vasoactive hormones (vasopresisn)

Ventricles have isovolumetric contraction and isovolumetric relaxation.
In this volume doesn't change but pressure does.

Cardiac Cycle (with reference to ventricles):
A) Mitral valves open
Pressure doesn't change but volume increases.
Ventricle gets filled with blood from the atria
Period of filling

B) Mitral valve closes
Pressure increases, volume stays the same
Isovolumetric contraction

C) Aortic Valve opens
Pressure increases, volume decreases
Blood flows out of ventricles
Period of ejection

D) Aortic Valve closes
Pressure decreases, Volume stays the same
Isovoluetric relaxation

A) Mitral Valve opens

A---->B: Filling period
B------->C: Isovolumetric contraction
C---------->D Ejection period
D----------> A: Isovolumetric relaxation

Cardiac Cycle takes 0.8 seconds.
Systole - 0.27 seconds
Diastole 0.53 seconds

There are also 3rd and 4th sounds which are very very soft. These are another diastolic and a late diastolic sound

More the venous blood that flows in, higher is the contraction force.

Druring diastole: Volume increases and pressure is mostly the same
During systole: Volume decreases

I: Filling period (V inc, P same)
II: Isovolumetric contraction (V same, P inc)
III: Ejection period (V dec, P increases a bit)
IV: Isovolumetric relaxation (V same, P decreases)

The resting length of cardiac muscle determines how powerful contraction would be.

Preload - Volume Value. (Volume of blood that flows into heart)
Afterload - Pressure Value (Pressur that the ventricle must overcome to circulate blood.)

Higher the venous return, higher the preload.

Increased heart rate alone will not increase cardiac output.
More the blood that flows into the heart, stronger will the contraction be (up to a certain limit)

Contraction force could increase without change in muscle length sue to sympathetic stimulation and an increase in external Ca2+ conc.

Rhythmic excitation of heart is due to natural pacemakers (SA node, AV node)

SA node --------> AV node ----------> AV bundle ----------> AV bundle branches ----------> Purkinje Fibres

Fast action potentials are Na+ channel dependent.

More negative, steeper, larger amplitude (0.3-0.4 m/s)
Slow action potential are not Na+ channel dependent.
Less negative, less steep, lower amplitude (0.1-0.2 m/s)

Slow action potential don't have a resting potential value.
Influx of Ca2+ causes depolarisation.

Heart rate decreases during during vagal nerve stimulation. (Parasympathetic). Vagal stimulation delays repolarisation and prevents Ca2+ ions from flowing in.

In the heart, sympathetic and parasympathetic works against each other.
Sympathetic innervation of heart is diffuse and more spread out.

Parasympathetic innervation (through vagus nerve) innervates the SA and AV node.

Neuronal regulation:
Vagal innervation decreases heart rate and contraction force.
Sympathetic innervation increases heart rate and contraction force

Humoral regulation:
Adrenaline increases heart rate and contraction force.

Ca2+ and K+ concentrations also regulates heart activity.
More the Ca2+ in cardiac muscle and extracellular fluid: higher the heart rate and contraction force.
Higher the K+ conc in extracellular fluid, lower is the heart rate and contraction force.

During ventricular systole: Pressure increases, volume decreases
Semilunar valve is open, so blood flows out of the ventricles.

Heart Action potential:
Steep depolarisation (influx of Na+)
Long plateau phase - delays repolarisation. Is due to slow Ca2+ channel opening and closing.
Long plateau phase delays repolarisation.

Velcoity of blood flow:
Aorta: 22.5 cm/s
Capillaries: 0.03 cm/s
Vena Cava: 11 cm/s
Velocity and cross sectional area are inversely proportional.
Capillaries have the highest cross sectional areas thus they have the lowest velocity of blood flow.
Aorta has the lowest cross sectional area thus it has the highest velocity of blood flow.

2/3 of total blood volume is in the venous system.
Blood volume distribution depends on pressure and compliance.

In invasive blood pressure determination, needle tipped cannula is inserted into artery and then blood pressure is measured.
In non invasive blood pressure determination, the first sound is systolic blood pressure.
Last sound is diastolic blood pressure.

Critical Reynold number: 2200
Greater than this then flow becomes turbulent.
Lesser than this, then the flow is laminar.

Cardiac cycle: 0.8 s
Systole: 0.27s
Diastole: 0.53s

Length of cardiac cycle (pulse rate) affects the mean arterial blood pressure.
Longer the cardiac cycle, longer the diastole and systole, higher the mean arterial blood pressure.

During diastole, aorta passively contracts and pushes blood forwards.

Aging decreases aortic elasticity.

On the right side of the heart:
During expiration, venous return decreases. During inspiration, venous return increases.
On the left side of the heart:
During expiration, venous return increases. During inspiration, venous return decreases.

Valsalva maneuver: Forced expiratory effort
Whenecer thoracohumeral muscles are used.
This maneuver evokes complex cardiovascular reflexes. There are large fluctuations in vebous flow during this manoeuvre.

Purpose of cardiovascular system:
Facilitates exchange of gases, fluids, electrolytes between cells and outside environment.

Flow output of right and left heart do not differ significantly.
Output of right and left heart are independent of each other.

Circulation of most major organ systems are in parallel.
Except portal circulation.
Because the circulation is parallel, adjustment of blood flow to 1 organ does not create major disturbances in the blood supply to other organs.

Pressure gradient is the energy that drives movement of the fluid.
Flow (Q): fluid volume flowing through the cross section of a vessel in a given time period ($\Delta V/\Delta T$)

Hagen Poiseuille Law:
$Q = \Delta P \times pi \times r^4 / 8 \times n \times l$
n = viscosity
l = length of vessel
r = radius of vessel

At a given pressure gradient, flow will be determined by hydraulic resistance.
Hydraulic resistance is determined by fluid viscosity, tube length and tube radius.
When this statement is applied for systemic circulation, it is called total peripheral resistance.

In parallel circuit, total resistance is less than sum of resistance

Organ blood flow is not driven by the output of the heart but instead by the pressure generated within the arterial system.

Blood is a non Newtonian fluid.

Transmurla pressure within the vessel exerts a force on the vessel wall causing it to be stretched

Local control of circulation: Maintains adequate blood flow to meet local metabolic and functional needs of tissues.

Local vascular resistance is the key determinant of local blood flow.

Basal tone of arteriolar smooth muscle is controlled by local vascular and tissue hormonal factors and myogenic tone.

Vasodilatory innervation can increase blood flow locally.

Myogenic tone - spontaneous contraction maintained by arteriolar smooth muscle.

Bayliss effect: Some arteriolar smooth muscles are sensitive to stretching. They respond to stretching with contraction. Thus blood pressure reduces.

Increased transmural pressure induces arteriolar contraction.

Endothelial factors regulating arteriolar smooth muscle tone can be dialators or constrictors.
Dialators: Nitric Oxide, prostacyclin, EDHF
Constrictor: Endothelin.
All this is produced by the endothelial cells.

Local vasodilator tissue metabolites are released from active cells that are not getting enough blood flow/ not getting enough oxygen (hypoxia) / getting too much CO2 or lactic acid (acidosis).

K+ ions, NO, PGI2, PGE2, ATP, ADP are all signals for vasodilation.

Hyperemia - Increased blood flow above the base line.
Can be active hyperemia (to meet metabolic/functional demands)
Or
Reactive hyperemia (following an interruption to flow)

Blood flow autoregulation is present in every organ and is most prominent in cerebral and coronary circulation. This is where systemic circulation doesn't happen.

Blood flow regulation is based on the parallel increase or decrease of local vascular resistance with changes in arterial blood pressure.

Change in perfusion pressure ----------> Sudden increase/decrease in local blood flow ----------> appropriate constriction/dilation of arterioles
(The appropriate constriction/dilation of arterioles is an autoregulatory response)
Autoregulation is unable to prevent sudden changes in blood flow is blood pressure changes drastically (more than 1 mm Hg/s)

Autoregulation:
1) Myogenic (Bayliss effect)
2) Metabolic (accumulation or washout of vasodilatory metabolites)

Long term accumulation (takes weeks to months) new vessel growth, vessel degenration

Active hyperemia:
Increase in tissue metabolism will proportionally increase tissue blood flow. Due to the release of vasodilatory tissue metabolites ----------> Arteriolar dilation ----------> Local vascular resistance decreases ----------> blood flow increases ---------> O2 and nutrient supply increases.
This only happens as long as tissue metabolic rate is increased.

During active hyperemia, endothelial cells of the arterioles proximal to the tissues will sense the increased flow due to increased shear stress. They will release NO inducing vasodilation. Due to this, even arterioles that are not exposed to the tissue metabolites are involved in active hyperemia.

Reactive hyperemia:

Renal physiology

Kidney functions:

- Homeostasis of fluid compartments

isosmia - regulation of osmotic concentration

isovolemia - regulation of blood pressure and blood plasma volume
isoionia - regulation of ion concentration in blood plasma
isohydria - regulation of pH in blood plasma

pH of blood plasma = 7.37-7.43

- Elimination of non required substances. Endogenous (metabolic end products) & Exogenous (organic and inorganic substances)
- Endocrine function (renin, erythropoietin, calcitrol)
- Gluconeogenesis

Functional unit of kidney is nephron.
1 kidney has approximately 1.2 million nephrons.
Nephrons have:
- glomerulus + Bowmans capsule
- Proximal Convoluted Tubule
- Loop of Henle
- Distal convoluted tubule
- Collecting Duct

All glomerulus + Bowmans Capsule is in the cortex.
Superficial nephrons are called cortical nephron.
Deep nephrons are called juxtamedullary nephrons.
Loop of Henle is always in the medulla

Cortical nephron (aka short looped nephron): Has a short loop of Henle. The loop gores to the border between inner and outer medulla.
Juxtamedullary nephron (aka long looped nephron): Has long loop of Henle. Loop goes into the inner medulla.

Malphigian Corpuscle: Ultrafiltration - 180 litre/day.
Proximal Tubule: Large quantities transported, gradient not built here. Transport processes are not regulated here. No hormones act here. Phosphate is an exception.

Juxtaglmerular apparatus - Renin and Adenosine production.

Glomerular filtration: 180 litre /day
Glomerular Filtration Rate: 100-130 ml/minute

Factors determining filtration:
1) Extension, permeability of glomerular membrane
2) Effective filtration pressure (this is the driving force of filtration cuz ultrafiltration is passive)
3) Properties of filtrating substances. (Diameter, radius, shape of substances)

Glomerular membrane (blood plasma transported through it) has:
- Capillary endothelieum
- Basal membrane
- Podocytes.

Capillary endothelium has large fenestrations.
Pores between fenestrated endothelial cells (50-100 nm)
Pores between podocytes (25 nm)

Ultrafiltration depends on pressure difference.

Glomerular capillaries have relatively high pressure for normal ultrafiltration

Vasoconstriction: Vasopressin, Angiotensin II, Adenosin
Vasodilation: PGE, PGI2

Proteins cannot be filtered through the glomerulus.
The glomerular filtrate is protein free and phospholipid free blood plasma.

Pressure in bowmans capsule is pretty much constant.

To check filterability, we use filtrate/plasma concentration ratios.
Lower the molecular weight, molecular radius and molecular diameter, greater the chances it'll be filtered.

Renin hormones also breaks down angiotensinogen to angiotensin I and then angiotensin II.
Angiotenisn II causes:
- vasoconstriction of arterioles
- Na+ reabsorption in proximal tubules
- increased vasopressin concentration
- increased aldosterone concentration

Both vasopressin and aldosterone increase blood pressure.

In the proximal tubules, epithelial cells have luminal and basolateral membrane.
Basolateral membrane has Na+/K+ pump.

Na+ reabsorption happens in the PCT using 3 mechanisms including Na+/proton antiporter on luminal membrane.
Na+ draws water with its movement.

Glucose is completely reabsorbed in proximal tubule.
Glucose and amino acids are reabsorbed in PCT using Na+ solute cotransporter.

If blood glucose level is above 10 mmol/l, not all glucose will be taken up by the cell as glucose transporters will be saturated. Glucose stays in the filtrate.

15% of filtrated water is reabsorbed in the descending limb of the loop of Henle.
The thick ascending limb of the loop of Henle is impermeable to water. It makes the filtarte hypoosmotic. Na+ and Cl- reabsorption happens here.

Distal convulated tubule does reabsorption of 15% of filtrated water. Reabsorption of Na+, Cl-, Ca2+ happens here.

There are 2 types of collecting ducts: Inner medullary and cortical.
Inner medullary collecting duct: Na+ reabsorption happens without K+ secretion.
Cortical collecting duct: Na+ reabsorption and K+ interstitium secretion are coupled.

Diuretic drugs do:

ANF causes:
- vasodilation
- increased GFR (due to dilation of afferent arteriole)
- inhibits renin, aldosterone, ADH secretion
- thus water and Na+ diuresis increases
- Due to increased urination there is decreased blood plasma volume in body and hence decreased blood pressure.

99% of filtered Na is reabsorbed by kidney.

Proximal tubule:
Paracellular passive transport (solvent drag mechanism)
Na+/proton antiport
Na+ - Solute symport

Loop of Henle:
Paracelular passive transport through tight junctions
Na+ - K+ - 2Cl- symport

Distal nephron:
Na+ channel
Na+ - Cl- symport

All these mechanisms which reabsorb Na+ from tubular fluid into blood will increase the blood pressure.

Water in urine output is 1000 - 2000 ml per day

Thirst sensation by angiotensin II, hypothalamic centers (barorevptord affect these - decrease in blood pressure sensed by baroreceptors causes thirst)

- Ca2+ dependent K+ channels open
- Slow hyperpolarisation
- Voltage gated Ca2+ channels close
- Ca2+ dependent K+ channels close

BER is created in the interstital cells of Cajal.

If BER crosses the threshold, there is influx of Ca2+ ions eventually leading to contraction of smooth muscle cells,

Number of Ca2+ spikes determine how long and how strong smooth muscle contraction is.

Peristaltic movement is all throughout the GI tract.
Segmental contractions are responsible for mixing only. No forward movement.

MMC (migrating myoelectric complex)
It is the periodic electrical and peristaltic activity in the EMPTY stomach, small intestine.
6-10 minutes active period. Then 1.5 hour long pause.
This moves undigested food to the colon.

If there's inhibition of GI motility, this could cause necrosis of intestinal wall.

Damaged part of GI tract gets sympathetic signals which could lead to paralytic ileus.

Arterial blood flow in the splanchnic circulatory bed almost all goes to portal circulation.

Biting and the 1st part of chewing is voluntary.
The rest of chewing is automated.
Thus chewing is partly automated, partly myotatic (stretch) reflex.

Swallowing takes place after food has been cut up sufficiently.

Oral cavity: Not much digestion happens here (only amylase breaks down starch here)

Initial part of swallowing is controlled by striated muscles.

Swallowing has 2 phases:
Voluntary phase (from mouth to pharynx)
Reflex phase: Once in the pharynx and upper esophagus.

Contact with esophageal mucosa causes peristalsis.

Center of swallowing is the medulla.
Efferents are CN 9 and 10

Issues with swallowing can be due to inflammation, narrowing, diverticulim of esophagus.

For swallowing, pharyngeal muscles, upper esophageal sphincter, soft palate, nasal muscles must all work together in a coordinated manner.

Acidic reflux happens when acid from the stomach enters the esophagus. This happens cuz lower esophageal sphincter doesn't close properly.

Primary peristalsis: Peristaltic wave initiated from pharynx (voluntary action)
Secondary perisatic waves: Removes residual bolus. Initiated in the esophagus.

At both esophageal sphincters there are changes in the pressure leading to opening and closings.

Volume clearance: Saliva from mouth goes down into the stomach
pH clearance: Alkaline saliva and the acidic stomach content neutralize each other.

Achalasia: Lower Esophageal Sphincter doesn't open.

Saliva
Saliva is not critical for digesting food.
However food must be made moist. Allows for easier swallowing of food. This lubrication is done by the saliva.

- Osmotic activity could increase leading to diahrrea
- Lipids, fat soluble vitamins are not digested

Chief cells secreate pepsinogen (proteolytic proenzymes) via exocytosis.
Chief cells also secreate gastric lipase which is made up of Free Fatty Acid and Glycerin.
Chief cell secretion is regulated by the vagus nerve (PSY) - Acetylcholie - M3 receptor, Gastrin, CCK, Secretin

Parietal cells secreate HCl.

Digestion of proteins begins with the denaturation of proteins by HCl.
HCl also converts pepsinogen (inactive form) to pepsin (active form) which can then digest proteins.

Exocrine portion of pancreas is made up of acinar and duct cells.
Acinar cells secreate digestive enzymes.
Duct cells secreate aqueous $NaHCO_3$ solutions.

Pancreatic juice secretion: 200-700ml/day
Contain proteolytic enzymes, lipases and pancreatic amylase.

Pancreatic enzymes are initially secreted into an acidic environment.
As they move through the ducts, the environment becomes more and more alkaline.
This mechanism makes sure pancreatic enzymes don't digest pancreatic cells itself.

Pancreatic duct cells have HCO_3^- and Cl^- transports facing the duct lumen.

Secretin (physiological antacid) has an important stimulating effect on the pancreas.

Cephalic phase - sight, smell, thought of food has a parasympathetic effect via the vagus nerve.
Stimulates the pancreatic juice secretion.

Bile from gall bladder:
Dark Green in color, acidic pH

There is enterohepatic recirculation of bile salts (reabsorbed from later parts of small intestine)

There is neural and humoral regulation of bile secretion.
Parasympathetic input stimulates bile production by the liver.

Choleretic factors (increase bile production):
Secretin
Bile acid recirculation

Cholekinetics factor (increase bile transport)
CCK
Vagus nerve

There is simultaneous contraction of gall bladder and relaxation of sphincter of Oddi.

Cholelithasis - Gall stones (bile contains too much cholesterol & not enough bile salts)

GI system does:
uptake of food, fluid
Transport, temporal storage of food, fluid
Digestion, Absorption of food, fluid
Waste management

Only the upper 1/3 of esophagus and external anal sphincter have skeletal muscle fibres with somatic motor innervation (controlled only by CNS)
Thus chewing, swallowing, defecation are all voluntary.

Alimentary wall in between contains only smooth muscle cells.

Warfarin: Anticoagulant (vitamin K competition)

Trace elements & minerals
Daily required uptake is very low.
Need more minerals than trace elements daily.

Overdose of:
Zinc/Selenium: prevents defense against free radicals
Calcium: interferes with utilization of iron, zinc, magnesium
copper: interferes with zinc absorption
Iron: excess storage of iron

Fiber
Food group that cannot be digested by the human system.
Eg: Cellulose, Lignin, polysaccharides.
Fibres have anti inflammatory effect, regulate microbiome, evoke the feeling of satiery and stretch the intestinal wall.

Energy metabolism: conversion of energy from one form to another form
Anabolism: Energy is used up to build up complex molecules
Catabolism: Energy is used to breakdown stuff leading to heat & energy production and physical work.

Energy in chemical form/storage is usable energy.
Energy put into structural maintenance is not usable energy.

Human body is an open system. There is energy absorption, output and storage.

1 mol Glucose ----------> 1 mol Glycogen
2780 kJ 1488 kJ
There is 46% heat disspation

Approximatley 1L pancreatic juice is produced per day

Endocrine pancreas:
Alpha cells produce glucagon
Beta cells produce insulin
Delta cells produce somatostatin - inhibitor of glucagon & insulin

Exocrine pancreas produces digestive enzymes.

Acinar cells - enzyme secretion
Ductal cells - modify the content of the fluid.

Pancreatic secretion is isotonic.

On the pancreatic ductal cells:
Luminal side has Cl-/HCO3- exchanger.
Cl- into cell, HCO3- into lumen

Basolateral side has Na+/K+ ATPase & Na+/H+ antiport exchanger.
K+ and Na+ brought into the cell. Na+ and H+ sent out to the blood

Carbonic acid (H2CO3) is present within the cell.
Comes from H2O + CO2 (enzyme is carbonic anhydrase).
H2CO3 breaks down to HCO3- & H+ which are sent out of the cell.

Pancreatic secretion has:
water, bicarbonates, inactive & active enzymes
Active enzymes: amylase, lipase, ribonuclease
Inactive enzymes: very strong proteases (trypsinogen, chymotrypsinogen
Active forms are trypsin & chymotrypsin)

Inactive enzymes become active in the duodenum due to the action of the enzyme enteropeptidases. These are present only in the lumen of the duodenum.

Regulation of pancreatic secretion:
By hormonal regulation, by CCK, neuronal regulation by vagus nerve (vago vagal reflex)

Parasympathetic activity (via vago vagal reflex) activates pancreatic cells, stimulates pancreatic secretion.
Sympathetic activity inhibits pancreatic secretion.

CCK A receptor is for CCK
CCK B receptor is for gastrin.

I cells produce CCK.
CCK acts on acinar cells leading to increased enzyme production.

Low pH acts on S cells.
S cells then produce secretin.
Secretin acts on ductal cells and thus aqueous secretion increases (more Na+ and HCO3- secreated)
HCO3- neutralizes acidic pH from stomach.

Carbohydrate digestion starts in saliva by alpha amylase enzyme.
In duodenum, pancreatic amylase does this too.
On intestinal mucosa, sucrase, maltase, lactase are active

Protein digestion starts in the stomach (has pepsin & HCl)
Pancreatic juice has trypsin, chymotrypsin and elastase which are strong proteases.
Protein digestion ends in intestinal mucosa (done by dipeptidases)

Trypsinogen (inactive) becomes trypsin (active) due to the action of enteropeptidases which are anchored to the intestinal brush border.
Trypsin then activates itself and other proenzymes in the small intestine.

Lipids are digested by pancreatic juices which have lipases.

Negative feedback common with hormones.
Positive feedback also present. Eg: high estradiol levels further stimulate higher LH release. This happens during the middle of the menstrual cycle.

Hormone producing organs are innervate by sympathetic and parasympathetic fibres.
Vasoconstriction and vasodilation also affect hormone release.

Permissive effect of hormones:
Eg: Requirement of glucocorticoids to be present for catecholamines to exert their effect
This is because glucocorticoids increase the production of catecholamines receptors.

Pathophysiology could be because hormone levels are too high or too less or because receptors levels are too less.

Hormone therapy treatment: glucocorticoids are anti-inflammatory and have immunosuppressive effect.

Adenohypophysis produces and secretes growth hormone, adrenocorticotrophic hormone, thyroid stimulating hormone, lutenizing hormone, follicle stimulating hormone, prolactin.
Supraoptic and periventricular nuclei of hypothalamus produce vasopressin and oxytocin and send it to the neurohypophysis for storage and release.
Hypothalamus creates releasing and inhibiting hormones and sends them to adenohypohysis.
All of the releasing and inhibit hormones are peptides except prolactin inhibiting hormone.

The adrenal gland sits omtop of both kidneys.
Adrenal cortex has:
zona glomerulosa - makes mineralocorticoids (aldosterone)
zona fasiculata - makes glucocorticoids (cortisol)
zona reticularis - makes androgens. (dehydroepiandrosterone)

ACTH acts on G proteins of target cells. Protein kinase is made which converts cholesterin ester to cholesterin. Cholesterin moves from within lipid droplets into the mitochondria. Thus ACTH main function: mobilize cholesterin and prepare it for cortisol production.

Strech marks, thin skin, fat pads, poor muscle development, red cheeks, poor wound healing ulcers are all symptoms of Cushing syndrome - too much glucocorticoids in the body.

Androgens also made from cholesterol.
Adrenal cortex has mostly DHEA (dehydroepiandrosterone) which is a weak androgen hormone.
Only 7% DHEA is free in the blood
90% transported by albumin. 3% transported by GBG

Without adrenal cortex: stress tolerance would be very low
Adrenal cortex may be destroyed by infection, cancer or autoimmune disease.

Hormones - chemical substances released by the endocrine glands, move via circulation and reach receptor organs.

Hormones are grouped by their chemical composition:
Protein/Peptide hormones
Amino Acid hormones
Steroid hormones (derived from cholesterol)

Steroid and thyroid hormones are fat soluble. Thus they have intracellular receptors.
Protein/peptide hormones are water soluble and have plasma membrane receptors.

For excretion, steroid hormones first become water soluble in the liver by conjugation.

Free hormones in the blood are biologically active.

eg of negative feedback: testosterone negatively influences/inhibits GnRH from hypothalamus. It can also inhibit LH coming from the anterior pituitary.
LH goes to testes and makes testosterone.

eg of positive feedback.
Mid ovarian cycle, estradiol (hormone) increases the activity of anterior pituitary cells which increases the release of FSH and LH and the cycle continues.

Ferguson reflex (example of positive feedback). Is a mixed reflex.
- Baby head stretches cervix, feedback sent to pituitary
- Pituitary secreates oxytocin into blood which travels to uterine muscle
- Oxytocin stimulates uterine contraction, pushes the baby down and stretches the cervix.
- Cycle repeats until the baby is born.

Estrogen is important in the action of oxytocin.

GnRH (Gonadotrophin releasing hormone) of hypothalamus causes FSH, LH to be released from anterior pituitary.
Dopamine (catecholamine) inhibits GnRH and prolactin.
TRH (thyrotrophin releasing hormone) of hypothalamus acts on TSH (thyroid stimulating hormone) releasing cells of the anterior pituitary.
TSH causes T3, T4 to be made from thyroid gland.
GHRH (growth hormone releasing hormone) of hypothalamus acts on GH (growth hormone) producing cells of the anterior pituitary.
ACTH is important for glucocorticoid and weak androgen release.
Angiotensin and renin needed for mineralocorticoid release.
Prolactin - production of milk.
Oxytocin - ejection of milk

Calcitonin from C cells of thyroid gland and parathyroid hormone are antagonistic.
Calcitonin decreases Ca^{2+} concentration of blood
Parathyroid hormone increases Ca^{2+} concentration of blood by removing calcium from bones.

Centers for feedback are hypothalamus and anterior pituitary.
eg of negative feedback: testosterone negatively influences/inhibits GnRH from hypothalamus. It can also inhibit LH coming from the anterior pituitary.
LH goes to testes and makes testosterone.

eg of positive feedback.
Mid ovarian cycle, estradiol (hormone) increases the activity of anterior pituitary cells which increases the release of FSH and LH and the cycle continues.

Ferguson reflex (example of positive feedback). Is a mixed reflex.
- Baby head stretches cervix, feedback sent to pituitary
- Pituitary secreates oxytocin into blood which travels to uterine muscle
- Oxytocin stimulates uterine contraction, pushes the baby down and stretches the cervix.
- Cycle repeats until the baby is born.

Estrogen is important in the action of oxytocin.

GnRH (Gonadotrophin releasing hormone) of hypothalamus causes FSH, LH to be released from anterior pituitary.
Dopamine (catecholamine) inhibits GnRH and prolactin.
TRH (thyrotropin releasing hormone) of hypothalamus acts on TSH (thyroid stimulating hormone) releasing cells of the anterior pituitary.
TSH causes T3, T4 to be made from thyroid gland.
GHRH (growth hormone releasing hormone) of hypothalamus acts on GH (growth hormone) producing cells of the anterior pituitary.
ACTH is important for glucocorticoid and weak androgen release.
Angiotensin and renin needed for mineralocorticoid release.
Prolactin - production of milk.
Oxytocin - ejection of milk

Calcitonin from C cells of thyroid gland and parathyroid hormone are antagonistic.
Calcitonin decreases Ca2+ concentration of blood
Parathyroid hormone increases Ca2+ concentration of blood by removing calcium from bones.

Controlled by
T4/T3 (balance of BMR)
Physical activity (balance of lifestyle)
Food intake (controlled by hormones)

Assesment of lean body mass vs body fat is more accurate than BMI.

Too much energy intake causes abnormal amount of fat in the liver - fatty liver - liver dysfunction. This leads to insulin resistance, high triglyceride, high LDL, low HDL. All this contributes to cardiovascular disease.

Adipokkines - hormones of adipose tissue.

Leptin
Stimulated by: Increased fat storage
Targets: hypothalamus
Effect: Decreases food intake, increases energy expenditure.

Adiponectin
Stimulated by: Decreased fat storage
Targets: muscle cells
Stimulates: Free fatty acid use.

TNF alpha is stimulated by increased fat storage.
Targets the liver and adipocytes
Is proinflammatory and insulin resistance.

Stimulation of NPY and AgRP neurons stimulates food intake.
MSH/CART neurons inhibits food intake.
All these neurons are in arcuate nucleus, project to periventricular nucleus. They control feeling of hunger.

Empty stomach has ghrelin. Ghrelin promotes hunger.
Streched stomach, PYY on hypothalamus, CCK on vagal afferents all promote satiety

Stress causes excess cortisol output.

Endocrine pancreas:
alpha cells (25%) make glucagon
beta cells (60%) make insulin
delta cells (10%) make somatostatin. Somatostatin inhibits both insulin and glucagon.

Insulin causes protein, fat and glycogen synthesis
GIP - gastric inhibiting peptide.

Insulin is released from beta cells by exocytosis. This is facilitated by Ca2+

Hyperglycemia, Arg & Leu, incretin all stimulate insulin release
Somatostatin and catecholamines inhibit insulin release.

Insulin like Growth Factor (IGF)
IGF 1 and IGF 2 from tissue have paracrine effect
IGF 1 from liver acts like a hormone.

Glucagon increases gluconeogenesis thus glucose increase in blood is countered by insulin.

Diabetes mellitus has type I and II
In type I: beta cells cant produce insulin. Is hereditary
In type II: sensitivity to insulin is decreased. There is resistance to insulin due to lifestyle.

Too much glucose in blood would cause a loss of lot of water as glucose would go into the urine and take water with it.
Due to this, the body cant support tissues properly leading to inflammation.

low insulin increases glucagon effect and causes decreased glycogenesis, lipogenesis.

20% of filtered Na+ is reabsorbed in Loop of Henle
9% of filtered Na+ is reabsorbed in the distal convoluted tubule and collecting duct.
Less than 1% if filtered Na+ will be excreted.

In the proximal convoluted tubule, there is passive and secondary active Na+ reabsorption. There is sodium solute transport on the luminal membrane. Solute usually glucose. Amino acids, phosphates, water soluble vitamins, bicarbonates, chloride and sulfate also used in Na solute transport

Sodium proton antiport also present on luminal membrane
Protons of Na+/proton antiport come from carbonic acid dissociation inside the cell.

These 2 mechanisms reabsorb half the Na+ in the proximal convulated tubule.
Passive Na+ reabsorption through tight junctions (through water channels) makes up the other half.

On the basolateral side there is Na+/K+ ATPase.

Descending segment of loop of Henle does concentration of fluid. Goes from 300-1200 milios/l. Descending segment is strongly permeable to water (water reabsorption occurs). Na+ is transported from interstitium to the tubular fluid.

Ascending limb has thin and thick segments.
Ascending limb is not permeable to water and freely permeable to Na+ and Cl-. Na+ flows to the interstitum, especially in the thick ascending segment.

Na+ and Cl- reabsorption into the interstitum, without water reabsorption builds up medullary gadient which is required later for H2O reabsorption from collecting duct.

In thick ascending segment, paracellular Na+ reabsorption present along with Na+ - Cl- - K+ symport.
Na+ - Cl- - K+ symport is driven by Na+/K+ ATPase on the basal membrane.

Distal convoluted tubule has no paracellular Na+ resorption. It has only
Na+ - Cl- cotransport driven by Na+/K+ ATPase.

Total Ca2+ in plasma is 2.1 to 2.6 mmol/L (50% is free, 40% is protein bound and 10% is in complex salt).

Ca2+ is needed for muscle contraction.
Hypocalcemia causes uncontrolled muscle spasms (tetany). Could be fatal if the muscles affected are laryngeal or respiratory muscles.

Voltage gated Na+ have a threshold.
If Ca2+ concentration decreases, voltage gates don't function properly and open on their own.
Thus in hypocalcemia, neuromuscular excitability is abnormally high

Hypercalcemia may cause precipitation of insoluble Ca2+ salt in the soft tissues.

In humans, there is positive calcium balance until bone formation ends.

Required Daily Intake of Ca2+ is 1g per day.
Net Ca2+ absorption is 5 mmol/day. Net Ca2+ secretion is also 5 mmol/day.
There is increased Ca2+ demand during pregnancy, growth, lactation.

Ca2+ balance is exclusively endocrine.
Ca2+ balance maintained by parathyroid hormone, Calcitrol (from vitamin D), calcitonin (From thyroid gland)
Ca2+ levels control these hormone production.

Bone exchanges Ca2+ with the extracellular fluid.

Parathyroid hormone acts on bone and kidney
Calcitriol acts on bone and GI tract
Both parathyroid hormone and calcitriol increase the plasma Ca2+ concentration.
Ca2+ reduces hormone activity by reducing gland activity.

Ca2+ inhibits parathyroid hormone through the stimulation of cell membrane Ca2+ sensor receptors. Triggers signals which causes high Ca2+ in cells inhibiting parathyroid hormone secretion.

85-95% inorganic phosphate is reabsorbed in the proximal convoluted tubule.
Has a glucose type reabsorption (secondary active transport with Na+)
Parathyroid hormone inhibits inorganic phosphate reabsorption.

Bone is a mineral reserve
Bone density in women decreases as they age.

Osteoblast: produce osteoid proteins like collagen, promotes mineralization and increases inorganic phosphate levels.
Osteoclast: dissolve and breaks down the bone

Osteoclast is activated by RANKL-RANK signalling.
This signalling causes bone degradation releasing Ca2+.

Parathyroid hormone and calcitriol activate osteoclasts using RANKL - RANK signalling.

Osteomalacia - bone softening. Happens when bone mineralisation is reduced.
Could be due to vitamin D deficiency, parathyroid hormone overproduction.
Osteoporosis: bones are fragile & brittle. Loss of bone mass
Due to loss of both mineral & organic materials,

98% of K+ is intracellular
2% if K+ is extracellular
Normal K+ levels in serum: 3.5 - 5.2 mmol/L

Hyperkalemia: > 5.5 mmol/L
Hypokalemia: < 3.5 mmol/L
Both lead to severe organ damage.

K+ is important in maintiang stable membrane potential.

Both hyperkalemia & hypokalemia cause depolarisation.
Both cause muscle weakness, seizures.

Kidney removes non volatile acids. This is done by the reabsorption of HCO3- and H+ secretion.
For every HCO3- reabsorbed, kidney must secreate a proton.
80-90% of HCO3- reabsorption happens in the proximal tubule.

In the proximal tubule, HCO3- is reabsorbed with Na+

In tubule lumen, HCO3- + H+ ----------> H2CO3 --------> H2O + CO2.
CO2 diffuses into the cell
CO2 + H2O ----------> H2CO3 ----------> H+ + HCO3-
Na+ and HCO3- are reabsorbed together via basolateral Na+ - HCO3- cotransporter.
Simulataneously H+ secretion is done by apical Na+/H+ antiporter.

In thick ascending limb of Loop of Henle, HCO3- is reabsorbed by Cl-/HCO3- basolateral exchanger.
Simultaneously, H+ secretion is done by apical Na+/H+ antiporter.

Collecting duct
(during acidosis - stimulated by low pH)
Intercalated type A cells have
HCO3- reabsorption by Cl-/HCO3- exchanger & H+ secretion by apical H+ ATPase.

(during alkalosis - stimulated by high pH)
Intercalated type B cells have:
H+ reabsorption by basolateral H+ ATPase & HCO3- secretion by apical Cl-/HCO3- exchanger.

Kidney must secreate HCO3- if there us excess base.
Kidney must reabsorb HCO3- if there is excess acid

Most of the H+ in urine combines with urinary buffers (phosphate, creatinine) or combines with free base NH3 to be excreted as NH4+

Blood pH should be 7.37 - 7.42.

Important buffer in the plasma is carbonic acid/bicarbonate system.
Uses kidney & respiration to regulate
Carbonic acid level is regulated by respiration.
Bicarbonate level is changed by kidney

In acidosis we do hyperventilation - CO2 decreases leads to respiratory Alkalosis.

In Alkalosis we do hypoventilation - CO2 increases leading to respiratory acidosis.

Hemoglobin acts as a buffer.
Hamburger shift happens heren

Renal regulation is possible for acidosis & Alkalosis.

Renal compensation for acidosis:
H+ secretion increases, HCO3- absorption increases.
This decreases H+ in the body & increases pH.

Renal compensation for Alkalosis:
H+ secretion decreases, HCO3- absorption decreases.
This increases H+ in the body & decreases the pH.

Thermophysiology

Poikilotherm - body temperature is affected greatly by the environment (cold blooded creatures)

Humans have a high, relatively constant core temperature and do lots of temperature regulation.

The core body temperature is only relatively constant. Relates to visceral organs and the brain.

Body temperature is highest in late afternoon and reduces and is at its lowest during REM sleep (1 degree fluctuation).
Postovulatory temperatures are higher than preovulatory temperatures.

Body temperature avegare: 36.6 degrees celsius (98 degree farenheit)
Physiological maximum (due to heavy exercise) is 40 degrees celsius (104 degree farenheit)

Perfect heat balance is impossible.

Has vasodilation and sweating

For thermoregulation, behavioural changes come first and then homeostasis.

If body temperature starts to fall almost 3x more heat production happens.

In different cells of the body, metabolic heat is produced in different proportions considering their different O2 consumption.

At rest, the heart, brain and liver produce the most heat.

Heat production depends on BMR
What we eat and how much exercise is done affects heat production

Non shivering thermogenesis: special brown adipose tissue.

White adipose tissue does storage of fat and provides insulation.
Brown adipose tissue has only 1 function: to provide hear
Is full of mitochondria, has rich blood supply and rich sympathetic innervation.

In brown adipose tissue, terminal oxidation and ATP synthesis are dissociated.
Normally protons go back to the mitochondrial matrix via ATP synthase.
In brown adipose tissue, uncoupling proteins allow protons to go back into the mitochondrial matrix bypassing ATP synthase. This produces heat.

Clothing is involved in behavioral thermoregulation.
Midday naps, sleeping both reduce heat production.

Skin is usually recieeving 5% of cardiac output

Lactate is also used up at type I fibers.
Lactate undergoes oxidation to pyruvate and gives off CO_2 + H_2O + ATP
Lactate can also undergo gluconeogenesis at the liver and skeletal muscle.

Lactate threshold (where production > elimination) is usually 50-60% of VO_2 max.
For elite athletes it could be 70-80% of VO_2 max.
Only training can increase lactate threshold (training causes higher elimination rate and higher tolerance to lactate)

During exercise, arm work causes the highest increases in systolic blood pressure.
Arm work also increases mean arterial blood pressure and diastolic blood pressure.
During leg work, diastolic blood pressure stays similar, mean arterial blood pressure increases slightly and systolic blood pressure increases significantly.

Blood pressure increases the most if work is static.

Effects of training:
Skeletal muscle blood vessels stay dilated (due to local metabolites and Beta 2 adrenergic receptors)
Muscle gets 15% cardiac output but can increase till 80% due to training.
Blood flow to splanchnic regions decrease (vasoconstriction) except kidney which has autoregulation.
In heart venous return increases, thus stroke volume increases so cardiac output increases
Coronary vessels get dilated, blood flow in the coronaries increases up to 5 times.

Long term effects of training will be that:
performance will be better
cardiac muscle becomes stronger and thicker (stronger contractions, increased stroke volume, more sustained work)
Size of heart ventricles increases to receive more blood
Muscle strength increases cuz there's an increase in cross sectional area and a slight increase in the ratio of type II fibers.

During dynamic exercise:
Skin perfusion increases
Plasma volume decreases (due to sweating)
Fluid & electrolyte replacement is important.
Eventually stroke volume decreases (due to reduced plasma volume)
Heart rate increases slowly
Blood pressure declines.

During static exercise:
Blood flow and oxygen supply is decreased so lactate is produced.

Muscle pain is due to lactic acid production.
Muscle soreness comes a few days later. Due to microtraumas in muscle causing inflammation, edema which affect pain receptors

Exercise stimulates bone density.
Strenous exercise inhibits remodelling, prevents osteoclast dominance and bone loss
Adequate Ca2+ intake and regular exercise stimulates bone density and reduces the risk of osteoporosis.

Exercise increases muscle strength and functional capacity.
Daily exercise decreases blood glucose levels and insulin responses to glucose ingestion.

Estrogen is important in bone homeostasis in young women.

High carbohydrate diet leads to increase in muscle glycogen content.
High carbohydrate diet causes increased tome to exhaustion compared to a low carbohydrate diet.

Consumption of carbohydrates with good timing increases performance (a carbohydrate & protein rich meal 2 hours before and after exercise. NO fiber and fat because they slow down the absorption of glucose.)

Muscle fatigue - loss of muscle power . Reversible by rest. It is due to the depletion of energy delivery system.

During follicular phase, cholesterol goes to theca cells from circulation.
The theca cells then produce weak androgen hormones. These diffuse to granulosa cells where they are further modified to estradiol

During luteal phase, LH stimulates progesterone to be made from cholesterol only.
Then from the progesterone, a small amount of estradiol can be made.

Transport of estradiol & progesterone
Free estradiol: 2%
Free progesterone: 2%
Albumin with estradiol: 60%
Albumin with progesterone: 50%
Gonadal steroid binding globulin: 38% for estradiol
Corticosteriod binding globulin: 48% for progesterone

Receptors for estradiol and progesterone are both intracellular.

Estradiol effects:
Oocyte maturation
Increased oocyte motility in oviducts
Increased mucous secretion secretion at the cervix
Proliferation of endometrieum
Increased excitability/sensitivity of the myometrium
More oxytocin receptors produced
Growth of ducts in mammary glands.

Estradiol also:
Does mineral deposition at the bone
Increases HDL:LDL ratio (anti atherosclerotic) effect
Increases hepatic protein synthesis (transport & clotting proteins)

Oral contraception contains modified estrogen and progesterone molecules.
These molecules can be absorbed from the GI tract easily and act on estrogen and progesterone receptors.
These molecules inhibit estrogen and progesterone binding and this causes:
Inhibition of ovulation
Thins the endometrial level
Increases mucus consistency/viscosity of the cervix.

Cyclic activity of the ovary stops when all follicles have been used up or have died (menopause).
Leading up to menopause, menstrual cycles become irregular and take longer.

After menopause, estradiol and progesterone are not secreted in the ovaries.
Estradiol and progesterone are not present so there is no negative feedback on GnRH, FSH, LH
Thus after menopause, LH, GnRH, FSH secretion increases leading to heat flushes (sweating, feeling hot)
Even after menopause, androgen hormones are still produced in normal quantities.

Sperm is stored for a few days in the epididymis.
Further maturation & incapacitation (receiving covering protein) & protection of sperm happens in the epididymis.

Seminal vesicle fluid + Prostate gland fluid + Sperm = ejaculate fluid (3ml). Contains 150 million sperm

Fertilisation: sperm and ovulated oocyte fuse

Diffusion: O2, CO2, steroid hormones
Facilitated diffusion: glucose
Active transport: Na+ Symport
Endocytosis of Immunoglobulins (IgG)

Maternal blood circulates through the intervillous space/ Fetal blood flows through the chorionic villi.

Pregnancy duration is 38 weeks post conception or 40 weeks post last mestruation

hCG (human chorionic gonadotropin) is the first hormone secreated. Reaches high concentration early in pregnancy.
Peaks in week 10
Produced by placenta
Is a glycoprotein hormone (like FSH, TSH, LH). All 4 have the sma ealpha peptide chain and different beta chains. Beta chain of LH and hCG are basically the same.
hCG increases till week 10. Due to this progesterone and estradiol don't decrease till week 10.
After 10 weeks of pregnancy, hCG drops. Cant support corpus luteum anymore. Corpus Luteum dies

hCG used in pregnancy test. Presence of hCG fragment is used to test if woman pregnant or not.
hCG fragments act as a bridge between the antigen and antibodies.
Control is always positive - always shows a one
If in the test region there is also a line that means pregnant.

Estradiol sensitizes the myometrium. Makes membrane potential excited.
Progesterone stabilizes and protects it.

Once the corpus luteum dies, progesterone and estradiol concentrations don't drop because now the fetoplacental unit produces the 2 hormones.
Feroplacental unit made up of mothers blood, placenta and fetus.
Mothers blood provides cholesterol for steroid hormone synthesis.

Thus eventually, progesterone, estradiol, estriol are present in all 3.

Progesterone activity overrides stimulating activity estradiol from week 10 towards the end.
In the last few weeks, there is a sharp increase in estradiol and estriol concentration.
Helps in preparation for delivery.

During parturition (delivery) there is increased estrogen and decreased progesterone effect.

Increased estrogen:
Increase in oxytocin receptors
Causes depolarisation
(These 2 increase excitability causing stimulus)
Increase gap junctions (cause conduction)
Increase contractile proteins (causing contraction)
Oxytocin also causes stimulation.

Contraction pushes endometrium towards the baby, baby head gets pushed against and dilates the cervix. Positive feedback of oxytocin.

Placenta also exits along with the baby during delivery.

After delivery, there is a very sudden drop in all steriod hormone concentrations.

During puberty:
Estradiol differentiates the duct system of the breast & deposits fats in the breats
Progesterone differentiates the alveoli of the breasts.

Durinf the 40 weeks of pregnancy, there is further growth & differentiation of mammary gland.
Estrogen and progetsone have the same effect on mammary glands during pregnancy as they did during puberty.
Insulin & glucocorticoids also have effects on mammary glands.

Female gonads: ovaries
This is the site of hormone production and development of oocytes.
Main hormones are estrogen and progesterone.
Oviduct: site of fertilisation
Uterus: site of implantation

GnRH secretion becomes pulsatile at the start of puberty.
GnRH induces FSH, LH release from the anterior pituitary.

FSH & LH act on the ovary.
Around the developing oocyte is thecal and granulosa cells.
This makes up the follicle.

Theca cells are similar to Leydig cells.
Granulosa cells are similar to Sertoli cells.

Follicles produce estrogen & progesterone.

During the follicular phase of the ovarian cycle, estrogen level is high.
There is positive feedback at the end of the follicular phase to anterior pituitary.
Progesterone increases just before ovulation due to LH peak.

In Luteal phase, corpus luteum produces the progesterone.

If estradiol level is low, there is negative feedback.

If frequency of GnRH pulses is high (like in luteal phase) then LH is produced mostly.
If frequency of GnRH pulses is low (like in follicular phase), then FSH is mostly produced.

Before puberty, estrogen values are low due to low activity of GnRH.

74 days are needed to produce mature spermatozoa from spermatogonia.

Testosterone can be converted to estrogen (17 beta estradiol) by aromatase enzyme or to DHT (dihydrotestosterone) by reductase enzyme.
DHT is a more potent androgen

Estrogen in males is used in bones for epiphysial closure.

Capability of movement by sperm happens in epididymis. (sperm maturation)
Storage of sperm in vas deferens.

Erection, Emission and Ejaculation.
Emission: Sympathetic contraction of smooth muscle in vas deferens, prostate and seminal vesicle causing sperm & seminal plasma to move to urethra.
Erection: Due to increased efferent parasympathetic activity leading to vasodilation.

In females, 1-2 million oocytes are present at birth.
100,000 remain at puberty.
Several follicles are stimulated together to develop at each month.
One follicle is more dominant than the other (is more sensitive to FSH). Other follicles die.

Hormone production also occurs in follicles.
Cholesterole is the main starting point for estrogen, progesterone, testosterone.
The direct precursor of estrogen is androgens via aromatase enzyme activity.

Developing follicles produce estrogen.

Menopause is due to not enough follicles present anymore.

Cerebral blood flow control is mostly due to autoregulation.
Cerebral blood flow is very sensitive to changes in CO2, O2, glucose.
If glucose or oxygen concentration decreases and if CO2 concentration increases then blood flow to the brain will increase by arteriolar vasodilation.
Now there is increased global cerebral blood flow
Hypercapnia - increased CO2
Hypoxia - decreased O2
Hypoglycemia - decreased glucose.

Global cerebral blood flow is stable. Local distribution is very variable. This variability is due to changes in function.

Stimulation leads to increased neuronal activity then increased glucose and O2 uptake by brain so increased cerebral blood flow.

Flow metabolism coupling:
Local increase in neuronal activity ---------- Local increase in metabolism causing vasodilation and increase in blood flow.
This is called active hyperaemia.
This is rapid - happens within a few seconds.

Activation of excitatory glutamergic neurons synapses play an important role.
Hypoxia, hypoglycemia, hypercapnia do not occur during the coupling metabolism.
Initiation of coupling is independent (feed forward) - there is release of NO, prostaglandins (vasodilators).
Initiation is independent of how long the stimulation is.
Maintanance of coupling is dependent (feedback)

Maintained activation goves rise to adenosine.
There is hyperpolarisation and relaxation of the smooth muscle of arterioles.
The coupling metabolism only affects the intraparenchymal vessels mainly.
Pial arterioles can also undergo vasodilation.

Local regulation is the most important and common of the cerebral blood flow regulations.

One single primary sensory neuron may provide information to multiple secondary order neuorns.
This is called divergence.

Inhibitory synapses exist which suppress activity in neighbouring neurons (lateral inhibition)

Mechanoreception senses touch, pressure, vibration, stretch. All are sensed by A beta fibre endings

Thermoreception senses cold (free nerve ending of A delta) or warmth (by free nerve endings of C fibers)

Nociception.
Fast pain sensed by A delta fibers.
Slow pain, itch sensed by C fibers.

Mechanoreceptors of the skin are encapsulated.
MErkel receptor, Meisnner corpuscle, Pacinian corpuscle, Ruffini endings are all present in hairless skin.
Hairy skin doesn't have Meisnner corpuscle.

Merkel receptor in the basal layer of epidermis. Synapses with A beta afferent nerve endings.

Meissner corpuscles have sheaths of Schwann cells and several afferents.

Ruffinin corpuscle - one single nerve fiber is present. Is encapsulated. Senses stretch.

Pacinian corpuscle - Schwann cells and connective tissue surround the nerve endings. Is sensitive to vibration. Present in the superficial subcutaneous tissue. Has very fast adaptation.
The nerve terminal itself is a slow adaptating structure. The surrounding structure makes the corpuscle a fast adapting structure

C fiber - slow pain

Conducting velocity and diameter reduces from top to bottom.
Myelination also reduces from top to bottom.

Sensory receptors are terminals of primary afferent neurons.
They convert stimulus into electrical signals.
This signal is meditated through opening and closing of ion channels.
If depolarisation occurs (actual potential increases), Na+ flows into the cell.
If Cl- flows into the cell, repolarisation occurs (actual potential decreases).

When intensity of stimulation reaches the threshold, action potential is formed and is propagated.
Action potential activate 2nd order neurons.
Modality (type), location, intensity, duration of stimulus are sensed and encoded.

Higher intensity stimulation causes higher firing of action potential on primary afferent fibers.

Rapidly adapting receptors are activated only at the start of the stimulus.
Slow adapting receptors are activated throughout the stimulus.

Meissner corpuscle is an encapsulated superficial receptor. Sense 2 point diacrimation. Is a rapidly adapting receptor.

Hair follicles are rapidly adapting receptors. They have a small receptive field.

Pacinian corpuscles sense vibrations.
Are rapidly adapting receptors.
Have a large receptive field.

Merkel cells are superficially located.
They have a small receptive field.

Astigmatism - when vertical curvature of the cornea is less than the horizontal curvature

Intraocular pressure is controlled by the production and draiage of aqueous humor.
Checked by tonometry.
Aqueous humor is made of plasma ultrafiltrate.
Produced by epithelial cells in the ciliary body. Production is ana active process.
Drainage is a passive process via transcellular vesicular transport.

Parasympathetic effect:
Contraction of the pupil
Increased aqueous outflow
Lens are more spherical (contraction of ciliary body, relaxation of zonula fibers)

Sympathetic effect:
Dilation of the pupil
Lens are more flat (relaxation of ciliary body, contraction of zonula fibers)

When we look close, parasympathetic tone is active.
When we look far, sympathetic tone is active.

Balance between drainage and production of aqueous humor keeps intraocular pressure normal (60 mm Hg)
If intraocular pressure is not normal, there's blurred vision and glaucoma.

Cup is usually within the optic disk.
Normal disc has a cup-disc ratio of 0.2.
In glaucoma: cup-disk ratio is 0.7 or more.
This effects eye functioning.

Eye movements can be conjugated or vergence.
Vergence movements:
Convergence: when object is close
Divergence: when object is far away.
Conjugated movements:

Ganglion cell layer (ganglion cells)

Receptive fields of ganglion cells depends on how many rods, cones give information to that 1 ganglion cell.
Receptive field is lower & resolution is higher in the fovea.
Receptive field is higher & resolution is lower in the periphery.

Receptor cells, horizontal cells, Off bipolar cells show hyperpolarisation in response to light.
On bipolar cells show depolarisation in response to light.
Like the 2 types of bipolar cells, there are also 2 types of ganglion cells - On and Off.

Cone sensitivity is super high.
In phototopic conditions - 550 nm is the optimum sensitivity
In scototopic conditions - 500 nm is te optimum sensitivity

Dark and light adaptation is done by the pupil
In dark, pupil is dilate to allow more light to come in

Fovea has high cone density.
Periphery has high rod density.

Visual receptive field - That area on the retinal surface from where a visual neuron can be stimulated.

Receptive field of ganglion cells have a centrum and periphery.

Only cone cells have connections with ON and OFF biploar cells both.

Light acts on cone cell.
Causes hyperpolarisation in the cone cell.

Metarhodopsin binds to arrestin instead of transducin.
Now hydrolysis of metarhodopsin.
11-trans-retinol becomes 11-cis-retinol again

Dark Current
In the dark, photoreceptors are depolarized.
cGMP gated Na+ & Ca2+ channels open.
Depolarization causes constant glutamate release.

In light, photoreceptors are hyperpolarized.
Due to metarhodopsin cGMP levels are low, Na+ and Ca2+ channels are closed.
Glutamate release is reduced.

Cone cells have iodopsin instead of rhodopsin.
There are 3 types of cones: blue, gree, red.
Each has its own peak stimulation at an optimum wavelength.

Horizontal pathways create lateral inhibition.
This increases contrast.
Horizontal cells in the horizontal pathway are excited by glutamate released from photoreceptors.
Horizontal cells then release GABA & inhibit adjacent photoreceptors. This is what increases contrast.

OFF bipolar cells
In dark:
Glutamate is released from photoreceptors,
Cation channels open, cell gets depolarized.
Glutamate is released to OFF ganglion cells.

Basically OFF bipolar cells activates OFF ganglion cells in the dark.

Conduction of vibration:
Sound can move through air or bone.
Air conduction is more sensitive than bone conduction.

Air conduction is through the ear.
Bone conduction is directly through the skull.

Air conduction:
Vibrations are collected by the outer ear, sent through the external canal, goes through the tympanic membrane and vibrates eardrum.
Vibration occurs in ossicles, passed onto oval window which causes waves to be made in the cochlear fluid

Outer ear has pinna (collects vibrations), external auditory meatus, tympanic membrane.
Outer ear: collects & funnels sound to the eardrum. Provides physical protection and has resonance function.

Middle ear has Eustachian tube (equilisation function), oval and round windows, ossicles (malleus, incus, stapes) and muscles.
Middle ear is essential for hearing and does amplification of the vibrations.
Without amplification, most vibrations would be reflected from the oval window.

Oval window is the border between middle and inner ear.
Middle ear is filled with air like the outer ear. Inner ear is filled with fluid

Stapedius muscle (facial nerve) and tensor tympani (trigeminal nerve) influence the movement of the ossicles.
If these muscles are contracted then ossicle movement is inhibited.
These muscles usually contract in response to loud sound (protective reflex).
This tympanic reflex prevents the amplification of loud sounds and reduces the transmission of these loud sounds to the inner ear.

- Motor cortex, basal ganglia, reticular formation, spinal cord via inferior olive (olivo cerebellar tract)
- Vestibular system via vestibular nuclei
- Reticular formation (reticulocerebellar pathway)
- spinal cord (dorsal spino cerebellar tract - proprioceptive)

In the cerebellum, Purkinje cells are inhibitory, act on cerebellar neurons.
Input to cerebellum comes via mossy fibers and climbing fibers.
Input via climbing fibers goes directly to Purkinje cells.
Input via mossy fibers excites unipolar brush cells (amplify the signal) & granule cells.
Granule cells become parallel fibers which activate basket & stellate cells.
Basket & stellate cells inhibit purkinje cells.

Paleocerebellum coordinates hand and finger movement.
Archiocerebellum coordinates equilibrium movement.
Neocerebellum provides feedback to the upper sensory sensory motor system to plan voluntary movements.

Vestibulocerebellum gets information from vestibular system & visual information.
Its motor response involves compensating eye & head movements.
Involves the fastigial nucleus, Deriters nucleus, flocculonodual lobe.

Spinocerebellum gets planned movement and actual movement as sensory information.
Compares the 2.A
Its motor response is smooth, coordinated movement.

Cerebrocerebellum gets movement plan as senseory information.
Motor response: planning of sequential movement and timing of movement

Motor thalamus gets information from the basal ganglia and cerebellum.

CNS

Cortical input goes to cerebellum from primary, suplementary & premotor cortex
Primary somatosensory cortex also projects to the cerebellum.
These cortical inputs run to the cerebellum via the pontine nuclei.

All sensory modalities provide input to the cerebellum indirectly.

Cerebellum also gets information from the ascending tracts.

From the cerebellum, information goes back to the cortex via the thalamus.
Cerebellum can also modify brainstem nuclei or descending tracts.

Cerebellum has as many neurons as the entire cerebral cortex.
Superficially there is a cerebellar cortex (gray matter).
Deep to that is the white matter.
White matter has afferent and efferent fibers.

White matter of cerebellum has Dentate nucleus, fastigial nucleus, interpositus nucleus (globus + emboliformis).
Output nucleus of the medial side is the Deiters nucleus (aka deep nucleus of cerebellum).
Not actually present in the cerebellum.

Deiters nucleus receives all sensory modalities and information from the cerebellum.

Cerebellar functions:
- Postural functions (by flocculonodular lobe)
- Coordination of intention & actual movement
- Comparison of afferent & efferent copy
- Cooridnation of muscles during movement
- Plays a role in implicit memory & motor learning.

Corticospinal tract (via pontine nuclei) sends input to the cerebellum.

From the spinocerebellum, half the output goes to the motor cortex. The other half goes to the red nucleus.
From the paleocerebellum, almost all output goes to the motor cortex.

All information from the cerebellum to the motor cortex goes via the motor thalamus.

Vestibulocerebellum does eye, head movement, gait, posture, balance.
Spinocerebellum does correction of movement patterns based on feedback.
Neocerebellum does planning, initiation, termination & timing of movements.

Cerebellar damage leads to balance disorders and coordination problems
Signs of cerebellar damage are ipsilateral (not contralateral like in the pyramidal tract)

Primary motor cortex is the primary input to the basal ganglia.
Caudate and putamen receives this input. They can send this information to the substantial nigra or to the externa/internal globus pallidus.

Caudate & putamen are the input structures of the basal ganglia.
Input from the cortex (corticostriatal) is excitatory input.
Input from the substantial nigra (nigrostiatal)

Output of basal ganglia:
- Globus Pallidus pars interna to the thalamus (VL, VM, CM nucleus)
- Substantia nigra pars reticulata the the thalamus (VL, VA)
- To the superior colliculus
- To the pontine tegmental nucleus.

Cortex projects to the caudate & putamen by glutamate neurons.
Globus pallidus pars interna & Substantia nigra pars reticulata project to the thalamus via GABAnergic neurons

From input nuclei to output nuclei there is:

Hypothalamus

Hypothalamus- key to homeostasis & survival. Can't live without it

It is an important crossroad.
All major ascending & descending tracts go through it. Can exert am effect on different pathways at the same time.

Hypothalamus can effect somatic nervous system, Autonomic Nervous system & pituitary gland.

Hypothalamic integration: Based on distinct hormonal & physiological needs, the hypothalamus turns on programs.

Programs include: temperature regulation, salt & water homeostasis, energy homeostasis (by feeding & Satiety control), growth & development, fight or flight reaction in response to stress, sleep wake cycle, cardiorespiratory response to exercise.

Hypothalamus usually gets information from peripheral sensors, intrinsic hormone sensors, intrinsic sensors.

Lateral hypothalamus has many structures.
Contains nerve endings & fibers running through it.

Hypothalamus have many nuclear groups.
Each is different from one another & have specific functions.

Paravebtricular & Supraoptic nuclei (both are magnocellular) make ADH & oxytocin & send it to the posterior pituitary.

There is photoendocrine system in the hypothalamus - pineal gland.
Endocrine clock is in response to dark & light.

Retina has special type of ganglion cell for dark & light recognition.