Human Physiology

Learning objectives for candidates preparing for the Wits Additional Placement Test (WAPT) - 2023

REFERENCES: textbooks

- Marieb EN, Hoehn K, Human anatomy & physiology (11th ed.) San Francisco: Pearson/ Benjamin Cummings
- Marieb EN. Essentials of human anatomy & physiology (13th ed.) San Francisco: Pearson/ Benjamin Cummings

NOTE:

- The previous editions of these two books will also give the information you need.
- In all text in the reference books above you may omit sections headed 'Homeostatic imbalance'

THE DETAILED OBJECTIVES

- There may be some overlap/ duplication between sections within Physiology, and between Physiology, Anatomy and Molecular Medicine
- It is strongly recommended that you study the anatomy and physiology of the same system at the same time.

Body Fluids

Body fluid compartments

Describe the organization of body fluid compartments with reference to:

- intracellular spaces
- extracellular spaces (including interstitial and intravascular spaces)

Constituents of body fluid compartments

Describe the constituents of body fluid compartments with reference to:

- differences in electrolyte concentrations in the different compartments
- differences in concentrations of organic substances, including albumin, in the different compartments

Movement of water and solutes through membranes

- Describe the generation of osmotic forces
- Define the concepts of osmolarity, osmolality and tonicity
- Define the following terms and describe what affects them:
 - hydrostatic pressure
 - oncotic (colloidal) pressure
- Describe the mechanisms of membrane transport including diffusion, osmosis, endocytosis, exocytosis and carrier-mediated transport
- Describe the factors that influence the movement of water solutes across cell membranes with reference to the role of:
 - osmotic gradients
 - ion channels
 - active transport systems
- Describe the factors that influence the movement of water solutes across capillary endothelial membranes with reference to the role of Starlings forces, specifically
 - capillary hydrostatic and oncotic pressures
 - interstitial hydrostatic and oncotic pressures
 - capillary membrane permeability
- List the blood electrolytes that contribute most towards extracellular osmolarity and those which contribute most towards intracellular osmolarity.
- Estimate blood osmolarity from measured electrolytes.
- Osmolarity is a measure of solute concentration, defined as the number of osmoles (Osm) of solute per litre (L) of solution (osmol/L or Osm/L).

Osmolality is a measure of solute concentration, defined as the number of the osmoles(Osm) of solute per kilogramme of solvent (osmol/kg or Osm/kg).

Tonicity: the ability of a solution to change the shape or tone of cells by altering their internal water volume The following equations can be used to calculate osmolarity:

- Calculated osmolarity = $2(Na^+) + 2(K^+) + Glucose + Urea$ (all in mmol/L) OR
- Calculated osmolarity = $2(Na^+) + Glucose + Urea$ (all in mmol/L).

Special body fluid systems

Describe the characteristic components of:

- sweat
- gastrointestinal fluids
- cerebrospinal fluid
- saliva

Blood

Plasma constituents of blood

- List the plasma constituents of blood:
 - organic components consisting of plasma proteins.
 - inorganic components consisting of electrolytes
- Briefly describe how plasma proteins are measured using electrophoresis
- Electrophoresis is a technique used to separate different elements (fractions) of a blood sample into individual components. All proteins have an electrical charge and the test is designed to make use of this characteristic. The sample is placed in or on a special medium (e.g., a gel), and an electric current is applied to the gel. The protein particles move through the gel according to the strength of their electrical charges, forming bands or zones. An instrument called a densitometer measures these bands, which can be identified. Serum protein electrophoresis (SPEP) is a screening test that measures the major blood proteins by separating them into five distinct fractions: albumin, alpha₁, alpha₂, beta, and gamma proteins. Protein electrophoresis can also be performed on urine.

Cellular constituents of blood: erythrocytes

- Describe erythrocytes in the context of their
 - unique cellular structure
 - unique metabolic features
 - role in O₂/CO₂ transport and the importance of haemoglobin in this process
- Describe the formation of erythrocytes with reference to
 - the stimulus for formation
 - the hormonal control of formation
 - haemoglobin synthesis
 - the role of iron, folate and vitamin B_{12} in erythrocyte formation
- Describe haemoglobin degradation and how this affects
 - iron transport
 - bilirubin production
- List the reasons for measuring:
 - haemoglobin concentration [Hb] and haematocrit
 - mean cell volume (MCV), mean cell haemoglobin (MCH), and mean cell haemoglobin concentrations (MCHC)
- Haemoglobin concentration [Hb]: the mass of haemoglogin in a blood sample in relation to the volume of the sample. It is measured to show whether there is too much or too little haemoglobin in the blood (for whatever reason)
- Haematocrit: the volume of erythrocytes in a sample of blood as a proportion of the total volume of the sample. It gives a rough indication of the number and volume of the erythrocytes in the blood.
- Mean cell volume (MCV): the average volume of one erythrocyte in a sample of blood. By showing whether the erythrocytes are too large or too small it directs attention to known reasons for such abnormal values.
- Mean cell haemoglobin (MCH): the average mass of haemoglobin in on erythrocyte in a sample of blood. By showing whether the erythrocytes have too much or too little haemoglobin in them it directs attention to known reasons for such abnormal values.
- Mean cell haemoglobin concentrations (MCHC): the average mass of haemoglobin in one erythrocyte in relation to the average volume of one erythrocyte in a sample of blood. By showing whether the haemoglobin concentration in erythrocytes is too high or too low it directs attention to known reasons for such abnormal values.

Cellular constituents of blood: leukocytes and platelets

- Classify leukocytes
- List the roles of each type of leukocyte
- List the general roles of platelets

Haemostasis

- Define 'haemostasis'
- Describe the vascular and platelet phases of haemostasis with respect to the role of
 - vessel constriction
 - platelet plug formation
 - prostaglandins
- Describe the coagulation phase of haemostasis and the pathways of clotting activation including the
 - intrinsic pathway: how the process is initiated and its endpoint
 - extrinsic pathway: how the process is initiated and its endpoint
 - the role of tissue factor in coagulation
- Describe the process of fibrinolysis including activation of the process, and the role of tissue plasminogen activator
- Describe the inhibition of coagulation, both in vivo and in vitro
- List the reasons for measuring bleeding time; clotting time; prothrombin time and prothrombin index; partial thromboplastin time
- Role of prostaglandins: they maintain the vasoconstriction that has been initiated by the initial injury to the vessel
- Bleeding time: assesses platelet function
- Clotting time: a rough test to assess the intrinsic pathway of coagulation
- Prothrombin time (PT): assesses the quality of the extrinsic and common pathways of coagulation
- Prothrombin index: the ratio between the PT of a blood sample taken from a person known to be normal, and the PT of a sample taken from the patient being investigated, using exactly the same reagents and process. In this way variations between different batches of reagents and in processes used in carrying out the test are compensated for.
- Partial thromboplastin time: assesses the quality of the intrinsic and common pathways of coagulation

Blood groups

Describe the ABO and rhesus (Rh) factor blood group systems with reference to:

- the antigens and antibodies involved
- inheritance of the ABO system

Excitable Tissue

The cell membrane

- Briefly describe the structure and function of the cell membrane with reference to the
 - Lipid structure and its permeability to ions
 - Role of ion channels
 - Role of ion pumps and exchangers
- Compare the distribution of Na⁺, K⁺, Cl⁻ and Ca²⁺ found in the intracellular and extracellular spaces
- Indicate and explain the direction of Na⁺, K⁺, Cl⁻ and Ca²⁺ movement across a cell membrane if the membrane were temporarily permeable to each ion
- List changes to the cell membrane that could temporarily change the permeability of the membrane to ions
- Define 'voltage gated' and 'ligand gated' ion channels and state how each is activated

Resting membrane potentials

- Define 'cell membrane conductance' and 'resting membrane potential (RMP)'
- Define the equilibrium potential for an ion
- State the ion that contributes most to RMP and explain its dominant effect over other ions
- Describe the role of the Na⁺-K⁺-ATPase pump in contributing toward RMP
- Cell membrane conductance: the capability of a cell to allow ions to permeate the cell wall.
- Equilibrium potential for an ion: the value of transmembrane voltage at which diffusive and electrical forces counterbalance, so that there is no net ion flow across the membrane

Action potentials

- Define 'threshold potential' and 'action potential'
- Explain the role of the following in generating action potentials:
 - Na⁺ channel 'm' (activation) gates
 - Na⁺ channel 'h' (inactivation) gates
 - K⁺ channel 'n' gates

- Briefly describe the role of the Na⁺-K⁺-ATPase pump in restoring ionic gradients
- Threshold potential: the membrane potential to which a membrane must be depolarized to initiate an action potential.

Excitatory and inhibitory potentials

- Briefly describe how 'excitatory' and 'inhibitory' transmembrane potentials influence action potentials
- Describe how increases or decreases in the 'openness' of Na⁺, K⁺, Ca²⁺ and Cl⁻ channels affect the resting membrane potential, excitability and action potentials

Neuronal and synaptic function

- Briefly describe the structure and function of the following parts of a neurone: soma; dendrites; axons; nerve terminals and pre- and post-synaptic membranes
- State how neuronal conduction velocity is affected by axonal diameter and the degree of myelination
- Briefly describe the role of the nodes of Ranvier
- Define 'generator potentials'
- Briefly describe the mechanisms of neuronal transmission in electrical, chemical and mixed synapses
- Chemical synapses
 - Briefly describe exocytosis with reference to the stimulus for the process; the effect of the process on transmission of electrical signals; and the role of presynaptic Ca²⁺ channels
 - Define the terms inhibitory and excitatory post-synaptic potentials (IPSP and EPSP)
 - List the ionic changes responsible for IPSPs and EPSPs
 - List the differences between ionotropic and metabotropic receptors
 - State the role of autoreceptors
 - Define 'second messenger system'
 - List the main components and effects of activation of the following second messenger systems: cyclic adenosine monophosphate (cAMP) and inositol trisphosphate (IP3) (the PIP₂ mechanism)
 - State what happens if the each of the two second messenger systems listed above is activated
 - State the principal enzyme responsible for degrading cAMP
- Briefly describe how glutamate and gamma amino butyric acid (GABA) affect ion channels and postsynaptic membrane potentials
- List five other major neurotransmitters found in the central and peripheral nervous system
- List the differences between the pre-synaptic and post-synaptic effects of neurotransmission and neuromodulation
- List five neuromodulators found in the central and peripheral nervous systems
- Define 'temporal' and 'spatial' summation of neuronal signals
- An autoreceptor, present at a nerve ending, is a receptor that regulates, via positive or negative feedback processes, the synthesis and/or release of its own physiological ligand
 - Enzyme degrading cAMP: phosphodiesterase

Muscle contraction

- Revise the structure of the sarcomere (see Anatomy)
- State the role of each of the following in muscle contraction:
 - The T-tubule system in striated muscle
 - Excitation-contraction coupling
 - The sarcoplasmic reticulum (SR) and Ca²⁺ release from the SR
 - Actin and myosin filaments
 - The troponin complex
 - Myosin-ATPase (enzyme hydrolyzing ATP into ADP and P_i)
 - The SR Ca²⁺-ATPase pump (which actively pumps Ca²⁺ back into the SP after excitation-contraction coupling is over)

Skeletal muscle and the neuromuscular junction

- List the components of a motor unit
- Briefly describe the following elements of neuromuscular junction in skeletal muscle:
 - The neurotransmitter involved
 - The post-synaptic receptor and ion channel involved
 - Termination of neurotransmitter actions

Cardiac muscle

Briefly describe the differences between cardiac and skeletal muscle contraction with reference to:

- The role of Ca²⁺-induced SR Ca²⁺ release
- The role of second messengers
- Energy requirements

Smooth muscle

Briefly describe the differences between smooth and skeletal muscle with respect to the

- Organization of myofilaments
- Dependence on excitation-contraction coupling
- Role of second messengers
- Effect of Ca²⁺-induced SR Ca²⁺ release (for vascular smooth muscle)

Role of second messengers:

- In cardiac muscle: the second messenger is cyclic AMP which activates protein kinase A. The release of cyclic AMP is stimulated or inhibited by excitatory or inhibitory G proteins, which in turn are stimulated by catecholamines (sympathetic stimulation) and acetyl choline (parasympathetic stimulation) respectively
- In smooth muscle: the second messenger inositol triphosphate stimulates calcium release from the sarcoplasmic reticulum; in vascular smooth muscle the second messenger diacylglycerol also activates protein kinase C

The Nervous System, Part I: The Autonomic Nervous System

- List the functional differences between the autonomic and somatic nervous systems
- Describe the basic functional design of autonomic neurones with reference to:
 - The length of the preganglionic and postganglionic neurones involved
 - Ganglionic (preganglionic) neurotransmitters
 - Postganglionic neurotransmitters and transmission

Neurochemistry and pharmacology of the autonomic nervous system

- List the principal steps in the synthesis, storage, release, breakdown, degradation and termination of the effects of noradrenaline and acetylcholine
- Describe the principal receptors, ion channels and second messenger systems involved in mediating the autonomic actions of:
 - noradrenalin on adrenergic receptors and target tissues
 - acetylcholine in ganglia and at target tissues
- Explaining the mechanism of action in each case, describe the changes in target tissue function that characterize the action of the stimulation of postganglionic alpha, beta and muscarinic receptors
- Noradrenalin receptors: G protein-coupled receptors resulting in a cAMP (cyclic AMP) second messenger cascade, which in turn stimulates protein kinase
- Acetylcholine receptors: 2 types
 - (1) Nicotinic: a ligand gated ion channel allows Na⁺ and K⁺ diffusion and depolarization
 - (2) Muscarinic: G protein-coupled receptor resulting in a second messenger cascade (mainly cyclic AMP and inositol triphosphate)
- Noradrenaline: synthesized from tyrosine; stored in vesicles in second neuron sympathetic nerve endings; released when an action potential reaches the nerve ending; most reabsorbed by the nerve endings (some stored in vesicles again, some degraded by mono-amine oxidase in mitochondria); a little bit is absorbed by the effector cells and metabolized by catechol-O-methyl-transferase
- Acetylcholine: synthesized from choline and acetyl coenzyme A; stored in vesicles in nerve endings; released as above; degraded by enzyme choline esterase (split into choline and acetic acid); the choline is actively reabsorbed by the nerve endings and re-used in synthesis

Autonomic control of specific organs/body functions

Listing the neurotransmitters, receptors and second messenger systems involved, describe and explain the effect of activation of the sympathetic or parasympathetic nervous systems on:

- Cardiac rate and contractility
- Blood vessels
- Sweat glands
- Bronchiolar smooth muscle and glands
- The pupils, lacrimal glands, lens and eyelid
- Gastrointestinal tract and gall bladder: motility, exocrine secretions, endocrine secretions
- Micturition and ureteric contraction
- Erectile capacity and ejaculation
- Salivary glands

The Nervous System, Part II: The Motor System

Motor control at a peripheral level

- Define a lower motor neurone (LMN)
- List the principal differences between intrafusal and extrafusal skeletal muscle fibres with reference to their main function and the motor neurons that control them

- List the main sensory functions of muscle spindles and Golgi tendon organs, and the stimuli for activating them
- Describe a simple muscle reflex (myotatic or monosynaptic stretch reflex) with reference to:
 - Inducing the reflex; the sensory receptors involved
 - The afferent and efferent pathways
 - The effector organ
- State the spinal levels at which the LMNs are located for the biceps, triceps, patellar and ankle reflexes
- Describe the plantar response: its overall function as a withdrawal response; the sensory receptors that are activated; the spinal level involved; and the motor response
- Explain the impact of muscle spindle firing on resting muscle tone and muscle bulk
- Biceps reflex level: C_5 - C_6 ; Triceps reflex level: C_6 - C_8 ; Patellar reflex level: L_2 - L_4 ; Ankle reflex level: S_1 - S_2
- Pacinian corpuscles are the sensory receptors activated in the plantar response

Motor control at a central level

- List the major direct (pyramidal) and indirect (extrapyramidal) descending pathways and tracts
- During flexion of a limb such as the arm, describe the effect of activation of cortical upper motor neurons (UMNs) on alpha and gamma motor neurones to the flexor muscles and inhibitory interneurones to the extensor muscles
- State the main functions of brainstem motor nuclei (reticular and vestibular nuclei and the red nucleus) and their descending tracts
- List the cranial nerve nuclei that receive an UMN supply from both cerebral hemispheres and those that receive an UMN supply from only one hemisphere
- UMN supply from both cerebral hemispheres: V_3 (mandibular division); VII (frontal division only), IX and X (skeletal/ striated muscles of the pharynx, larynx and upper oesophagus), XII (intrinsic tongue muscles)
- UMN supply from one cerebral hemisphere: II, IV, VI, VII (all divisions except frontal), XII (extrinsic tongue muscles)
- *UMN supply unclear (whether it is ipsilateral, contralateral or bilateral) : XI*

The function of the cerebellum

- List the main sensory inputs to the cerebellum as derived from the dorsal columns of the spinal cord, vestibular nucleus, pretectal nucleus and inferior olive
- List the targets of outputs from the cerebellar cortex and the deep cerebellar nuclear cells
- State the main inhibitory neurotransmitter released from the cerebellar cortex to deep cerebellar nuclear cells
- Describe how outputs from the cerebellum affect the brainstem motor nuclei that control postural muscle function, the thalamus and consequently the motor cortex
- The pretectal nuclei relay visual information to the cerebellum; the inferior olive relays sensory information on the state of stretch of muscles and joints to the cerebellum
- The inhibitory neurotransmitter is

The function of the basal ganglia

- State the neuronal targets of outputs from the basal ganglia, and their role in motor control
- Define the term 'motor memory'
- Describe the function of the premotor cortex, supplementary motor cortex, and central pattern generators in the brainstem and spinal cord
- Describe the microcircuits that link the basal ganglia together.
 - State the main neurotransmitters released in the
 - Impact of dopamine and muscarinic cholinergic receptor activation on thalamic neuronal firing
- Functions of the secondary motor cortices:
 - the posterior parietal cortex, responsible for transforming visual information into motor commands
 - the premotor cortex, responsible for motor guidance of movement and control of proximal and trunk muscles of the body
 - the supplementary motor area (or SMA), responsible for planning and coordination of complex movements such as those requiring two hands.
- Neurotransmitters in the basal ganglia and their effect:
 - In the basal ganglia most neurons (e.g. from the striatum, pallidum, and substantia nigra pars reticulata)
 use GABA as neurotransmitter and have <u>inhibitory</u> effects on their targets (so the basal ganglia basically
 function through inhibition and disinhibition).
 - The inputs from the cortex and thalamus to the basal ganglia use glutamate.
 - Dopamine has a modulating effect usually stimulatory within the basal ganglia, but mildly inhibiting the thalamus. Acetylcholine has the opposite effect.

The Nervous System, Part III: The Somatic Senses

List the 7 types of somatic sensations

Pain, temperature, proprioception, vibration, light pressure/touch, deep pressure/stretch, two-point discrimination

Nociceptor activation and pain sensation

- Briefly describe the roles of the following chemical substances in mediating the nociceptor response:
 - phospholipase and cyclo-oxygenase enzymes
 - prostanoids and prostaglandins
 - histamine
 - inflammatory mediators (e.g. cytokines)
- Explain how nociceptors differ from other sensory receptors in terms of threshold for stimulation and rate of adaptation
- Describe the different forms of pain sensation conveyed by A-delta and C-fibre afferents
- Describe descending inhibitory pain pathways in terms of:
 - The neurotransmitters and neuromodulators involved, including endogenous opioids, noradrenaline and serotonin
 - Their effects on spinothalamic tract firing
 - The effects of trauma or stress on the activity of the pathway
- Prostanoids are lipid mediators formed by the action of phospholipase A2 (PLA₂), cyclooxygenase (COX) and prostanoid synthases, which converts arachidonic acid into various prostanoids. The prostanoids serve pivotal functions in pain signalling at the site of inflammation and at the level of the spinal cord. The spinal prostanoids are important in inflammation-induced pain, and probably also in postoperative pain and in the early phase of nerve-injury induced pain.
- At the periphery, the responsiveness of pain receptors is enhanced by the presence of prostaglandins. These prostaglandins are formed in response to tissue trauma. This means that the receptors will respond to a lesser stimulus than before they were sensitised. A number of endogenous compounds (e.g., histamine, serotonin) may be responsible for the actual pain sensation.
- Nociceptor stimulation threshold is higher than for other sensory receptors.
 - 'Windup': Following an injury, dorsal horn cells are bombarded by stimuli originating from pain receptors. Over a period of time, the receptive field of these cells increases. This process of increasing central sensitisation of dorsal horn cells is called windup.
 - Nociceptors adapt. This adaptation varies in terms of direction (most showing a declining response rate with time, a few showing short-term increases in firing rate during stimulation) and time (most adapt rapidly, fewer more slowly).
- The midbrain's periaqueductal grey area has inputs from the thalamus, the hypothalamus and the frontal cortex. From it serotoninergic axons descend to end in synaptic contact with enkephalinergic interneurons situated in the dorsal horn. They release endogenous opiate neuromodulators which close the 'pain gate' gate by inhibiting the release of substance P. There are also opioid serotoninergic and non-opioid noradrenergic descending mechanisms which are capable of blocking upward transmission of pain generated impulses. In these ways the spinal interneurons are activated to inhibit dorsal horn transmission cells responsible for projecting nociceptive information received.
- Pain intensity and unpleasantness are not simply determined by the magnitude of the painful stimulus, but 'higher' cognitive activities can influence perceived intensity and unpleasantness
- Describe the afferent and efferent components of the corneal and gag reflexes
- Corneal reflex: afferent ophthalmic division of trigeminal (V^{th}) nerve; efferent facial (VII^{th}) nerve
- Gag reflex: afferent glossopharyngeal (IXth) nerve; efferent vagus (Xth) nerves

The thalamus and the primary somatosensory cortex

- Describe the course, components and functions of the following ascending (sensory) pathways:
 - Dorsal column pathways
 - Anterolateral pathways
 - Spinocerebellar pathways
- List the main function of the thalamus

The Nervous System, Part IV: The Special Senses

Hearing

- List the elements of the central neural auditory pathway
- Describe the mechanisms responsible for sound transduction; sound localization; detection of sound intensity and sound pitch

Equilibrium and balance: the vestibular apparatus

- Describe the pathways of the balance and orientation system of the body, from receptors to effector organs
- Describe the general function of the vestibular apparatus in maintaining the body's static and dynamic equilibrium
- Describe the central pathways from the vestibular apparatus including:
 - The cranial nerve and nucleus conveying the signals
 - Brainstem connections with the cerebellum, cranial nerves, vestibulospinal tracts, the vomiting centre

Vision

- Define visual accommodation; indicate its purpose and describe the process of visual accommodation
- Describe the roles of the following cells in the retina:
 - rods in photo-transduction and scotopic (dark) vision
 - cones in colour vision and photopic (light) vision
- Describe and explain the 'pupillary reflexes' (response when a light is shone in the same or opposite eye); state the purpose of these reflexes and name their afferent and efferent components
- Explain how the left and right visual fields are projected onto the visual cortex
- Describe the role of the lateral geniculate nucleus in vision
- Pupillary reflexes: Afferent component = optic (IInd) nerve fibres to pretectal nucleus in the midbrain; efferent component = parasympathetic fibres in oculomotor (IIIrd) nerve

The Nervous System, Part V: Higher Brain Functions and Emotion

Consciousness

- State the location of the reticular activating system
- List the major targets of the outputs from the reticular activating system
- List the principal physiological functions of the reticular activating system

Learning and memory

- List the differences between declarative and non-declarative memory, and between short-term and long-term memory
- Briefly describe memory processing in the brain and the neuronal circuits that support it

Emotion

- List the principal functions of the limbic system
- Explain the role of the limbic system in the causation of psychosomatic illness

Language, speech and reading

- State the cerebral hemisphere usually responsible for language, speech and reading
- Identify the location of the following and describe their functions: Broca's area, Wernicke's area, the angular gyrus

Endocrine Physiology

Introduction to endocrinology

- Define the following terms: endocrine, paracrine, autocrine
- State the two chemical classes of hormones; describe their mechanisms of action; and give examples of each
- Briefly describe the three main stimuli for hormone release
- Describe the basic mechanism of control of hormone release (negative feedback)

Hormones of the pituitary

- Describe the role of the hypothalamus in the control of pituitary hormone secretion
- Anterior pituitary hormones: growth hormone (GH, somatotropin), thyrotropin (thyroid stimulating hormone, TSH), adrenocorticotrophic hormone (ACTH), follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin

For each of these hormones:

- State where it is synthesised and released
- List its physiological effects/ actions and briefly describe how these are mediated
- List the principal factors regulating its secretion and briefly describe their regulatory action
- Posterior pituitary hormones: antidiuretic hormone (ADH), oxytocin

For each of these hormones:

- State where it is synthesized and released
- List its physiological effects/ actions and briefly describe how these are mediated
- List the principal factors regulating its secretion and briefly describe their regulatory action

Hormones of the thyroid gland

 Briefly describe the synthesis and secretion of thyroid hormones, referring to the roles of iodine and thyroglobulin

- List the principal factors regulating thyroid hormone secretion and briefly describe their regulatory action
- List the functions/actions of thyroid hormones, referring effects on metabolism and development

Hormones of the adrenal gland

- List the principal hormones secreted by the adrenal cortex and medulla respectively
- State the substrates for the synthesis of steroid hormones and catecholamines
- List the functions/actions of cortisol (glucocorticoid) on carbohydrate, protein and fat metabolism, and on stress and inflammation
- List the principal factors regulating adrenal steroid hormone secretion and briefly describe their regulatory action

For functions/ actions of aldosterone and catecholamines refer to the notes on the renal and autonomic nervous systems

• Substrate for steroid hormones: cholesterol; for catecholamines: tyrosine (an amino acid) which forms dopamine (a neurotransmitter), then the 2 adrenal medullary hormones

Hormones of the pancreas

- Briefly describe the functions/actions of insulin with on carbohydrate, protein and fat metabolism, and growth
- List the functions/actions of glucagon
- List the principal factors regulating pancreatic hormone secretion and briefly describe their regulatory action

The calciotropic hormones

- Briefly describe the metabolism of calcium: absorption, distribution, excretion, bone-extracellular fluid exchange
- List the main physiological actions of calcium in the body
- List the sources of the hormones involved in calcium homeostasis: parathyroid hormone, vitamin D and calcitonin
- Briefly describe the regulation of the calciotropic hormones with reference to the role of plasma calcium
- List the functions/actions of calciotropic hormones on bone, kidney, the gastrointestinal tract and plasma Ca²⁺ and phosphate concentrations

The reproductive hormones

- The male reproductive hormones: testosterone and inhibin
 - List the sites of their production
 - List the physiological functions/ actions of these hormones in males
 - Briefly describe the regulation of these hormones
- Functions of the female reproductive system
 - List the steps in the process of ovulation
 - List the changes in the endometrium during the menstrual cycle
 - List the steps involved in fertilization and implantation of a fertilized ovum
 - List the factors involved in maintenance of pregnancy
 - Describe the physiological regulation of parturition and lactation
- The female reproductive hormones: oestrogen and progesterone
 - List the sites of their production
 - List the physiological functions/ actions of these hormones in females
 - Briefly describe the regulation of these hormones
- Compare the serum levels of FSH, LH, oestrogen and progesterone:
 - during the menstrual cycle, relating them to ovulation and menstruation
 - in the weeks following implantation of the fertilized ovum

The Cardiovascular System

Compare and contrast the systemic and pulmonary systems

Describe the coordinated electrical activity of the heart:

- Trace an impulse from the SA node to the end of repolarisation
- Define pacemaker; compare resting membrane potential with pacemaker potential
- Define spontaneous depolarization of cardiac tissue and list the ionic currents responsible for this electrical activity of the heart
- Describe the role of the AV node in transmitting and filtering impulses
- Compare the rates of depolarization and action potentials of the different cardiac conduction cells

Describe the cardiac cycle in the left heart:

- Define the terms systole and diastole
- Describe one cardiac cycle in terms of volumes and pressures in the left atrium, left ventricles and the aorta;
 compare these to the myocardial events

Describe the valvular events in the cycle, the trans-valvular pressure gradients and the generation and timing
of the first and second heart sounds

Discuss the electrocardiograph (ECG):

- Describe the cardiac electrical events that correspond to the P wave, P-R interval, QRS complex, Q-T interval and T wave of the ECG recording
- Identify atrial depolarization on the electrocardiogram
- Describe the relationship between the ECG recording and the cardiac cycle

Discuss cardiac function:

- Define cardiac output, stroke volume, and the relationship between cardiac output, stroke volume and heart rate
- Define inotropic, lusitropic and chronotropic
- Define preload, contractility and afterload, and describe how stroke volume is regulated in terms of these three
- Explain how changes in ventricular pressure, volume, radius and wall thickness affect ventricular wall tension/ stress
- Explain how stretching cardiac myofilaments can increase stroke volume (Frank-Starling relationship)
- Explain how changes in wall stress affect myocardial oxygen demand
- Explain how sympathetic activation affects myocardial contractility/ inotropy, in terms of circulating adrenaline, the receptors involved, cAMP and calcium ion movement
- Explain the effect of parasympathetic activation on the heart and the 'normal' vagal tone of the heart
- Briefly explain why the RMP and action potentials in the 4 tissues above are different
- Inotropic: affecting the force of muscle contraction
- Lusitropic: related to myocardial relaxation
- Chronotropic: affecting the heart rate

Compare the right and left heart:

- Compare differences in pressures generated in the right versus the left ventricle in systole and diastole
- Compare flow and resistance, and cardiac output in the right and left heart

Describe the general systemic circulation

- Describe the relationship between flow, pressure and resistance, and between resistance, length and radius
- Define the terms systemic arterial blood pressure, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and total peripheral vascular resistance (TPR)
- Describe changes in blood pressures noted in the systemic circulation from aorta to capillaries to veins
- Explain the pulsatile nature of aortic and small artery pressures and non-pulsatile nature of smaller vessel pressures
- Define autoregulation of blood flow by body tissues and list the common mechanisms of such control.
- List the extrinsic and extrinsic mechanisms controlling arteriolar smooth muscle in the systemic circulation

Describe the control of arterial blood pressure:

- Summarise the factors involved in maintaining systemic arterial blood pressure.
- List the four neural short-term control mechanisms and briefly explain their mechanisms of action (what stimulates them and what effect they have)
- List the principal short-term hormonal control mechanisms, their effects and sites of action
- Briefly explain the renal blood pressure regulation mechanism.

Describe the capillary circulation:

- List the four routes by which different molecules may move across the endothelium of fenestrated capillaries, relating this to the microscopic structure of the capillary
- Describe how changes in capillary hydrostatic and oncotic pressures regulate the flow of fluid across the capillary wall.

Describe the functioning of the venous system:

- Explain why the venous system is called a capacitance system
- Describe how changes in venous return affect cardiac output with reference to the Frank-Starling relationship
- Describe and explain the effect on venous return (and hence cardiac output) of changes in blood volume and in systemic arteriolar and venous smooth muscle tone
- Describe and explain the effect on venous return of changes in posture
- Describe how normal inspiration, contraction of skeletal muscle and venous valves affect venous return

Describe the changes in cardiac output that occur with exercise, with reference to:

- Alterations in contraction of skeletal muscle around veins
- Venous return on the Frank-Starling relationship
- Autonomic effects on cardiac contractility and heart rate

The Respiratory System

- State the general role of the lungs in O₂ and CO₂ exchange
- Define the terms PaO₂, PAO₂, PaCO₂ and PACO₂
- Define and differentiate between 'internal respiration' and 'external respiration'

Ventilation

- Define the terms 'intrapleural pressure', 'lung compliance' and 'surfactant'
- State the relationship between volume change and pressure change, and between intrapulmonary pressure and air flow
- Describe the mechanics of pulmonary ventilation:
 - The role of the respiratory muscles in inspiration
 - The role of lung elasticity in normal expiration
 - The importance of alveolar and pleural pressures in ventilation
- Explain the impact of surfactant on lung compliance
- Define the terms 'minute ventilation' (V_E) and 'alveolar ventilation' (V_A)
- Compare the composition of alveolar air and atmospheric air and explain the differences noted

Lung volumes and capacities

- Define the following lung volumes: tidal volume; inspiratory reserve volume; expiratory reserve volume; residual volume
- Define the following lung capacities: vital capacity; total lung capacity; dead space

Alveolar diffusion

- Define the term 'alveolar diffusion'
- Indicate how the partial pressures of gases (O₂ and CO₂) differ in the alveoli as compared to the blood
- List the factors which influence the rate of gas diffusion through the respiratory membrane

The transport of O2 and CO2 in blood

- List the ways in which O₂ and CO₂ are transported in the blood, and in which proportions
- State the chemical components of haemoglobin that bind O₂ and CO₂ respectively, and give the names of the resulting compounds
- Draw the normal oxygen-haemoglobin dissociation curve (with named x and y axes):
 - Explain how changes in 2,3-diphosphoglycerate, pH and P_{CO2} influence it
 - Explain how a rightward shift of the curve (the Bohr effect) affects O₂ delivery to tissues

The ventilation-perfusion ratio

- Define what is meant by the alveolar ventilation:perfusion (V_A:Q) ratio in the lungs
- Explain how autoregulation in the lungs attempts to maximize the V_A:Q ratio by modifying arteriolar and bronchiolar diameters
- Explain why the apex of the lungs tends to have a higher V_A:Q ratio than the bases, in an erect person

Regulation of respiration

- State the areas of the body that contain chemoreceptors that control respiration
- Identify the location of the respiratory control centres in the central nervous system, state which chemical
 changes they primarily respond to, and describe the nature of this response
- Identify the location of the peripheral chemoreceptors in the body, state which chemical changes they respond
 to, and describe the nature of this response
- State the most potent chemical influencing respiration
- List the neural influences on the brainstem respiratory centres.

Renal Physiology

NOTE: it is very important to revise the microscopic anatomy of the nephron, the renal capillary beds and the juxtaglomerular apparatus before studying renal physiology.

Glomerular filtration

- Describe what is meant by glomerular filtration the actual process that takes place
- Compare the composition of the glomerular filtrate with that of blood and interstitial fluid
- State how glomerular filtration is affected by the capillary hydrostatic and oncotic pressures, and the permeability of the basement membrane
- Briefly describe the following intrinsic regulatory mechanisms of glomerular filtration:
 - The myogenic mechanism (related to systemic blood pressure)

- Tubuloglomerular feedback (related to the tubular NaCl concentration)
- Describe the process of autoregulation of renal blood flow and glomerular filtration
- Briefly describe the following extrinsic regulatory mechanisms of glomerular filtration:
 - Sympathetic nervous system/ alpha adrenergic stimulation of mesangial cells and arteriolar smooth muscle
 - The renin-angiotensin mechanism
- Explain how the differential effect of angiotensin II on the smooth muscle of afferent and efferent arterioles helps maintain filtration
- Explain why renal clearance of creatinine can reasonably be used to estimate the glomerular filtration rate (GFR)
- State the formula for the calculation of creatinine clearance
- State the normal GFR and the amount of fluid filtered in a day

Renal tubular reabsorption

- State the substance which when reabsorbed provides the energy and means for the reabsorption of most of the others
- State the portion of the tubule that reabsorbs most Na⁺ and water, as well as almost all nutrients
- Describe the process of proximal tubular Na⁺ and water reabsorption with reference to active transport with the Na⁺-K⁺-ATPase pump, facilitated diffusion through channels, and the presence of aquaporins
- Briefly describe how nutrients are reabsorbed through secondary active transport (co-transport with Na⁺) and
 diffusion, also explaining the role of specific transporters in determining the T_m (transport maximum) for each
 substance
- Briefly describe how lipid soluble substances, Ca²⁺, K⁺, Cl⁻ and urea are reabsorbed passively by diffusion in the proximal tubule
- Regarding reabsorption in the loop of Henle:
 - State the difference in reabsorption capability of the descending and ascending limbs of the loop, for solutes and water
 - Briefly explain how this difference leads to concentration of urine and extracellular fluid in the renal medulla (the so-called counter-current mechanism or exchange)
 - Explain how the vasa recta contribute to maintaining this osmotic gradient
- Explain how aldosterone secretion is affected by plasma K⁺ and Na⁺ concentrations and the renin-angiotensin mechanism.
- Explain how aldosterone and atrial natriuretic peptide (ANP) affect the reabsorption of Na⁺ (and K⁺ secretion) in the distal convoluted tubules and the collecting ducts
- Explain how ADH promotes the reabsorption of water in the collecting ducts, and thereby affects urine and plasma osmolarity
- Explain how the high osmolarity in the renal medulla together with the action of ADH regulates the concentration of urine
- Briefly describe how creatinine is cleared from the plasma by renal filtration and secretion
- Briefly describe how and where urea is filtered and reabsorbed in the renal tubular system

Renal tubular secretion

- List the differences between renal tubular reabsorption and secretion
- List the substances that are normally secreted by the renal tubules
- State where K⁺ is mainly secreted and what controls this secretion

Acid-Base Balance

- Explain briefly why the correct H⁺ concentration in the body is so important for its normal functioning
- State the normal pH for arterial blood, venous blood and intracellular fluid, and explain why venous blood and intracellular fluid (ICF) have lower pH values
- Define the terms acidosis, acidaemia, alkalosis and alkalaemia
- List the four main sources of acid production in the body
- List the three mechanisms that the body uses to regulate the H⁺ concentration in the blood and body fluids
- Compare the relative speeds and buffering power of the three mechanisms

Chemical buffer systems in the body

- State the principal difference between weak and strong acids and bases
- Define a chemical buffer and state the relationship between the power of a buffer and its concentration in a solution
- Discuss each of the three major chemical buffer systems in the body (bicarbonate, phosphate and protein) under the following headings:
 - The components of the buffer system

- The body fluid compartment(s) in which it operates
- Briefly describe how haemoglobin functions as an 'amphoteric' protein buffer

Respiratory regulation of H⁺ concentration

- Write the equation showing the equilibrium between H₂O, CO₂, H₂CO₃, H⁺ and HCO₃⁻
- Explain in detail how an increase in plasma H⁺ concentration (from increased CO₂ concentration or other metabolic causes) is controlled by changes in ventilation
- Explain how an increase in plasma pH is controlled by changes in ventilation

Renal mechanisms for maintaining acid-base balance

- List the acids commonly produced by the normal body metabolism, that are excreted by the kidney
- Briefly explain how the kidney compensates for (conserves) the HCO₃⁻ in the urinary filtrate that cannot be reabsorbed
- Explain how metabolism of glutamine in the tubular cells produces new HCO₃- for the body and acidic NH₄+ for excretion in urine
- Explain the role of the phosphate buffer system in the kidney:
 - State the two mechanisms by which renal tubular cells excrete H⁺ into the urine to be buffered by HPO₄²⁻
 - Briefly explain how the system generates new HCO₃- for the body
- Explain what is meant by respiratory and metabolic acidosis and alkalosis
- Explain the difference between 'actual' and 'standard' HCO₃- levels in the plasma, and how this distinguishes between respiratory and metabolic acidosis and alkalosis
- Standard bicarbonate concentration is the bicarbonate concentration in the blood at a pCO₂ of 5.33kPa, full oxygen saturation and 37°C. If this is abnormal it indicates a metabolic acidosis or alkalosis.

Gastrointestinal and Liver Physiology

• Briefly describe the general functions of the gastro-intestinal tract (GIT): ingestion, propulsion (peristalsis and segmentation), digestion (mechanical and chemical), secretion, absorption and defaecation.

Regulation of GIT function

- Briefly describe the mechanical and chemical stimuli that regulate GIT function
- Briefly describe the intrinsic and extrinsic neural control of GIT function and the role of short and long reflexes
- Describe the hormones that act on digestion in terms of their source, stimulus for secretion and action

Saliva

 Discuss the composition of saliva and the functions of its constituents with specific reference to enzymes, antimicrobial substances, bicarbonate, mucins and anti-nutritional factor inhibitors

The stomach

- List the substances produced by the 4 types of cells in gastric glands
- Describe the cellular mechanisms responsible for the control of gastric acid secretion with special reference to the role of
 - the autonomic nervous system.
 - the proton pump
 - histamine
- Describe how the gastric mucosa is protected from corrosion by acid

The exocrine pancreas

- List the main constituents of pancreatic juice and describe their functions including pro-enzymes, enzymes and electrolytes
- Explain briefly how pro-enzymes are activated

Bile salts

- Briefly describe their synthesis
- Identify the site of their storage and describe the factors that control their release into the small intestine
- Describe the role they play in the emulsification of fat
- Briefly describe the entero-hepatic recycling of bile salts

The small intestine

- Describe the digestion (via the enzymes in brackets) of the major macronutrients listed below; identify the products of digestion of these nutrients; and describe their absorption:
 - Fat (lipases, co-lipase)
 - Protein (peptidases)
 - Carbohydrates (saccharidases)
- Indicate the origins of the enzymes listed above
- Describe the absorption of the following:

- Water and fat soluble vitamins
- Minerals and electrolytes including iron, Ca²⁺ and Na⁺

Large intestine

- Describe the major motility patterns of the large intestine with reference to the role of peristalsis, haustrations and mass movements
- Describe the defaecation reflex
- Discuss the importance of resident intestinal bacteria with regards to the synthesis of vitamins
- List the substances normally absorbed in the large intestine

Hunger and satiety

- State the area of the brain which controls appetite and food intake
- State how the following affect the appetite centres:
 - Hormones: insulin, leptin, ghrelin, adrenalin and glucagon
 - Distension of the GI tract
 - Plasma glucose, amino acids and fatty acids

Liver functions

- Describe the metabolism in the liver of carbohydrates, proteins and lipids
- Describe the storage in the liver of glycogen, fats, iron and vitamins
- Describe the synthesis in the liver of glucose, proteins and lipids
- Briefly explain the biotransformation/ detoxification function of the liver (using the examples of alcohol, hormones and cholesterol)
- Describe the function of the Kupffer cells in defense/immunity

Bile pigments

Describe the production and excretion of the following bile pigments:

- Bilirubin (conjugated and unconjugated)
- Stercobilin
- Urobilinogen

Nutrition

- Define the term 'nutrient' and list the groups of major and minor nutrients
- Define the following terms:
 - Essential and non-essential nutrients
 - Recommended dietary allowance
- Recommended Dietary (Daily) Allowance (RDA): the amounts of selected nutrients considered adequate to meet the known nutrient needs of healthy people
- Define the term 'energy value' of a foodstuff and state the energy yield of each of fat, protein, and carbohydrate
- State the ideal proportion of energy obtained from each of dietary fats, proteins, and carbohydrates
- Define the term 'respiratory quotient' (RQ) and state the respiratory quotient for the complete biological oxidation of fats, carbohydrates, and proteins
- Define the term 'basal metabolic rate' (BMR) and state its normal value
- Define the term 'specific dynamic effect/ activity' (SDE/A) and state its average value
- Energy value of a foodstuff: the amount of energy available from food that is available through respiration Energy values for specific foods (in kcal/g): fats 9; ethanol 7; proteins and most carbohydrates 4; polyols and organic acids <4
- $RQ = CO_2$ eliminated / O_2 consumed
 - RQ for selected foods: carbohydrates 1; proteins 0.8-0.9; fats 0.7
- SDE is the increment in energy expenditure above resting metabolic rate due to the cost of processing food for storage and use. Its average value is 10% of the caloric intake over a given time period

Macronutrients

- With respect to carbohydrates:
 - Distinguish between complex and simple carbohydrates
 - Describe the function of dietary fibre
 - Briefly describe how glucose is metabolized through glycolysis, the Krebs cycle and the electron transport chain to produce ATP
- With respect to lipids:
 - Briefly describe their metabolism and storage
 - Define 'essential fatty acids' and explain the term 'essential'

- List the functions of fatty acids and triacylglycerols
- List the physiological functions of cholesterol
- With respect to proteins:
 - Briefly describe their metabolism
 - Define 'essential amino acids' and explain the term 'essential'
 - Define the terms 'biological value' of amino acids and 'limiting amino acids'
 - State the differences in the biological values of meat, cereal, legume and egg proteins, and explain why
 combining proteins from different dietary sources increases their biological value
- Simple carbohydrates: sugars; complex carbohydrates (long chains of sugars): starches and fibre
- Essential fatty acids and amino acids: necessary components of important body compounds, but cannot be formed in the body so have to be ingested in the diet
- Biological value of proteins: a protein has high biological value if it consists of amino acids in the same proportion as the human body's needs for amino acids i.e. almost all the amino acids will be used after digestion to form proteins and few will be deaminated and used as an energy source. Another term for such proteins is 'complete proteins'. Animal proteins tend to have high biological values and plant proteins have low biological values.

Micronutrients

- List the fat-soluble and water-soluble vitamins
- Briefly describe the role of vit.A in metabolism and vision
- With respect to the B vitamins:
 - List their general functions in metabolism
 - List the specific roles of each of the following:vit.B₁₂, folic acid, vit.B₆ and biotin
- List the functions of vit.C in the body
- Briefly explain how the plasma concentration of active vit.D is affected by sunlight, the kidney, and factors that determine its GIT absorption
- List the metabolic and haemostatic functions of vitamin K
- State the function of vitamin E
- With respect to iron:
 - Briefly describe its distribution in the body
 - Describe the absorption of iron from the GIT
- List the functions of iodine in the body
- With respect to fluoride:
 - List the tissues in which this mineral is found
 - State the function of this mineral

Diet

- Define a 'balanced diet'
- List the best food sources of each of the major vitamins and minerals, and of proteins, carbohydrates, and fats.
- A balanced diet is a diet containing the amounts of nutrients that will supply the metabolic needs of a person's body more or less exactly over a given period of time, while avoiding nutrients known to contribute to ill-health

Temperature Regulation

Body temperature

- Define body temperature, including core and surface (shell) temperature, and state its normal range
- Briefly describe the effect of body temperature increase and decrease on cell function

Control of body temperature

- List and briefly explain the mechanisms of heat exchange between the skin and the external environment
- List and briefly explain the body's physiological and behavioural heat promoting and heat loss mechanisms
- Outline the mechanisms of neural control of body temperature with respect to
 - Peripheral thermoreceptors
 - Central integration in the hypothalamus
 - The reflexes initiated by the hypothalamus