Medical Physiology Curriculum Core

Overview of physiology

Definition of physiology
Concept of the internal environment
Volumes of body fluid compartments
Indicator-dilution principle
Ionic composition of extracellular fluids (plasma, interstitial fluid)
  Electroneutrality in solutions
Ionic composition of intracellular fluid (skeletal muscle cells)
Definition of homeostasis
Distinction between steady state and equilibrium
Negative feedback control system
Positive feedback
Feedforward control

Membrane transport

Structure of the plasma membrane
Mechanisms of solute transport
  Phagocytosis and endocytosis
  Exocytosis
Simple diffusion
  Fick’s law of diffusion
Facilitated diffusion via carrier proteins
Diffusion through ion channels
  Voltage-gated channels
  Ligand (or chemically)-gated ion channels
Active transport
  Primary active transport
    Na⁺/K⁺-ATPase
    Ca²⁺-ATPase
    H⁺-ATPase
    H⁺/K⁺-ATPase
  Secondary active transport
Movements of solutes and water across epithelial cell layers
Osmosis
  van’t Hoff equation
  Osmotic pressure
  Tonicity
  Reflection coefficient (s)
  Aquaporins
Cell volume regulation
  Role of sodium pump
Neurophysiology

Structure of neuron
- Dendrites, soma, axon, axon hillock, synaptic cleft

Properties of ion channels
- Voltage-gated ion channels

Resting membrane potential
- Diffusion potential
- Equilibrium potential
  - Nernst equations
- Magnitude of resting membrane potential in nerve
  - Goldman-Hodgkin-Katz equation or chord conductance equation
- Effects of changing membrane conductance or permeability to $\text{Na}^+$ or $\text{K}^+$ on membrane potential
- Effects of changing extracellular or intracellular $[\text{K}^+]$ on resting membrane potential
- Role of $\text{Na}^+$/K$^+$-ATPase in maintenance of resting membrane potential

Nerve action potential
- All-or-none nature
- Threshold
- Changes in sodium and potassium conductances
- Upstroke of action potential (opening of $\text{Na}^+$ channel activation gates)
- Overshoot
- Repolarization
  - Inactivation of $\text{Na}^+$ channels
  - Opening of voltage-gated potassium channels
  - Undershoot or hyperpolarizing afterpotential
- Ionic basis of absolute and relative refractory periods

Propagation of nerve action potential
- Electrotonic conduction
  - Local currents
  - Time and space constants
- Conduction velocity
  - Effect of myelinization and nerve fiber diameter
  - Saltatory conduction
  - Calculation of nerve conduction velocity

Synaptic and neuromuscular transmission
- Types of synapses: chemical and electrical
- Structure of a chemical synapse between nerve cells
- Release of chemical transmitter
  - Role of calcium
Synaptic vesicle activities: mobilization, trafficking, docking, fusion
and pore formation, release (exocytosis), membrane
incorporation, membrane extraction, reloading

Neuromuscular transmission
Structure of the neuromuscular junction
Nicotinic acetylcholine receptor
Role of acetylcholinesterase
Miniature end-plate potential (mepp)
Endplate potential
Margin of safety
Chemical agents that alter neuromuscular transmission
Myasthenia gravis

Excitatory postsynaptic potential (epsp)
Inhibitory postsynaptic potential (ipsp)
Summation of potentials on a nerve cell body
Temporal and spatial summation
Electrotonic spread of potentials to axon hillock (initial segment)

Directly-gated ion channels (ionotropic)
Indirectly-gated ion channels (metabotropic)
Gap junctions

Basics of sensory physiology
Types of receptors
Mechanoreceptors and proprioceptors
Touch
Audition
Vestibular apparatus
Baroreceptors
Muscle spindles
Golgi tendon receptors
Joint receptors

Photoreceptors
Chemoreceptors
Olfaction
Taste
Arterial blood PO₂
Cerebrospinal fluid pH

Thermoreceptors
Nociceptors (pain)

Generator (receptor) potential
Relation between stimulus intensity and frequency of action potentials in a
single sensory nerve fiber
Relation between stimulus intensity and number of nerve fibers activated
Two-point discrimination
Slowly and rapidly adapting receptors
Autonomic nervous system
The three divisions of the autonomic nervous system: sympathetic (thoracolumbar division), parasympathetic (craniosacral division), and enteric (intrinsic innervation of the digestive tract)

Differences between sympathetic and parasympathetic divisions
Preganglionic and postganglionic nerve fibers and the transmitters they release

Adrenal medulla

Effects of sympathetic and parasympathetic divisions on organ functions

Fight-or-flight response

Muscle physiology

Classification of muscles
Striated muscle
Skeletal
Cardiac
Smooth muscle
Multi-unit
Unitary

Skeletal muscle structure
Whole muscle
Fasciculus
Muscle fiber
Myofibril
Sarcomere
Z-line
A band
I band

Membrane systems in a skeletal muscle fiber
Sarcolemma
Transverse (T)-tubules
Sarcoplasmic reticulum (SR)
Terminal cisterna
Longitudinal elements

Contractile machinery in a skeletal muscle fiber
Thick filaments
Myosin
Thin filaments
Actin
Tropomyosin
Troponins C, I, and T

Electrophysiology of skeletal muscle
Contractile activation (excitation-contraction coupling) and relaxation in skeletal muscle
  Roles of calcium and ATP
  Rigor mortis
Calcium release mechanism
  Ultrastructure of a triad
  Coupling of the signal from the T-tubule to SR
    Voltage sensor
    Calcium release channels
Contraction mechanism and force generation
  Sliding filament model
  Cross-bridge cycle
Mechanics of skeletal muscle contraction
  Muscle twitch
  Isometric tension
    Overlap of thick and thin filaments and force generation
    Force-tension curves for skeletal and cardiac muscle
Isotonic contraction
  Force-velocity curve
  Power output curve
Temporal and spatial summation
  Tetanus
  Definition of motor unit
  Recruitment of motor units

General structure of smooth muscle cells
Sources of calcium in different types of muscle
Calcium regulation of smooth muscle contraction
  Thick filament-linked regulation
  Calmodulin
  Myosin light chain kinase (MLCK)
  Interaction of myosin and actin
  Myosin light chain phosphatase
Latch state
Comparison between resting membrane potentials, action potential shapes and durations, ionic basis of action potential, latency in activation of contraction, and rate of tension development in skeletal, cardiac and smooth muscles
Mechanics of smooth muscle contraction
  Force-velocity curve
  Stress relaxation
Control of rhythm in unitary smooth muscle
  Slow waves

Anatomy of the heart: 4 chambers and 4 valves
Structure of cardiac muscle cells
Electrical coupling
Spread of excitation in the heart
Cardiac action potentials
  Action potential in a ventricular muscle cell and the ionic basis of phases 0 to 4
  Significance of plateau phase (phase 2)
SA nodal cell action potential
  Ionic basis of different phases
  Effects of changing rate of diastolic depolarization, shifting threshold potential, or changing maximum diastolic potential on heart rate
  Effects of sympathetic (cardioaccelerator) and parasympathetic (vagus) nerves on rhythm of pacemaker cells
Calcium release mechanisms in cardiac muscle cells
Length-tension relationship for cardiac muscle (Starling’s law of the heart)

**Electrocardiogram (EKG)**

Cellular origin of the EKG
Resultant dipole representing spread of electrical activity in the heart
  Scalar recordings and vectors
Phases of the EKG
  P wave
    Atrial depolarization
  P-R segment
  QRS complex
    Septal depolarization
    Apical depolarization of ventricle
    Basal depolarization of ventricle
  S-T segment
  T wave
    Ventricular repolarization
Measurement of EKG
  Electrode conventions and standard values for amplitude and speed of EKG tracing
  Bipolar limb leads
    Einthoven triangle
    Calculation of mean QRS electrical axis
  Unipolar limb leads
  Unipolar chest (precordial) leads
  Complete set of 12 traces in an EKG
Arrhythmias
  Respiratory sinus arrhythmia
  Paroxysmal atrial tachycardia
  Atrial flutter
Atrial fibrillation
A-V block
   First-degree
   Second-degree
   Third-degree
Premature ventricular complex (PVC)
Ventricular fibrillation
EKG changes with right and left bundle-branch block, right or left ventricular hypertrophy, myocardial ischemia (current of injury)

**Cardiovascular physiology**

Hemodynamic principles of the cardiovascular system
   Relationships between blood flow, pressures, and resistance (Ohm’s law)
   Series and parallel resistances
   Poiseuille’s law
      Effects of vessel radius, blood viscosity, and tube length on resistance
   Streamline (laminar) flow
   Reynold’s number and turbulent flow
   Effects of gravity on pressure in a column of blood
   Fahreaus-Lindqvist effect
   Total blood volume and its distribution in the circulation

Cardiac cycle
   Phases
      Atrial systole
      Isovolumetric contraction of ventricles
      Rapid ventricular ejection
      Reduced ventricular ejection
      Isovolumetric relaxation of ventricles
      Rapid filling of ventricles
      Reduced filling of ventricles
   Functions of heart valves
      Atrioventricular (tricuspid, mitral)
      Semilunar (pulmonic, aortic)
   Four heart sounds
      Timing and causes of sounds
      Splitting of second heart sound
   Venous pressure waves (a, c, and v waves)

Cardiac mechanics
   Cardiac output depends on stroke volume and heart rate
   Measurement of cardiac output
Comparison between pumping activity (pressures and flows generated) by right and left ventricles

Frank-Starling relationship in the heart
  - Ventricular preload
  - Ventricular function (Starling) curve

Left ventricular pressure-volume loop
  - End-diastolic volume, end-systolic volume, and stroke volume

Effects of changes in cardiac contractility, hypertrophy, afterload, ventricular radius, and diastolic compliance on stroke volume

Effects of sympathetic nerve stimulation on heart rate, cardiac contractility, ventricular work, cardiac metabolism, cardiac oxygen consumption, and cardiac output

Venous return
  - Coupling of cardiac output and venous return
  - Factors affecting venous return
    - Muscle pump
    - Respiratory pump

Stroke work
Ejection fraction

Arterial blood pressure
  - Systolic and diastolic blood pressures
  - Estimation of mean arterial blood pressure
  - Pulse pressure
  - Compliance and elastic recoil of large arteries

Effects of changes in stroke volume, heart rate, arterial compliance, and systemic vascular resistance on arterial blood pressures

Measurement of arterial blood pressure by sphygmomanometry
  - Errors introduced by inappropriate cuff width
Normal range of arterial blood pressures
Changes of arterial distensibility (compliance) with age

Microvascular regulation
  - Functions of arterioles, capillaries, and venules
  - Myogenic vascular regulation
  - Effects of sympathetic nerve stimulation on the microvasculature
  - Endothelial synthesis of nitric oxide (NO) and the interaction of NO with vascular smooth muscle cells
  - Effects of endothelin, vasodilator or vasoconstrictor prostaglandins, and angiotensin II on blood flow

Autoregulation of blood flow
  - Myogenic mechanism
  - Metabolic mechanism

Effects of tissue metabolism on blood flow (active hyperemia)
Reactive hyperemia
Transcapillary exchange of water and solutes
   Capillary structure and capillary exchange
   Diffusion of metabolites and O\textsubscript{2} and CO\textsubscript{2}
   Starling-Landis equation for transcapillary fluid exchange
     Colloid osmotic (oncotic) and hydrostatic pressures
     Capillary filtration coefficient
     Effects of precapillary and postcapillary resistances on capillary hydrostatic pressure
   Edema formation
   Absorption of interstitial fluid after hemorrhage
Lymphatic system

Special circulations
   Coronary circulation
   Cerebral circulation
   Small intestine circulation
   Hepatic circulation
   Skeletal muscle circulation
   Cutaneous circulation
   Fetal and placental circulation

Neural regulation of the cardiovascular system
   Effects of sympathetic nerve stimulation on the heart, systemic vascular resistance, and venous tone
   Effects of vagus nerve stimulation on heart rate
   Arterial baroreceptors and blood pressure control
   Stretch receptors in the cardiac atria and ventricles
   Brain centers that affect blood pressure and heart rate
     Medullary centers
     Hypothalamus
     Higher brain centers
   Consequences of loss of neural vascular control
   Effects of brain ischemia on arterial blood pressure

Altered circulatory states
   Shock
     Types of shock
       Hypovolemic (hemorrhagic) shock
       Cardiogenic shock
       Peripheral vascular collapse
       Neurogenic shock
     Compensatory mechanisms
     Decompensatory phase of shock
   Hypertension
     Definition
Essential hypertension
  Labile and sustained stages
Other causes of hypertension
  Obesity
  Renal disease
  Pheochromocytoma
Treatment of hypertension
  Diabetes mellitus
  Heart failure

Congenital and acquired heart anatomical abnormalities
  Cardiac murmurs
  Atrial septal defect
  Ventricular septal defect
  Tricuspid valve stenosis
  Tricuspid valve insufficiency
  Pulmonic valve stenosis
  Pulmonic valve insufficiency
  Mitral valve stenosis
  Mitral valve insufficiency
  Aortic valve stenosis
  Aortic valve insufficiency

Respiratory physiology

Primary and secondary functions of the lungs
  Gas exchange
  Defense
  Regulation of blood pH
  Blood filter
  Metabolic reactions
Conducting and respiratory zones of the lungs
  Airway tree
  Blood flow to these two zones
  Development of respiratory zone with age
Respiratory defense mechanisms
  Removal of particulates by impaction, sedimentation, and diffusion
  Site of deposition of particles
  Mucociliary escalator
  Alveolar macrophages
Structure of alveolar-capillary membrane
Spirometry
  Measurement of minute ventilation
  The four lung volumes (V_T, RV, ERV, IRV) and four lung capacities (TLC, VC, FRC, IC)
Helium dilution method to measure functional residual capacity (FRC)
Open-circuit nitrogen washout method to measure FRC
Whole body plethysmography

Mechanics of breathing
Obstructive and restrictive disorders, and their effects on FVC, FEV\textsubscript{1.0}, and FEV\textsubscript{1.0}/FVC
Muscles involved in breathing
- Diaphragm
- External intercostals
- Internal intercostals
- Abdominal muscles
- Other accessory muscles
Alveolar, pleural, transpulmonary, and transairway pressures
Reason why pleural pressure is usually subatmospheric
Pneumothorax
Changes in pleural pressure, alveolar pressure, and air flow during a normal quiet breathing cycle
Definitions of elasticity and compliance
- Static pressure-volume curve for lungs
- Relation between lung elastic recoil and pulmonary compliance
- Compliance curves and recoil tendencies for lungs and chest wall
- Alterations in lung elasticity and compliance in emphysema and restrictive disorders
Surface tension
- Origin of surface tension
- Laplace’s law
- Site of synthesis, chemical nature, and action of pulmonary surfactant
- Role of pulmonary surfactant in decreasing surface tension, reducing the work of breathing, stabilizing alveoli of different sizes, and keeping the alveoli dry
  - Infant respiratory distress syndrome (IRDS)
  - Acute (adult) respiratory distress syndrome (ARDS)
Alveolar interdependence
Airways resistance
- Laminar, turbulent, and transitional flow
- Major sites of resistance along airway tree
Dependence of airways resistance on lung volume, smooth muscle tone, gas density, and airways compression during forced expiration
- Bronchodilator effects of sympathetic stimulation and increased P\textsubscript{CO\textsubscript{2}} in small airways
- Flow-volume curve during forced expiration and forced inspiration
Dynamic airways compression
Equal pressure point
Effect of abnormally high pulmonary compliance, as in
the patient with emphysema

Work of breathing

Pulmonary ventilation
Definition of partial pressure
Dalton's law of partial pressures
Effect of high altitude on atmospheric pressure and partial pressure of oxygen
Composition of atmospheric air and alveolar gas
Dead space ventilation and alveolar ventilation
Effects on alveolar ventilation of increasing dead space volume at constant minute ventilation
Effects on alveolar ventilation of increasing breathing frequency at constant minute ventilation
Anatomical and physiological dead space
Definitions and methods of measurement
Effects of changes in alveolar ventilation on arterial blood $P_{CO_2}$ and $P_{O_2}$
Distinction between hyperventilation and hyperpnea
Causes of hypoventilation and hyperventilation
Causes of uneven ventilation in lung disease
Effects of gravity on regional ventilation in the upright lung

Pulmonary diffusion
Henry's law (solubility of a gas in a liquid)
Fick's law for diffusion of gases
Pulmonary diffusing capacity
Measurement of diffusing capacity using a single breath of carbon monoxide
Factors that affect the pulmonary diffusing capacity for oxygen
Uptake of $N_2O$, $O_2$, and CO by pulmonary capillary blood
Perfusion- versus diffusion-limited uptake
Effects of exercise or thickened alveolar membrane on uptake of $O_2$

Pulmonary circulation
Pressures, blood flow, and resistance of the pulmonary circulation, contrasted to the systemic circulation
Calculation of pulmonary vascular resistance
Factors that influence pulmonary vascular resistance
Lung volume
Right ventricular output (cardiac output)
  Recruitment and distension of pulmonary vessels
Gravity
  Zones 1, 2, and 3 in the lungs
Alveolar hypoxia
  Hypoxic pulmonary vasoconstriction
Inspired nitric oxide
  Nerves and hormones
Pulmonary edema

Bronchial circulation

Ventilation/Perfusion (V/Q) Ratio
  Average V/Q ratio in a normal person
  Effects of mismatched (abnormally high or abnormally low) V/Q ratios on the composition of alveolar and pulmonary end-capillary PO₂ and PCO₂
  Effects of gravity on V/Q ratios and alveolar PO₂ and PCO₂ values at the top and base of the lungs of a standing individual

Shunts
  Anatomical
  Physiological
  Alveolar-arterial O₂ difference (gradient)

Simplified alveolar air (gas) equation

Definitions of hypoxia and hypoxemia

Causes of hypoxemia and how these may be distinguished
  Ventilation-perfusion mismatch
  Anatomical shunt
  Generalized hypoventilation
  Diffusion impairment
  Low inspired PO₂

Transport of oxygen and carbon dioxide
  Definition of oxygen content, oxygen carrying capacity, and oxygen saturation of blood
  Physically dissolved oxygen in blood
  Oxygen chemically combined with hemoglobin
  Oxyhemoglobin dissociation curve (hemoglobin-oxygen equilibrium curve)
    Effects of the shape of this curve on the uptake and delivery of oxygen
    Binding affinity for oxygen of fetal (HbF) versus adult hemoglobin (HbA)
    Effects of temperature, pH, PCO₂, and 2,3-diphosphoglycerate (DPG)
    Effects (if any) of anemia and carbon monoxide poisoning on the oxyhemoglobin dissociation curve, oxygen content of the blood, and arterial oxygen tension

Cyanosis
Forms in which carbon dioxide is carried by the blood
Bicarbonate
Carbaminohemoglobin
Physically dissolved CO₂
Percentage of total CO₂ transported in each form
Roles of red cell carbonic anhydrase and chloride-bicarbonate exchange (chloride shift) in CO₂ transport
Carbon dioxide equilibrium curve for blood
Haldane effect

Control of breathing
Organization of the medullary respiratory center
Effects of pontine, hypothalamic, and cerebral cortical centers on breathing
Afferent (sensory) neural inputs that affect breathing
  Slowly adapting receptors in lungs
  Rapidly adapting receptors in lungs
  C-fiber endings in lungs
  Mechanoreceptors and chemoreceptors in upper airways
  Pain fibers
  Temperature receptors
  Joint, muscle mechanoreceptors
  Carotid sinus and aortic arch baroreceptors
Response to oxygen lack (hypoxia)
  Signs and symptoms of hypoxia
  Acclimatization to chronic hypoxia
  Peripheral arterial chemoreceptors: carotid (and aortic) bodies
  Minute ventilation as a function of alveolar PO₂
    Interaction with CO₂
  Sequence of events by which hypoxia causes hyperventilation
Response to carbon dioxide
  Carbon dioxide as a stimulus for ventilation
  Effects of CO₂ on central (most important) and peripheral (less important) chemoreceptors
  Effects of CO₂ on pH of cerebrospinal fluid
  Effects of sleep, narcotics, chronic obstructive pulmonary disease (COPD), deep anesthesia, or metabolic acidosis on the response to CO₂
Responses to fixed acids and bases

Gastrointestinal physiology

Gastrointestinal (GI) motility
  Organization of smooth muscle in the digestive tract
    Outer longitudinal muscle layer
    Inner circular muscle layer
Muscularis mucosae
Role of interstitial cells of Cajal as pacemaker cells
Slow waves and action potentials (spikes)
Basic electrical rhythm (BER)
Extrinsic innervation of the GI tract (parasympathetic and sympathetic nerve fibers)
The enteric nervous system
Local, short, and long reflexes in the GI tract
  Peristaltic reflex
  Vagovagal reflexes
  Gastroileal reflex
Patterns of GI motility
  Peristalsis
  Rhythmic segmentation
  Tonic contractions
    Proximal stomach
    Sphincters
Swallowing
  Oral, pharyngeal, and esophageal phases
  Upper esophageal sphincter (UES)
  Lower esophageal sphincter (LES)
  Primary and secondary peristaltic waves
Differences in motility of proximal and distal stomach
  Reservoir function of proximal stomach
    Receptive relaxation
    Gastric accommodation
  Propulsion, grinding, and retropulsion in the distal stomach
  Effects of vagotomy on stomach motility
Determinants of the rate of gastric emptying
Motility patterns in the small intestine during the fasted and fed states
  Migrating motor (myoelectric) complex
  Segmentation
Vomiting reflex
Ileocecal valve
Motility patterns in the large intestine
  Haustration
  Peristalsis
  Mass movements
  Defecation
    Rectosphincteric reflex
    External anal sphincter
Disorders of colonic motility
  Incontinence
  Hirschsprung's disease (congenital aganglionosis)
  Constipation
  Diarrhea
Major hormones of the GI tract
  Gastrin
  CCK (cholecystokinin)
  Secretin
  Incretins
    GIP (gastric inhibitory peptide, glucose-dependent insulinotropic polypeptide)
    GLP-1 (glucagon-like peptide-1)
  Motilin

Salivary secretion
  Lubricating, protective, and digestive functions of saliva
  Organic constituents of saliva
    Mucus
    Lysozyme
    Lactoferrin
    Immunoglobulin A and its binding glycoprotein
    Salivary amylase (ptyalin)
    Haptocorrin
  The three principal pairs of salivary glands, their innervation, histologic type, and relative contributions to the total output of saliva
  The salivon
  Ionic composition and osmolality of saliva as a function of the rate of salivary secretion
  Effects of parasympathetic and sympathetic stimulation on salivary blood flow and secretion

Gastric secretion
  Oxyntic gland anatomy
  Pyloric gland anatomy
  Effects of gastric secretion rate on the ionic composition of gastric juice
  Production of HCl by gastric parietal cells
    Cell model
    $\text{H}^+/\text{K}^+\text{-ATPase and proton pump inhibitors}$
    Alkaline tide
  Effects of gastrin, acetylcholine, and histamine on gastric acid secretion
    Potentiation
    Enterochromaffin-like (ECL) cells
  Three phases of gastric secretion: cephalic, gastric, and intestinal
  Organic constituents of gastric juice
    Pepsinogens/Pepsins
    Intrinsic factor
    Mucins
    Gastric lipase
  The gastric mucosal barrier
Causes of peptic ulcer disease

Pancreatic secretion
The pancreatic acinus
Effects of pancreatic secretion rate (stimulated by secretin) on the ionic composition of pancreatic juice
Electrolyte secretion by pancreatic ductule cells
   Effects of defect in cystic fibrosis transmembrane conductance regulator (CFTR)
   Importance of pancreatic bicarbonate in neutralizing acidic chyme in the duodenum
Stimulation of an enzyme-rich secretion by CCK
Pancreatic acinar cell secretory products
   Zymogens: trypsinogen, chymotrypsinogen, proelastase, procarboxypeptidase, phospholipase A2
   Active digestive enzymes: a-amylase, carboxylester hydrolase (cholesterol esterase), lipase, ribonuclease, deoxyribonuclease
   Trypsin inhibitor
   Procolipase
   Monitor peptide
   Na+, Cl−, water
Conversion of trypsinogen to trypsin by enteropeptidase (enterokinase) and activation of other pancreatic zymogens by trypsin
Three phases of pancreatic secretion in response to a meal

Biliary secretion
Functions of bile
Comparison of the composition of human hepatic and gallbladder bile
   Functions of the gallbladder
Stimulation of bile secretion by secretin
Synthesis of primary bile acids from cholesterol in the liver
Structure of the biliary tree
Cell model for hepatocyte bile salt uptake, conjugation, and secretion into bile canaliculi
Formation of micelles by aggregation of bile salts
   Amphipathic nature of bile salts
Formation of secondary bile acids by colonic bacteria
Enterohpatic circulation of bile salts
Bile pigments
   Role of CCK in causing gallbladder contraction and relaxation of the sphincter of Oddi

Factors that affect food intake
Signals from adipose tissue (leptin), GI tract (ghrelin, CCK, peptide YY₃₋₃₆), and brain

Adaptations of the small intestine to increase surface area

Digestion and absorption of carbohydrates
  Salivary and pancreatic amylases
  Brush border oligosaccharidases (sucrase, lactase, maltase, isomaltase)
  Lactase deficiency (lactose intolerance)
  Cell model for enterocyte glucose absorption (SGLT-1 and GLUT-2)
  Glucose-galactose malabsorption

Digestion of proteins and absorption of tripeptides, dipeptides, and amino acids
  Recommended daily allowances for proteins in infants and adults
  Pepsins and pancreatic proteolytic enzymes
  Brush border and cytosolic peptidases in enterocytes
  Cell membrane dipeptide/tripeptide transporter and amino acid transporters

Digestion and absorption of lipids
  Hydrolysis of triglycerides by gastric and pancreatic lipases
  Emulsification of fat in the stomach
  Pancreatic lipase and colipase
  Role of bile salts in solubilizing products of lipid digestion in mixed micelles
  Unstirred water layer
  Resynthesis of triglycerides and phospholipids in enterocytes and formation of chylomicrons
  Transport of chylomicrons by intestinal lymphatics
  Fate of chylomicrons
  Production and absorption of short-chain fatty acids in the large intestine

Absorption of the fat-soluble vitamins: A, D, E, and K

Absorption of vitamin B₁₂ (cobalamin)

Absorption of iron

Absorption of calcium
  Regulation by 1,25-dihydroxvitamin D₃

Intestinal absorption and secretion of salt and water
  Magnitude of secretion and absorption of water along the GI tract
  Comparison between sodium and water absorption in the small and large intestine
  Cell models for sodium and water absorption
Effects of aldosterone on colonic Na\textsuperscript{+} absorption and K\textsuperscript{+} secretion
Secretion of fluid by intestinal crypt cells
Effects of cholera toxin and \textit{E. coli} heat-stable enterotoxin

Causes of diarrhea

Dietary fiber

Hepatic physiology
Blood supply of the liver
Hepatic lobule
Structure
Metabolic zonation
Cells of the liver
Hepatocytes
Endothelial cells
Stellate cells
Cholangiocytes
Kupffer cells
Carbohydrate metabolism in the liver
Glycogen synthesis and storage
Glycogenolysis
Gluconeogenesis
Glycolysis
Fructose, galactose, and pentose metabolism
Protein metabolism in the liver
Catabolism of amino acids
Transamination reactions
Synthesis of urea
Synthesis of serum albumin and clotting factors
Lipid metabolism in the liver
Uptake of chylomicron remnants
Lipid oxidation
Synthesis of lipoproteins (VLDL, HDL)
Cholesterol synthesis and excretion
Fatty acid synthesis
Ketone body production during starvation
Synthesis of triglycerides and phospholipids
Liver metabolism in the fed versus fasted state
Hydroxylation of vitamin D
Storage of vitamin A
Drug metabolism in the liver: phase I and phase II biotransformations
Symptoms of liver disease

Renal physiology
Role of the kidneys in regulating the composition and volume of the internal environment

Functional anatomy of the kidneys
- Cortex and medulla
- Nephron and collecting duct system
- Kidney blood vessels: afferent arteriole, glomerulus, efferent arteriole, peritubular capillary network, vasa recta
- Cortical and juxtamedullary nephrons
- Juxtaglomerular apparatus

Special substances produced by the kidneys
- Erythropoietin
- 1,25-dihydroxyvitamin D$_3$ (1,25-dihydroxycholecalciferol, calcitriol)
- Prostaglandins and thromboxane
- Renin
- Kallikrein

Methods to assess whole kidney function
- Definition of renal plasma clearance
- Use of inulin clearance to measure glomerular filtration rate (GFR)
- Endogenous creatinine clearance
- Relation between plasma creatinine concentration and GFR
- Use of p-aminohippurate (PAH) clearance to estimate renal plasma flow
- Calculation of renal blood flow from renal plasma flow and hematocrit ratio
- Calculation of the rates of tubular reabsorption or secretion of a substance
- Tubular transport maximum (Tm)
- Glucose threshold

Renal blood flow
- Magnitude of kidney blood flow
- Comparison of blood flow to kidney cortex and kidney medulla
- Autoregulation of renal blood flow and GFR
  - Myogenic mechanism
  - Tubuloglomerular feedback mechanism
- Factors that affect renal blood flow
  - Renal sympathetic nerves
  - Hormones

Glomerular filtration
- Anatomy of the glomerulus and ultrastructure of the glomerular filtration barrier
- Ultrafiltration
  - Influence of size, shape, and electrical charge on filterability of a macromolecule
- Causes and consequences of proteinuria
- Pressures involved in glomerular filtration
Magnitude of glomerular filtration in people
   Gender differences
   Age differences

Tubular reabsorption and secretion
   Changes in composition and volume of tubular fluid along the proximal convoluted tubule
   Isosmotic nature of proximal tubule reabsorption
   Dependence of water reabsorption on sodium reabsorption
   Use of tubule fluid/plasma inulin concentration ratio to indicate fractional water reabsorption
   Cell model for transport in the proximal convoluted tubule
   Role of peritubular capillary Starling forces in uptake of reabsorbed fluid
   Secretion of organic anions and cations by the proximal tubule
   Nonionic diffusion of lipid-soluble organic acids and bases (e.g., phenobarbital, ammonia)
   Water permeability of descending and ascending limbs of Henle’s loop
   Cell model for transport by thick ascending limb cells
      Na/K/2Cl cotransporter
   Cell model for transport by distal convoluted tubule cells
      Na/Cl cotransporter
   Cell model for sodium reabsorption and potassium secretion by cortical collecting duct principal cells
      Epithelial sodium channel (ENaC)
   Cell model for H+ secretion by α-intercalated cells and HCO3- secretion by β-intercalated cells
   Comparisons between proximal convoluted tubule and distal nephron with respect to transport capacity, water permeability, transepithelial gradients for small ions, tight junctions, and control

Water balance
   Fluid compartments of the body
      Total body water
      Extracellular water
         Plasma water
         Interstitial fluid-lymph water
         Transcellular fluid
      Intracellular water
   Osmotic equilibrium between intracellular and extracellular water
      Effects of addition of pure water, isotonic saline, or hypertonic saline on osmolality and distribution of water between cell and extracellular compartments
   Input and output of water from the body
      Water needs of infant compared to adult
   Thirst mechanism
   Antidiuretic hormone (arginine vasopressin [AVP] in people)
Chemical nature
Site of synthesis and release
Factors that increase or decrease AVP release
  Osmoreceptors in anterior hypothalamus
  Stretch receptors in left atrium and arterial baroreceptors
Relation between plasma AVP and plasma osmolality
Relation between urine osmolality and plasma AVP
Relation between plasma AVP and blood volume loss
Action of AVP on collecting duct cells
  \( V_2 \) receptor
  G protein
  Adenylyl cyclase
  cAMP
  Aquaporin-2

Production of an osmotically dilute or concentrated urine
  Value of being able to produce an osmotically concentrated urine
    Limits of urine osmolality in healthy people
    Minimum daily (or hourly) urine output
Calculation of free water production (clearance) from urine flow rate and osmolal clearance
Countercurrent mechanism
  Osmotic gradient in medulla
  Countercurrent multiplication by loops of Henle
  Countercurrent exchange in vasa recta
  Collecting ducts as osmotic equilibrating devices
  Special role for urea in the concentrating mechanism
Factors that affect the ability of the kidneys to produce an osmotically concentrated urine
  Neurogenic diabetes insipidus
  Nephrogenic diabetes insipidus

Sodium balance
  Magnitude of filtration, reabsorption, and excretion of ions (\( \text{Na}^+, \text{Cl}^-, \text{K}^+, \text{HCO}_3^- \)) and water
  Magnitude of reabsorption of sodium (as percentage of filtered load) along the nephron
Factors that affect sodium excretion
  Glomerular filtration rate
    Effect of shock (low arterial blood pressure)
    Glomerulotubular balance
  Mineralocorticoids (aldosterone)
    Renin-angiotensin-aldosterone system
  Intrarenal physical forces
  Natriuretic hormone
    Atrial natriuretic peptide
Other natriuretic peptides
Renal sympathetic nerves
Estrogens
Osmotic diuretics
Poorly reabsorbable anions
Diuretic drugs
Sodium salts as the main contributor to the osmolality of the extracellular fluid and as the main determinant of the amount of water (hence volume) of the extracellular fluid (ECF)
Input and output of sodium from the body
Effects of changes in dietary sodium intake
Regulation of the effective arterial blood volume (EABV) by changing sodium excretion
Renal sodium retention in congestive heart failure and other edematous states

Potassium balance
The amount of potassium in the body and its distribution
Effects of potassium imbalances
Hypokalemia
Hyperkalemia
Factors that affect the distribution of potassium between extracellular and intracellular fluid compartments
Input and output of potassium
Potassium handling along the nephron
Cell model for secretion of potassium by cortical collecting duct principal cell
Factors that affect renal potassium excretion
Dietary intake
Mineralocorticoids (aldosterone)
Acid-base disturbances
Excretion of poorly reabsorbed anions
Sodium excretion (and increased tubule fluid flow rate)

Phosphate balance
Input and output of phosphate and its distribution in the body
Reabsorption of phosphate by a Tm-limited mechanism in the proximal tubule
Effect of parathyroid hormone (PTH) on tubular phosphate reabsorption

Calcium balance
Input and output of calcium and its distribution in the body
Sites of reabsorption of calcium along the nephron
Effect of PTH on tubular calcium reabsorption

Magnesium balance
Acid-base balance

Definitions of acid, base, buffer, and pH
Normal range of arterial blood pH
Importance of constancy of blood pH
Isohydric principle
Chemical buffers present in intracellular and extracellular fluids and in bone
Henderson-Hasselbalch equation for the bicarbonate/CO₂ system
Why the bicarbonate/CO₂ system is so important in pH buffering in the body
The four simple acid-base disturbances
  Respiratory acidosis
  Respiratory alkalosis
  Metabolic acidosis
  Metabolic alkalosis
Anion gap
pH-bicarbonate diagram
Mixed acid-base disturbances

Renal regulation of acid-base balance
Sources of nonvolatile acids
The three processes involved in urinary acidification
  Reabsorption of filtered bicarbonate
  Formation of titratable acid
  Renal synthesis and excretion of ammonia
Net renal acid excretion
pH of tubular fluid along the nephron and collecting duct system
Cell models for the three processes involved in urinary acidification
Factors that influence renal secretion and excretion of hydrogen ions
Renal compensations for the four simple acid-base disturbances

Endocrinology

Endocrine control mechanisms and hypothalamic-pituitary interactions
Endocrine, paracrine, neurocrine, and juxtacrine actions
Properties of hormones
Amino acid derivatives
  Thyroxine
  Catecholamines
Peptide and protein hormones
  Insulin family
    Insulin, IGF-I, IGF-II, relaxin
  Secretin family
    Secretin, glucagon, GIP
Growth hormone family
  GH, prolactin, placental lactogen
Glycoprotein hormone family
  TSH, LH, FSH, hCG
Synthesis of peptide and protein hormones from preprohormones
  ACTH production by proteolytic processing of POMC
  Melanocyte-stimulating hormone (MSH)
Steroid hormones
Properties of endocrine glands
Transport of hormones in the blood
Hormone metabolism, degradation, and excretion
  Metabolic clearance rate (MCR)
Endocrine control systems
  Negative and positive feedback
  Inhibitory hormones
  Metabolic control
Hormone receptors and signaling pathways
  Plasma membrane receptors
  Cytoplasmic and nuclear receptors
Hormone assays
  Competition assay (e.g., Radioimmunoassay [RIA])
  Sandwich assay (e.g., Enzyme-linked immunosorbent assay [ELISA])
Pituitary gland
  Embryological origin
  Structure
    Adenohypophysis
      Pars tuberalis
      Pars distalis (anterior lobe)
      Pars intermedia
    Neurohypophysis
      Median eminence
      Infundibular stalk
      Pars nervosa (posterior lobe)
Hypothalamus-pituitary axis
  Hypothalamo-hypophyseal portal system and short portal system to the anterior pituitary
Hypothalamic releasing hormones
  Growth hormone releasing hormone (GHRH)
  Somatostatin (SRIF)
  Dopamine
  Corticotropin releasing hormone (CRH)
  Thyrotropin-releasing hormone (TRH)
  Gonadotropin-releasing hormone (GnRH = LHRH)
Anterior pituitary hormones
  Growth hormone (GH)
Prolactin (PRL)
Adrenocorticotropic hormone (ACTH)
Thyroid-stimulating hormone (TSH)
Gonadotropins
  Luteinizing hormone (LH)
  Follicle-stimulating hormone (FSH)
Posterior pituitary hormones
  Synthesis in hypothalamic nuclei
  Hypothalamo-hypophyseal tract
  Arginine vasopressin (AVP) = Antidiuretic hormone (ADH)
  Diabetes insipidus
  Syndrome of inappropriate ADH secretion (SIADH)
Oxytocin
  Role in parturition and milk let-down

The adrenal glands
Anatomy and histology of the adrenal glands
  Adrenal cortex
    Zona glomerulosa
    Zona fasciculata
    Zona reticularis
  Adrenal medulla
Adrenal cortex
  Steroidogenic pathways and major steroid hormone produced in the different zones of the adrenal cortex
  Mineralocorticoids
  Glucocorticoids
  Androgens
  Regulation of adrenal cortical function
  Hypothalamo-hypophyseal-adrenal axis
  Trophic and steroidogenic effects of ACTH
  Regulation of cortisol secretion
    Circadian rhythm
    Stress-induced cortisol secretion
Transport and metabolism of adrenal steroids
  Glucocorticoid and mineralocorticoid hormone receptor signaling
Physiological effects of glucocorticoids
  Metabolic effects
  Effects on vascular reactivity
Pharmacological effects of glucocorticoids
  Anti-inflammatory
  Immunosuppressive
Clinical findings in hypersecretion or hyposecretion of adrenal steroids
Cushing’s syndrome (hypersecretion)
  Cushing’s disease
  Adrenal tumor
  Ectopic ACTH-producing tumor
Adrenal insufficiency
  Primary adrenal insufficiency (Addison’s disease)
  Secondary adrenal insufficiency

Adrenal medulla
  Relationship of medulla and sympathetic nervous system
  Biosynthesis of epinephrine (adrenaline) and norepinephrine (noradrenaline) by chromaffin cells
  Pathway of epinephrine and norepinephrine degradation
  Actions of epinephrine
    Metabolic
    Cardiovascular and pulmonary
Adrenal medullary dysfunction
  Hypofunction
  Hyperfunction
    Pheochromocytoma

The thyroid gland
  Anatomy and histology of the thyroid gland
  Embryological development of the thyroid
  Thyroid hormone formation
    Chemical structure of thyroid hormones
      Thyroxine (T₄)
      Tri-iodothyronine (T₃)
    Thyroglobulin synthesis and secretion
    Sodium/iodide symporter protein
    Oxidation, organification, and coupling
      Thyroid peroxidases
    Microvilli and endocytosis of colloid
    Lysosome migration and phagolysosome formation
    Deiodination
    Anti-thyroid compounds
  Hypothalamo-hypophyseal-thyroid axis
  Transport and metabolism of thyroid hormones
    Plasma concentrations of T₄ and T₃
    Binding of thyroid hormones to plasma proteins
    Peripheral metabolism of T₄
      Conversion of T₄ to T₃ or reverse T₃
      Formation of inactive diiodothyronines
  Thyroid hormone receptor signaling
  Physiological effects of thyroid hormones
    Calorigenic effect (increased oxygen consumption and basal metabolic rate [BMR])
Effects on cardiac output
Effects on carbohydrate metabolism
Effects on lipid metabolism
Effects on protein synthesis
Effects on growth
Effects on development and maturation of the nervous system

Thyroid dysfunction
  Hyperthyroidism
    Graves’ disease
  Hypothyroidism

Endocrine pancreas
  Normal range of blood glucose
  Effects of hypoglycemia
  Effects of hyperglycemia

Synthesis and secretion of islet hormones
  Beta cells: insulin
  Alpha cells: glucagons
  Delta cells: somatostatin
  F cells: pancreatic polypeptide

Stimulation of insulin by increased blood glucose
  Proinsulin synthesis
    Insulin
    C-peptide
  Factors that stimulate or inhibit insulin secretion

Stimulation of glucagon secretion by decreased blood glucose
  Proglucagon synthesis
  Factors that stimulate or inhibit glucagon secretion

Effects of insulin
  Insulin receptor
  Intracellular signaling pathways
  Translocation of GLUT 4 to the plasma membrane
  Stimulation of glycogen synthesis
  Stimulation of glycolysis
  Lipogenic and antilipolytic effects of insulin
  Stimulation of protein synthesis and inhibition of protein degradation

Effects of glucagon
  Glucagon receptor
  Increased glycogenolysis in the liver
  Increased gluconeogenesis in the liver
  Stimulation of ureagenesis in the liver
  Stimulation of lipolysis in the liver
  Stimulation of ketogenesis in the liver

Insulin/glucagon ratio
Diabetes mellitus
Type 1 diabetes mellitus
Type 2 diabetes mellitus
The diabetes epidemic

Calcium, phosphate, and bone homeostasis
- Physiological actions of calcium
- Physiological actions of phosphate
- Distribution of calcium and phosphate in tissues
- Forms of calcium in blood plasma
  - Ionized (physiologically important form)
  - Complexed with small anions
  - Bound to plasma proteins
- Forms of phosphate in blood plasma
- Calcium balance and the distribution of calcium in the body (ECF, cells, bone)
- Phosphate balance and the distribution of phosphate in the body (ECF, cells, bone)
- Regulation of plasma ionized calcium
  - Parathyroid hormone (PTH)
  - Calcitonin
  - 1,25-dihydroxyvitamin D$_3$
- Structure of the parathyroid glands
- Calcium-sensing receptor
- Parafollicular cells (C cells) of the thyroid gland: produce calcitonin
- Pathway of synthesis of 1,25-dihydroxyvitamin D$_3$
- Effects of PTH and calcitonin on kidney, bone, and small intestine and on plasma calcium and phosphate concentrations
- Functions of osteoblasts and osteoclasts
- Effects of 1,25-dihydroxyvitamin D$_3$ on intestinal calcium absorption
- Negative feedback between 1,25-dihydroxyvitamin D$_3$ and PTH
- Changes in bone calcium content as a function of age in males and females
- Abnormalities of bone mineral metabolism
  - Osteoporosis
  - Osteomalacia and rickets
  - Paget's disease
  - Osteogenesis imperfecta

Prenatal and postnatal growth
- Differences between prenatal and postnatal growth
- Prenatal (fetal) growth factors
  - IGF-I
  - IGF-II
  - Insulin
EGF/TGFa
Postnatal growth
  Three phases of postnatal growth
    Epiphyseal fusion
  Normal growth and its assessment
Hormonal control of postnatal growth
Growth hormone
  Structure
    Hypothalamo-hypophyseal growth hormone axis
      Somatotrope
      GHRH and somatostatin
      Ghrelin
  Pulsatile secretion
  Physiological effects of growth hormone
    GH-IGF axis
Insulin-like growth factors (IGFs)
  IGF-I
  IGF-II
Thyroid hormone
Gonadal steroids
Glucocorticoids
Local growth factors
  Epidermal growth factor
  Nerve growth factor
  Platelet-derived growth factor
  Angiogenic and antiangiogenic factors
Effects of growth hormone deficiency or excess
  Dwarfism
  Gigantism
  Acromegaly
Growth disorders
  Etiologies of short stature
  Etiologies of tall stature

Reproductive physiology

Hypothalamic-pituitary-gonadal axis
  Components of the reproductive endocrine system
    Higher centers
    Hypothalamus
      GnRH-secreting neurons
      Pulse generator
    Pituitary
      Gonadotropins
    Gonads
Sex steroids and peptide hormones
Negative feedback
Control of puberty
Dual mechanisms of control (gonadotropin-dependent and
gonadotropin-independent)
Factors that affect the onset of puberty
Normal puberty
Gonadarche versus andrenarche
Menarche in girls
Clinical characteristics of puberty in boys and girls
The pubertal growth spurt

Male reproductive physiology
Organs of male reproduction
Testes
Epididymis
Vas deferens
Seminal vesicles
Prostate
Penis
Structure of testes
Blood-testis barrier
Seminiferous tubules
Germ cells to spermatozoa
Sertoli cells: functions
Leydig cells: functions
Bidirectional interactions between Sertoli and Leydig cells
Effects of LH and FSH on the testes
Spermatogenesis
Primordial germ cell
Spermatogonium
Primary spermatocyte
Meiotic division I
Secondary spermatocyte
Meiotic division II
Spermatids
Mature spermatozoa (sperm)
Spermiogenesis
Spermiation
Structure of mature sperm
Role of testosterone in spermatogenesis
Capacitation
Steroidogenesis
Synthesis of testosterone
The LH receptor on Leydig cells
Properties of circulating testosterone
Binding to plasma proteins
Conversion of testosterone to dihydrotestosterone via 5α-reductase
Conversion of testosterone to estradiol via aromatase
Conversion of testosterone to biologically inactive compounds
Decline of plasma testosterone with age in adult men

Actions of androgens
  Cellular mechanism of action
  Male sexual differentiation
  Secondary sexual development in both males and females
On the brain
Disorders of male reproduction
  Hypothalamic-pituitary hypogonadism
    Kallman syndrome
  Primary hypogonadism
    Klinefelter syndrome
  Androgen insensitivity
    Testicular feminization
  Evaluation of male infertility

Female reproductive physiology
Hypothalamic-pituitary-ovarian axis
Female reproductive organs
  Ovaries
  Oviducts (Fallopian tubes)
  Uterus
  Vagina
Folliculogenesis
  Primary follicle to Graafian follicle
  Oocyte
  Granulosa cells
  Theca cells
  Role of FSH in folliculogenesis
  Inhibin
Number of oocytes as a function of a woman’s age
Germ cell meiosis
Ovarian steroidogenesis
  Synthesis of estradiol and progesterone
  Effects of LH on theca and granulosa cells and FSH on granulosa cells
  Interplay between theca and granulosa cells in steroidogenesis
Cellular mechanisms of action of estradiol and progesterone
Menstrual cycle
  Menses
  Follicular phase
Ovulation
- LH surge
Luteal phase
- Corpus luteum
Changes in plasma levels of FSH, LH, estradiol, progesterone, and inhibin, follicle diameter, basal body temperature, vaginal cornification and pyknotic index, cervical mucus ferning, and endometrial thickness

Menopause
Disorders of female reproduction
- Primary amenorrhea
- Secondary amenorrhea
  - Polycystic ovary syndrome
- Evaluation of amenorrhea
Fertilization
Implantation
Pregnancy
- Placental hormones (hCG)
  - Interactions between placenta and fetal adrenal cortex in the production of estrogens
Parturition
- Oxytocin, relaxin, and prostaglandins
Lactation
- Mammary glands
- Prolactin
- Suckling reflex
  - Oxytocin
Physiological bases for infertility actions of contraceptive steroid hormones

Sexual differentiation
Normal sexual differentiation
- Genetic sex
  - SRY
Gonadal differentiation
- Differentiation of internal reproductive structures
  - Bi-potential duct systems
  - Gonadal hormones
  - Testosterone
  - AMH (Antimüllerian hormone = müllerian inhibiting substance)
  - Involution of Müllerian ducts in males and Wolffian ducts in females
- Differentiation of external genitalia
  - Bi-potential
  - Role of dihydrotestosterone
Gender role and gender identity
Etiologies of ambiguous genitalia
- Overvirilization of a genetic female
- Congenital adrenal hyperplasia
- Undervirilization of a genetic male
- Gonadal differentiation defect
- Syndromic/mechanical/idiopathic causes

**Thermal regulation**

Balance between heat production and heat loss
- Normal range of body temperature
- Diurnal cycle

Factors affecting metabolic rate
- Exercise
- Thermogenic effect of food
- Hormones
- Body size
- Age/gender
- Disease
- Ambient temperature

Routes of heat loss
- Convection
- Radiation
- Evaporation (sweating)
- Conduction

Core, shell, and mean body temperatures
Cutaneous cold and warm receptors

Regulation of body temperature
- Increase in set point during fever

Measurement of basal metabolic rate (BMR) by direct and indirect calorimetry
- BMR as a function of age

Heat acclimatization

Responses to cold
- Shivering
- Cutaneous vasoconstriction

Hypothermia

Hyperthermia
- Heat syncope
- Heat exhaustion (heat collapse)
- Heatstroke
- Malignant hyperthermia

**Exercise physiology**
Metabolic systems that provide energy during exercise
Energy sources as a function of exercise duration
Relation between oxygen consumption and exercise intensity
Maximal $O_2$ consumption
  Factors affecting
  Physiological limitations of $V_O^{\text{max}}$
Oxygen debt
Respiratory changes during exercise
  Factors stimulating hyperpnea
  Changes in tidal volume, respiratory frequency, pulmonary diffusing capacity, and pulmonary blood flow during exercise
  Arterial and mixed venous $P_O$, $P_CO_2$, and pH during exercise
Effect of diet on fuels used during exercise
Changes in circulatory dynamics during exercise
  Heart rate
  Stroke volume
  Cardiac output
  Arterial blood pressure
  Systemic vascular resistance
  Distribution of blood flow
Changes in heat production and dissipation and body temperature during exercise
Effects of static versus dynamic exercise on blood pressure
Effects on exercise performance of training, muscle fatigue, $V_O^{\text{max}}$, anaerobic threshold, gender, and age
Benefits of daily exercise in weight control, bone strength, insulin sensitivity, optimal blood lipid profile, and in pregnancy