

D Human physiology

Introduction

- health depends on physiological mechanisms working efficiently
- hormones must be secreted at variable rate to achieve equilibrium
- chemical composition of blood is regulated by liver
- red blood cells transport respiratory gases and these influence blood pH

D.1 Human nutrition

Essential nutrients

- some nutrients are essential as food is only possible source of nutrient
- other nutrients are non-essential, either another nutrient can fulfill same purpose or it can be made in body from another nutrient
- some essential nutrients are conditionally essential (adults produce vitamin K, infants do not)

Essential fatty acids and amino acids

- half of 20 amino acids in proteins are essential in humans; cannot be synthesized in sufficient quantities; others can be made from simpler nitrogen compounds
- threonine and arginine are conditionally essential; threonine can be synthesized if phenylalanine is present; synthesis pathway of arginine is not active in prematurely born infants
- some omega-3 and omega-6 fatty acids are essential in diet (α -linolenic and linolenic acid)

Essential amino acids are needed for protein synthesis

- if there is shortage of one or more essential amino acids, body cannot make enough proteins: protein deficiency malnutrition (either general lack or imbalance in diet)

Essential minerals

- minerals are needed in very small quantities (mg)
- minerals are chemical elements, usually in ionic form (e.g. Ca^{2+} ions)
- consequences of deficiency diseases can be serious (iodine: needed by thyroid gland for synthesis of hormone thyroxin which stimulates metabolic rate)

Vitamins

- organic compounds need in very small amounts as they cannot be synthesized by body
- serve variety of co-factors for enzymes, anti-oxidants, hormones
- are often broadly categorized as fat soluble (can be stored in body) and water soluble (must be constantly consumed, excess is lost in urine)

Types of malnutrition

- poor diet causes malnutrition; low in quantity or unbalanced; often associated with poverty
- starvation is consequence of diet lacking adequate protein and carbohydrates
- obesity is consequence of unhealthy diets with excess fat and refined carbohydrates

The appetite control center

- hypothalamus of brain is responsible for making us feel satisfied: appetite control center
- small intestine secretes hormone PYY3-36 when containing food, pancreas secretes insulin, adipose tissue secretes hormone leptin: when appetite control center receives these hormones it reduces the desire to eat

Consequences of being overweight

- nutrition related diseases are diabetes and hypertension
- auto-immune destruction of insulin-secreting cells (type I diabetes) and decreased responsiveness of body cells to insulin (type II diabetes)
- epidemiology: study of rates and distribution of disease

- studies of type II diabetes implicate increased blood concentrations of fatty acids, linked to risk factors: fat-rich and fiber-poor diet, overeating or lack of exercise for obesity, genetic factors affecting fat metabolism
- main symptoms of type II diabetes: elevated blood glucose, glucose in urine, dehydration
- diabetes can cause other health problems: atherosclerosis, hypertension, CHD
- seems to be link between cardiovascular problems and blood lipid concentrations: links between high concentrations of cholesterol, high LDL concentrations, low HDL concentrations
- clear correlation between excess weight gain and hypertension (high blood pressure): weight gain leads to higher cardiac output, abdominal obesity can increase vascular resistance, associated with arteries becoming stiffer and narrower

Effects of starvation

- starvation occurs due to severe lack of intake of essential and non-essential nutrients
- body first accesses glycogen stores; if no glucose is available, body breaks down its own muscles to use resulting amino acids as energy source: result is loss of muscle mass

Ascorbic acid is an essential nutrient in some animals

- ascorbic acid (vitamin C) is needed for the synthesis of collagen fibers
- most animals can synthesize vitamin C
- in all cases the inability to synthesize vitamin C is due to mutations in the GLO gene which codes for the production of the enzyme L-gulono- γ -lactone oxidase; this catalyses the final reaction of the pathway
- variety of symptoms arising from vitamin C deficiency are collectively known as scurvy; these can be alleviated by intake of dietary sources of the compound

Anorexia

- anorexia means reduced appetite; psychiatric illness; involves voluntary starvation and loss of body mass; amounts of carbohydrate and fat consumed are too small to satisfy energy needs
- protein and other chemicals are broken down: wasting of muscles
- as body weight falls, not only skeletal muscle is digested but heart muscle deteriorates
- lack of dietary intake alters electrolyte balance (e.g. calcium, potassium, sodium): skeletal and cardiac muscle do not contract normally under these circumstances

Phenylketonuria

- phenylketonuria (PKU) is a recessive genetic disease; mutation of genes coding for enzyme that converts phenylalanine into tyrosine
- phenylalanine accumulates in the body and there can be a tyrosine deficiency
- high phenylalanine levels cause reduced growth of head and brain with mental retardation of young children and severe learning difficulties, hyperactivity, seizures in older children, lack of skin and hair pigmentation
- PKU babies are unaffected at birth: mother's metabolism kept levels normal
- treatment is a diet low in phenylalanine, tyrosine supplements

Vitamin D deficiency

- vitamin D is needed for calcium absorption from food in the intestines
- symptoms are similar to those of calcium deficiency; skeletal deformities (rickets)
- can be synthesized in the skin if ultraviolet light (290-310nm) strikes the skin
- few dietary sources of vitamin D
- UV light has some harmful consequences, including mutations that can lead to skin cancer; dark skin protects against cancer, but allows less vitamin D synthesis

Blood cholesterol and heart disease

- cholesterol is a normal component of plasma membranes
- research has shown correlation between high levels of cholesterol and coronary heart disease
- unclear whether a lower cholesterol intake will lower risk of CHD
- research covert total cholesterol levels but only cholesterol in low density lipoprotein (LDL) is implicated in CHD; reducing intake has a small effect on blood levels; liver can synthesize

cholesterol; genetic factors are more important than dietary intake; drugs can be more effective to lower blood cholesterol levels; could be saturated fats and not cholesterol

D.2 Digestion

Regulation of digestive secretions

- under natural conditions there are gaps between meals; to conserve energy animals do not have digestive systems active constantly
- nerves and hormones ensure resources are devoted to digestion only when needed

Regulation of gastric secretions

- nerves and hormones are involved in controlling secretion of digestive juices (e.g. gastric juice)
- sight or smell of food causes brain to send nerve impulses via vagus nerve from medulla to stimulate gland cells in stomach to secrete components of gastric juice
- hormone gastrin stimulates secretion of acid and pepsinogen by exocrine gland cells
- two other hormones (secretin, somatostatin) inhibit gastric secretion if pH falls too low

Exocrine glands

- alimentary canal: passage through which food passes from mouth to anus
- digestive juices are secreted by exocrine gland cells in alimentary canal at several points with composition being different
- exocrine glands secrete into ducts (unlike endocrine glands); secretory cells are in groups (acinus) around duct branch
- extensive endoplasmic reticulum for synthesis of enzymes and numerous mitochondria

Adaptations of the villus

- ileum: site of significant amount of absorption in small intestine
- inner surface of ileum has numerous folds with projections (villi) covered with epithelial cells
- epithelial cell adheres to neighbors through tight junctions
- cell surface membrane on intestinal lumen has many extensions (microvilli): increase surface area
- mitochondria required to produce ATP for active transport processes
- pinocytic vesicles present due to absorption by endocytosis
- apical surface (faces lumen of intestine) and basal surface (faces blood vessels): have different types of proteins involved in material transports

The role of acid conditions in the process of digestion

- acid is secreted by parietal cells of stomach; acid disrupts extracellular matrix, holding together cells in tissues; denatures proteins, exposing polypeptide chains (for pepsin)
- pepsin is released by chief cells as inactive pepsinogen: ensures that cells producing pepsinogen are not digested at same time as protein in diet

Egestion

- dietary fiber: edible part of plants, resistant to being digested (e.g. cellulose, lignin)
- fraction of ingested food never leaves digestive tube and secretion in to it occurs
- excretory products, unabsorbed water, undigested dietary fiber are egested as feces

The role of dietary fiber

- cellulose, lignin, pectin cannot be readily digested; two categories: soluble and insoluble
- dietary fiber draws water into intestine
- the higher water content of intestine, the faster the movement of fecal matter
- advantage of dietary fiber in diet: presence of bulky material in stomached intestines may increase feeling of satiety, slow down absorption of sugars, prevent constipation

Bacterial infection as a cause of ulcers

- stomach ulcers are open sores, caused by partial digestion of the stomach lining by enzymes pepsin and hydrochloric acid
- bacterium is found as a significant cause for development of stomach ulcers

Proton pump inhibitors

- stomach acid is corrosive: body produces a natural mucus barrier which protects the stomach lining; in some people this barrier may have broken down: acid damages stomach causing bleeding: ulcer
- other people may have a non functioning circular muscle at the top of the stomach: acid escapes and irritates the esophagus: “acid reflux”
- acidic environment is achieved by proton pump called H^+ , K^+ -ATPase; uses one ATP to exchange two potassium ions in lumen surrounding the parietal cell
- proton pump inhibitors (PPI) bind irreversibly to a single pump; pumps are recycled and replaced with new pumps naturally; decrease acidity
- PPIs are consumed in inactive form, are activated in acid conditions in vicinity of parietal cells

Dehydration due to cholera

- cholera is a disease caused by a bacterial infection; bacterium releases a toxin that binds to a receptor on intestinal cells and brought in by endocytosis
- toxin trigger efflux of Cl^- and HCO_3^- ions into the intestine; water follows leading to watery diarrhea; water is drawn from blood
- quickly severe dehydration can result in death if patient does not receive rehydration

D.3 Functions of the liver

Processing of nutrients by the liver

- liver regulates quantity of nutrients circulating blood; key role in regulation of glucose (either storing as glycogen or breaking it down to glucose); processes nitrogenous waste
- body cannot store proteins or amino acids: excess is broken down in liver for energy source
- manages circulating lipids; processes lipids in one form and distributes in other forms
- very low density lipids (VLDL) are synthesized to hepatocytes; surplus cholesterol to bile salts

Storage of nutrients in the liver

- when levels of glucose are high, insulin is released: insulin stimulates hepatocytes to take up glucose and store it as glycogen
- when glucose levels fall, glucagon is released, which results in breakdown of glycogen, glycerol, amino acids, fatty acids in liver release glucose to blood
- iron, retinol (vitamin A), calciferol (vitamin D) stored in liver (excess) and released (deficit)

Recycling of red blood cells

- lifespan of erythrocyte (red blood cell) is about 120 days
- old erythrocyte changes plasma membrane which make them susceptible to recognition by macrophages: are removed from circulation and broken down in spleen and liver
- liver involved in breakdown of erythrocytes and hemoglobin: products are recycled

The role of Kupffer cells in the breakdown of erythrocytes

- with aging, erythrocytes swell and some are engulfed by Kupffer cells (macrophages) which line sinusoids in liver; Kupffer cells have long arm-like extensions (filopodia)
- in Kupffer cells, hemoglobin molecule is split to globing chains and heme group; amino acids from globing chains are recycled, heme group is broken down to iron and bilirubin
- Kupffer cells release bilirubin into blood, iron is bound to transferrin and transported to liver and spleen for storage or to bone marrow for synthesis of new red blood cells

The transport of iron to bone marrow

- hemoglobin synthesized in red blood cells; here iron is added to heme group
- iron essential for red blood cell to function but toxic at high concentrations
- iron is transferred in blood bound to transferrin (protein)
- red blood cells are formed from stem cells in bone marrow; developing erythrocytes have high levels of transferrin receptors; once bound, receptor-iron complex enters cells and iron is either incorporated into heme molecule or transferred to storage molecule (ferritin)

Conversion of cholesterol to bile salts

- cholesterol is absorbed from food in intestine but also synthesized by hepatocytes (liver cells)
- cholesterol is needed for synthesis of vitamin D and steroid hormones; it is a structural component of membranes and used in production of bile
- liver secretes cholesterol and phospholipids in bile
- excess saturated fat in diet increases production of cholesterol

Production of plasma proteins by hepatocytes

- rough endoplasmic reticulum of hepatocytes in liver produce 90% of proteins in blood plasma
- albumin is carrier protein binding to bilirubin and maintains osmotic balance in blood
- fibrinogen is protein essential for blood clotting
- hepatocytes are actively involved in protein synthesis so show extensive networks of endoplasmic reticulum and Golgi body

Detoxification by the liver

- detoxification as important role of liver: absorbs toxic substances from blood and converts them to non-toxic or less toxic substances using chemical conversions
- alcohol to less toxic substance by ethanol dehydrogenase; toxic ammonia to urea; detoxifies biochemicals foreign to body (poisons, drugs)
- liver converts hydrophobic compounds to more easily excreted hydrophilic compounds

Jaundice

- red blood cells are broken down and hemoglobin is released which is digested by macrophages into heme and globin; globin is digested into amino acids which are recycled, heme group is further converted to iron and yellow pigment (bilirubin)
- bilirubin is transported to the liver bound to albumin
- bilirubin is relatively insoluble, so in the liver it is reacted with glucuronic acid to make it soluble
- along with water, electrolytes, bicarbonate, cholesterol phospholipids, salts it is called bile
- when a disease interferes with the normal metabolism or excretion of bilirubin, it can build up in the blood: condition is called jaundice (yellow skin and eyes)
- jaundice is not a disease itself, but a symptom of many disorders of the liver
- jaundice in newborns is relatively common: either high turnover of red blood cells, liver still developing, lack of intestinal contents and bilirubin is reabsorbed
- treatment is the exposure to ultraviolet light (artificial or sun)

D.4 The heart

Cardiac muscle cells

- cardiac muscle is unique to heart; appear striated, arrangement of contractile proteins actin and myosin is similar to skeletal muscle; cells are shorter and wider with one nucleus per cell
- contraction is not under voluntary control
- cells are Y-shaped to create interconnected network of cells: where they meet there is specialized junction (intercalated disc): consists of double membrane containing gap junctions providing channels of connected cytoplasm: allows for rapid movement of ions and low electrical resistance: allows wave of depolarization to pass easily from cell to network of other cells leading to synchronization of muscle contraction

The sinoatrial node

- contraction of heart's chambers is systole and relaxation is diastole
- in wall of right atrium is collection of uniquely structured cardiac cells (sinoatrial node) that spontaneously initiate action potentials without stimulation by nerves: occurs rhythmically
- SA node is referred to as pacemaker
- gap junctions allow electric charges to flow freely between cells: contraction originating from SA node spreads rapidly across entire atrium: atria undergoes systole
- signals cannot pass directly from atria to ventricles; instead signal reaches atrioventricular node from where signal spreads through heart via specialized tissue (Purkinje fibers)
- ventricles undergo systole: atrioventricular valves are shut; after ventricles empty, semilunar valves close
- ventricles begin diastole, atrioventricular valves open and ventricles start filling with blood

The atrioventricular node

- mechanisms that stagger contraction of atria and ventricle: fibers connecting SA node to AV node carry action potential slowly (delay of 0.12 seconds)
- cells of AV node take longer to become excited; AV node cells have smaller diameter (conduct slower), reduced number of Na^+ channels (more negative potential, prolonged refractory period), fewer gap junctions, more non-conductive tissue

The delay in conduction

- delay of initiation of contraction caused by AV node is important: ensures that atria contract and empty blood to ventricles before ventricles contract
- contraction of ventricles too early would lead to too small volume of blood entering ventricles

Coordination of contraction

- atrioventricular bundle receives impulse from AV node and conducts signal rapidly to point where it splits to right and left bundle branches
- at apex of heart, bundle branches connect to Purkinje fibers which conduct signals even more rapidly to ventricles
- fibers have modifications to facilitate fast conducting: fewer myofibrils, bigger diameter, higher densities of voltage-gated sodium channels, high number of mitochondria
- contraction of ventricle begins at heart apex (bottom)

Causes of the sound of the heartbeat

- normal heartbeat has two sounds: caused by closing of valves
- atrioventricular valves snapping shut as first, then semilunar valves as second sound

Artificial pacemakers

- surgically fitted into patients with a malfunctioning sinoatrial node which initiates the heartbeat
- purpose is to maintain the rhythmic nature of the heart beat
- either provides a regular pulse or only discharges when a beat is missed

Explaining the use of a defibrillator

- cardiac arrest occurs when heart tissue is deprived of oxygen; consequence is ventricular fibrillation due to rapid and chaotic contraction of individual muscle cells
- paddles are applied in a diagonal line with the hear tin the middle
- device checks for fibrillation; an electric discharge is given off to restore a normal heart rhythm

Hypertension and thrombosis

- atherosclerosis is hardening of arteries caused by the formation of plaques (atheromas), which develop due to high circulating levels of lipids and cholesterol, reducing the speed of the blood
- triggers a clot (thrombosis) which blocks the blood flow and denies the tissue access to oxygen
- if this occurs on the surface of the heart, the consequence can be a myocardial infarction (heart attack)
- greater resistance to blood flow causes a greater pressure on arteries (hypertension)
- consequences of hypertension: damage to cells lining the arteries, constant high blood pressure can cause a section of artery to enlarge (aneurysm) which can burst and cause bleeding, can lead to a stroke by weakening blood vessels in the brain, kidney failure as it damages leading to the kidney and the capillaries in the glomerulus
- risk factors: genetic precondition, old age, post-menopause due to fall in estrogen, males that generally have lower estrogen, skimming, high-salt diet, too much saturated fat and cholesterol in diet, height affects blood pressure