MINERALS

BY FATIMA HAIDER

KGMC

- Chromium increase the effect of insulin
- Ceruloplasmin - carrier of copper
- Menkes disease is a lethal multisystemic disorder of copper metabolism
- Wilson's disease is a rare inherited disorder that causes copper to accumulate in liver, brain and other vital organs
- Deficiency of potassium might lead to paralytic ileus
- Zinc is present as a cofactor in carbonic anhydrase
- Solubility of calcium is highly pH dependant. Low pH promotes calcium absorption
- Fluoride should be added regularly in traces to diet to avoid dental caries
- Macrominerals
    - Calcium
    - Phosphorus
    - Magnesium
    - Sodium
    - Potassium
    - Chloride
    - Sulfur
- Trace minerals (needed in less than 100 mg)
    - Iron
    - Zinc
    - Copper
    - Iodine
    - Fluorine
    - Chromium
    - Cobalt
    - Selenium
    - Manganese
    - Molybdenum
- Tetany is caused by low calcium levels
- Physiologically active form of calcium is ionized calcium
- Hemochromatosis, or iron overload, is a condition in which body stores too much iron
- Selenium acts as antioxidant
- Plasma calcium and inorganic phosphorus are decreased in osteomalacia
- Intestinal absorption of calcium is hampered by phytate
- Iron is better absorbed in acidic medium
- Acrodermatitis enteropathica is a disorder of zinc metabolism
- Iron in mucosal cells bind with protein ferritin
- Cobalt is a constituent of Vitamin B_{12}

- Molybdenum is a component of Xanthine oxidase
- Rennin acts on casein of milk in infants in presence of Ca^{+2}
- A diabetic patient was given an insulin infusion. The patient suddenly developed cardiac arrhythmias due to:
  Ans: Hypokalemia
- The antioxidant mineral selenium is absolutely essential for normal development of spermatozoa
- Addison's disease i.e. diminished secretion of aldosterone results in
  Hyperkalemia + Hyponatremia + Hypochloremia

MACROMINERAL	FUNCTIONS	DEFICIENCY
Sodium	-Principal extracellular cation -buffer constituent -water and acid base balance -cell membrane permeability -uptake of glucose, galactose and amino acids	-dehydration -acidosis -excess leads to edema and hypertension
Potassium	-principal intracellular cation -buffer constituent -water and acid base balance -neuromuscular irritability	- muscle weakness - paralysis and mental confusion - acidosis
Chloride	-principal extracellular anion -electrolyte -osmotic balance -acid base balance -gastric HCl formation	- deficiency secondary to vomiting and diarrhea
Calcium	-constituent of bone and teeth -blood clotting -regulation of nerve, muscle and hormone function	- tetany - muscle cramps - convulsions -osteoporosis and rickets
Phosphorus	-constituent of bone and teeth, nucleic acids, NAD, FAD, ATP etc. -required for energy metabolism	- growth retardation - skeletal deformities - muscle weakness - cardiac arrhythmia
Magnesium	-cofactor for phosphate transferring enzymes -constituent of bones and teeth -muscle contraction -nerve transmission	- muscle spasms - tetany - confusions - seizures
Sulfur	-constituent of proteins, bile acid, GAG, vitamins like thiamine, lipoic acid -involved in detoxication reactions	Unknown

MICROELEMENT	FUNCTION	DEFICIENCY
Chromium	Potentiate the effect of insulin	Impaired glucose metabolism
Cobalt	Constituent of Vitamin B_{12}	Macrocytic anemia
Copper	-constituent of oxidase enzymes e.g. tyrosinase, cytochrome oxidase, ferroxidase, ceruloplasmin - iron absorption and mobilization	-microcytic hypochromic anemia -depigmentation of skin, hair - excessive deposition in liver in **Wilson's disease**
Fluoride	-constituent of bone and teeth -strengthens bone and teeth	Dental caries
Iodine	-constituent of thyroid hormones (T_3 and T_4)	- **Cretinism** in children - **goiter** in adults
Iron	-constituent of heme and non-heme compounds -transport and storage of O_2	Microcytic anemia
Manganese	Cofactor for number of enzymes e.g. arginase, carboxylase, kinase etc.	Not well defined
Molybdenum	Constituent of xanthine oxidase, sulfite oxidase and aldehyde oxidase	**Xanthinuria** (excess urinary excretion of xanthine)
Selenium	-antioxidant -cofactor for glutathione peroxidase -protects cell against membrane lipid peroxidation -found as selenocysteine in selenoproteins	Cardiomyopathy
Zinc	-cofactor for enzymes in DNA, RNA and protein synthesis -constituent of insulin, carbonic anhydrase, carboxypeptidase, LDH, alcohol dehydrogenase, alkaline phosphatase	- growth failure - impaired wound healing - defects in taste and smell - loss of appetite

NUCLEOTIDES AND NUCLEIC ACIDS

- Pseudouridine is a modified base present in tRNA
- Nucleosome is a double stranded DNA with all histones except H_1
- Cap of mRNA present at 5' end have high guanine content
  Tail of mRNA present at 3' end is poly-Adenine tail
- Pyrimidine nucleus contains two nitrogen atoms and four carbon atoms
- Purine nucleus contains four nitrogen atoms and five carbon atoms
- Purines and pyrimidines are attached to sugar in a nucleotide through N-glycosidic linkage
- tRNA Regions:
  1. Acceptor arm – CCA sequence present at 3' end
  2. D arm – presence of base dihydrouridine (D)
  3. Anticodon arm
  4. T φ C arm – contains both ribothymidine (T) and pseudouridine
- Chargaff's rule states that DNA from any species of any organism should have 1:1 stoichiometric ratio of purine and pyrimidine bases
- Cyclic AMP is formed from ATP
- Smallest RNA is tRNA
- Most abundant free nucleotide in mammalian cells is ATP
- Precursor mRNA comprises the bulk of heterogenous nuclear RNA (hnRNA)
- Allopurinol is a competitive inhibitor of xanthine oxidase
- Nucleic acid synthesis would be reduced most directly by deficiency of folic acid
- The number of base pairs present in each turn of B form of DNA helix is 10
- Chargaff's rule is only applicable for double stranded DNA molecule. It is not applicable for single stranded DNA or RNA molecule
- Uracil and ribose form uridine

BLOOD

- **Hemoglobin synthesis**
  1. Succinyl Co-A + Glycine $\longrightarrow$ ALA (alpha levulinic acid)
     This is a rate limiting step and involves enzyme ALA synthase
  2. 2 ALA condensation $\longrightarrow$ Prophobilinogen
     Enzyme: ALA dehydrogenase
  3. 4 Prophobilinogen condensation $\longrightarrow$ Uroporphyrinogen
     Enzyme: Uroporphyrinogen Synthetase + Co-synthetase
  4. Uroporphyrinogen III $\longrightarrow$ Coproporphyrinogen III
     (in mitochondria)
     Coproporphyrinogen III $\longrightarrow$ Protoporphyrinogen III
     (in cytosol)
  5. Protoporphyrinogen III $\xrightarrow{\text{lose 6 H}}$ Protoporphyrin III (Protoporphyrin IX)
     Enzyme: Ferrochelatase
  6. Protoporphyrin III + Fe^{+2} $\longrightarrow$ Heme
  7. Heme + Globin $\longrightarrow$ Hemoglobin

- Lead inhibits enzymes
  - ALA dehydrogenase
  - Ferrochelatase

- HEMOLYTIC JAUNDICE
  - Massive lysis of RBCs in hemolytic anemia e.g. sickle cell anemia
  - Bilirubin is produced in a rate faster than the rate of conjugation by liver
  - Increased blood unconjugated bilirubin
  - In urine, urobilinogen is increased
  - No bilirubin in urine as it is bound to albumin (color of urine is normal)
  - Dark color stool due to increased stercobilin (produced from increased urobilinogen)

- HbS is formed by substitution of amino acid at position 6 in β-chain

- Gower 1 Hb is a form of hemoglobin existing in embryonic life and is primary embryonic hemoglobin. It is composed of two zeta chains and two epsilon chains

- VARIEGATE POPHYRIA
  - Autosomal dominant genetic disorder
  - Due to deficient activity of mitochondrial enzyme protoporphyrinogen oxidase

- The first bile pigment formed in heme catabolism is biliverdin

- Porphyrins emit red fluorescence because of double bond joining two pyrrole rings

- Biliverdin is converted into bilirubin by the action of enzyme biliverdin reductase
- Unconjugated bilirubin is increased in Crigler Najjar syndrome
- Normal individuals have four α globin genes and two genes coding for β chain
- The four pyrrole rings are connected by four methylene bridges
- Unconjugated bilirubin is transported in plasma bound to albumin. Albumin has two bilirubin binding sites.
- The conjugated primary bile acid is glycochenodeoxycholic acid
- Conjugated hyperbilirubinemia seen in Dubin Johnson Syndrome
- Kernicterus is a type of brain damage that can result from high levels of bilirubin in baby's blood
- The catabolism of hemoglobin involves the oxidative cleavage of porphyrin ring
- Normal brown color of feces occur due to the presence of bilirubin
- Serum = Albumin + Globulin
- Plasma = Albumin + Globulin + Fibrinogen
- Infective hepatitis show slight decrease in albumin and significant increased γ-globulins
- Liver cirrhosis show elevations in $\beta\ and\ \gamma$-globulins with a decrease in albumin
- Nephrosis shows low level of albumin, significantly elevated α_2-globulin and elevated β-globulin
- Multiple myeloma shows marked increase in γ-globulin
- Albumin is the most abundant protein found in plasma accounting for 50% of plasma protein mass
- Very low albumin concentration develop edema
- Immunoglobulin
    - Two light chains, two heavy chains
    - Four chains linked by disulfide bonds
    - Light chain have one variable and one constant region
    - Heavy chain have one variable and three constant regions

- Negative acute phase reactants
  - Albumin
  - Prealbumin
  - Transferrin

- Acute phase proteins
  - C-Reactive protein
  - Ceruloplasmin
  - Antiprotease inhibitors
  - α_1-acid glycoprotein
  - Fibrinogen
  - Heptoglobin

- Fab is a region on antibody that binds to antigens

- IgG can cross placental membrane

- IgM antibodies are the largest antibodies

- Apo C-II acts as cofactor activator for lipoprotein lipase

- Colostrum contains IgA

- The main site of production of plasma proteins is liver

- The most effective buffer of plasma is $NaHCO_3$ / H_2CO_3

- The major carriers of triacylglycerols are chylomicrons and VLDL

TYPES	PER-CENTAGE	CHARACTERISTICS	FUNCTIONS
IgG	70%	-main antibody in the secondary response -it is only immunoglobulin which crosses the placenta and is the only maternal antibody which protects the fetus	-neutralizes bacterial toxins and viruses -opsonizes bacteria, making them easier to phagocytize -activates complements which enhances bacterial killing
IgA	20%	-major component of colostrum -also occurs in saliva, tears and respiratory, intestinal and genital tract secretions	-secretory IgA prevents attachment of bacteria and viruses to mucous membranes and helps protect mucous surface from antigenic attack -prevents access of foreign substances to the circulation
IgM	8 – 10%	-main antibody in the primary response to an antigen -produced by fetus	-activate complement, promotes phagocytosis and causes lysis of antigenic cells -antigen receptor on the surface of B lymphocytes
IgD	Less than 1%	Labile molecules. These facts have made the study of IgD function difficult	-uncertain. May function as an antigen receptor -no known antibody function
IgE	0.004%	Binds mast cells and basophils, leads to rupture of the cell membrane, degranulation and release of histamine	-antiallergic and antiparasitic -mediates immediate hypersensitivity by causing release of histamine from mast cells and basophils upon exposure to antigen -main host defence against parasites like helminthes, provides protection in the disease schistosomiasis

CELL AND PH

- In biochemistry, dialysis is an operation to separate dissolved molecules based on molecular weight

- The pressure which stops the osmosis of pure solvent into solution through a semipermeable membrane is known as osmotic pressure

- The sulfonamides are a group of synthetic antimicrobial agents that are structural analogs of para-amino benzoic acid (PABA). They are competitive inhibitors of folic acid metabolism

- The H^+ ion concentration of pure water is equal to $1x10^{-7}$ M

- The major buffer systems of body
  1. Carbonic acid bicarbonate buffer system (H_3PO_4/ $H_2PO_4^-$)
  2. Phosphate buffer system (H_3PO_4 / $H_2PO_4^-$)
  3. Protein buffer system

- Normal pH range = 7.35 – 7.45

- A buffer is a combination of a weak acid and its salt with strong base

- The most important buffer of plasma is carbonic acid – bicarbonate buffer

- At isoelectric pH protein molecule has no net charge

- Bicarbonate ions and carbonic acid are present in the blood in 20:1 ratio if the blood pH is within normal range

- Histidine (amino acid) provide efficient buffering in Hb buffer system

- Most reliable method for measuring GFR (Glomerular Filtration Rate) is inulin clearance test

- Diabetic acidosis develops when substances called ketone bodies (which are acidic) build up during uncontrolled diabetes

ENZYMES

- Alkaline phosphatase is an enzyme in blood that helps break down proteins. It plays a particular important role in liver function and bone development
- Five isozymes of normal LDH, can be identified by electrophoresis at pH 8.6
- Creatine phosphokinase found mainly in heart, brain and skeletal muscle
- The most commonly used serum enzymes in pancreatic diseases are total amylase, pancreatic isoamylase, lipase and trypsin
- Km (Michaelis constant) – The substrate concentration at which the reaction rate is 50% of the v_{max}

  Km is a measure of the affinity an enzyme has for its substrate, as the lower the value of Km, the more efficient the enzyme is at carrying out its function at a lower substrate concentration
- Competitive inhibitors
  - Increase Km
  - Do not change V_{max}
- Non-Competitive inhibitors
  - Does not Km
  - Decrease V_{max}
- Elevated serum levels of acid phosphatase are seen in patients with carcinoma of prostate
- All amino transferases require the co-enzyme pyridoxal phosphate
- Hydrolases - Enzymes which breaks a biomolecule by the addition of water molecule
  Lyases – Enzymes which breaks a molecule without addition of water
- Group specificity means that the enzyme will act only on molecules that have specific functional groups such as amino, phosphate and methyl groups e.g. pepsin, hexokinase
- Absolute specificity – in which enzyme acts upon one specific substrate e.g. urease attacks only on urea
- Relative specificity – The enzymes bind with a group of similar substrates and catalyzes a group of similar reactions
- Ligase is also called synthetase

CARBOHYDRATES

- Glycosaminoglycans or mucopolysaccharides
    - Heparin
    - Chondroitin sulfate
    - Hyaluronic acid
    - Dermatan sulfate
    - Keratan sulfate
    - Blood group polysaccharides
- Most of monosaccharides belong to D-series
  Most of amino acids belong to L-series
- D glucose is dextrorotatory that is why glucose is called Dextrose
  D fructose is levorotatory
- Sucrose is called invert sugar.
  Sucrose is dextrorotatory. On hydrolysis sucrose yields a mixture of dextrorotatory glucose and leverotatory fructose. Because of the strong levorotatory nature of fructose, the magnitude of levorotation is more. Hence sucrose is called invert sugar.
- Deoxy sugars
    - L-fucose
    - Deoxy ribose
- Sugar acids – Uronic acid, glucuronic acid, Galacturonic acid, Mannuronic acid
- Uronic acid important in animals include D-Glucuronic acid and L-iduronic acid. Both are abundant in connective tissue
- Reducing sugar have a free anomeric carbon
  Non-reducing sugar lack a free anomeric carbon
- Amylose – linear polymer of D-Glucose
  Amylopectin – branched polymer of D-Glucose
  Dextrin – formed by partial hydrolysis of starch
  Glycogen – branched polymer of glucose
  Cellulose – unbranched polymer of glucose
  Inulin – polymer of D-fructose
  Dextran – branched polymer of D-glucose
  Agar – sulfuric acid ester of a complex both D and L galactonic units
- Glycosaminoglycan (GAG) is an unbranched heteropolysaccharides made up of repeating diasaccharides
  Components of GAG
  1. Amino sugar – either D-Glucosamine or D-Galactosamine
  2. Uronic acid – either L-Glucuronic acid (HA, chondroitin sulfate) or L-iduronic acid (Dermatan sulfate, heparin, heparan sulfate)

  Creatine sulfate has no uronic acid

  GAG is a polymer of (uronic acid-amino sugar). This polymer is attached covalently to extracellular proteins called core proteins (except hyaluronic acid) to form proteoglycans

With exception of HA, all GAGs contain sulfate group

- HA + Keratan sulfate → N-acetyl glucosamine
  Chondroitin sulfate + Dermatan sulfate → N-acetyl glucosamine
  Heparin → Glucosamine
  Heparan sulfate → Glucosamine + some acetylated glucosamine