Trace Elements

Objective: principal of biochemistry, functions & disorders of most common trace elements

Trace elements TEs TES are expressed in µg/dl in fluids and mg/kg in tissues. The ultraTE are expressed in ng/dl in fluids and µg/kg in tissues. They are essentials when the sign and symptoms induced by an element deficiency are reversed only by adequate supply of that element. TEs are important or essential for many critical biochemical processes, deficiencies are often associated with decreased activities of the Enzymes Es that require TEs for optimal activity. Function can be restored by dietary replacement, but must be in care from toxicity. A chemical element required in minute quantities by an organism to maintain proper physical functioning.
Dose-Effect relationships: In low intake of an element the biological function of humans decreased (determinantal effects), with continues supply or intake of element the biological functions improved with approaching the plateau region (constant optimal human function even with increased element concentrations), but with increased element levels the biological functions decline (Toxicity region, which depend on element and its chemical structure in the diet).
Iron

Iron is widely distributed throughout the human body with ≈3-5 g in 70 kg human body, 1. in Hb of RBCs (2g), 2. storage iron in the form of Ferritin and hemosiderin. Ferritin is found in all tissues mainly hepatocytes and in bone marrow and spleen. This stored iron may be first depleted in iron deficiency states. This stored iron is ready for Hb and other heme proteins formation and in this form iron shielded from oxidative toxicity (ionic Fe+3 is toxic; prooxidant).
3. Tissue iron, this represents the amount of iron in enzymes or cofactors for enzymes; peroxidases, cytochromes (heme proteins), many CAC enzymes. 4. Myoglobin resembles Hb but monomer and deals with storage of O2 in muscles. **Transferrin** is the carrier protein (transporter) of iron in blood and intracellular compartments. Dietary requirement is \( \approx 1 \text{mg/day} \) to compensate that lost from body, mainly in feces. Excretion increased in menstruating women 20 mg/cycle.
Intestine is the **regulatory step** in homeostasis of iron. In iron deficiency (decreased body iron content), the amounts of the intestinal absorbed iron and their release into the circulation are increased to compensate the body’s deficiency. The inverse in case of iron overload (increase of iron body content), most of the absorbed iron is sloughed during the shedding of the enterocytes.
Functions of iron mainly in transporting (as part of Hb) of O2 from lung to the tissues, and returning of CO2 to the lung excretion in ventilation. Iron in Hb must be in Fe +2, if Fe+3 is nonfunctional Hb = metHb. Peroxidase and catalase to remove of H2O2 and free radical as H2O. Thyroperoxidase involved in formation of thyroid Hs.

Disorders:
Iron deficiency; Anemia. It is the most common disease, affects ≈15% of worldwide population.
Menstruating, pregnant, lactating women, neonate (low milk iron content), children, and adolescents at higher risk of iron deficiency. Increased blood loss and low dietary iron intake = decreased iron body stores and so iron deficiency (anemia): investigations: low serum iron (in most but not all), increase Total Iron Body Capacity TIBC (unoccupied sites on transferrin), decrease RBCs, MCHC and microcytic anemia. But now the more sensitive and reliable test in iron deficiency is serum ferritin.
Iron overload: secondary in poisoning of iron by oral ingestion or parenteral administration. In Primary, hemochromatosis and hemosiderosis. In iron overload, serum iron increased and TIBC is decreased, serum ferritin is not reliable in this disorder.
Primary Hemochromatosis: overload of iron due to genetic defect in which there is increased absorption of intestinal iron even with normal dietary content. Symptoms: which are due to toxic accumulation of iron in organs are: D M, bronzing of skin and cirrhosis. Hemosiderosis: iron overload, but without tissues injuries (due to excess iron medication).
Copper (Cu):

Is an important element found in +1 and +2. It is found in meats; liver and kidney, also, in shellfish, nuts, whole grain cereals... . Lower amounts in dairy products; cow’s milk and white meats. Absorbed Cu is transported to liver by albumin, where it incorporated in cuproenzymes and proteins, the major one is apoceruloplasmin + Cu = ceruloplasmin. 2/3 of body Cu (80-100 mg) in skeleton and muscle, in
blood 90% of Cu incorporated in ceruloplasmin (glycoprotein). Excretion mainly by bile-intestine (0.5-2 mg) = feces, so in bile obstruction = increased of Cu accumulation.

Functions: Essential component of cuproenzymes and structural proteins: 1. Cytochrome C oxidase of respiratory chain = ATP production, 2. Lysyl oxidase involved in structural proteins; collagen and elastin, so important in connective tissues formation; skin, skeleton, 3. Dopamine hydroxylase and monoamino oxidases involved in catecholamine synthesis (adrenaline and noradrenaline) so important for CNS function,
4. Tyrosinase involved in melanin synthesis 5. IC and EC superoxide dismutase SOD involved in antioxidant defence. 5. Ceruloplasmin (ferroxidase) is important in normal iron metabolism and Hb formation. **Disorder is Menkes’ syndrome** recessive X-linked genetic defect in copper transport from intestinal mucosa(normal absorption), so Cu cannot be transported to liver and results in Cu deficiency= mental defect, failure to thrive, diminished Cu containing enzymes, connective tissues abnormalities, kinky hair and early death. Anemia due to defect in normal metabolism of Iron.
**Wilson’s disease**.. Cu overload disorder. It is autosomal genetic defects in incorporation of Cu into apoceruloplasmin=accumulation of the abosorbed,transported Cu into liver(not exported into circulation from liver), kidney, cornea, brain... =liver cirrhosis, brain lesions, Kayser Fleischer rings; low S.Cu(<50 µg/dl), high urinary Cu excretion, low S.ceruloplasmin(<200 mg/l). Liver biopsy: normally Cu 8-40 µg/kg, in this disease >250µg/kg. S.Ceruloplasmin is acute phase reactant so increased in acute inflammation and OC pills.
Zinc  **Zn**: it found in meat, fish and dairy products. RDA 8-11 mg/day, pregnant and children increase requirement. Absorbed Zn transported to liver bound to albumin and α2-macroglobulin. Excretion mainly bile-intestine. **Zn** is an important cofactor for >300 enzymes. Also, integral component of important enzymes;ALP, Alcohol DH, carbonic anhydrous( the latter predominant in RBCs) .Zn enzymes are essential for DNA and RNA(polymearses enzymes so essential for growth,wound healing), integrity of connective tissues, reproductive function, the immune system and protection from free radical damage(SOD). Insufficient dietary Zn is important cause of deficiency, PO4 and fiber=decrease Zn absorption.
Zn deficiency; clinical features: growth retardation (dwarfism), skin lesions, alopecia, slow wound healing, diarrhea, impotence, and tendency to infections (decrease T-cell function).

Acrodermatitis Enteropathica characterized by low blood Zn; dermatitis, alopecia and diarrhea.
Chromium

RDA is ≈ 50-200µg/d. forms Cr +3 and +6, the Cr+6 is toxic (oxidant, damage tissue damage). Processed meats, whole grain products, green beans are good sources, but fruit and dairy products are not. After intestinal absorption transported by transferrin with equal affinity to Fe+3. It is essential as it is a potent activator of Insulin, Cr deficiency is associated with Insulin resistance and impaired glucose tolerance and Cr supplementation improved glucose tolerance and decreased total cholesterol in Type 2 DM.
Cr $+6$ is carcinogenic; contamination (leather tanning and dyestuff industries) with this ion = increased incidence of lung cancer, dermatitis and skin ulcers.

**Selenium**

It has essential functions: cofactor for glutathione peroxidase GPX (Antioxidant enzymes) and iodothyronine deiodinase (ENZYMES of thyroid hormones synthesis). It has antioxidant function (component of GPX), and involved in thyroid Hs metabolism ($T_4 \rightarrow T_3$).
Se soil contents is important in incidence of element deficiency. Deficiencies Disorders are Keshan disease is endemic cardiomyopathy in children and young adults, Kashin-Beck disease it is severe arthritis, Thyroid diseases: endemic goiter (hypothyroidism with low T3),
Floride F is important in preventing dental caries, incorporated into bone crystal, increasing bone mass in vertebrae. F from GIT→bone+teeth. Renal excretion is major route of excretion. Measurement by Ion-selective electrodes. Sources by addition of F to water and sugar and salt. Toxicity mottling of teeth and calcifications of soft tissues.
Manganese

Present in +2 and +3. It is activator for several enzymes; arginase (urea cycle), pyruvate carboxylase (gluconeogenesis), and SOD. Its deficiency features is rare, but may be seizures and epilepsy.
Cobalt Co

It is essential for human only as integral component of vit.B12 (cobalmin), however, B12 must be supplied as that in diet and Co cannot interacts with pool of body vit.B12. The physiological signs of severe vitamin B\textsubscript{12} deficiency are megaloblastic anemia, spinal cord demyelination, and peripheral neuropathy.
Iodine

This trace element has one known function in higher animals and humans; it is a constituent of thyroid hormones (thyroxine, $T_4$) and triiodothyronine ($T_3$). Iodine prevented goiter, enlargement of thyroid gland, and increased iodine intake was associated with decreased endemic cretinism, the arrested physical and mental development caused by the lack of thyroid hormone. Today, the consequences of iodine deficiency still are a major public health problem in the world.