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Micronutrients

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1. Describe the concept of essential mineral elements and how their content in the body is regulated.
    a. Required to maintain normal physiology and health.
    b. Occur in diet, sometimes as trace elements.
    c. Variable absorption, may be regulated
    d. Intestinal absorption = body losses
2. Describe the factors influencing intestinal mineral absorption.
    a. Intraluminal pH
    b. Redox state of metals
    c. Formation of chelates to enhance solubility.
    d. Formation of insoluble complexes w/ other dietary components.
3. Describe the cellular mechanism of iron absorption and its regulation.
    a. Dietary iron in heme or non-heme iron compounds.
    b. Nonheme iron in 3+ form requires gastric acid for solubilization.
        i. Reduced to Fe2+ via ferrireductase at brush border
        ii. Absorbed by DMT1 (divalent metal transporter)
    c. Heme Fe absorbed via receptor mediated endocytosis via HCP1
    d. Free Fe binds to ferritin to be stored, or binds to transport protein to be secreted
        i. Intestinal ferritin increased when iron stores are high
        ii. Iron response proteins bind to iron response element in ferritin mRNA
        iii. Results is iron storage in enterocytes instead of absorption
        iv. Excess ferritin sloughs back into lumen and is excreted
    e. Ferroportin exports Fe2+, Hephaestin oxidizes to Fe3+ basolaterally
    f. Fe binds to transferrin in plasma to be sent to storage/utilization
    g. Liver is storage site for excess iron
        i. Hepcidin secreted by hepatocytes to inhibit iron absorption by gut and release from Mphages
        ii. Hepcidin production decreased by iron deficiency; increased w/ iron loading/inflammation
        iii. Hepcidin interacts w/ ferroportin to lead to degradation
4. Describe the consequences of iron deficiency and abnormal increased absorption.
    a. Deficiency
        i. Microcytic/hypochromic anemia, poor growth, impaired energy metabolism
        ii. Caused by dietary, excess phytate/oxylate, gastric achlorhyrdria, hookworm infestation, excessive bleeding
        iii. Tx. w/ iron supplements
    b. Increased absorption (hereditary hemochromatosis)
        i. Usually related to mutation in HFE protein --> decreased hepcidin
        ii. Iron deposition in liver, heart, pancreas and joints
5. Have a general understanding of their function and how different classes of vitamins are absorbed by the intestine.
    a. Water soluble --> facilitated diffusion
        i. Generally are coenzymes, vit C is an antioxidant
        ii. Metabolized to coenzyme form
    b. Fat soluble absorbed like other lipids (Vit A, D, E, K)
        i. Vitamin deficiency in cases of fat mal-absorption
6. Describe the function and absorption of folates.
    a. Conenzymes in 1-C transfers; nucleic acid synthesis and amino acid metabolism
        i. Deficiency --> megaloblastic anemia
        ii. Related to neuronal tube defects --> pregnant women should consume more folates

b. In diet, generally are polyglutamated
    i. Hydrolyzed at brush border to monoglutamated form by folate conjugase
        1) Inhibited by ethanol and some drugs (dilantin, sulfaslazine)
        2) I think conjugase is actually bacterial
    ii. Folate:OH exchange mechanism to absorb
    iii. W/in enterocyte, folic acid is reduced and methylated
    iv. Exported basolaterally as folic acid or in reduced/methylated from

7. Describe the function and dietary source of vitamins E and K.
    a. Vitamin E
        i. Lipid soluble antioxidant in plasma membranes
        ii. Vegetable oils, wheat germ, nuts, green leafy veggies
    b. Vitamin K
        i. Cofactor in post-translational modifications for proteins, esp. blood clotting factors
        ii. K1 most abundant in green leafy veggies
        iii. Bile salts important for absorption
        iv. Bacterially derived K2 prevents severe deficiency
8. Describe the function, dietary source and absorption of Vitamin A and Beta-carotene.
    a. Compounds related to all-trans-retinol
        i. Required for vision, growth, cellular differentiation, reproduction and integrity of immune system
        ii. Deficiency --> xeropthalmia (present initially as night blindness that turns into total); also increased susceptibility to infection
        iii. Hypervitaminosis --> increased intracranial P, skin lesions, hepatic injury b/c Vit A stored in liver
        iv. Some carotenoids are antioxidants and other things
    b. Retinoids in milk, carotenoids in carrots and green leafy veggies
    c. Absorption
        i. Retinol
            1) Retinyl esters in diet are de-esterified by non-specific cholesterol esterase
            2) Absorbed as retinol
            3) Esterified by ARAT (similar to ACAT) to retinyl esters to be released into lacteals as part of chylomicrons
        ii. Beta-carotene
            1) Absorbed
            2) Split into two retinals
            3) Retinal --> retinol
    d. Metabolism/storage
        i. Chlyomicron remnants taken up from blood by hepatocytes w/ retinol in them
        ii. Retinol secreted by hepatocytes bound to RBP
        iii. Stored in stellate cells in sinusoids
    e. Retinol uptake into target cells
        i. Bound to RBP as rational or albumin as retinoic acid
        ii. Absorbed by target cells, then bind to cellular retinol binding protein
        iii. Travel to nucleus to activate genes