Anemia of decreased production

Nutritional deficiency

Iron deficiency anemia: most common anemia (chronic anemia)

- Some nice information about iron
  - 80% of functional body iron is present in hemoglobin with the remainder located in myoglobin and iron containing enzymes (catalase, cytochtomes....). 2– iron is stored in ferritin(small, soluble) and hemosiderin (large, insoluble) in bone marrow, liver, spleen and they form 15–20% of total iron. 3– hemosiderin consist of large iron particle, granular in shape, intercellular, visible in light microscope. 4– serum ferritin is derived from stored ferritin. 5–normal loss of body iron is by shedding skin and mucosal epithelium(no excretion). 6– dietary iron is either hem(red meat, bioavailability 20%) or non hem(inorganic, vegetarian, bioavailability 1%). 7– hepcidin: hormone secreted from liver, inhibits iron absorption (degrade ferroportin on enterocytes). 8–hepcidin increases in situations of high serum iron and inflammation (effect of IL–6). 9–hepcidin decreases in iron deficiency, thalssemia major , primary hemaochromatosis.
- Causes
  - 1–chronic blood loss
  - Decreased absorption
  - Diatery: vegetarians, infants(no iron in mother's milk), tenagers(junk food)
  - Increased demands; growing children, pregnancy, myeloproliferative neoplasms)
  - Hypotransferritinemia
  - Enzymatic deficiency
- Symptoms:
  - Pica
  - Glossitis, stomatitis.
  - Spooning of fingernails
  - Restless leg syndromes
  - Hair loss
  - Blue sclera
  - Weakened immunity
  - Cognitive impairment
- Indicators of iron status
  - Bone marrow aspirate: eariest change, invasive procedure, perl's prussian blue stain (low in IDA)
  - Serum ferritin level(low in IDA)
    - Is affected by inflammation, fasting, vitamin c status and pregnancy so it is not accurate
  - Serum iron level (low in IDA)
  - Transferritin saturation (low in IDA) , normaly 30%
  - Total iron binding capacity (high in IDA)
  - Serum transferritin and transferritin receptor (high in IDA)
  - Reticulocye hemoglobin content(CHr) (low in IDA)
  - Mean reticulocyte volume(MRV) ,(low in IDA)
- Morphology ...refer to slides 10–11
  - RBCs apear small and empty (hypochromic microcytic)
  - Different shapes of RBCs apear(poikelocytosis)
  - Target cells
  - Low reticulocytosis (Erythropoietin is high, but inffective)
  - Thrombocytosis is common (low iron medium in bone marrow shift progenitor cells to megakaryocytic lineage instead of erythroid)

Megaloblastic anemia

- Causes:
  - Deficiency in vitamin b12
    - Mainly present in animal products, resistant to cooking, synthesized by bacteria in bowel, enormous stores in the liver, dietary deficiency occurs most commonly in vegetarian
    - Causes:
      - More commonly: defective absorption
      - Pernicious anemia: atoimmune gastritis in which autoreactive T–lymphocytes causing injury to parietal cells and activates B lymphocytes and palsma cells to synthesize and secrete auto antibodies that further damage parietal cells and block binding of vitamin b12 to intrinsic factors
      - Gastrectomy
      - Small bowel disease (malabsorption)
      - Elderly people are susceptible (decreased gastric acids and pepsin, thus decreased reslease of vitsmin b12 from food)
    - Functions of vitamin b12
      - Recycling or tetrahydrofolate
      - Synthesis of myelin sheath
      - Metabolism of hemocysteine (toxic to neurons)
      - Degree of neuronal damage does not correlate with the degree of anemia
  - Deficiency in folate :
    - Normally, minimal amount of folate is stored in human body. Folate is vastly present in food(green leaves), but it is destroyed by cooking
    - Causes:
      - Decreased dietary intake
      - Increasd demands (pregnancy, chronic hemolytic anemia)
      - Intestinal disease
      - Beans, legume, alcohol, phenytoin (inhibit absorption)
      - Methotrexate: inhibits folate mrtabolism and cellular usage
- Pathogenesis
  - 1– Both vitamin b12 and folate are required for synthesis of thymidine, thus DNA replication is impaired leading to abnormalities in all rspidly dividing cells, but hematopoietic cells are most severely affected.
  - 2– maturation of RBCs progenitors is deranged, many undergo apoptosis inside bone marrow(ineffective erythropoiesis, mild hemolysis
  - 3– viable nucleated RBCs take a longer time to mature, resulting in typical morphology (megaloblastoid)
- Morphology: macroovalocyte (characteristic of megablastic anemia). (Refer to slide 22)
- Symptoms
  - Chronic, general symptoms of anemia
  - Glossitis (beefy tongue)
  - Mild jaundice
  - In vitamin b12 deficiency
    - Posterior and lateral columns degeneration of spinal cord (paresthesia, loss of proprioception)
    - Peripheral neuropathy
    - Neuropsychotic symptoms

Chronic inflammation

- Also called anemia o of chronic disease
- Seen in chronic infections, cancer , chronic immune diseases
- Common in inpatients
- Chronic inflammation inhibits synthesis of erythropoietin from kidenys
- High IL–6 ➡️ high hepcidin➡️block iron absorption
- Lab finding
  - Low levels of
    - Serum iron, transferrin saturation
    - Reticulocytes
    - Serum transferritin
    - Total iron binding capacity
  - High levels of
    - Bone marrow iron stores
    - Serum ferritin
  - Normal
    - Morphology of RBCs but then hypochromic micocytic
    - Transferrin saturation
    - Transferrin receptor

Bone marrow failure

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