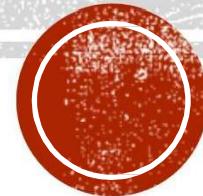


PATHOLOGY OF BLOOD AND LYMPHATIC SYSTEM – LECTURE 2

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ANEMIA OF DECREASED PRODUCTION

General causes:

- Nutritional deficiency
- Chronic inflammation
- Bone marrow failure

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IRON DEFICIENCY ANEMIA

- Most common type of anemia
- Affects 10% of people in developed countries and 25-50% of people in developing countries
- Iron storage pool: iron is stored in ferritin (soluble) and hemosiderin (insoluble) in bone marrow, liver and spleen, forming 15-20% of total iron
- Hemosiderin consists of large iron particles, granular in shape, intracellular, visible by light microscope
- Serum ferritin is derived from stored ferritin



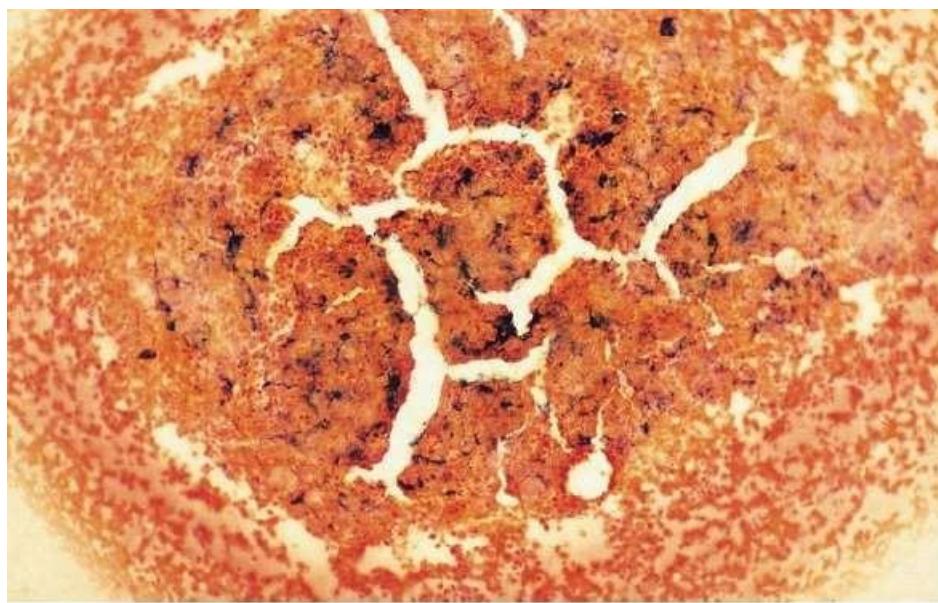
INDICATORS OF IRON STATUS

- Bone marrow aspirate: earliest changes, invasive procedure, Perl's Prussian blue stain (\downarrow in IDA)
- Serum ferritin level (\downarrow in IDA)*
- Serum iron level (\downarrow in IDA)
- Total iron binding capacity (\uparrow in IDA)
- Reticulocyte hemoglobin content (CHr): (\downarrow in IDA)
- Mean reticulocyte volume (MRV): (\downarrow in IDA)

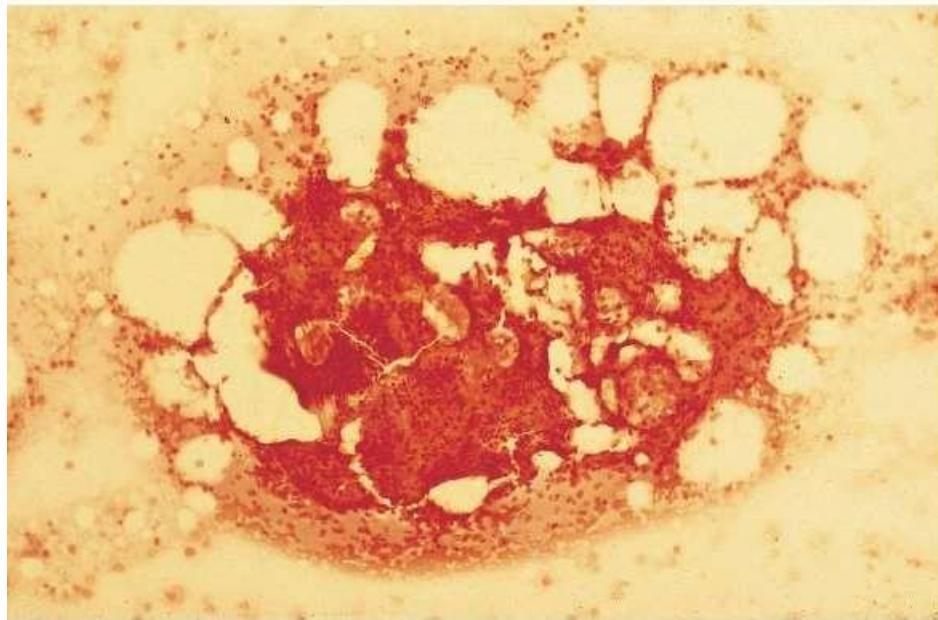
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* Affected by inflammation, fasting, vitamin C status and pregnancy





Aspirate of normal bone marrow (BM): bluish-black iron (haemosiderin) in macrophages in a fragment. Perls' stain $\times 40$.



Aspirate of normal BM: a fragment with no stainable iron. Perls' stain $\times 40$.



IRON HOMEOSTASIS

- Normal loss of body iron: shedding skin and mucosal epithelium (no excretion)
- Dietary iron is either hem (red meat) or non-hem (inorganic, vegetarian)
- 20% of hem and 1 % of non-hem iron are absorbed in duodenum



IRON HOMEOSTASIS

- Hepcidin: hormone secreted from liver, inhibits iron absorption (degrade ferroportin on enterocytes)
- Hepcidin increases in situations of high serum iron and inflammation (effect of IL-6)
- Low hepcidin: iron deficiency. Very low: thalassemia major, primary hemochromatosis



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CAUSES OF IRON DEFICIENCY

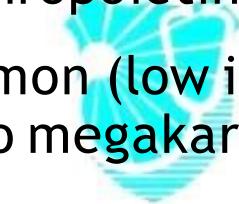
- Chronic blood loss
- Dietary: vegetarians, infants, teenagers
- Decreased absorption: gastrectomy, hypochlorhydria, intestinal diseases, elderly
- Increased demands: growing children, pregnancy, myeloproliferative neoplasms
- Hypotransferritinemia: decreased synthesis of transferritin, secondary to liver disease, protein deficiency (diet, malabsorption) or loss in urine (nephrotic syndrome)
- Enzymatic deficiency



MORPHOLOGY

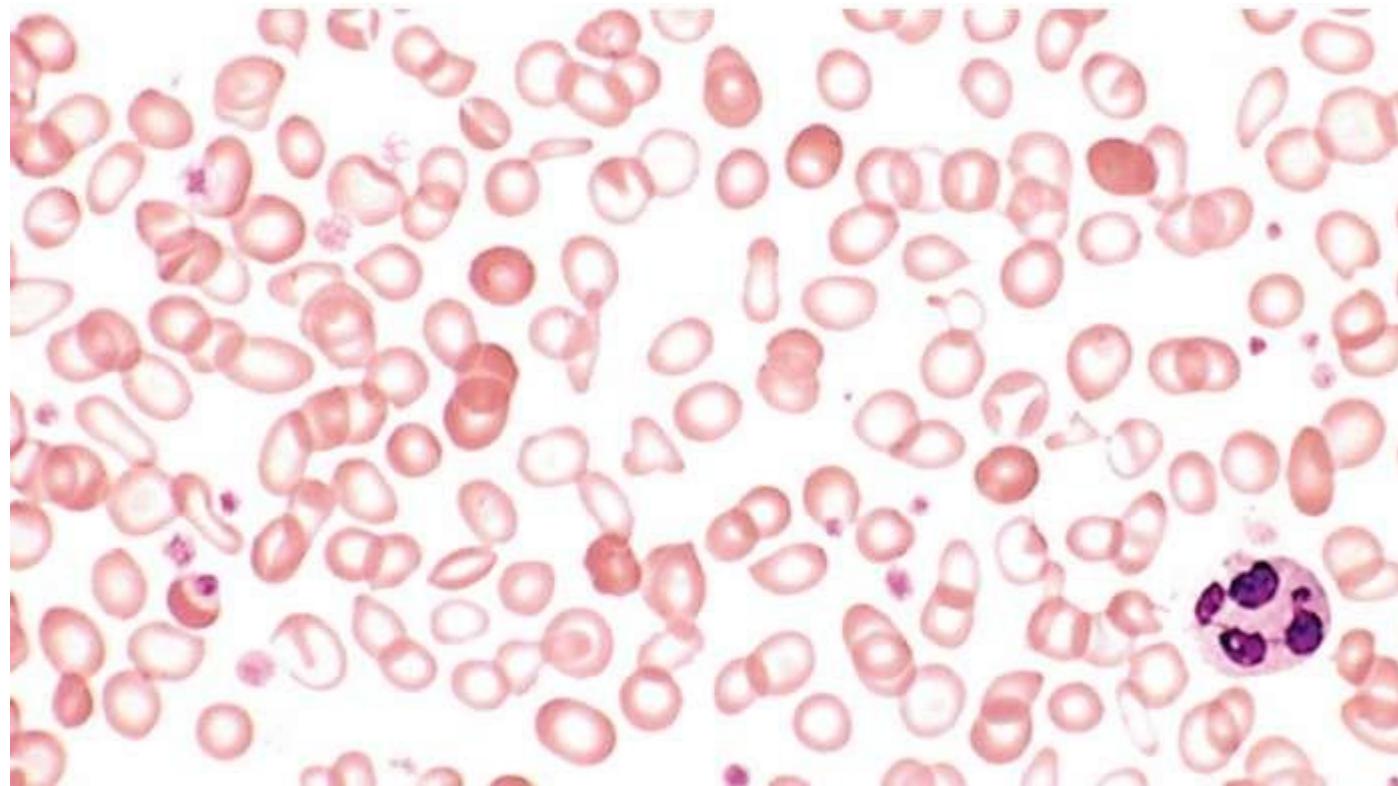
- RBCs appear small and empty (hypochromic microcytic)
- Different shapes of RBCs appear (poikilocytosis)
- Target cells
- Low reticulocytes (Erythropoietin is high, but ineffective)
- Thrombocytosis is common (low iron medium in bone marrow shifts progenitor cells to megakaryocytic lineage instead of erythroid)

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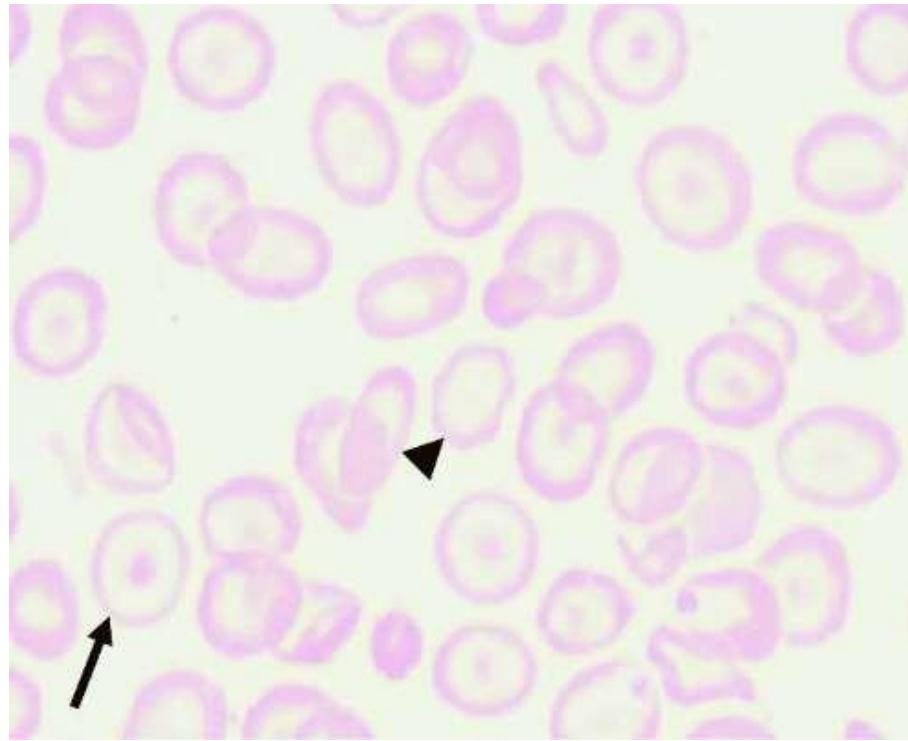




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□IDA: note the hypochromia and poikilocytosis





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□IDA: note the target cells (arrow)



SYMPTOMS

- IDA is a chronic anemia
- General symptoms of anemia
- Pica
- Glossitis, stomatitis
- Spooning of fingernails
- Restless leg syndrome
- Hair loss
- Blue sclera
- Weakened immunity
- Cognitive impairment

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ANEMIA OF CHRONIC INFLAMMATION

- Also called anemia of chronic disease
- Seen in chronic infections, cancer, chronic immune diseases
- Common in inpatients
- Chronic inflammation inhibits synthesis of erythropoietin from kidneys
- High IL-6 □ high hepcidin □ blocks iron transfer from macrophages to RBC precursors in bone marrow (degrade ferroportin on macrophages)



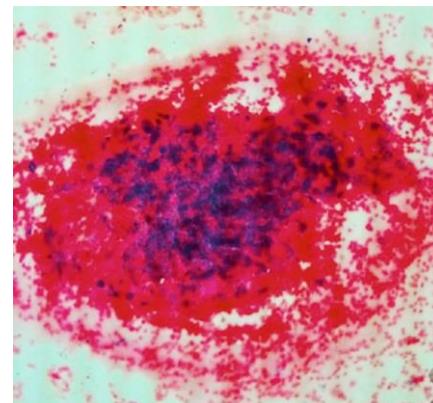
LABORATORY FINDINGS

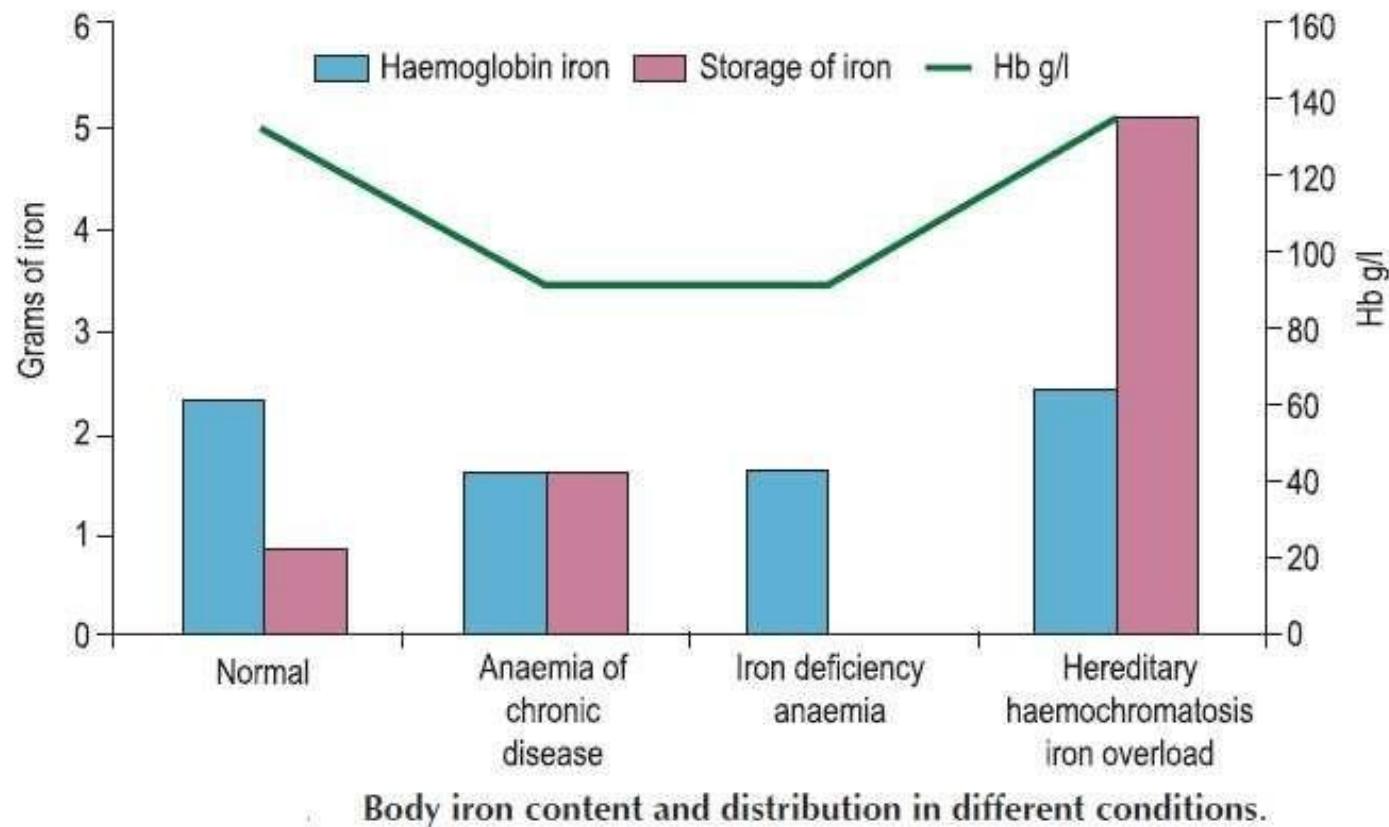
- Similar to IDA: serum iron is low
- RBCs: normal morphology, then hypochromic microcytic
- Reticulocytes ↓

In contrast:

- Bone marrow iron stores ↑
- Serum ferritin ↑

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MEGALOBLASTIC ANEMIA

- Caused by deficiency in vitamin B12 or folate
- Both are required for synthesis of thymidine, thus DNA replication is impaired
- Abnormalities occur in all rapidly dividing cells, but hematopoietic cells are most severely affected
- Maturation of RBC progenitors is deranged, many undergo apoptosis inside bone marrow (ineffective erythropoiesis, mild hemolysis)
- Viable nucleated RBCs take a longer time to mature, resulting in typical morphology (megaloblastoid)



FOLATE DEFICIENCY

- 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 of deficiency:

- Decreased dietary intake
- Increased demands (pregnancy, chronic hemolytic anemia)
- Intestinal diseases
- Beans, legume, alcohol, phenytoin (inhibit absorption)
- Methotrexate: inhibits folate metabolism and cellular usage

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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 vegetarians
- More commonly: deficiency results from defective absorption

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PERNICIOUS ANEMIA

- Autoimmune gastritis
- Autoreactive T-lymphocytes, causing injury to parietal cells
- Activates B-lymphocytes and plasma cells to synthesize and secrete auto antibodies that further damage parietal cells, and blocks binding of vitamin B12 to intrinsic factors



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OTHER CAUSES OF VITAMIN B12 DEFICIENCY

- Gastrectomy
- Small bowel diseases (malabsorption)
- Elderly people are susceptible (decreased gastric acids and pepsin, thus decreased release of vitamin B12 from food)
- Metformin (inhibits absorption)



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OTHER FUNCTIONS OF VITAMIN B12

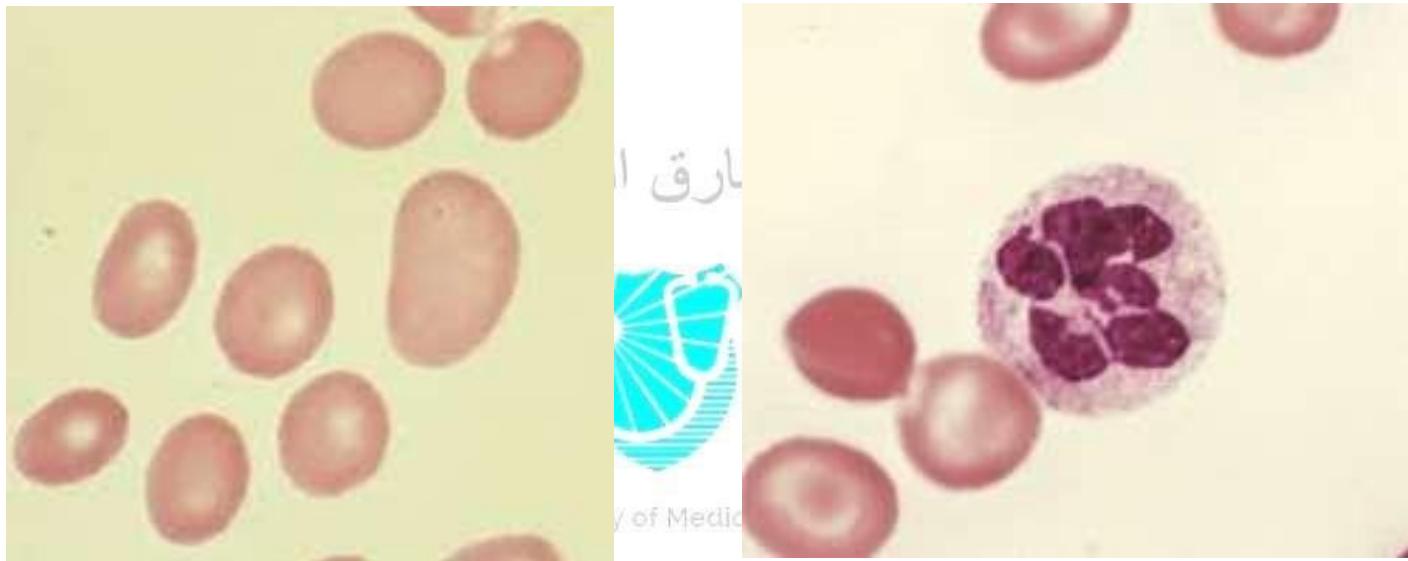
- Recycling of tetrahydrofolate
- Synthesis of myelin sheath
- Synthesis of neurotransmitters (dopamine, serotonin)
- Metabolism of homocysteine (toxic to neurons)
- Degree of neuronal damage does not correlate with the degree of anemia



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MORPHOLOGY OF MEGALOBLASTIC ANEMIA



□ Macroovalocyte: characteristic of megaloblastic anemia



SYMPTOMS

- Chronic, general symptoms of anemia
- Glossitis (beefy tongue)
- Mild jaundice
- In severe cases: pancytopenia

In vitamin B12 deficiency:

- Posterior and lateral columns degeneration of spinal cord (paresthesia, loss of proprioception)
- Peripheral neuropathy
- Neuropsychotic symptoms

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