

PATHOLOGY OF BLOOD AND LYMPHATIC SYSTEM – LECTURE 2

Dr. Tariq Al-Adaily, MD د. طارق العديلي

Associate Professor

Department of Pathology

The University of Jordan

Email: TNALADILY@ju.edu.jo



School of Medicine



ANEMIA OF DECREASED PRODUCTION

General causes:

- Nutritional deficiency
- Chronic inflammation
- Bone marrow failure

د. طارق العديلي

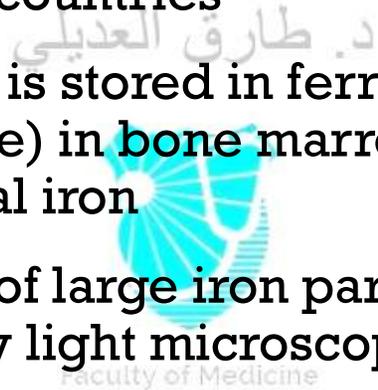


Faculty of Medicine



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

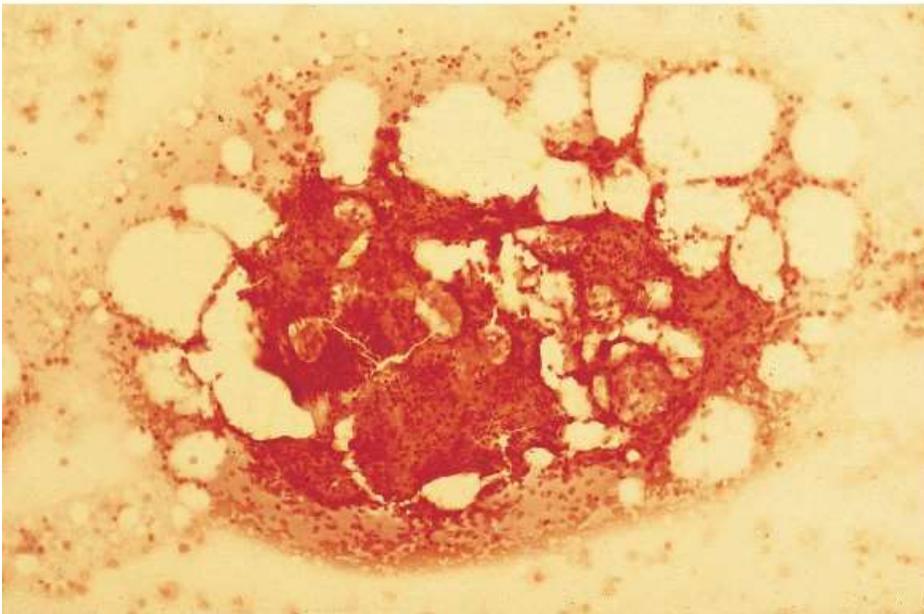
- Bone marrow aspirate: earliest changes, invasive procedure, Perl's Prussian blue stain (↓ in IDA)
- Serum ferritin level (↓ in IDA)*
- Serum iron level (↓ in IDA)
- transferrin saturation (serum iron/ serum transferrin) (normally 30%, ↓ in IDA)
- Total iron binding capacity (↑ in IDA)
- Serum transferrin and transferrin receptors (↑ in IDA)
- Reticulocyte hemoglobin content (CHr): (↓ in IDA)
- Mean reticulocyte volume (MRV): (↓ in IDA)

** 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 $\times 40$.

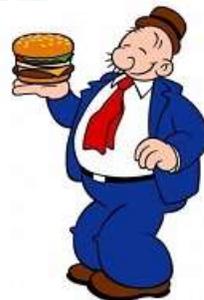


Aspirate of normal BM: a fragment with no stainable iron. Perls' stain $\times 40$.



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



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



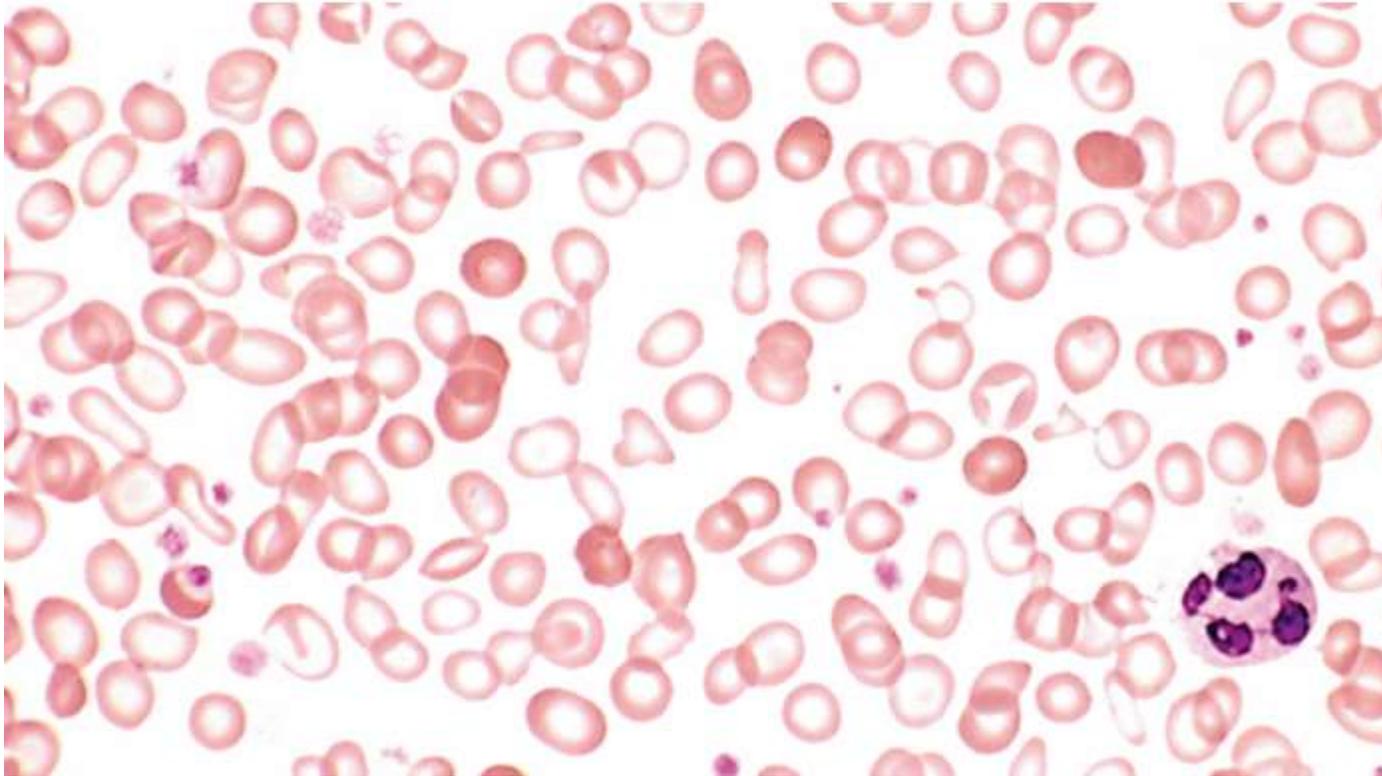
MORPHOLOGY

- 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)

د. طارق العديلي

Faculty of Medicine

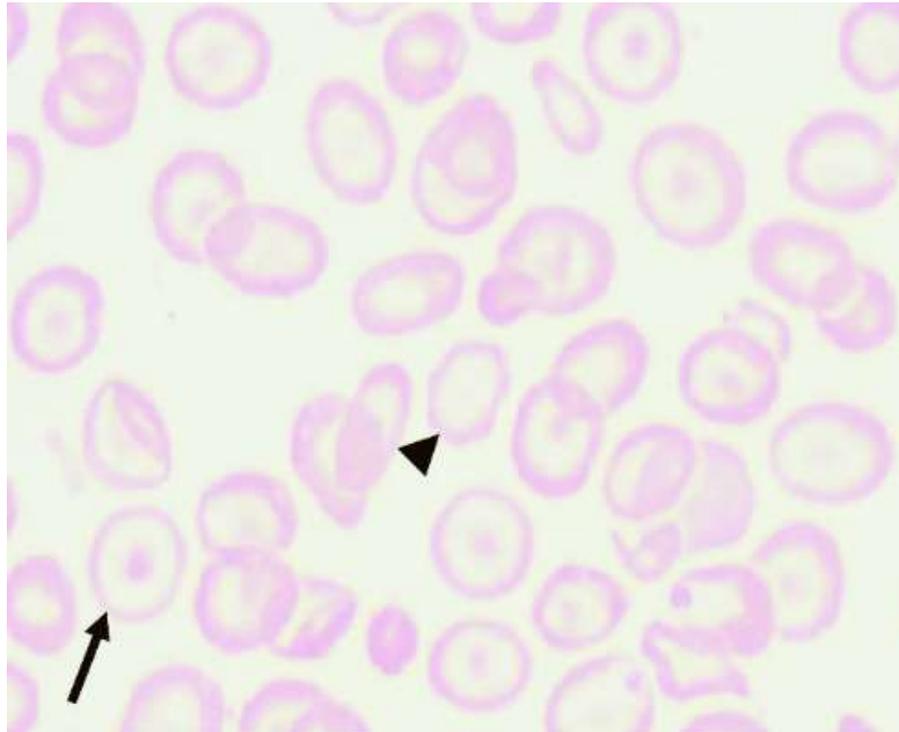




Faculty of Medicine

- IDA: note the hypochromia and poikilocytosis





Faculty of Medicine

- 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



د. طارق العديلي



Faculty of Medicine



ANEMIA OF CHRONIC INFLAMMATION

- Also called anemia of chronic disease
- Seen in chronic infections, cancer, chronic immune diseases
- Common in inpatients د. طارق العديلي
- 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) of Medicine



LABORATORY FINDINGS

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

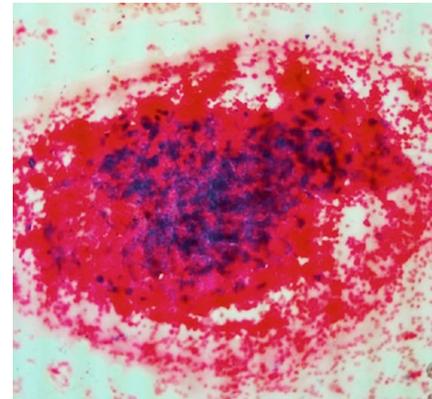
In contrast:

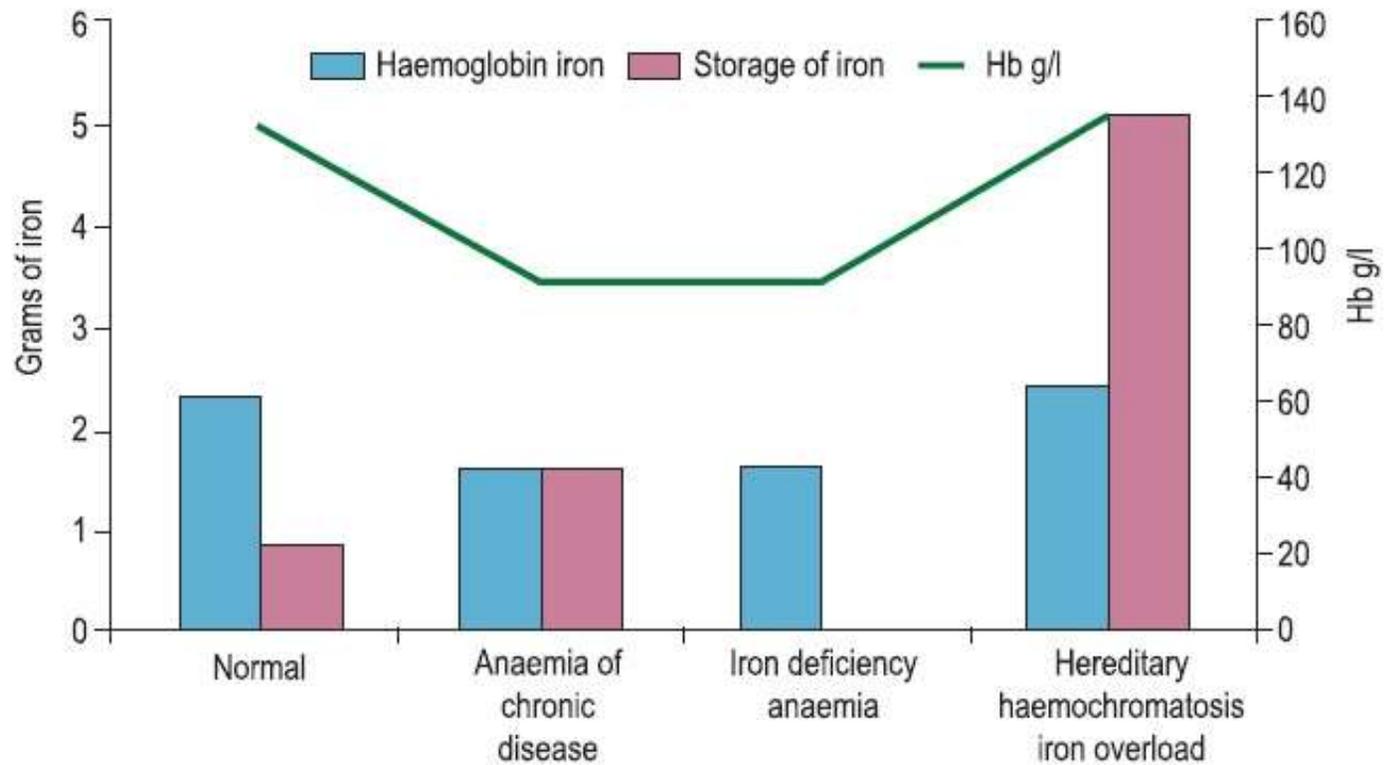
- Bone marrow iron stores ↑
- Serum ferritin ↑
- Serum transferrin ↓
- Total iron binding capacity ↓
- Transferrin saturation: normal
- Transferrin receptor: normal

د. طارق العديلي



Faculty of Medicine





Body iron content and distribution in different conditions.



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

د. طارق العديلي
Faculty of Medicine



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



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

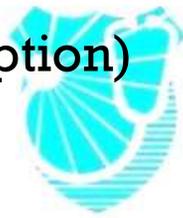


Faculty of Medicine



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)



Faculty of Medicine



OTHER FUNCTIONS OF VITAMIN B12

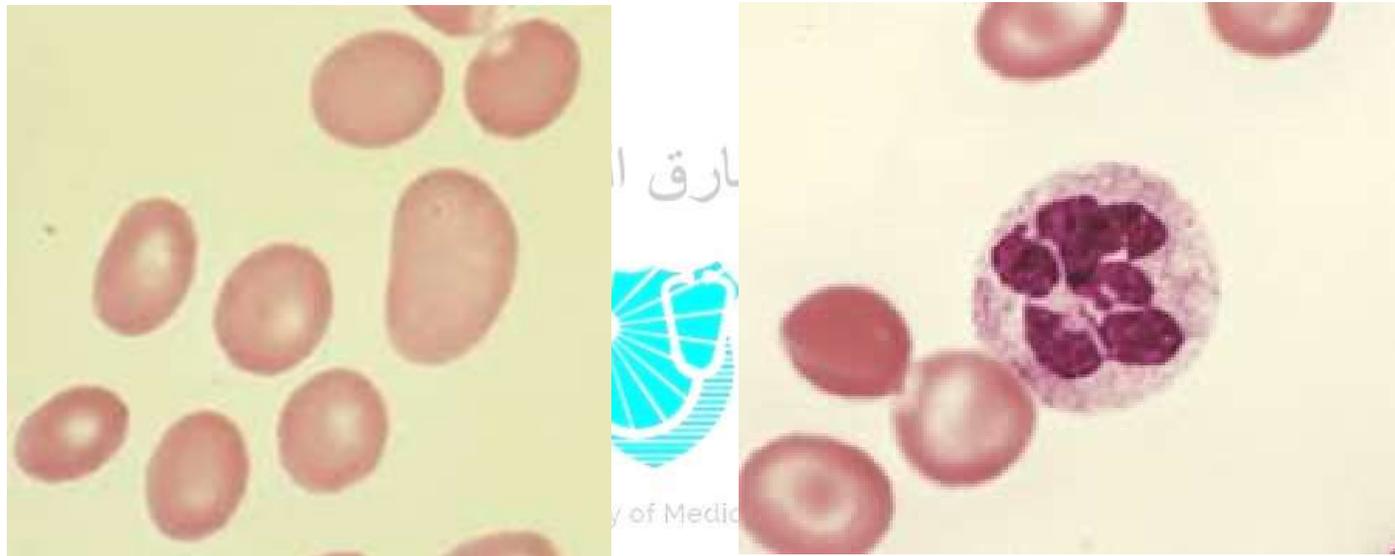
- Recycling of tetrahydrofolate
- Synthesis of myelin sheath
- Synthesis of neurotransmitters (dopamine, serotonin)
- Metabolism of homocysteine (toxic to neurons)
- Degree of neuronal damage does not correlate with the degree of anemia



Faculty of Medicine



MORPHOLOGY OR 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

د. طارق العديلي



Faculty of Medicine

