* هدول السلايدات من ارشيف احسان
السلايدات اللي مؤخت عزيم الدكتورة نفسرهم بس شايلة منهم بعض
السلايدات (محففيته يعني) ← فالسلايدات اللي عليها هاي العلامة "#"
هي السلايدات اللي الدكتورة شايلاتهم

Anemia

Muna Kilani, MD

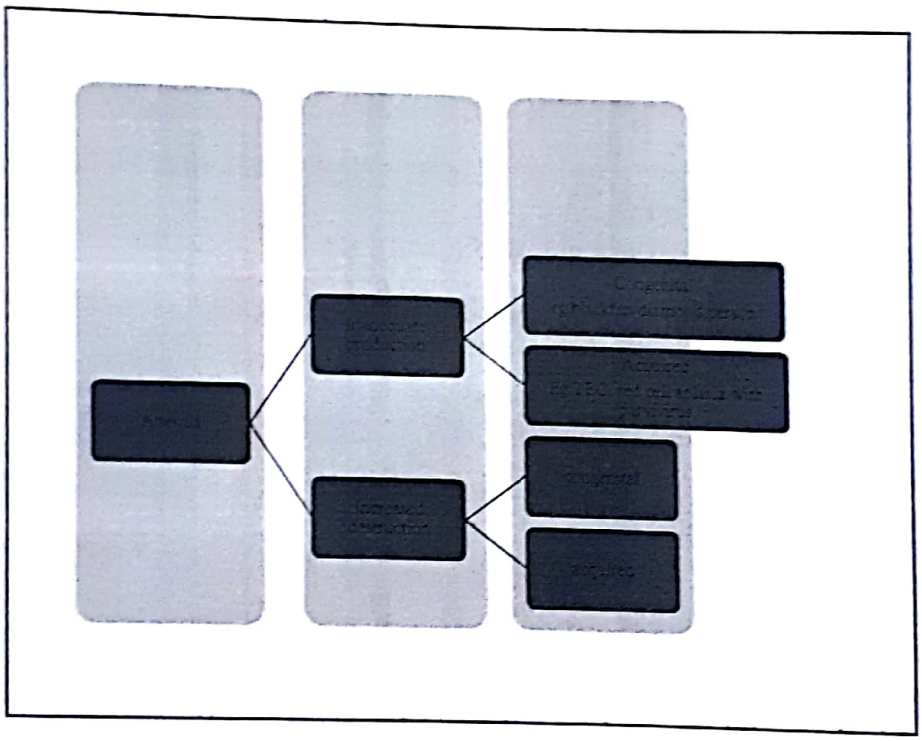
Anemia

- Is defined as a reduction of the hemoglobin concentration or hematocrit below the range of values occurring in healthy persons.
- "Normal" hemoglobin and hematocrit vary with age and sex race.

Table 447-1 Normal Mean and Lower Limits of Normal for Hemoglobin, Hematocrit, and Mean Corpuscular Volume

Age (yr)	HEMOGLOBIN (g/dL)		HEMATOCRIT (%)		MEAN CORPUSCULAR VOLUME (μM³)	
	Mean	Lower Limit	Mean	Lower Limit	Mean	Lower Limit
0.5-1.9	12.5	11.0	37	33	77	70
2-4	12.5	11.0	38	34	79	73
5-7	13.0	11.5	39	35	81	75
8-11	13.5	12.0	40	36	83	76
12-14 female	13.5	12.0	41	36	85	78
12-14 male	14.0	12.5	43	37	84	77
15-17 female	14.0	12.0	41	36	87	79
15-17 male	15.0	13.0	45	38	86	78
18-49 female	14.0	12.0	42	37	90	80
18-49 male	16.0	14.0	47	40	90	80

From Bruguera C, Cline FJ, Nathan DG. Nathan and Oski's hematology of infancy and childhood, ed 7. Philadelphia, 2009, WB Saunders, p. 456.



How the body will adapt :

(Symptoms of anemia)

- - Increased cardiac output .
- - Augmented oxygen extraction .
- - Shunting of blood flow toward vital organs and tissues.
- - Shift to the right" of the oxygen dissociation curve reduces the affinity of hemoglobin for oxygen and results in more complete transfer of oxygen to the tissues.
- - Higher levels of erythropoietin (EPO) and consequent increased red cell production .

•Clinical manifestation

HISTORY

Symptoms of Anemia

- Age, sex, race and ethnicity.
- Irritability, hypoactivity and decreased exercise tolerance, weakness, tachypnea, shortness of breath on exertion, palpitation, headache, dizziness or syncope.
- Pallor, jaundice, change in color of urine or stool
- Hx of petechial skin rash ,ecchymosis, bleeding .

History

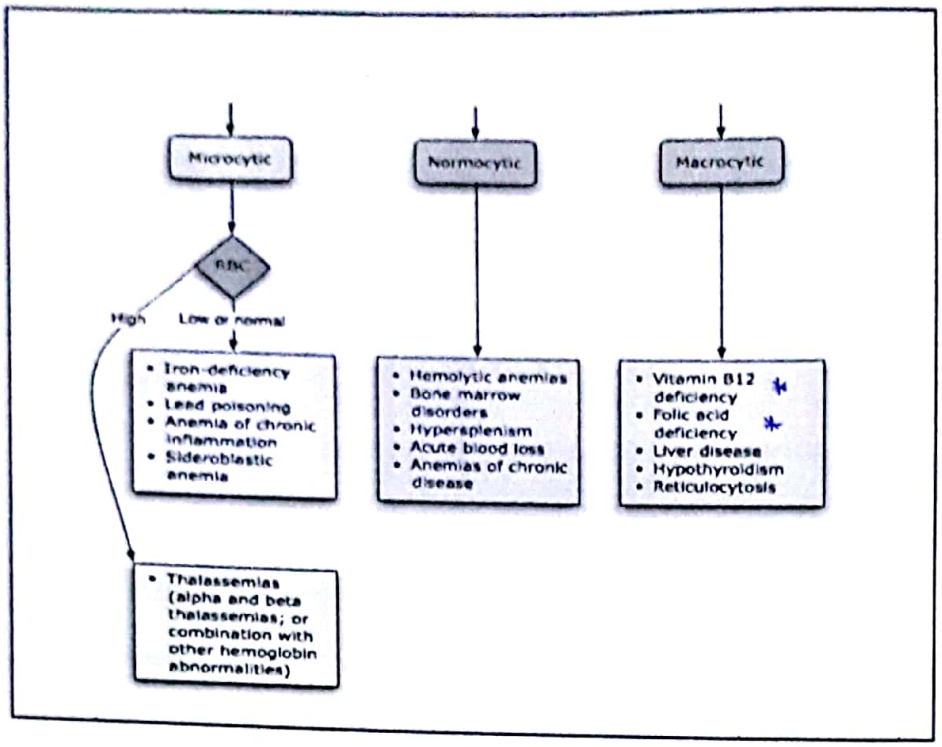
- Diet. → important
- Medications . (some meds cause hemolysis)
- Chronic diseases, infections .
- Travel. (Malaria)
- A family history of anemia ,Jaundice, splenomegaly, splenectomy, G6PD deficiency, sickle cell anemia, Thalassemia, frequent gall bladder stones.
- Previous hx of blood transfusion .

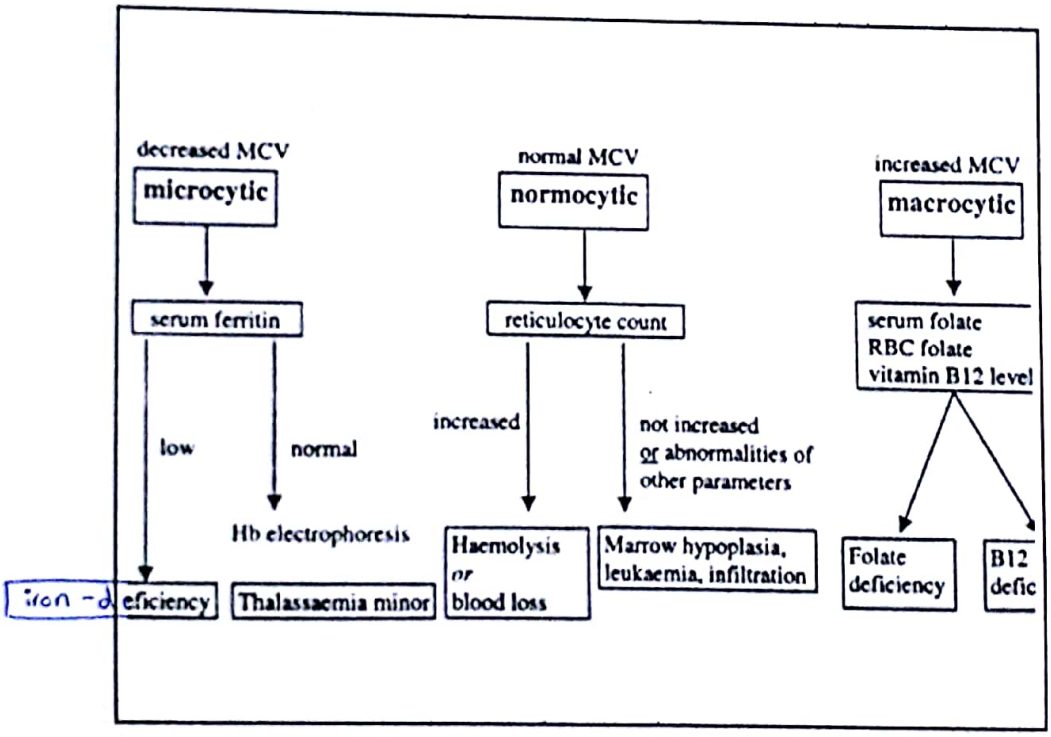
PHYSICAL EXAMINATION

- There often are few physical symptoms or signs .
- Clinical findings generally do not become apparent until the hemoglobin level falls to <7-8 mg/dL.
- Clinical features can include pallor, jaundiced , sleepiness , frontal bossing, dysmorphic feature.
- Growth parameters (wt,ht,head circumferance)
- Lymphadenophathy .
- Tachycardia ,heart murmur, heart failure
- Hepato-spenomegally .

LABORATORY STUDIES

- Initial laboratory testing should include:
  - Hemoglobin, hematocrit, and red cell indices (CBC)
  - White blood cell count and differential,
  - Platelet count .
  - Reticulocyte count.
  - Peripheral blood smear.
  - The need for additional laboratory studies is dictated by the history, the physical, and the results of this initial testing





MCV for Characterize Anemia

(>85fl)

***Macrocytic**

- Normal newborn
- Increased erythropoesis
- Post splenectomy
- Liver disease
- Aplastic anemia
- Megaloblastic anemia
- Down S.
- Obstructive jaundice

Low(<70 fl)

-Hypochromic/Microcytic

-Iron deficiency anemia

-Thalassemia

-Sideroblastic anemia

-Lead poisoning

-Inborn errors of Fe metabolism

-Severe malnutrition

-Copper deficiency

- **Normocytic**
  - Acute blood loss
  - Infection
  - Renal failure
  - Connective tissue disorders
  - Liver disease
  - Disseminated malignancy
  - Early iron deficiency
  - Aplastic anemia
  - Bone marrow infiltration
  - Dyserythropoietic anemia

Etiologic classification

I Impaired red cell formation

A/ Deficiency

- Decreased dietary intake
- Increased demand
- Decreased absorption
- Increased loss

B/ Bone marrow failure

- Failure of a single or all cell lines
- Infiltration

C/Dyshematopoietic anemia

II Blood loss

III Hemolytic anemia

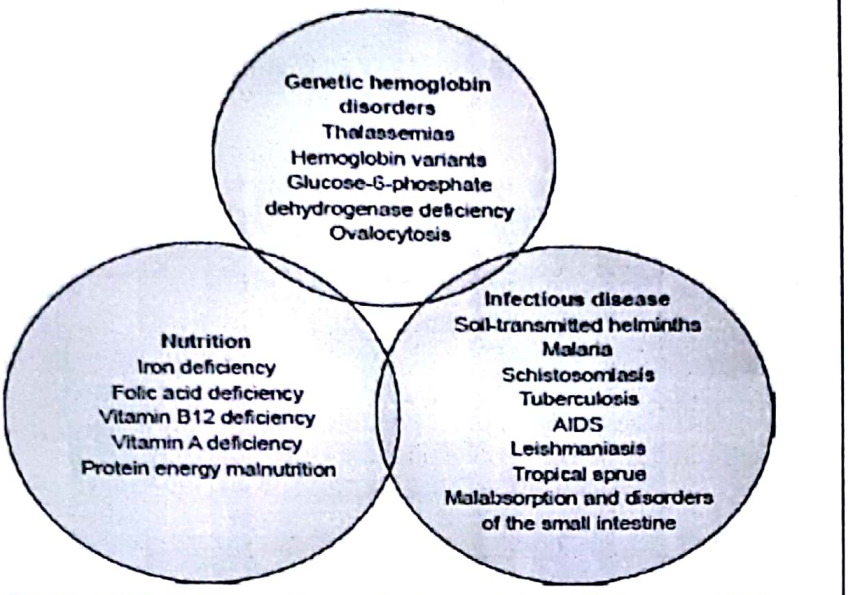
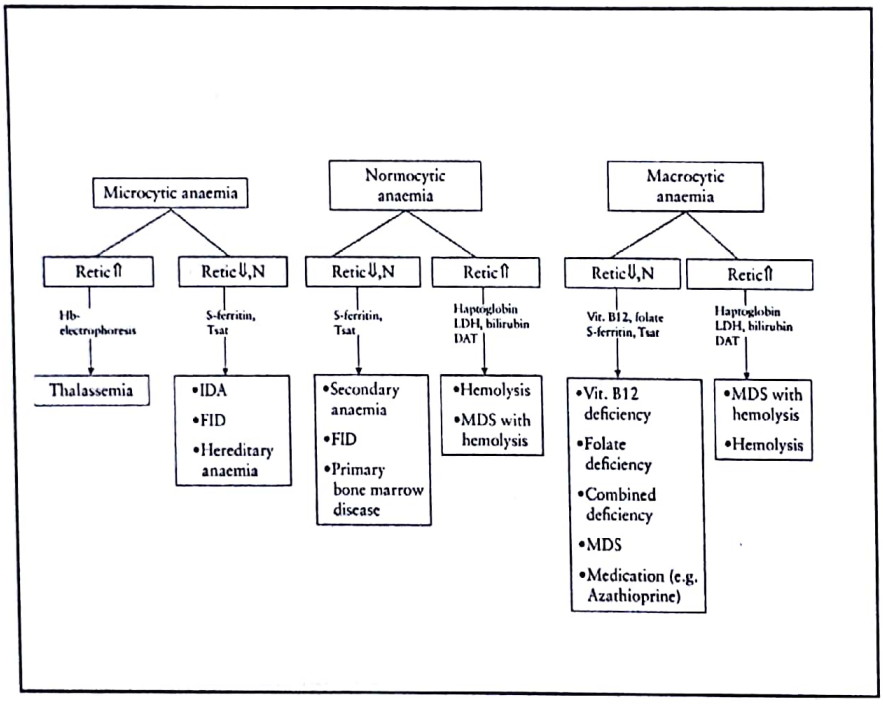
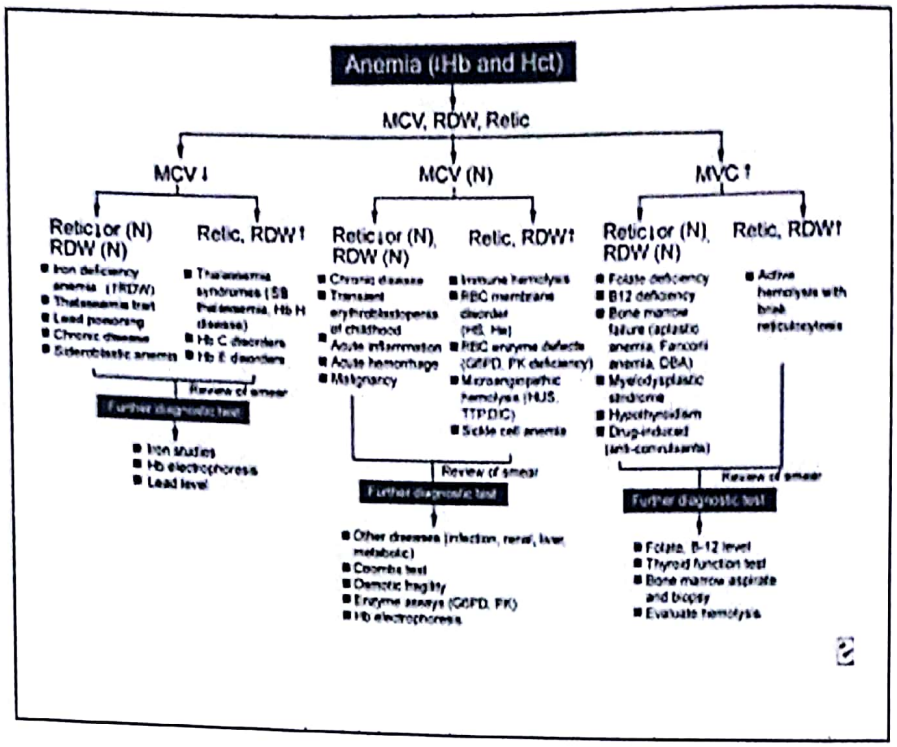


Figure 447-2 Causes of anaemia in countries with low or middle incomes. *(From Balarajan Y, Ramakrishnan U, Özaltin E, et al: Anaemia in low-income and middle-income countries. Lancet 378:2123–2134, 2011. Fig. 3.1*





↳ An anemia of ↓ production

Iron Deficiency Anemia

- Symptoms
- GI: Anorexia, poor weight gain, pica, atrophic glossitis
- CNS: fatigue, irritability
- Cardiac: increased cardiac output, cardiac hypertrophy
- Dry skin, thin hair, pallor, nail ridges

Extra note

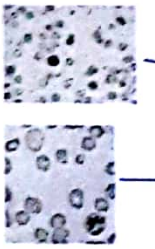
* In infants, the introduction of cow's milk in the first year of life is the greatest dietary risk factor for developing iron defeciency anemia
  - Cow's milk is low in iron and its iron is poorly absorbed
  - It also decreases the absorption of iron from other dietary sources.

Iron Deficiency Anemia

Etiology

- Store depletion in term infant at age 6-9 months.
- ~~Early cord clamping <30 sec.~~
- Diet (cows milk protein , malnutrition)
- Blood loss particularly in older children and adolescents(lesion of the gastrointestinal (GI) tract, such as peptic ulcer, meckel diverticulum, polyp, hemangioma, or inflammatory bowel Disease)
- Infection with hookworm, Plasmodium, and Helicobacter pylori .
- Growth spurt and menstrual blood loss in adolescent girls → Peak growth leading to ↑ demand.

Iron Deficiency Anemia



Mini Osce

-Characteristics of peripheral blood smear
- microcytic
- hypochromic

*MCV and Hgb– decreased
Ferritin – decreased (<13mg/dL)
- TIBC - high

-Serum iron –decreased (N 50-150 µg/dL)

Iron Deficiency Anemia

Laboratory test:

- Tissue iron stores are depleted → reduced serum ferritin→ serum iron levels decrease, the iron-binding capacity of the serum (serum transferrin) increases, transferrin saturation decrease → microcytic hypochromic anemia and increase of RDW → Red Cell distribution width
- REITCULOCYTOPENIA → why? ↓ iron → ↓ production → ↓ reticulocytes
- Normal WBC ,normal or high platelet .

Treatment :

- iron supplement usually for 2-3 month.

→ Prevention is very important because some symptoms of iron deficiency anemia are irreversible once they occur (ex. impaired psychomotor and/or mental development)

Transient erythroblastopenia of childhood (TEC)

- Is the most common acquired red cell aplasia occurring in children.
- This syndrome of severe, transient hypoplastic anemia occurs mainly in previously healthy children between 6 mo and 3 yr of age .
- The suppression of erythropoiesis has been linked to immunoglobulin IgG, IgM, and cell mediated mechanisms.
- Familial cases have been reported, suggesting a hereditary component.

Transient erythroblastopenia of childhood (TEC)

- The temporary suppression of erythropoiesis results in reticulocytopenia and moderate to severe normocytic anemia.
- Some degree of neutropenia occurs in up to 20% of cases.
- Platelet numbers are normal or elevated.
- Virtually all children recover within 1-2 mo. RBC transfusions may be necessary for severe anemia in the absence of signs of early recovery.
- Corticosteroid therapy is of no value .

Diamond-Blackfan anemia (DBA)

↳ Congenital anemia
↳ ↓ production

* Very rare

- Is a rare, congenital bone marrow failure syndrome that usually becomes symptomatic in early infancy.
- Is characterized by anemia, usually normochromic and macrocytic, reticulocytopenia, and insufficient or absent of red blood cell (RBC) precursors in an otherwise normally cellular bone marrow.

يعني بس الـ RBCs إللي بتأثروا

Diamond-Blackfan anemia (DBA)

- ETIOLOGY

-DBA associated gene mutations that encodes a component protein of the small 40S ribosomal subunit.

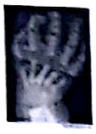
- EPIDEMIOLOGY

-DBA affects about 7 individuals per 1 million live births

- It is primarily an autosomal dominant disease, with substantial phenotypic diversity .
- CLINICAL MANIFESTATIONS :
- Profound anemia usually becomes evident by 2-6 mo of age .
- Approximately 50% of patients have congenital anomalies

Clinical features

- 25% have prenatal or postnatal growth failure and associated congenital defects, including short stature, abnormalities of thumbs, skeletal anormalities, congenital heart defects, webbed neck, urinary tract abnormalities and craniofacial dysmorphism
- Chromosomal studies generally normal
- No hepatosplenomegaly



Diamond-Blackfan anemia (DBA)

TREATMENT

- Corticosteroids
- blood transfusions at intervals of 3-5 wk to maintain a hemoglobin greater than 8 g/dL
- Hematopoietic stem cell transplantation (HSCT) can be curative.
- PROGNOSIS
  - It has been identified as a cancer predisposition syndrome.
  - The risk is increased for myelodysplastic syndrome, acute myeloid leukemia, colon carcinoma, osteogenic sarcoma, and female genital cancers.

Diamond-Blackfan anemia
congenital pure red cell aplasia

The erythroid progenitor cell is intrinsically abnormal in the following aspects:

- **Decreased sensitivity to erythropoietin (EPO)**
- **Decreased sensitivity to EPO not corrected by IL-3 and GM-CSF**

***caused by*:**

- **Functional abnormalities in the erythropoietin receptors**
- **Erythroid progenitors are abnormally sensitive to a deprivation of erythropoietin, resulting in an accelerated rate of apoptosis**

Fanconi anemia

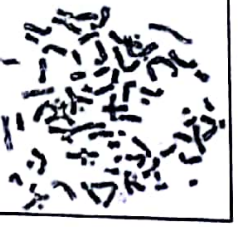
congenital aplastic anemia

- Rare inherited disorder, autosomal-recessive trait
- Pancytopenia: develops between 4 and 12 years of age
- It may present with isolated anemia or leukopenia or anemia + thrombocytopenia
- Macrocytosis (high MCV), high HbF, high erythropoetin, presence of I antigen – characteristic of stress erythropoiesis

Fanconi anemia

congenital aplastic anemia

- Diepoxybutane (DEB)-induced chromosomal breakages * One of the tests they do for Dx is chromosomal breakage studies
- Hypocellularity and fatty replacement in bone marrow
- Congenital anomalies: patchy brown pigmentation of the skin → Café au lait spots, short stature, skeletal anomalies, hyperreflexia, hypogenitalism, microcephaly, microphthalmia, strabismus, ptosis, nystagmus, abnormalities of the ears, deafness, mental retardation, renal and cardiac anomalies
- *Chromosomal breakages and structural abnormalities, chromatoid exchange*
- High incidence of AML, carcinoma



Fanconi anemia

FANCONI ANEMIA

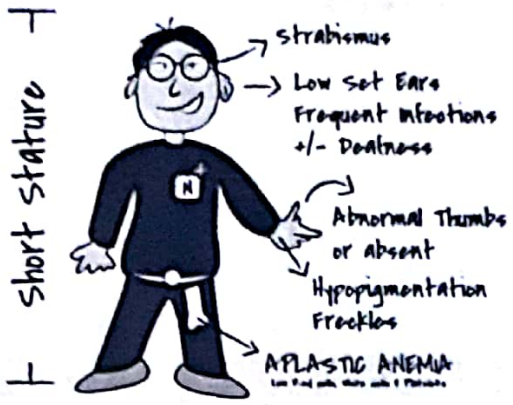
Clinical Features

Autosomal Recessive Genetic Disorder

- Due to chromosomal breakage
- Common in Ashkenazi Jews

Rx

Bone Marrow Replacement



mitochondrial disorder that presents w/ hypoplastic anemia

اهم اشي نعرف إنه هو مثال على

Pearson Syndrome

- Pearson marrow-pancreas syndrome is a rare mitochondrial disorder that presents with a hypoplastic anemia .
- The marrow failure usually appears in the neonatal period and is characterized by a macrocytic anemia and, occasionally, neutropenia and thrombocytopenia.
- There are vacuolated erythroblasts and myeloblasts in the bone marrow.
- The hemoglobin F level is elevated.
- There is multiorgan involvement manifested by failure to thrive and symptoms of exocrine pancreas dysfunction, liver and renal tubular defects, malabsorption, and myopathy.
- This disorder is caused by a mitochondrial DNA deletion of variable size and location .
- Therapy for the hematologic manifestations of the disease is primarily supportive and includes red cell transfusions to correct anemia and granulocyte colony-stimulating factor to reverse episodes of severe neutropenia.

* اجا مريض مرة كان Pearson بين DD× في Cystic fibrosis و

Acquired Aplastic Anemia

pathophysiology

- Immunologically mediated, tissue-specific, organ-destructive mechanism
- Exposition to an antigen → cells and cytokines of the immune system destroy stem cells in the marrow → pancytopenia
- Gamma –interferon plays a central role in the pathophysiology of AA (Aplastic Anemia)
- T cells from AA patients secrete gamma-IFN and TNF – potent inhibitors of both early and late hematopoietic progenitor cells
- Cytotoxic T cells secrete also IL-2, which causes polyclonal expansion of the T cells

Causes of acquired AA

Idiopathic (70%)

Secondary:

- Drugs: cytostatics, antibiotics (sulfonamides, chloramphenicol), anticonvulsants (hydantoin), antirheumatics, antidiabetics, antimalarian
- Chemicals: insecticides
- Toxins: benzene, carbon tetrachloride, glue, toluene
- Irradiation
- Infections: viral (hepatitis A, B, C, HIV, EBV, CMV, parvovirus) * Parvovirus B19
- Immunologic disorders: GvHD
- Preleukemia, MDS, thymoma
- Malnutrition
- Paroxysmal nocturnal hemoglobinuria

RED CELL APLASIA ASSOCIATED WITH PARVOVIRUS B19 INFECTION

- Parvovirus B19 is a common infectious agent that causes erythema infectiosum (fifth disease)
- It can cause RBC aplasia in patients with chronic hemolysis, patients who are immunocompromised, and fetuses in utero.
- In addition to decreased or absent erythroid precursors, characteristic nuclear inclusions in erythroblast and giant pronormoblasts may be seen under the light microscope in bone marrow specimens.

The anemia of chronic disease

- Anemia of inflammation .
- Is found in conditions where there is ongoing immune activation.
- It occurs in a wide a range of disorders including
  - infections,
  - malignancies
  - autoimmunity, and graft-versus-host disease.
  - chronic kidney disease. and end-stage renal failure
- It is typically a mild to moderate normocytic, normochromic, hypo proliferative anemia associated with a decreased serum iron and low transferrin saturation.

Physiologic Anemia of Infancy

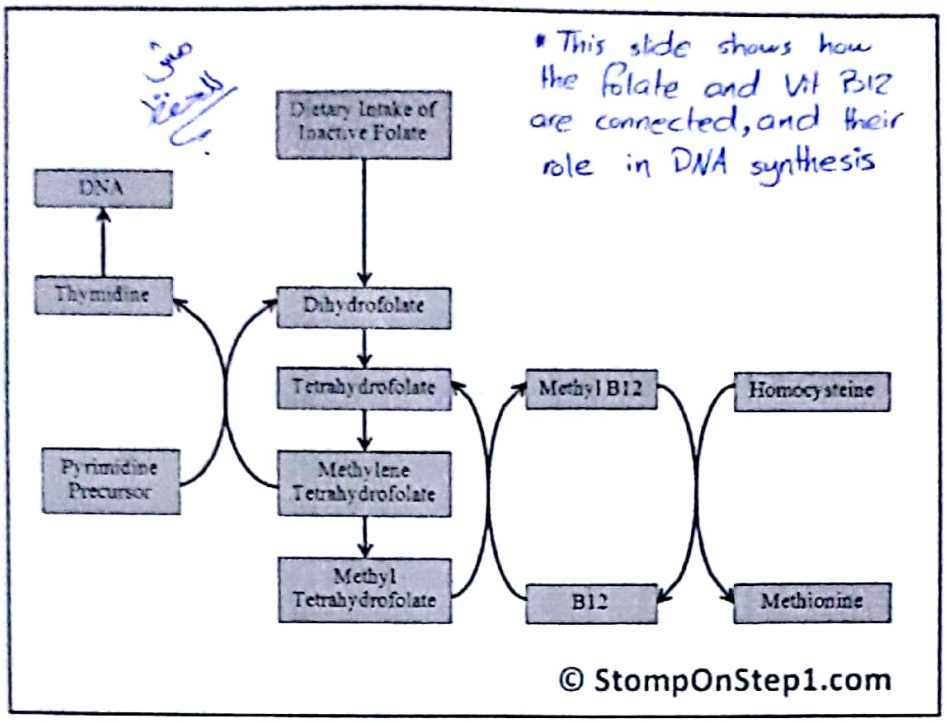
- This "anemia" considered as physiologic adaptation to extrauterine life, reflecting the excess oxygen delivery relative to tissue oxygen requirements.
- There is no hematologic problem, and no therapy is required unless physiologic anemia of infancy is exacerbated by other ongoing processes .
- At birth, normal full-term infants have higher hemoglobin (Hb) levels and larger red blood cells (RBCs) than do older children and adults and, supression of erytropiotin
- So, within the 1st wk of life There is progressive decline in Hb level begins and then persists for 6-8 wk.
  ↳ The Hb can go as low as 9

* The intrauterine life is a relatively hypoxic stage → The pressure of O_2 (PaO_2) is in the 70's, so for the body to ~~stabt~~ adapt and ↑ the O_2 carrying capacity → the EPO level is high increasing the RBC count
* When the child is born (extrauterine life) → The $PaO_2 = 100$ → so there is suppression of erythropoeisis and ↓ Hb.

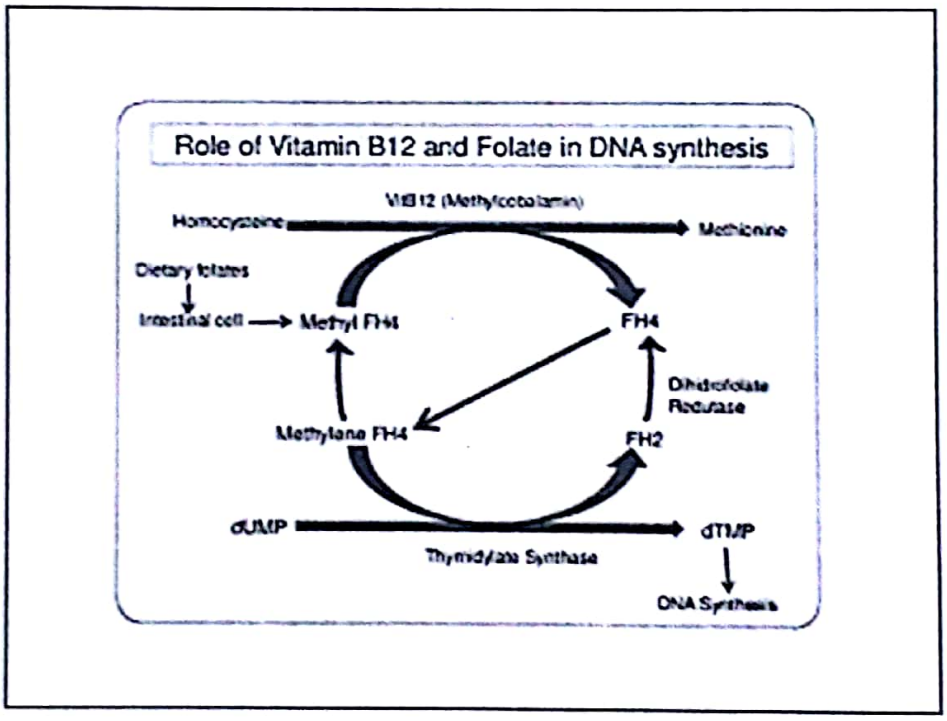
Megaloblastic anemia

- Describes a group of disorders that are caused by impaired DNA synthesis.
- Red blood cells (RBCs) are larger than normal
- There is often an associated thrombocytopenia & leukopenia
- The peripheral blood smear is notable for large, often oval, RBCs with increased mean corpuscular volume.
- Neutrophils are characteristically hypersegmented, with many having >5 lobes.
- Most cases of childhood megaloblastic anemia result from a deficiency of folic acid or vitamin B12 (cobalamin),
- Rarely, these anemias may be caused by inborn errors of metabolism. (congenital cause)

However environmental (aquired) causes are way more common.



• This slide shows how the folate and Vit B12 are connected, and their role in DNA synthesis



Folic Acid Deficiency

Folic acid deficiency can occur :

- - Inadequate folate intake(malnutrition, pregnancy, periods of accelerated growth, and/or chronic hemolysis) .
- -Decreased folate absorption(malabsorption,celiac, chronic enteritis ,hx of intestinal surgery, antiepileptic drugs) .
- - Acquired and congenital disorders of folate metabolism or transport.
- Congenital disorders may be associated with hypogammaglobulinemia, severe infections, failure to thrive, neurologic abnormalities, and cognitive delays .

Vitamin B12 (Cobalamin) Deficiency

- Vit B deficiency can occur:
  - - Inadequate dietary intake of cobolamin (nutritional, resulting from low Cbl levels in the breast milk of B12-deficient mothers)
  - -Lack of intrinsic factor IF (pernicious anemia)
  - - Impaired intestinal absorption of IF-Cbl(celiac ,IBD, previous surgery Pancreatic insufficiency).
  - - Absence of vitamin B12 transport protein

Vitamin B12 (Cobalamin) Deficiency

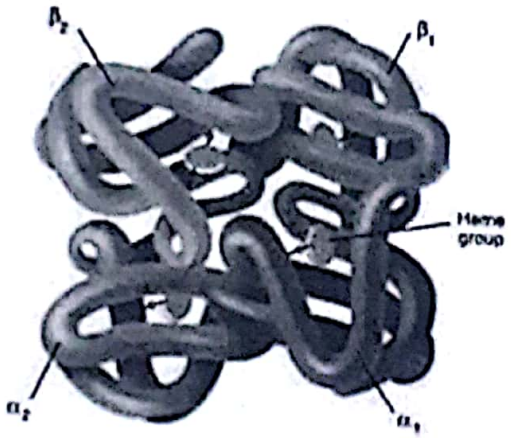
- CLINICAL MANIFESTATIONS:
  - Weakness, lethargy, feeding difficulties, failure to thrive,and irritability.
  - Other common findings include pallor, glossitis, vomiting, diarrhea, and icterus.
  - Neurologic symptoms can include
    - paresthesia,
    - sensory deficits .
    - hypotonia .
    - seizures .
  - Developmental delay, developmental regression, and neuropsychiatric changes.
  - (they may occur in the absence of any hematologic abnormalities).

Anemia because of increased destruction of RBC's

(Hemolysis)

Hemoglobinopathies

- The major hemoglobin in adults is hemoglobin A, a tetramer consisting of :
- one pair of alpha globin chains
- one pair of beta globin chains
- Thalassemia refers reduced or absent production of one or more globin chains .



The most common of the hemoglobinopathies.

Sickle Cell Disease

- Autosomal recessive disorder
- Arises from a mutation substituting thymine for adenine in the sixth codon of the beta-chain gene.
- This change encodes valine instead of glutamine in the 6th position in the β-globin molecule. → causing the Hb to be unstable leading to sickling.
- HbSS disease or sickle cell anemia (the most common form) homozygous mutation

Sickle Cell Disease

- Sickle cell anemia (HbSS), homozygous HbSS, occurs when
- both β-globin alleles have the sickle cell mutation (βs).

CLINICAL MANIFESTATION OF SICKLE CELL ANEMIA(HB SS)

Important

- Fever and Bacteremia

Fever in a child with sickle cell anemia is a medical emergency, requiringprompt medical evaluation and delivery of antibiotics becauseof the increased risk of bacterial infection and subsequent high mortalityrate.

- Infants with sickle cell anemia, as early as 6 mo of age,develop abnormal immune function due to splenic infarction. → So children are put on prophylactic Abx.
- By 5 yr of age, most children with sickle cell anemia have complete functional asplenia.
- Children need to be on prophylactic antibiotics

Sickle cell anemia

- Aplastic Crisis

Caused mainly by Human parvovirus B19.

The acute anemia of an aplastic crisis is treated conservatively using red blood cell transfusion when the patient becomes hemodynamically symptomatic or has a concurrent illness, such as acute chest syndrome .

Splenic Sequestration

- A life-threatening complication occurring
- Occurs in children between the ages of 6 mo and 2 yr .
- it is associated with rapid spleen enlargement causing left-sided abdominal pain and a decline in hemoglobin of at least 2 g/dL from the patient's baseline
- Sequestration may be triggered by fever, bacteremia, or viral infections

Treatment

- Isotonic fluid or blood transfusion
- Repeated episodes of splenic sequestration are common
- Prophylactic splenectomy performed after an acute episode has resolved .

Sickle cell anemia

Sickle Cell Pain

- Dactylitis, referred to as hand-foot syndrome, is often the first manifestation of pain in infants and young children with sickle cell anemia,
  - occurring in 50% of children by their 2nd year of age
  - often manifests with symmetric or unilateral swelling of the hands and/or feet

due to infarcts in the bones and swelling of the fingers

يشكل عام sickle cell disease من أعراض

Sickle cell anemia

- The cardinal clinical feature of sickle cell anemia is acute vasoocclusive pain.
  - Characterized as unremitting discomfort that can occur in any part of the body but most often occurs in the chest, abdomen, or extremities.
- These painful episodes are often abrupt and cause disruption of daily life activities
- The exact etiology of pain is unknown ?? tissue ischemia.

  Avascular necrosis (AVN)

  Most commonly, the femoral head is affected

Neurologic Complications :

- Acute ischemic stroke with focal neurologic deficit .
  - headaches , seizures, cerebral venous thrombosis . reversible
- Posterior leukoencephalopathy syndrome.
  - Treatment
    - exchange transfusion

Cognitive and Psychological Complications

Acute Chest Syndrome

Pulmonary Complications

- Lung disease in children with sickle cell anemia is the second most common reason for hospital admission and is associated with significant mortality.
- Defined as a new radiodensity on chest radiography (pneumonia يعني) plus any 2 of the following: fever, respiratory distress .
- Causes :??
- -Infection is the most well-known etiology, most common pathogens are S. pneumoniae, Mycoplasma pneumoniae,and Chlamydia sp.
- -Fat emboli

→ fever is the 1st most common cause of hospital admission

← يعني hypoxic و بنعطيه O2 عشان dehydration و بنعطيه fluids عشان Abx و بنعطيه

#

- Renal Disease and Enuresis
- Renal disease:
- (1) gross hematuria,
- (2) papillary necrosis,
- (3) nephrotic syndrome,
- (4) renal infarction,
- (5) hyposthenuria,
- (6) pyelonephritis,
- (7) renal medullary carcinoma.

Thalassemia Syndromes

- Thalassemia refers to a group of genetic disorders of globin chain production in which there is an imbalance between the α-globin and β-globin chain production.
- β-Thalassemia syndromes result from a
  - Decrease in β-globin chains, which results in a relative excess of α-globin chains.

Hemoglobin defects

Thalassemias

- Alpha chains hemoglobinopathies:

  Deletion of two genes –alpha Thalassemia minor
- Beta chain hemoglobinopathies (Hgb S, C,E, D)

  Beta Thalassemia Major (impaired beta chain synthesis)

→Sickle Cell Disease : Hgb SS disease, Hgb S-C disease, Hgb S-beta

Thalassemias

Beta-thalassemia – impaired beta-chain production

Alpha-thalassemia – impaired alpha-chain production

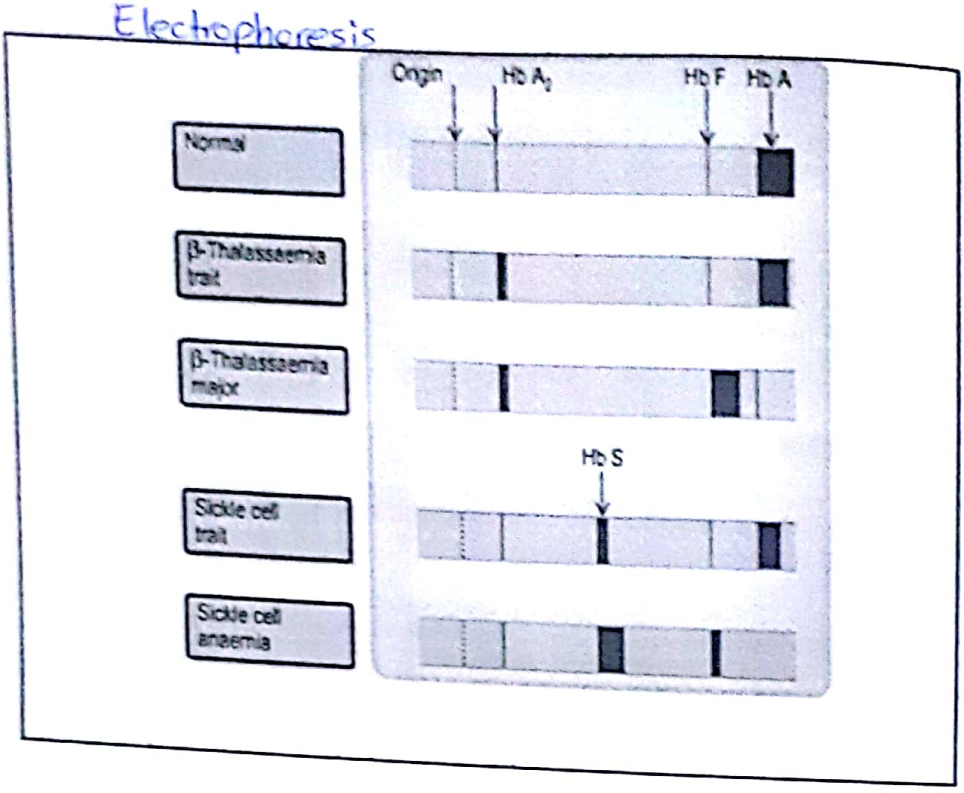
Genetic defects:

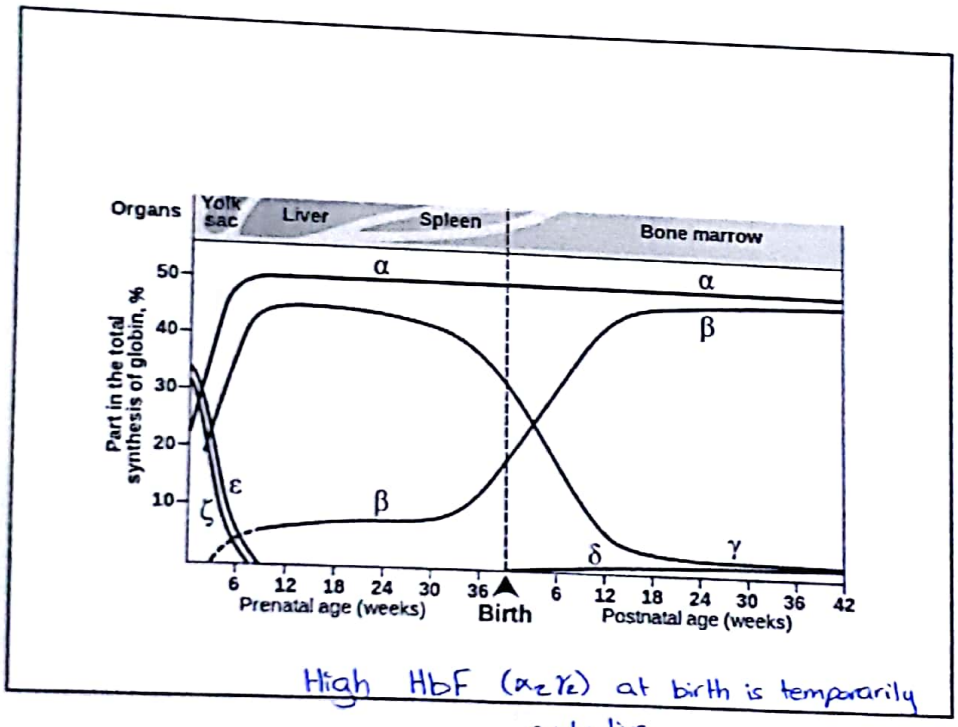
- **Two genes for Beta-globin synthesis (one on each chromosome 11) B-thalassemias are due to point mutations in one or both genes**
- **Four genes for a- globin synthesis (two on each chromosome 16) Most a-thalassemias are due to deletion of one or more a-genes**

- globin Chains:α、β、δ、γ、ε、ζ
- α-type chains: α, ζ ----141 amino acids
  β-type chains: β、δ、ε、γ ($^{G}\gamma$、$^{A}\gamma$) -----146 amino acids

Adult	Hb A	$\alpha_2\beta_2$	97 ~ 98%
	Hb A_2	$\alpha_2\delta_2$	2 ~ 3%
	Hb F	$\alpha_2\gamma_2$	< 1%
Fetal	Hb F	$\alpha_2\gamma_2$	
Embryonic (12 weeks)	Hb Gower I	$\zeta_2\varepsilon_2$	
	Hb Gower II	$\alpha_2\varepsilon_2$	
	Hb Portland	$\zeta_2\gamma_2$	

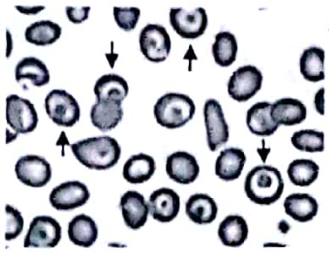
Electrophoresis





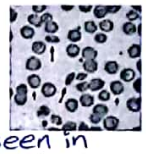
High HbF ($\alpha_2\gamma_2$) at birth is temporarily protective

Thalassemia



→ Mini Osce

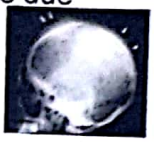
- Hypochromic, microcytic anemia
- Reticulocytosis
- Leukopenia, thrombocytopenia
- Blood smear: target cells and nucleated cells, extreme anisocytosis, contracted red cells, polychromasia, punctate basophilia, circulating normoblasts
- HbF raised, HbA2 – increased
- Bone marrow: megaloblastic (due to folate depletion), erythroid hyperplasia



- Decreased osmotic fragility → Classically seen in spherocytosis
- High serum ferritin
- Raised bilirubin
- Evidence of liver dysfunction (late, as cirrhosis develops) → because of repeated blood transfussions → ↑ iron
- Endocrine abnormalities (diabetes, hypogonadism)

Clinical features

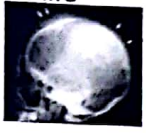
- Failure to thrive in early childhood
- Anemia
- Jaundice, usually slight, gallstones
- Hepatosplenomegaly, hypersplenism
- Abnormal facies: prominence of malar eminence, frontal bossing, depression of bridge of the nose, exposure of upper central teeth
- Skull radiographs showing hair-on-end appearance due to widening of diploid spaces

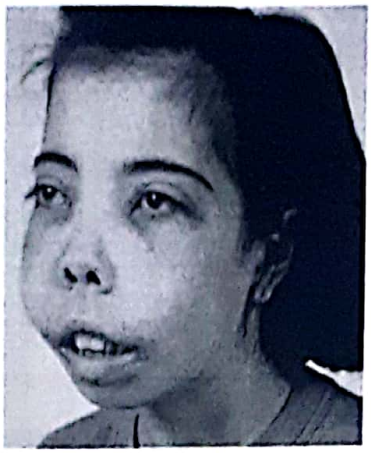


Clinical features

- Fractures due to marrow expansion and abnormal bone structure
- Osteoporosis
- Growth retardation, primary amenorrhea, delayed puberty in males
- Leg ulcers
- Skin bronzing
- If untreated, 80% of patients die in the first decade of life

→ They usually die due to cardiac causes due to iron overload from repeated transfussions





Chipmunk Appearance

Complications

Develop as a result of:

- Chronic anemia
- Chronic transfusion → hemosiderosis and hemochromatosis
- Poor compliance with chelation therapy

Complications

- Endocrine disturbances: growth retardation, pituitary failure with impaired gonadotropins, IDDM, adrenal insufficiency, hypothyroidism
- Liver failure, cirrhosis
- cardiac failure due to iron myocardial iron overload
- Bony deformities due to extramedullary hematopoiesis
- Osteoporosis

→ To differentiate b/w Thalassemia and Iron defficiency anemia

- Metzner index MCV over RBC count. $\frac{MCV}{RBC}$

It's not diagnostic, but it helps.

- If less than 13 Thalassemia carrier diagnosis more likely than iron deficiency anemia.

Management

- Transfusion therapy (when Hb falls <7g/dl)
- Hypertransfusion program used to maintain a pretransfusion Hb between 10.5 – 11.0 g/dl - corrects the anemia and suppresses ineffective erythropoiesis
- Chelation therapy to maintain serum ferritin close to 1000 ng/ml
- Splenectomy to reduce the transfusion requirements
- Bone marrow transplantation
- Gene therapy in future
- Increase HbF synthesis (trials): 5-Azacytidine, hydroxyurea, cytosine arabinoside, busulfan, butyric acid analogues

Hemolytic anemia

- Hemolysis is defined as the premature destruction of red blood cells(RBCs) (a shortened RBC life span).
- Anemia results when the rate of destruction exceeds the capacity of the marrow to produce RBCs.

Corpuscular defects → بتخص ال RBC نفسها

→Membrane defects

→Enzyme defects

→Hemoglobin defects

→Congenital dyserythropoietic anemias

Extracorpuscular defects → أشياء خارجية بتأثر على ال RBC

→Immune

→Nonimmune

Clinical features suggesting a hemolytic process

- Ethnic factors: incidence of sickle gene factor in the black population (8%), high incidence of thalassemia in people of Mediterranean ancestry, high incidence of glucose-6-phosphate dehydrogenase deficiency among Sephardic Jews
- Age factors: anemia and jaundice in an Rh+ infant born to a mother Rh- or a group A or group B infant born to a group 0 mother → ABO compatabilites and ABO subgroup compatabilities
- History of anemia, jaundice, or gallstones in family - Urine color
- Persistent or recurrent anemia associated with reticulocytosis
- Intermittent bouts or persistent indirect hyperbilirubinemia
- Splenomegaly
- Hemoglobinuria
- Presence of multiple gallstones

هاي الأشياء لما نسأل عنها بالهيستوري بتوجهنا لل Hemolysis

Corpuscular hemolytic anemias

Membrane defects

- Morphologic abnormalities: hereditary spherocytosis, elliptocytosis, stomatocytosis, acanthocytosis
- *Spectrin* is responsible for maintaining red cell shape, regulates the lateral mobility of integral membrane proteins and provides structural support for the lipid bilayer.

Hereditary spherocytosis

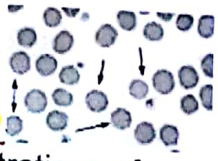
Genetics

- Autosomal-dominant inheritance (75%), non-family history –25%
- Most common in people of northern European heritage
- Incidence of 1 in 5000

Pathogenesis

- Membrane instability due to dysfunction or deficiency of a red cell skeletal protein: ankyrin (75-90%) and/or spectrin (50%)

- Anemia mild to moderate;
  in erythroblastopenic crisis Hb may drop to 2 – 3g/dl
- MCV usually decreased, MCHC raised → هاي بتبين على ال CBC
- Reticulocytosis
- Blood film – microspherocytes, hyperdense cells , polychromasia
- Coomb's test negative



- Increased red cell osmotic fragility
  spherocytes lyse in higher concentrations of saline than normal red cells, occasionally only demonstrated after incubation of blood sample at 37 C for 24 hours
- Reduced red cell survival
- Marrow- normoblastic hyperplasia, increased iron

Clinical features

- Anemia and jaundice- severity depends on rate of hemolysis, degree of compensation of anemia by reticulocytosis, and ability of liver to conjugate and excrete indirect hyperbilirubinemia
- Splenomegaly
- Presents in newborn (50% of cases) with hyperbilirubinemia, reticulocytosis, normoblastosis, spherocytosis, negative Coomb's test, and splenomegaly
- Presence before puberty in most patients
- Sometimes diagnosis made much later in life by chance

Complications

- Hemolytic crisis – with pronounced jaundice due to accelerated hemolysis (may be precipitated by infection)
- Erythroblastopenic crisis – dramatic fall in Hb level and reticulocyte count, usually associated with parvovirus B19 infection
- Folate deficiency caused by increased red cell turnover, may lead to superimposed megaloblastic anemia
- Gallstones in 50% of untreated patients, incidence increases with age
- Rarely hemochromatosis

Treatment

- Folic acid supplement 1mg/day
- Leukocyte-depleted packed red cell transfusion for severe erythroblastopenic crisis
- Splenectomy for moderate to severe cases

Enzyme defects

↱ Rare

- *Pyruvate Kinase deficiency:* defective red cell glycolysis
- Red cell rigid, deformed and metabolically and physically vulnerable
- Autosomal –recessive inheritance
- Nonspherocytic hemolytic anemia
- Variable severity: moderate severe anemia
- Neonatal jaundice, splenomegaly, heosiderosis
- Splenomegaly
- Gallstones, hemosiderosis, bone changes

Treatment: folic acid supplementation, transfusions, splenectomy

ما حكيت بكتبه (بس أول نقطة ذكرت)

Enzyme defects

Glucose-6-Phosphate Dehydrogenase deficiency

- Sex-linked recessive mode of inheritance
- Disease fully expressed in hemizygous males and homozygous females
- Most frequent among blacks and those of Mediterranean origin
- Associations : hemolysis may be produced by drugs, fava (broad) bean, infections

So basically anything that ↑ the oxidative load.

Clinical features

Drug induced hemolysis :

-Analgetics and antipyretics

-Antimalarian agents

-Sulfonamides

-Nitrofurans

-Sulfones

To be more specific…

- Drugs causing hemolysis in G6PD:
- Mnemonic is "PAINS"
  - Primiquine
  - Aspirin
  - Isoniazide
  - Nalidixic acid
  - Nitrofurontoin
  - Sulphamethaxole

Clinical features

- Favism:
  - Acute life-threating hemolysis often leading to acute renal failure caused by ingestion of fava beans
    Associated with mediterranean and Canton varieties

Neonatal jaundice

Chronic nonspherocytic anemia

Treatment:

Avoid drugs deleterious in G6PD, splenectomy

Sickle Cell Disease (SCD)

- Most common abnormal hemoglobin found in US (8% of the black population)
- at birth the incidence is 1 in 625

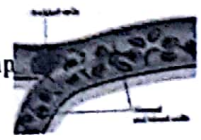
Genetics:

- transmitted as an incomplete autosomal-dominant trait
- Homozygotes (two abnormal genes) do not synthetize Hb A, red cell contain 90-100% Hb S
- Heterozygotes (one abnormal gene) have red cell containing 20-40% Hb S

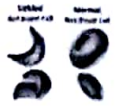
Pathophysiology:

A single amino acid substitution: valine for glutaminic acid (in the beta-polypeptide chain) ⟶

- Different electrophoretic mobility
- HbS is less soluble than HbA
- Sickle cells are prematurely destroyed causing a hemolytic anemia
- Sickle cells result in increased blood viscosity and imp flow and initiate thrombi



Clinical features



- Anemia- moderate to severe normochromic, norm
- Reticulocytosis
- Neutrophilia common
- Platelets often increased
- Blood smear: sickle cells, increased polychromasia, nucleated red cells, and target cells
- Erythrocyte sedimentation rate (ESR) – low
- Hemoglobin electrophoresis: HbS migrates slower than HbA, giving the diagnostic SS pattern

Crises

- Vaso-oclusive or symptomatic crisis:
  - hand – foot syndrome (dactylitis) – hand-foot swelling
  - bone crises - osteonecrosis
  - CNS crises -thrombosis/ bleeding
  - pulmonary crises -dyspnea, severe hypoxemia
  - priapism - hematuria,
- - intrahepatic vasoocclusive crisis
- Splenic sequestration crisis due to of pooling large amount of blood in the spleen) – splenomegaly, abdominal pain of sudden onset
- Erythroblastopenic crisis (cessation of red cell production)
- Hyperhemolytic crisis, unusual, in association with certain drugs or acute infections

Organ dysfunction

- Central nervous system (acute infarction of the brain) –motor disabilities, seizures, speech defects, deficit in IQ
- Cardiovascular system (cardiomegaly, myocardial dysfunction)
- Lungs (reduced PaO_2, reduced saturation, increased pulmonary shunting, acute chest syndrome)
- Kidneys (increased renal flow, increased GFR, enlargement of kidneys, hyposthenuria, proteinuria, nephrotic syndrome)
- Liver and biliary system (hepatomegaly, cholelithiasis)
- Bones (dactylisis, avascular necrosis)

Extracorpuscular hemolytic anemias

- Immune hemolytic anemia
  - Warm autoimmune hemolytic anemia - responsible antibodies IgG class
  - Cold autoimmune hemolytic anemia –IgM antibodies are cold agglutinins, and cold hemagglutinin disease,
    cold hemagglutinin disease usually occurs during *Mycoplasma pneumoniae* infection
- Nonimmune hemolytic anemia
  - Microangiopathic hemolytic anemia caused by renal, cardiac, liver disease, infections. Like hemolytic uremic syndrome...
    (HUS)

- Thanks you!!!!!!