433 Teams

MEDICINE

2 | ANEMIA

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Objectives:

1. Describe the Anemia
2.How to investigate Anemia
3.Describe the types of Anemia
4.Describe the types of Anemia

Overview:

1- Anemia is defined as a reduction in Hct or Hb concentration.

2. When red cell mass (as measured by Hb or less precisely by Hct) decreases, several compensatory mechanisms maintain oxygen delivery to the tissues.

These mechanisms include:

- Increased cardiac output (heart rate and stroke volume)
- Increased extraction ratio
- Rightward shift of the oxyhemoglobin curve (increased 2,3-diphosphoglycerate[2,3-DPG])
- Expansion of plasma volume.

Anemia develops rapidly, symptoms are more likely to be present, because there is little time for compensatory mechanisms.

Clinical features

1. A variety of nonspecific complaints—headache, fatigue, poor concentration,diarrhea, nausea, vague abdominal discomfort
2. Pallor—best noted in the conjunctiva
3. Hypotension and tachycardia
4. Signs of the underlying cause—jaundice if hemolytic anemia, blood in stool if GIbleeding.

Diagnosis

1. Hemoglobin and Hematocrit
   a. Formula for converting Hemoglobin to Hematocrit:

Hemoglobin level∗ 3 = Hematocrit

(So we can predict that 1 unit of packed RBCs[PRBCs] increases Hb level by 1 point, and Hct by 3 points)

Packed cell volume (PCV) or haematocrit	
Male	0.40–0.54
Female	0.37–0.47
Haemoglobin	
Male	13–18 g/dL
Female	11.5–16.5 g/dL

b. If the patient has good cardiac function and intravascular volume is adequate, low Hb and Hct levels are tolerated—even an Hb of 7 or 8 provides sufficientoxygen-carrying capacity for most patients. But anemia is not tolerated aswell in patients with impaired cardiac function .

2. Reticulocyte index

a. The reticulocyte count is an important initial test in evaluating anemia becauseit indicates whether effective erythropoiesis is occurring in the bone marrow or not.

b. A reticulocyte index >2% implies excessive RBC destruction or blood loss.

Thebone marrow is responding to increased RBC requirements.

c. A reticulocyte index <2% implies inadequate RBC production by the bone marrow.(bone marrow is not functioning well)

3. Blood smear and RBC indices (especially mean corpuscular volume [MCV]),
   a. Anisocytosis: Variation in size between cells
   b. Poikilocytosis: Variation in shape between cells

Treatment :

If anemia is severe, it is treated with packed red blood cell.

Q/ at what hematocrit do we transfuse patient?

1- when patient is symptomatic.

2- if hematocrit is very low in elderly or one with heart disease.

The types of Anemia

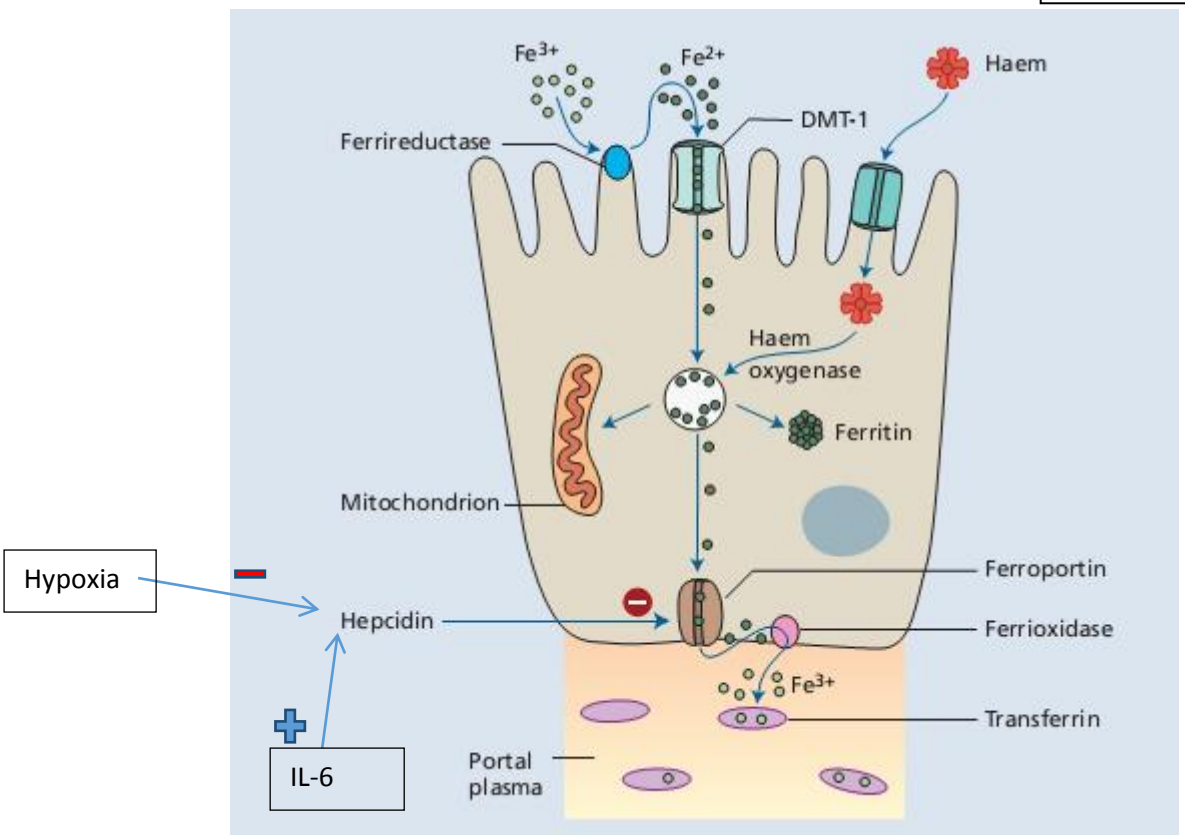
1-Microcytic Anemias(MCV< 80)"Mean cell volume"

- **Iron Deficiency Anemia**

Because Iron stops RBCs deviation, therefore decreased Iron leads to MICROCYTIC anemia

A. Background

- Most common cause of anemia worldwide



From the illustration above, it is important to remember the following starting from the top:

- Iron is absorbed in the Ferrous form (Fe^{2+})
- Inside the enterocyte Iron is either:
  - Stored as Ferritin
  - Released into the plasma
- Iron is released in the Ferric form (Fe^{3+})
- Iron release is inhibited by Hepcidin which binds to ferroportin.
- IL-6 (inflammatory) enhance Hepcidin function.
- Iron is transported in the plasma through Transferrin.

- Factors that Increase and Reduce Iron Absorption:

Table 3.2 Iron absorption.

Factors favouring absorption	Factors reducing absorption
Haem iron	Inorganic iron
Ferrous form (Fe^{2+})	Ferric form (Fe^{3+})
Acids (HCl, vitamin C)	Alkalis – antacids, pancreatic secretions
Solubilizing agents (e.g. sugars, amino acids)	Precipitating agents – phytates, phosphates, tea
Reduced serum hepcidin, e.g. iron deficiency	Increased serum hepcidin, e.g. iron excess
Ineffective erythropoiesis	Decreased erythropoiesis
Pregnancy	Inflammation
Hereditary haemochromatosis	
Increased expression of DMT-1 in duodenal enterocytes	Decreased expression of DMT-1 in duodenal enterocytes

B. Causes:

a. Chronic blood loss

- Most common cause of iron deficiency anemia in adults
- Menstrual blood loss is the most common source. **In the absence of menstrualbleeding, GI blood loss is most likely.**

b. Dietary deficiency/increased iron requirements—primarily seen in these threeage groups:

- **Infants and toddlers**—Occurs especially if the diet is predominantly humanmilk (low in iron). Children in this age group also have an increased requiremenfor iron because of accelerated growth. It is most common between6 months and 3 years of age.
- **Adolescents**—Rapid growth increases iron requirements. Adolescent womenare particularly at risk due to loss of menstrual blood.
- **Pregnant women**—Pregnancy increases iron requirements.

c.Erythropoietin Therapy

C. Clinical features

1. Pallor
2. Fatigue, generalized weakness
3. Dyspnea on exertion
4. Orthostatic lightheadedness
5. Brittle nails
6. Spoon-shaped nails (koilonychia)
7. Atrophy of the papillae of the tongue
8. Angular stomatitis
9. Brittle hair
10. A syndrome of dysphagia and glossitis

D. Diagnosis

1. Laboratory tests

a. Decreased serum ferritin—most reliable test available

b. Increased TIBC/transferrin level.

c. increased red cell distribution of width (RDW)

d. Microcytic, hypochromic RBCs on peripheral smear

2. Bone marrow biopsy—the gold standard, but rarely performed. Indicated if laboratory evidence of iron deficiency anemia is present and no source ofbloodloss is found.

3. If GI bleeding is suspected—colonoscopy. Colon cancer is acommon cause of GI bleeding in the elderly.

peripheral smear is not useful for microcytic anemia because the cells will be hypochromic

E. Treatment

1. Oral iron replacement (ferrous sulfate)

a. A trial should be given to a menstruating woman.

b. Side effects include constipation, nausea, and dyspepsia.

2. Parenteral iron replacement

a. Iron dextran can be administered IV or IM.

b. This is rarely necessary because most patients respond to oral iron therapy.

3. Blood transfusion is **not** recommended unless anemia is severe or the patient hascardiopulmonary disease.

- **Thalassemias:**

A. General characteristics

Inherited disorders characterized by inadequate production of either the α- or β-globin chain of hemoglobin.

1. β-thalassemias

a. β-chain production is deficient, and the synthesis of α-chains is unaffected.

b. Excess α-chains bind to and damage the RBC membrane.

c. It is most often found in people of Mediterranean, Middle Eastern, and Indian ancestry.

d.Severity varies with different mutations.

Diagnosis:

• Hemoglobin electrophoresis—**Hb F and Hb A2 are elevated.**
(most accurate test)

Treatment:

Frequent PRBC transfusions are required to sustain life.

2. a-thalassemias

a. There is a decrease in α-chains, which are a component of all types ofhemoglobins.

b. The β-globin chains form tetramers, which are abnormal hemoglobins.

c. The severity depends on the number of gene loci that are deleted/mutated—itranges from an asymptomatic carrier state to prenatal death.

Diagnosis:genetic studies is the most accurate test

- **Sideroblastic Anemia:**

the only type on microcytic anemia has high iron circulating.

• Caused by abnormality in RBC iron metabolism

• Hereditary or acquired—Acquired causes include drugs (chloramphenicol, INH,alcohol), exposure to lead, collagen vascular disease, and neoplastic disease(myelodysplastic syndromes).

•diagnosis :

a- laboratory: Increased serum iron and ferritin, normal TIBC, Transferrin saturationis normal or elevated, which distinguishes it from iron deficiency.

b- Prussian blue staining is the most accurate test

• Treatment:

Remove offending agents. Consider pyridoxine.

#Iron Study :

unique findings on iron studies are the best initial test on Microcytic anemia

Unique Features and Diagnoses of Iron Studies	
Unique feature	**Diagnosis**
Low ferritin	Iron deficiency
High iron	Sideroblastic anemia
Normal iron studies	Thalassemia

How to Answer "What Is the Most Likely Diagnosis?" for Anemia	
Feature in the history	**What is the most likely diagnosis?**
Blood loss (GI bleeding)	Iron deficiency
Menstruation	Iron deficiency
Cancer or chronic infection	Chronic disease
Rheumatoid arthritis	Chronic disease
Alcoholic	Sideroblastic
Asymptomatic	Thalassemia

Table 8.3 Microcytic anaemia: the differential diagnosis

	Iron deficiency	Anaemia of chronic disease	Thalassaemia trait (α or β)	Sideroblastic anaemia
MCV	Reduced	Low normal or normal	Very low for degree of anaemia	Low in inherited type but often raised in acquired type
Serum iron	Reduced	Reduced	Normal	Raised
Serum TIBC	Raised	Reduced	Normal	Normal
Serum ferritin	Reduced	Normal or raised	Normal	Raised
Serum soluble transfer receptors	Increased	Normal	Normal or raised	Normal or raised
Iron in marrow	Absent	Present	Present	Present
Iron in erythroblasts	Absent	Absent or reduced	Present	Ring forms

TIBC, total iron binding capacity.

2- Normocytic Anemias (MCV 80-96):

- Anemia of Chronic Disease

• Occurs in the setting of chronic infection (e.g., tuberculosis) cancer (e.g., lung, breast, Hodgkin's disease), inflammation (rheumatoid arthritis, systemiclupus erythematosus [SLE]), or trauma. The release of inflammatory cytokineshas an enhancing effect on **hepcidin** which in turn has a suppressive effect on erythropoiesis.

• It may be difficult to differentiate from iron deficiency anemia.

•Laboratory findings:

Low serum iron, low TIBC, and low serum transferrin level. Serum ferritin levels are increased.

•The anemia is usually normocytic and normochromic, but may **be microcytic andhypochromic as well.**

• No specific treatment is necessary other than treatment of the underlying process.

Do not give iron. The anemia is usually mild and well-tolerated.

- Aplastic Anemia:

A. General characteristics:

1- Bone marrow failure leading to **pancytopenia** (anemia, neutropenia,thrombocytopenia) , Causes :

a. Idiopathic—majority of cases
b. Radiation exposure
c. Medications
d. Viral infection
e. Chemicals

B. Clinical features:

1. Symptoms of anemia—fatigue, dyspnea
2. Signs and symptoms of thrombocytopenia (e.g., petechiae, easy bruising)
3. Increased incidence of infections (due to neutropenia)
4. Can transform into acute leukemia

C. Diagnosis

1. Normocytic, normochromic anemia
2. Perform a bone marrow biopsy thatwill reveals hypocellularmarrow and the absence of progenitors of all three hematopoietic cell lines.

D. Treatment

1. Bone marrow transplantation
2. Transfusion of PRBCs and platelets, if necessary (use judiciously)
3. Treat any known underlying causes.

3-Macrocytic Anemias *(MCV >100):*

- **Vitamin B12 Deficiency:**

A. Causes (almost all cases are due to impaired absorption)

1. Pernicious anemia (lack of intrinsic factor)
2. Gastrectomy
3. Poor diet, alcoholism
4. Crohn's disease, ileal resection

5- pancreatic insufficiency.

Pernicious anemia: is an autoimmune disorder, lacking of inadequate production of intrinsic factors which leads to decreased Vit B12 absorption in the terminal ileum

B . Clinical features

1. Anemia
2. Sore tongue (stomatitis and glossitis)
3. Neuropathy—can distinguish between vitamin B12 deficiency and folate deficiency.

C . Diagnosis

1. Peripheral blood smear
a. Megaloblastic anemia—macrocytic RBCs
b. Hypersegmented neutrophils (distinguish it from alcoholic anemia)
2. Serum vitamin B12 level is low.
3. Serum methylmalonic acid and homocysteine levels is elevated.
4. Antibodies against intrinsic factor can help in the diagnosis of pernicious anemia.

D . Treatment: Parenteral therapy is preferred—cyanocobalamin (vitamin B12) IM once\month.

Folate Deficiency:

A . Causes

1. Inadequate dietary intake such as “tea and toast” (most common cause)
2. Alcoholism
3. drugs like (phenytoin, sulfate and oral antibiotics)
4. Increased demand
5. Pregnancy
6. Hemolysis

B . Clinical features

similar to those in vitamin B12 deficiency but without the neurologicsymptoms

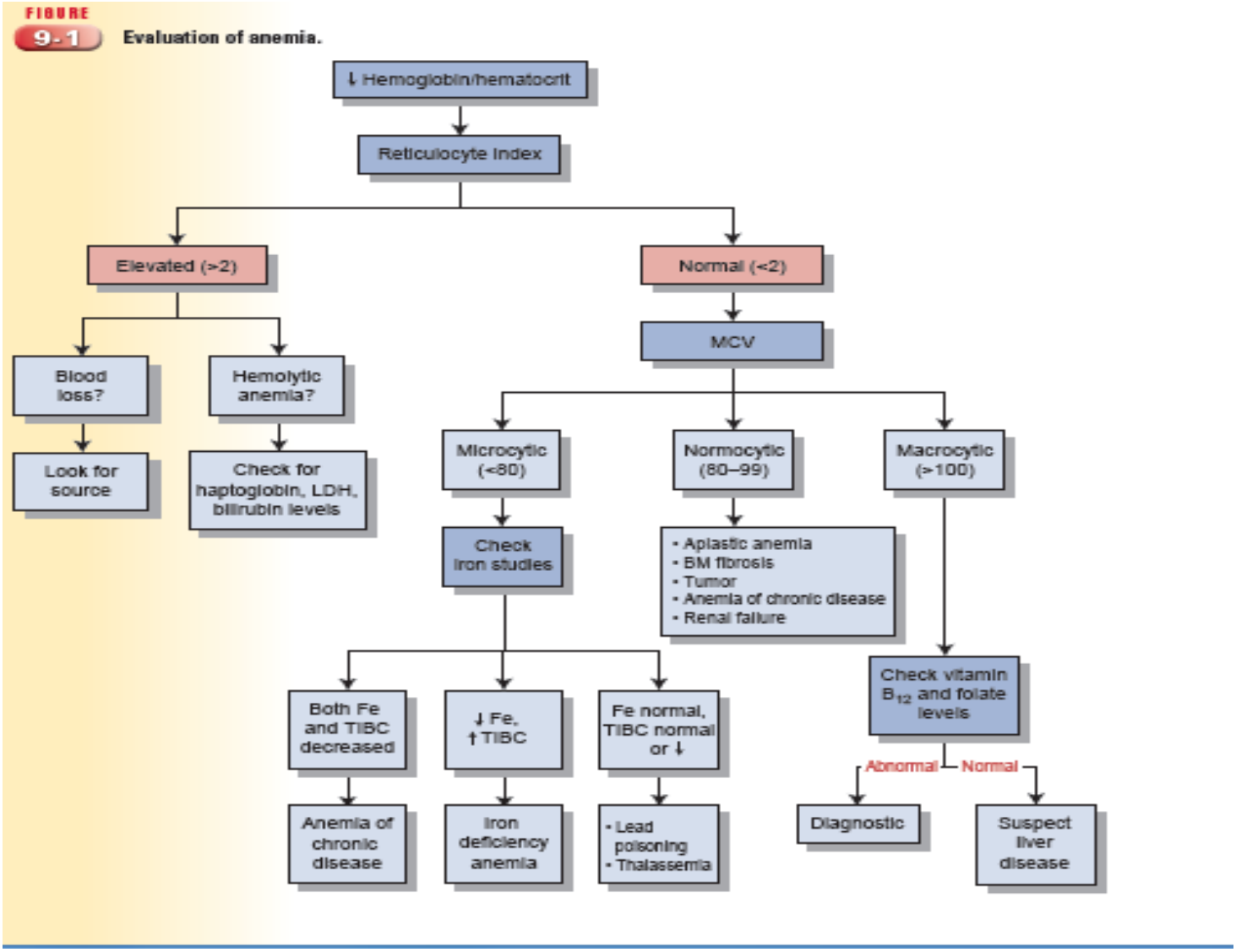
C . Treatment

Daily oral folic acid replacement

- Differences between Vit B12 and Folate deficiencies:

	VitB12 deficiency	Folate deficiency
Neurologic symptoms	+	-
Increased homocysteine	+	+
Increased methylmalonic acid	+	-

Diagnosing the cause of anemia (general approach) :



#Hemolytic Anemia:

A. General characteristics

1. Premature destruction of RBCsthat may be due to a variety of causes.
2. Bone marrow is normal and responds appropriatelyby increasing erythropoiesis,leading to an elevated reticulocyte count. However, if erythropoiesis cannot keepup with the destruction of RBCs, anemia results.
3. Hemolytic anemias can be classified based on mechanism, as follows:
    a. Hemolysis due to factors external to RBC defects—**most cases are acquired.**
    - Immune hemolysis.
    - Mechanical hemolysis (e.g., prosthetic heart valves, microangiopathichemolytic anemia).
    - Medications.

    b. Hemolysis due to intrinsic RBC defects—**most cases are inherited**
    - Hemoglobin abnormality:sickle cell anemia, hemoglobin C disease, thalassemias
    - Membrane defects: hereditary spherocytosis, paroxysmal nocturnalhemoglobinuria
    - Enzyme defects: glucose-6-phosphate dehydrogenase (G6PD) deficiency, pyruvate kinase deficiency
4. Hemolytic anemias can be classified based on the predominant site of hemolysis,as follows:
    a. Intravascular hemolysis—within the circulation.
    b. Extravascular hemolysis—within the reticuloendothelial system .

B. Clinical features

1. Signs and symptoms of anemia
2. Signs and symptoms of underlying disease (e.g., bone crises in sickle cell disease)
3. Jaundice
4. Dark urine color (due to hemoglobinuria, not bilirubin) may be present
5. Hepatosplenomegaly, cholelithiasis, lymphadenopathy (in chronic cases)

C. Diagnosis

1. Hb/Hct—level depends on degree of hemolysis and reticulocytosis
2. Elevated reticulocyte count due to increased RBC production
3. Peripheral smear
    a. Schistocytes suggest intravascular hemolysis ("trauma" or mechanical hemolysis)
    b. Spherocytes or helmet cells suggest extravascular hemolysis (depending on thecause).
    c. Sickled RBCs—sickle cell anemia
    d. Heinz bodies in G6PD deficiency
4. Haptoglobin levels—**low** in hemolytic anemias . (Haptoglobin bind to free hemoglobin in the plasma.)
5. LDH level is elevated—LDH is released when RBCs are destroyed.
6. Elevated indirect (unconjugated) bilirubin levels due to degradation of hemebecause RBCs are destroyed.
7. Direct Coombs test (detects antibody or complement on RBC membrane),positive in autoimmune hemolytic anemia

D. Treatment

1. Treat underlying cause.
2. Transfusion of PRBCs if severe anemia is present or patient is hemodynamicallycompromised.
3. Folate supplements

Sickle Cell Anemia

1. Causes:

a. **Autosomal recessive** disorder that results when the normal Hb A is replaced bythe mutant Hb S. Sickle cell disease is caused by inheritance of twoHb S genes(homozygous).

b. Hb S may be distinguished from Hb A by electrophoresis because of the substitutionof an uncharged valine for a negatively charged glutamic acid at the 6thposition of the β-chain.

c. Under reduced oxygen conditions (e.g., acidosis, hypoxia) the Hb molecules polymerize, causing theRBCs to sickle. Sickled RBCs obstruct small vessels, leading to ischemia.

B. Clinical features:

1. Severe, lifelong **hemolytic anemia**

   a. Jaundice, pallor

   b. Gallstone disease (very common)—pigmented gallstones.

   c. High-output heart

2. Findings secondary to vaso-occlusion

   a. **Painful crises** involving **bone**—This is themost common clinical manifestation.

   b. **Hand–foot syndrome** (dactylitis)

   - Painful swelling of dorsa of hands and feet seen in infancy and early childhood
   - Often the first manifestation of sickle cell disease

   c. **Acute chest syndrome**

   - Due to repeated episodes of pulmonary infarctions.
   - Associated with chest pain, respiratory distress, pulmonary infiltrates, and hypoxia

d. Repeated episodes of splenic infarctions—These lead to **autosplenectomy**.

e. Avascular necrosis of joints—most common in hip

f. Priapism

- Usually subsides spontaneously, after urine is passed, after light exercise, orafter a cold shower.

g. CVAs (stroke)—the result of cerebral thrombosis; primarily affects children

Diagnostic test :

- The **best initial** test is peripheral smear .
- The **most accurate** test is HB electrophoresis.

Treatment :

- Begin with oxygen,hydration ,analgesia.
- In case of fever or leukocytosis ,give antibiotics like ceftriaxone.
- Folic acid replacement on chronic basis.
- Pneumococcal vaccination because of splenectomy.
- **Hydroxyurea** prevent reccurent of sickle cell crises by increasing the non-mutated fetal hemoglobin

Case 1

You received a case in the emergency dept. 17 years old lady presented with fatigue ,chest pain, palpitation, dizziness. Examination: Pulse 115/min, RR 24/min , BP 116/76, NO LAN (no lymph adenopathy) , NO organomegally ,No jundice but Pallor.

1- What is the most single important history ?

all are right but the most one

A-Nutritional status.

B-Family history.

C-GI symptoms.

D-Medications.

E-Pregnency.

F-Menstrual abnormalities.

G-Chronic disease.

- ✓ She reported a history of menorrhagia
- ✓ All other items are negative

▶ Investigations:

- CBC : WBCs 8000 HGb 75gm MCV 50 MCH12 RDW 25%
- Plat 615000.

2-What is the single most important diagnostic test for this lady ?

A-Renal panel

B-Hepatic Pannel

C-Retic count

D-Coombs test

E-Ferritin level

G-Peripheral blood morphology

6-What is the further treatment for this lady ?

A-Oral iron tablets

B-IV iron injections

C-Blood transfusion

D-Observation

3-What you are expecting her iron indecies ?

A-low ferritin,High TIBC with low iron and TS

B-High ferritin ,Normal TIBC with low iron and TS

- C-High ferritin ,Low TIBC with low iron and TS

4-Would you do GI workup ? **no**

5- What is the best initial treatment for this lady ?

A-Oral iron tablets

B-IV iron injections

C-Blood transfusion (because this condition is serious)

D-Observation

Acute phase reactant , elevated in acute infections and stressful situation so useful to do CRP,ESR

7-Important further workup for this case ?

A-Coagulation profile (PT, PTT, INR) and pelvic US

B-Bone marrow biopsy

C-Tumor markers

D-Erytheropoiten level

Case 2

You receive a new referral in your clinic , 55 years old lady who discovered to have low Hb .

Examination: Pulse 75/min, RR 16/min , BP 116/76 , NO LAN, NO organomegally ,No jaundice.

1-What is the most single important history ?

A-Nutritional status

B-Family history

C-GI symptoms

D-Medications

E-Pregnency

F-Menstrual abnormalities

- She is known case of DM,HTN,HF,CKD
- All other items are negative

Investigations

- CBC : WBCs 8000 Hb:85gm MCV:87 MCH:30 RDW:12%
- Plat 180000
- Urea35 high, creatinine 650 high
- Coombs test -ve ? in this case we did coombs test

because autoimmune hemolytic anemia is one

of DDx of normocytic anemia

2- What is your provisional diagnosis?

A-IDA

B-Autoimmune hemolytic anemia

C-Anemia of CD

D-Aplastic anemia

E-Acute leukemia

3-What you are expecting her iron indecies ?

A-low ferritin,High TIBC with low iron and TS

B-High ferritin ,Normal TIBC with low iron and TS

C-High ferritin ,Low TIBC with low iron and TS

4-Would you do GI workup ? **Yes** because of her age

5- What is the best initial treatment for this lady ?

A-Oral iron tablets

B-IV iron injections

C-Blood transfusion

D-Observation

E-Treatment of underlying cause

F-Erytheropoietin injections

6-What is the further treatment for this lady "CKD" ?

A-Oral iron tablets

B-IV iron injections

C-Blood transfusion

D-Observation

F-Erytheropoietin injections

7-Important further workup for this case ?

A-Coagulation profile and pelvic US

B-Bone marrow biopsy

C-Tumor markers

D-Erytheropoiten level

MCQs

note: at the end there is an explanation for each question

1- A 55-year-old man is being evaluated for constipation. There is no history of prior gastrectomy or of upper GI symptoms. Hemoglobin is 10 g/dL, mean corpuscular volume (MCV) is 72 fL, serum iron is 4 µg/dL (normal 50-150 µg/dL), iron-binding capacity is 450 µg/dL (normal 250-370 µg/dL), saturation is 1% (normal 20%-45%), and ferritin is 10 µg/L (normal 15-400 µg/L). Which of the following is the best next step in the evaluation of this patient's anemia?

a. Red blood cell folate

b. Serum lead level

c. Colonoscopy

d. Bone marrow examination

e. Hemoglobin electrophoresis with A2 and F levels

2- A 50-year-old woman complains of pain and swelling in her proximal interphalangeal joints, both wrists, and both knees. She complains of morning stiffness. She had a hysterectomy 10 years ago. Physical examination shows swelling and thickening of the PIP joints. Hemoglobin is 10.3 g/dL, MCV is 80 fL, serum iron is 28 µg/dL, ironbinding capacity is 200 µg/dL (normal 250-370 µg/dL), and saturation is 14%. Which of the following is the most likely explanation for this woman's anemia?

a. Occult blood loss

b. Vitamin deficiency

c. Anemia of chronic disease

d. Sideroblastic anemia

e. Occult renal disease

3- A 35-year-old woman presents with several days of increasing fatigue and shortness of breath on exertion. She was recently diagnosed with Mycoplasma pneumoniae. Physical examination reveals BP 113/67, HR 114 beats/minute, and respiratory rate 20 breaths/minute. She appears icteric and in mild respiratory distress. Her hemoglobin is 9.0 g/dL and MCV is 110. Which of the following is the best next diagnostic test?

a. Serum protein electrophoresis

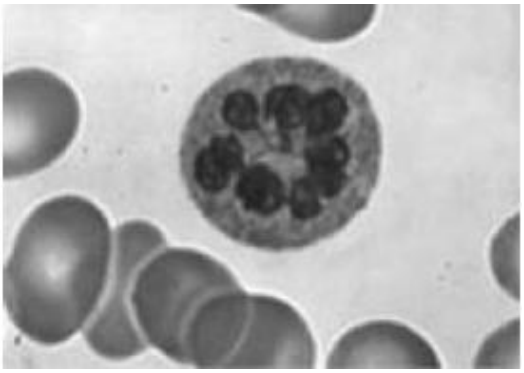
b. Flow cytometry

c. Peripheral blood smear

d. Glucose-6-PD level

e. Bone marrow biopsy

4- A 60-year-old man develops numbness of the feet. On physical examination he has lost proprioception in the lower extremities and is noticed to have a wide based gait with a positive Romberg sign. His past medical history includes hypertension, hypothyroidism, and previous gastrectomy for gastric cancer. The peripheral blood smear is shown below. What is the most likely cause of his symptoms?



a. Folic acid deficiency

b. Vitamin B12 deficiency

c. Vitamin K deficiency

d. Iron deficiency

e. Thiamine deficiency

5- A 30-year-old black man plans a trip to India and is advised to take prophylaxis for malaria. Three days after beginning treatment, he develops pallor, fatigue, and jaundice. Hematocrit is 30% (it had been 43%) and reticulocyte count is 7%. He stops taking the medication. The next step in treatment should consist of which of the following?

a. Splenectomy.

b. Administration of methylene blue.

c. Administration of vitamin E.

d. Exchange transfusions.

e. No additional treat0ment is required

Answers: 1- C 2-C 3- C 4- B 5- E

1- The patient has a microcytic anemia. A low serum iron, low ferritin, and high iron-binding capacity all suggest iron-deficiency anemia. Most iron-deficiency anemia is explained by blood loss. The patient's symptoms of constipation point to blood loss from the lower GI tract. Colonoscopy would be the highest-yield procedure. Barium enema misses 50% of polyps and a significant minority of colon cancers. Even patients without GI symptoms who have no obvious explanation (such as menstrual blood loss or multiple prior pregnancies in women) for their iron deficiency should be worked up for GI blood loss

2- Patients with chronic inflammatory or neoplastic disease often develop anemia of chronic disease. The inflammatory reaction, however decreases the iron-binding capacity (as opposed to iron-deficiency anemia, where the iron-binding capacity is elevated), so the saturation is usually between 10% and 20%. The anemia is rarely severe (Hb rarely < 8.5 g/dL). The hemoglobin and hematocrit will improve if the underlying process is treated.

3- Macrocytic anemia and indirect hyperbilirubinemia suggest hemolysis, which in this patient is likely due to immune-mediated IgM antibodies which may follow Mycoplasma infections. These antibodies are also called cold-reacting antibodies. Examination of the peripheral blood smear is the first step in evaluation of hemolytic anemia.

4- This is a classic presentation of a patient with vitamin B12 deficiency. This is commonly seen in patients with gastric resection and malabsorption. Patients with gastric resection lose intrinsic factor production from parietal cells. Loss of intrinsic factor leads to decreased absorption of vitamin B12.

Megaloblastic anemia with hypersegmented neutrophils (as seen on this patient's peripheral blood smear) can be found in both folic acid and vitamin B12 deficiency. Folic acid deficiency does not produce neurologic findings. B12 deficiency may cause a bilateral peripheral neuropathy or degeneration (demyelination) of the posterior and pyramidal tracts of the spinal cord and, less frequently, optic atrophy or cerebral symptoms. Iron deficiency anemia would show micro-cytic and hypochromic red blood cells on peripheral blood smear.

5- This patient has developed a hemolytic anemia secondary to an antimalarial drug. Toxins or drugs such as primaquine, sulfamethoxazole, and nitrofurantoin cause hemolysis in patients with G6PD deficiency, which occurs most commonly in African Americans. Since the G6PD gene is carried on the X chromosome, most affected patients are males. The drugs that cause hemolysis in G6PD deficiency are oxidizing agents. Oxidant stress on red blood cells is normally counteracted by reduced glutathione. NADPH (which is required to regenerate reduced glutathione after it has been oxidized) is produced by the hexose monophosphate shunt. G6PD is the first enzyme in this
metabolic pathway. If this enzyme is less active, the cell cannot replace reduced glutathione and succumbs
to oxidizing stress. Clinically this can range from mild to life-threatening hemolysis. In mild cases, no treatment is necessary; once the offending drug is eliminated, the hemolysis resolves.

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