OUTLINE

I) OVERVIEW

(A) DEFINITION

Anemia is defined as a low carrying capacity condition due to decrease in hemoglobin concentration.

→ The diagnostic criteria is based on low hemoglobin (Hb), low hematocrit (Hct), or decreased RBC count.

Table 1. Diagnostic criteria for anemia in males and females [LabPedia.net].

RBCs values	Male	Female
Hemoglobin	14-17 g/dL	12-15 g/dL
Hct % Hematocrit **PCV** Packed cell volume	40-52% Normally → 45%	36-48% 40%
MCV Mean cell volume	80-100 fL	80-100 fL
MCH Mean cell hemoglobin	27-34 pg	27-34 pg
MCHC % Mean cell hemoglobin concentration	33 %	30-37%
Reticulocytes count	0.5-1.5%	0.5-1.5%

Avg. Contentment of Hb per unit of RBC → = Hb/Hct x100%

(B) CLASSIFICATION

There are several types of classifications for anemia, but two of the widely accepted are based on:

→ The etiology
→ The morphology

(i) Classification based on etiology

1) Increased RBC's destruction (hemolysis).
2) Increased blood loss, which may be acute or chronic.
3) Defective maturation of erythropoiesis.

(ii) Morphological classification

1) Normochromic and normocytic anemia (normal MCV and MCHC).
2) Hypochromic and microcytic anemia (low MCV, MHC and MCHC).
3) Normochromic and macrocytic (high MCV, normal or increase MHC and normal MCHC).

→ MCV determines size of erythrocytes.
→ MHC and MCHC determine color. → on Blood Smear

Table 1-2. Types of anemia according to their morphology [LabPedia.net].

	Microcytic hypochromic	Normocytic normochromic	Macrocytic
MCV	<80 fl	80-100 fl	>100 fl
MCH	<27 pg	>27 pg	↑/ N
MCHC	<32% → low	N	N
E.g.	• Iron deficiency • Thalassemia • Sideroblastic anemia • Chronic diseases • Lead poisoning	• Hemolytic anemias • Acute blood loss • Bone marrow failure • Renal diseases • Chronic D.	• Vit B12 deficiency • Folic acid deficiency • Aplastic anemia

(C) COMMON CLINICAL PRESENTATION

→ **Main symptoms are due to cardiovascular system adaptation**
→ Increased stroke volume, tachycardia and changes in the Hb O2 dissociation curve → shift to Right! → Release ↓ Affinity of Hb to O_2
→ Weakness and fatigue.
→ Dizziness and headaches.
→ Pallor of face, tongue and conjunctives.
→ Shortness of breath.

(D) DIFFERENTIAL DIAGNOSIS STUDIES

(i) Red cell distribution width (RDW)

→ Variation of Red cell volume → Normally → 11.5 - 14.5 %

- Helps in the differential diagnosis of iron deficiency anemia and thalassemia.

(ii) Serum iron

- Helps differentiating between hemochromatosis and hemosiderosis. → Packed Ferritin

(iii) Transferrin

- Cand help in diagnosis of anemia of chronic disease and differential diagnose with iron deficiency anemia.

(iv) Transferrin saturation

- Cand help in diagnosis of anemia of chronic disease and differential diagnose with iron deficiency anemia.

(v) Ferritin → Apo-ferritin + Fe^{+2}

- It correlates with total body iron stores.

(vi) Total Iron binding capacity (TIBC)

- Always done along serum iron levels.

(vii) Peripheral blood smear → We see it on Microscope

- Informs abnormalities of the RBC shape, size and inclusions.

(viii) Bone marrow examination

- Helpful study when there are signs and symptoms of aplastic anemia.

(ix) Coombs test

- Very useful to differentiate between hereditary spherocytosis and autoimmune hemolytic anemia.

II) IRON DEFICIENCY ANEMA

(1) Etiology

- Excessive bleeding.
- Menorrhagia. → Heavy Menstruation
- Iron deficiency in diet (common in vegetarians).
- Increased demand by the body
  - Infancy, pregnancy, lactation.

→ One of the most common causes of anemia.

(2) Pathogenesis

- Absence of iron:
  - Protoporphyrin can't form heme
    - Dysfunctional hemoglobin.
      - Erythrocyte volume decrease:
        → Microcytic red blood cells.

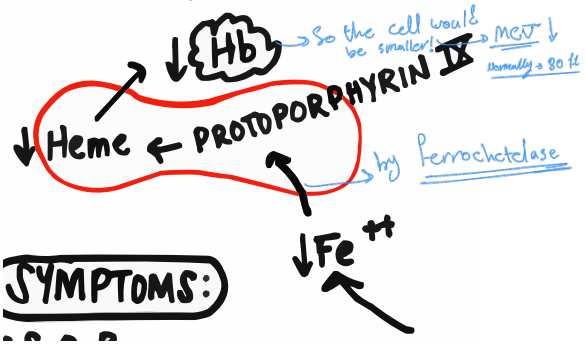


Figure 1. Pathogenesis of iron deficiency anemia.

(3) Specific symptoms

- Koilonychia: Spoon-shaped nails.
- Hair loss.
- Pica: Some patients may like to eat clay, ice and starch.
- Glossitis (smooth, red tongue).
- Stomatitis.
- Angular cheilitis.

→ Many times is asymptomatic.

⊗S.O.B
- Fatigue
- ↑ Work load on heart
- Tachycardia
- dizziness

(4) Diagnosis

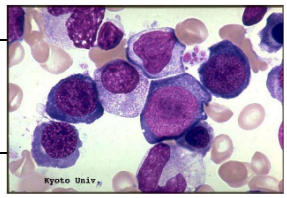
- History of patient.
- Physical examination.
- Blood test with complete blood count (CBC).
- Levels of serum ferritin, iron, TIBC and/or transferrin.

Table 1-3. Useful tests in the diagnosis of iron deficiency anemia [Hematología. La sangre y sus enfermedades].

RBC **Hg** **Hct**	↓↓↓↓ → Anemia
MCV	↓ Microcytic
MCH	↓ Hypochromic
MCHC	N
Reticulocytes	N / ↑
Leukocytes	N / ↓
Blood smear	Hypochromic and microcytic RBC, elliptocytes.
Platelets	N
Serum iron	↓
Ferritin	↓
TIBC	↑
RDW	↑ → Nutritional deficiency

III) PERNICIOUS ANEMIA

(1) Etiology



- Autoimmune.
- Deficiency in diet.

(2) Pathogenesis

(i) B12 deficiency

Autoimmune condition where the body creates **antibodies against Intrinsic Factor**.

- In order to be absorbed, **B12 binds to intrinsic** factor inside the GI tract.

→ Antibodies block B12 absorption
→ Decreased B12 within the blood stream
→ Red blood cells DNA **can't mature and condense → Macrocytic RBC**
→ Abnormal function of hemoglobin, risk of hemolysis inside the capillaries.

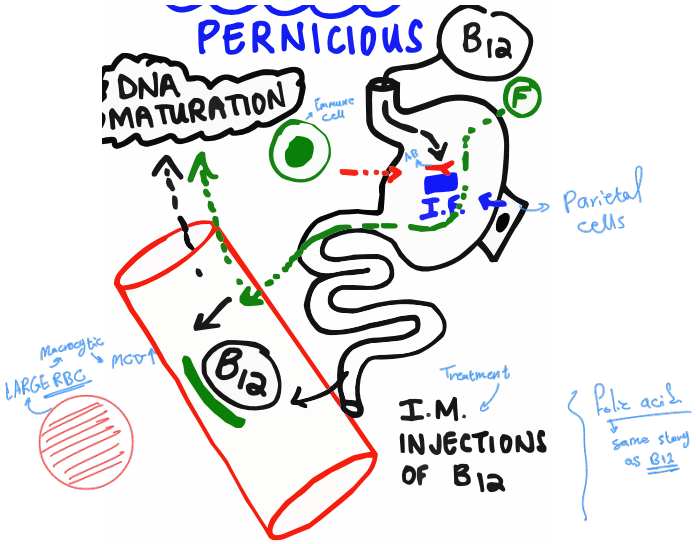


Figure 1-2. Pathogenesis of pernicious anemia.

(ii) Folic acid deficiency

Usually due to folic acid deficiency in diet.

- Folic acid is also needed for RBC to condense and mature

→ Its absence leads to macrocytic and unfunctional RBC.

(3) Diagnosis

Table 1-4. Useful tests in the diagnosis of pernicious anemia [Hematología. La sangre y sus enfermedades].

RBC **Hg** **Hct**	↓↓↓↓ → Anemia
MCV	↑ → Macrocytic
MCH	**N** → Normochromic
MCHC	N
Reticulocytes	N / ↑
Leukocytes	↓↓↓↓
Blood smear	Macrocyte RBC, teardrop cells
Platelets	↓↓↓↓

test B12, Folate!

→ Myeloid S.C Problem so?

(4) Treatment

→ **IM injections of B12**

IV) HEREDITARY SPHEROCYTOSIS

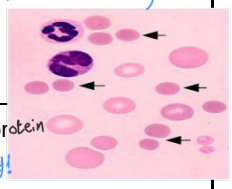
(1) Etiology

- Hereditary condition with mutations in membrane proteins and erythrocyte cytoskeleton.

→ Spectrin, ankrin, band 3 or protein 4.1

→ Most common is mutation of spectrin β, ankrin or band 3.

→ Autosomal dominant inheritance.



(2) Pathogenesis

- Abnormal erythrocyte membrane due to protein mutations.

→ Takes a spherical form

→ Poor ability to tolerate osmotic changes

→ Membrane stiffness

→ Cought in spleen → Splenomegaly → Hemolysis.

(3) Diagnosis

Table 1-5. Useful tests in the diagnosis of hereditary spherocytosis [Hematología. La sangre y sus enfermedades].

RBC Hg Hct	↓↓↓↓
MCV	↓
MCH	N / ↑
MCHC	↑↑
Reticulocytes	↑↑↑↑
Blood smear	Microspherocytes
Platelets	N / ↑
Coombs Test	**Negative**

V) G6PDH

Glucose 6-phosphate Dehydrogenase deficiency

(1) Etiology

Hereditary condition → X-linked

(2) Pathogenesis

- In order to obtain energy, RBC can **only** do glycolysis:

Glucose → Glucose 6-phosphate —*Glucose-6-phosphate dehydrogenase*→ 6-Phosoho-glucanolactone

NADP → NADPH

GSSG (oxidized glutathione) → **GSH (reduced glutathione)**

Effects of this process:

- Erythrocytes generate energy.
- The NADPH obtained thanks to the action of the G6PD enzyme, reduce glutathione allowing it to catch free radicals that are harmful for the RBC.

→ In the absence of G6PD there won't be NADPH production.

→ Glutathione won't get reduced.

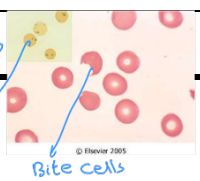
→ Free radicals won't get cached by glutathione.

→ Damage to RBC membrane

→ **Heinz bodies**

(3) Diagnosis

→ **Heinz bodies on blood smear.**



VI) SICKLE CELL ANEMIA

(1) Etiology

- Hereditary condition: Missense mutation → Glu → Val → 6th position on β chain of Hb

→ Production of abnormal Hb S

(2) Pathogenesis

- Sickle cell anemia occurs due to a substitution on the position 6 of the β chain of Hb A_1
  - Glutamine is substituted by valine
    - → Valine is a hydrophobic amino acid so it changes the structure of RBCs to sickle forms every time it polymerizes.
  - They only take a sickle form when they're not bound to O2 → every time they get oxygenated, RBCs go back to their normal structure.
    - → This process is called **sickling.**
  - On their sickle form they can undergo hemolysis or occlude blood vessels causing a **vaso-occlusive crisis**
    - Priapism: Vessels of the penis get clogged with sickle cells, causing a painful erection.
    - Splenomegaly due to the hemolysis
      - In some cases splenectomy will be needed.

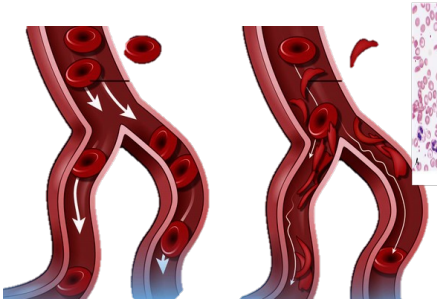


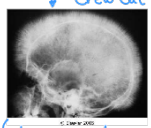
Figure 1-3. Red blood cells: Normal form and sickle form [MedlinePlus].

Nice to know

People with sickle cell anemia have been found to be resistant to malaria.

(3) Treatment

- Transfusions.
- Oxygen.
- Opioids depending on the severity of the pain.
- Fluids
- Hydroxy urea – helps producing fetal hemoglobin



VII) HEMORRAGIC ANEMIA

(1) Etiology

- Peptic ulcers due to H. pylori or aspirin
- Aneurisms
- Traumas
- Cancer
- Hemorrhoids

(2) Pathogenesis

- Excessive bleeding → ↓ RBC's

→ ↓ Oxygen → Anemia

(3) Treatment

→ It will depended on the severity of the anemia.

- Transfusions
- Fluids
- Surgery to stop bleeding

VIII) APLASTIC ANEMIA

(1) Etiology

Hematopoietic failure! / Pancytopenia

- Idiopathic in 65%
- Drugs (e.g. chloramphenicol, benzenes, streptomycin, etc.).
- Viruses (CMV, EBV).
- Radiation.

(2) Pathogenesis

- Destruction of the myeloid stem cells

→ decreased production of RBC's, WBC's and platelets.

→ **Pancytopenia**

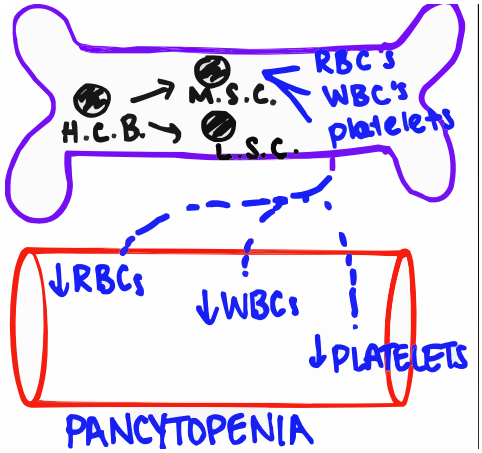


Figure 1-4. Aplastic anemia.

(3) Specific symptoms

- Current infections due to leucopenia.
- Petechiae (↑ bruising).
- Bleeding.

NO Splenomegaly!

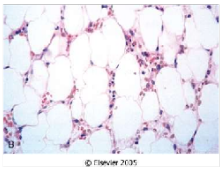
(4) Diagnosis

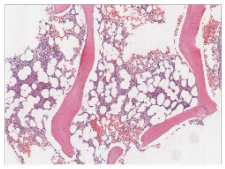
Table 1-6. Useful tests in the diagnosis of aplastic anemia [Hematología. La sangre y sus enfermedades].

RBC Hg Hct	↓↓↓↓
MCV	**N** → Normocytic but could be Macrocytic!
MCH	**N**
MCHC	N
Reticulocytes	N / ↑
Leukocytes	L: ↑ N: ↓
Platelets	↓↓↓↓
Bone marrow examination	Hypocellularity

(5) Treatment

- Bone marrow transplant.
- Transfusions.
- Respond well to immunosuppressives!





IX) THALASSEMIA

(1) Etiology

- Hereditary condition where there is an absence of a globin chain
  - If there is an α-chain missing → α-thalassemia.
  - If there is a β-chain missing → β-thalassemia. → Mutation in RNA splicing

→ More common within the Mediterranean ancestry.

Nice to know

Hemoglobin is formed with two α-chains and two β-chains.

(2) Pathogenesis

- Low functional hemoglobin due to its structure mutation
  - MCV >90 ft
    - Microcytic anemia.

(3) Diagnosis

Table 1-7 Differential diagnosis of thalassemia and iron deficiency anemia [Hematología. La sangre y sus enfermedades].

	Thalassemia	Iron deficiency
RDW	N	↑
Serum ferritin	N / ↑	↓
Serum iron	N	↓
Transferrin saturation	N	↑

(4) Treatment

- Transfusions.
- Iron supplements.
- Oxygen.
- Bone stem cell transplant.

Anemia of chronic Diseases

- Impaired Red cell production associated w/ chronic diseases that produce systemic inflammation.
- Most common Anemia among hospitilized pt.
- ↓Hb and Hct
- Could be ↔ hypochromic microcytic / normochromic normocytic
- ↑↑ ferritin
- ↓↓ TIBC

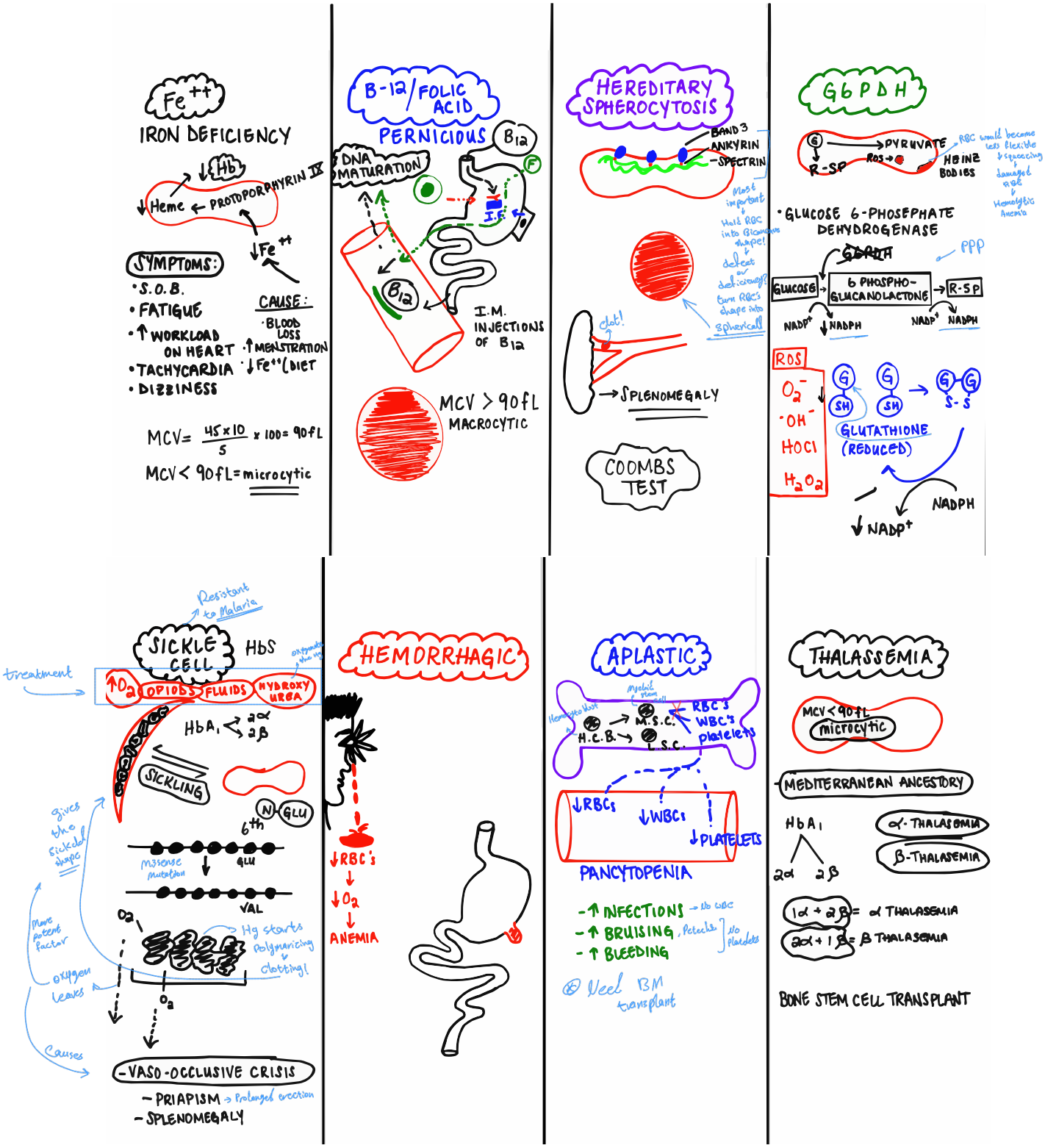


Figure 5. Summary of types of anemias.

XI) REVIEW QUESTIONS

1) A 31 year old woman is presented with history of fatigue, dizziness and headaches since three months ago.

A blood test was performed and results showed Hb 10 g/dL; Hct 40%; MCV 78 fl; MHC 25 pg and MCHC 30%.

According to laboratory findings, how would you morphologically classify this type of anemia?

a) Microcytic normochromic.
b) Macrocytic hypochromic.
c) Microcytic hypochromic.
d) Normochromic normocytic.

2) The following test comes to be very useful in the differential diagnosis of hereditary spherocytosis and autoimmune hemolytic anemia:

a) RDW
b) Peripheral blood smear
c) TIBC
d) Coombs test

3) G6PDH deficiency is a condition where glucose can't turn into 6-phospho-glucanolactone due to lacking of G6PDH, which leads damage to RBC's membranes.

What is exactly the mechanism of this damage?

a) NADP can't turn into NADPH so glutathione can't be oxidized, leading to increased free radicals.
b) NADP can't turn into NADPH so glutathione can't be reduced, leading to increased free radicals.
c) NADPH can't turn into NADP so glutathione can't be reduced, leading to increased free radicals.
d) NADPH can't turn into NADP so glutathione can't be oxidized, leading to increased free radicals.

4) If you're suspecting of pernicious anemia on your patient, which finding on a blood smear test would support your diagnosis?

a) Teardrop cells.
b) Elliptocytes.
c) Heinz bodies.
d) Microspherocytes.

5) The followings are specific symptoms of iron deficiency anemia EXCEPT for:

a) Pica.
b) Tachycardia.
c) Koilonychia.
d) Angular cheilitis.

CHECK YOUR ANSWERS

XII) REFRENCES

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