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Haematopoiesis and anemia

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CBC, Coagulation in ER

Definition of haematopoiesis:

- It is the process of blood cell formation.
- The processes that regulate haemopoiesis and the early stages of formation of red cells (erythropoiesis).
- Granulocytes and monocytes (myelopoiesis).
- Platelets (thrombopoiesis).

Site of haemopoiesis:

Table 1.1 Sites of haemopoiesis.	
Fetus	0–2 months (yolk sac) 2–7 months (liver, spleen) 5–9 months (bone marrow)
Infants	Bone marrow (practically all bones)
Adults	Vertebrae, ribs, sternum, skull, sacrum and pelvis, proximal ends of femur

Stages of haemopoiesis:

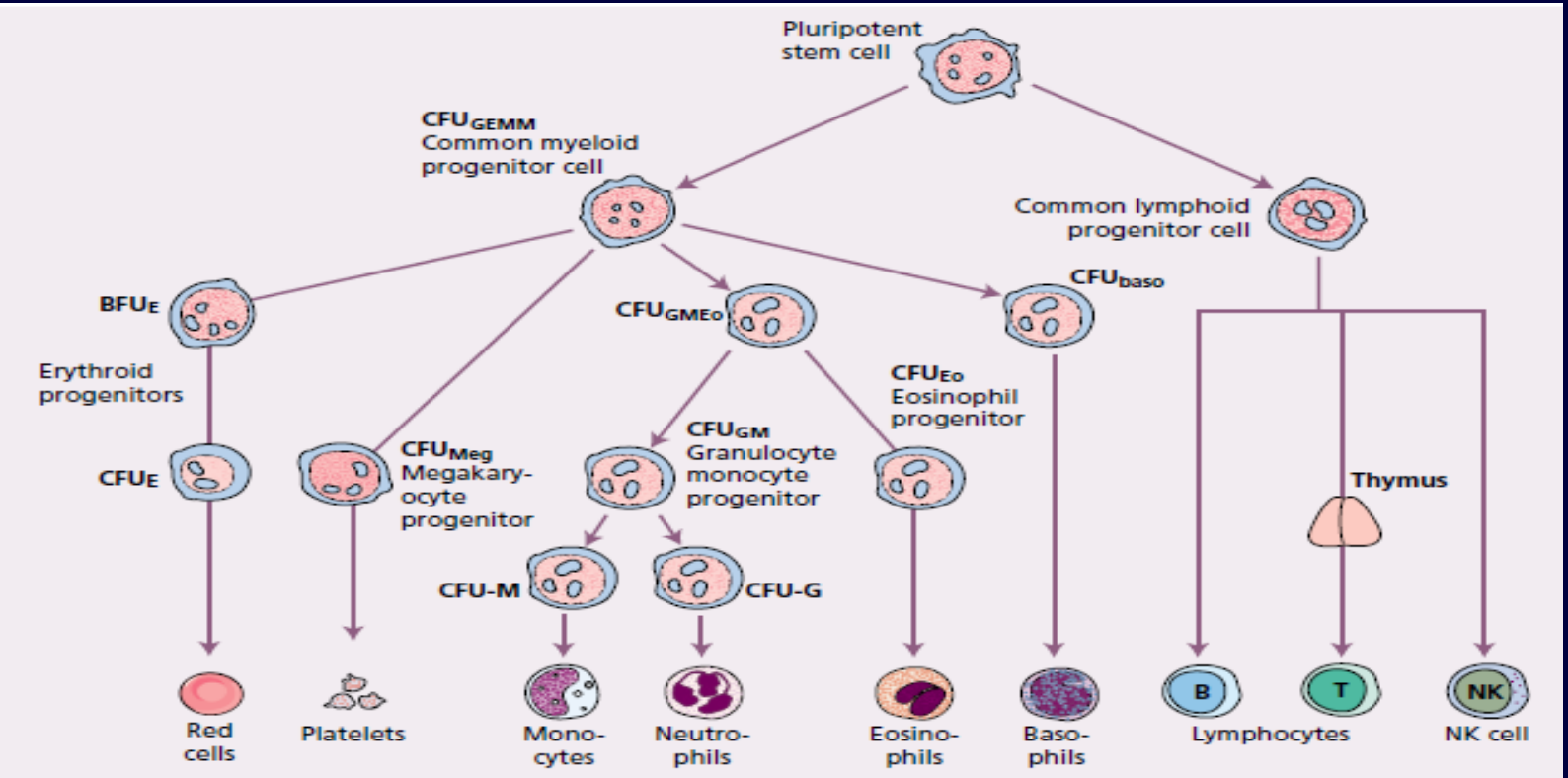


Figure 1.2 Diagrammatic representation of the bone marrow pluripotent stem cell and the cell lines that arise from it. Various progenitor cells can be identified by culture in semi-solid medium by the type of colony they form. It is possible that an erythroid/megakaryocytic progenitor may be formed before the common lymphoid progenitor diverges from the mixed granulocytic/monocyte/eosinophil myeloid progenitor. Baso, basophil; BFU, burst-forming unit; CFU, colony-forming unit; E, erythroid; Eo, eosinophil; GEMM, granulocyte, erythroid, monocyte and megakaryocyte; GM, granulocyte, monocyte; Meg, megakaryocyte; NK, natural killer.

Stem cell:

- Stem cells reside in the bone marrow in niches formed by stromal cells and circulate in the blood,
- The ***haemopoietic stem cell*** is rare, perhaps 1 in every 20 million nucleated cells in bone marrow.

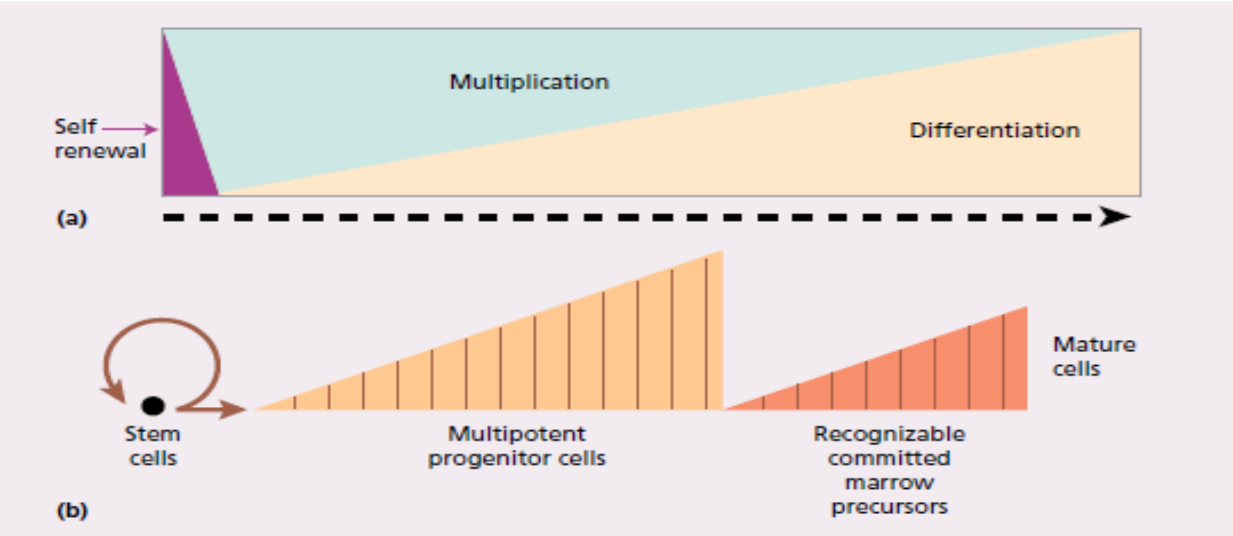


Figure 1.3 **(a)** Bone marrow cells are increasingly differentiated and lose the capacity for self-renewal as they mature. **(b)** A single stem cell gives rise, after multiple cell divisions (shown by vertical lines), to $>10^6$ mature cells.

Stem cell:

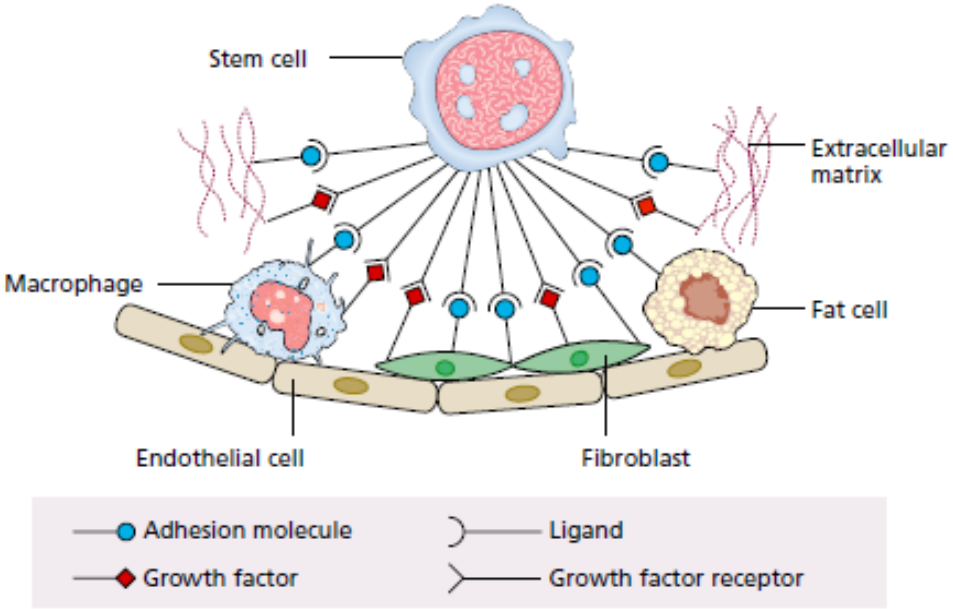


Figure 1.4 Haemopoiesis occurs in a suitable microenvironment ('niche') provided by a stromal matrix on which stem cells grow and divide. There are specific recognition and adhesion sites (see p. 13); extracellular glycoproteins and other compounds are involved in the binding.

Erythropoiesis:

- Erythropoiesis is the process by which hematopoietic stem cells divide, differentiate, and mature into enucleated RBCs.
- Erythropoietin (Epo) is the primary cytokine that controls erythropoiesis.
- Epo is produced primarily in the kidney (90%) and 10% in the liver and elsewhere.

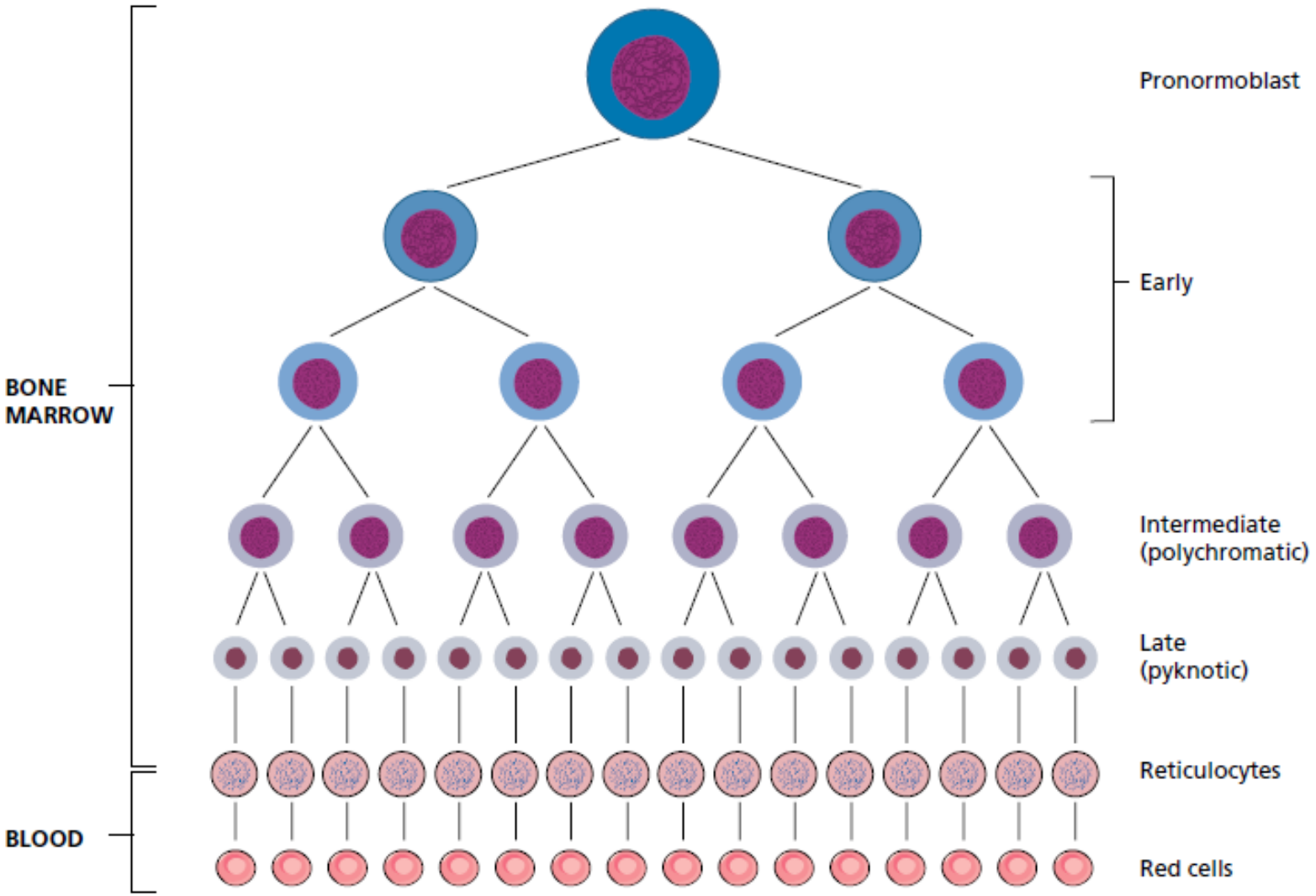
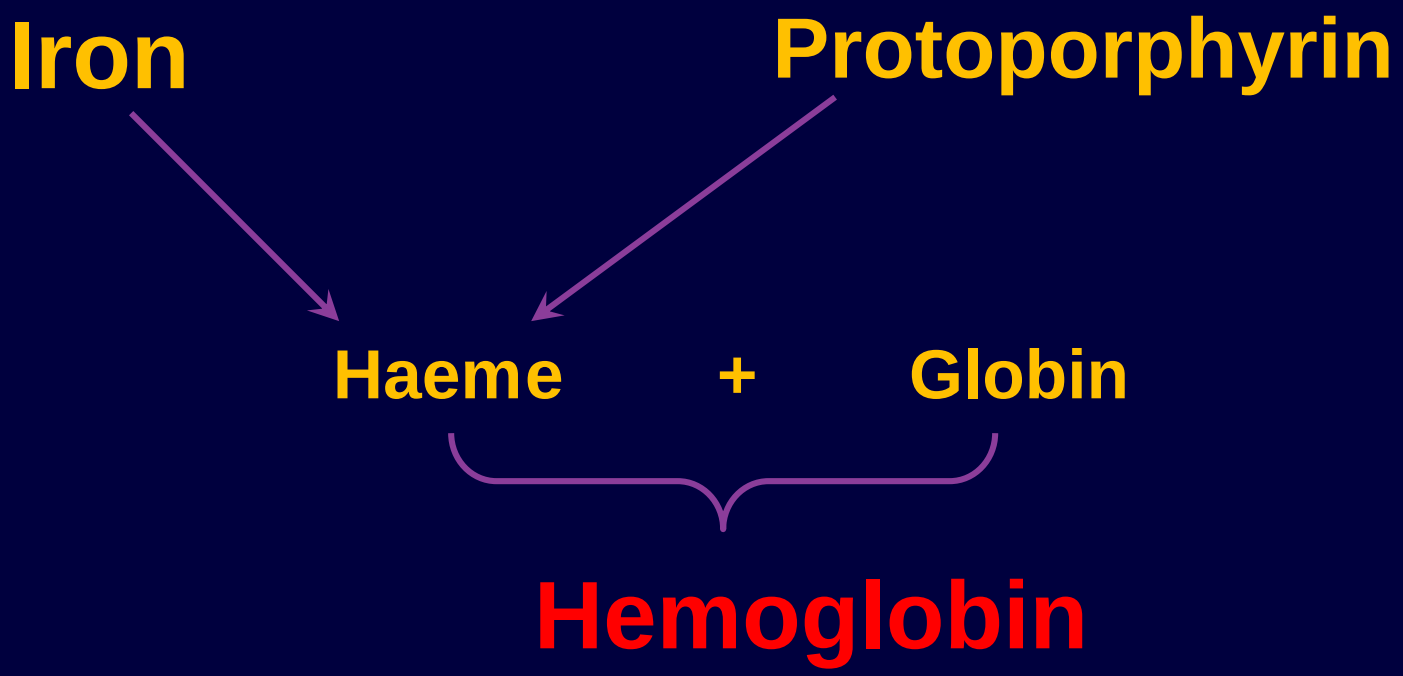


Figure 2.2 The amplification and maturation sequence in the development of mature red cells from the pronormoblast

Heme is a complex of ferrous iron and protoporphyrin



Anemia:

- Reduction in the concentration of circulating HB or oxygen carrying capacity of blood below the level for healthy person of the same age &sex in the same in environment.
- Anaemia is defined by the WHO as:
  - Hb < 12 g/dL in women and
  - Hb < 13 g/dL in men

- Iron deficiency is the most frequent cause of anaemia, closely followed by anaemia of chronic disease.

Normal adult red cell values:

	Male	Female
Haemoglobin(g/dl)	13.5 – 17.5	12.5- 15.5
PCV	40-52	36-48
Red cell count ($x10^{12}$ /l)	4.5-6.5	3.9-5.6
MCH (pg)	27-34	
MCV(fL)	80-95	
MCHC(g/dL)	30-35	
Reticulocyte count ($x10^{9}$ /L)	50-150	

Classification of anemia :

- Until recently classification was based on the red blood size (MCV).
- Now depend on the automated reticulocyte count, to assess RBC regeneration, :
  - Hypo-regenerative.
  - Regenerative anaemia.

Reticulocyte:

- Reticulocyte (%) = [Number of Reticulocytes / Number of total Red Blood Cells] X 100.

- Corrected reticulocyte count = [(reticulocyte percent × patient's hematocrit)/normal Hct] .
- If < 2 → Marrow is not responding to the degree of anemia.

I. Etiological classification:

Table 1: **Classification of anaemias**

Hyporegenerative	Regenerative
Aplastic anaemia	Haemolysis
Pure red cell aplasia	Immune
Myelodysplastic syndrome	Non-immune • Congenital: membrane, SS, thalassaemia, enzymopathies, unstable Hb • Acquired: PNH, drugs (Pb, Zn and Cu poisoning), microangiopathy, hypersplenism
Deficiency states • Iron • Vitamins	
Marrow infiltration/fibrosis	Haemorrhage (bleeding)
Inflammatory anaemia (anaemia of chronic disease)	
Erythropoietin underproduction	

II: Morphological classification of anaemia:

Microcytic (<80fl)	Normocytic (80-100)		Macrocytic(>100 fl)	
Iron deficiency A	RC:N	RC:low	meg	Non meg
Thalassemia	Haemolytic anamia.	A.A	Vit B12.	Liver disease
Sideroblastic A	Recent blood loss.	Chronic renal failure	Folic acid	H .anaemia
Naemia of chronic disease		Anaemia of chronic disease		MDS
Anaemia of lead poisoning		hypothyroidism		hypothyroidism
		Myelopthesic anaemia		

Clinical manifestations of anemia:

Depends on:

- Speed of onset.
- Severity of anemia.
- Age of patient.
- Underlying diseases especially CVS.

A) Symptoms:

1) CVS:

- Low COP symptoms.
- Exertional dyspnea & palpitation.
- Angina and intermittent claudication.
- Symptoms of heart failure in severe cases.

2) Neurological:

- Lack of concentration.
- Headache, tinnitus, blurring of vision.

3) Skeletal:

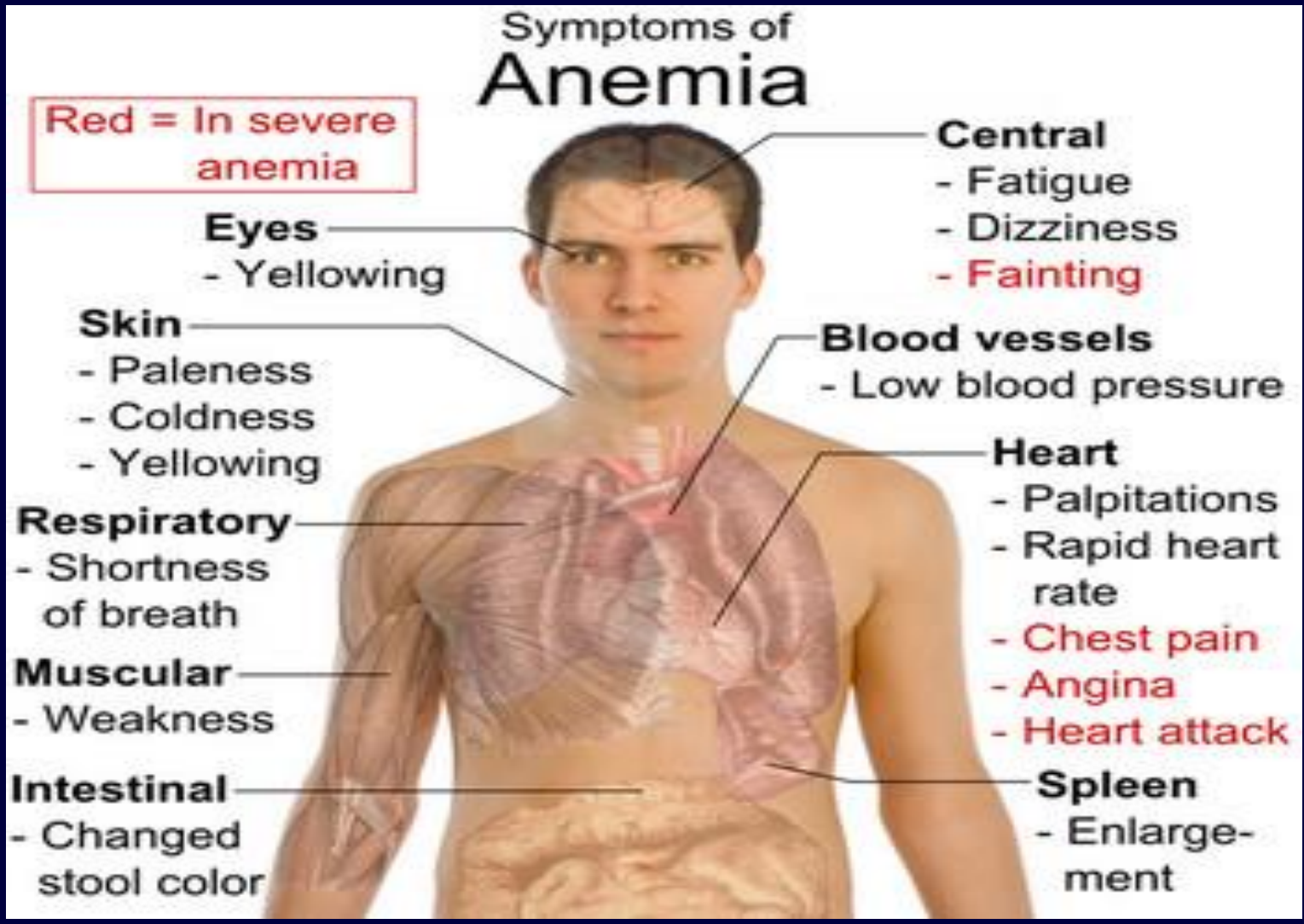
- Bone ache
- Fatigability.

4) Genital:

- Menstrual disturbance esp menorrhgia.
- ↓ Libido.

5) Renal:

- Polyuria.


Symptoms of
Anemia
Red = In severe anemia
Central
- Fatigue
- Dizziness
- Fainting
Eyes
- Yellowing
Skin
- Paleness
- Coldness
- Yellowing
Blood vessels
- Low blood pressure
Heart
- Palpitations
- Rapid heart rate
- Chest pain
- Angina
- Heart attack
Respiratory
- Shortness of breath
Muscular
- Weakness
Intestinal
- Changed stool color
Spleen
- Enlarge-ment

B) Signs:

1- Pallor: MM, nail bed, simian creas other causes of pallor …. (SBE, Rh fever, MI, Myxoedema).

2- CVS

- Tachycardia (hyperdynamic circulation).
- Hemic murmur: on aortic, soft midsystolic, no thrill.
- Collapsing pulse.
- Capillary pulsation.
- Congestive Ht failure

3- Oedema LL:

- ↑ capillary permeability.
- HF.

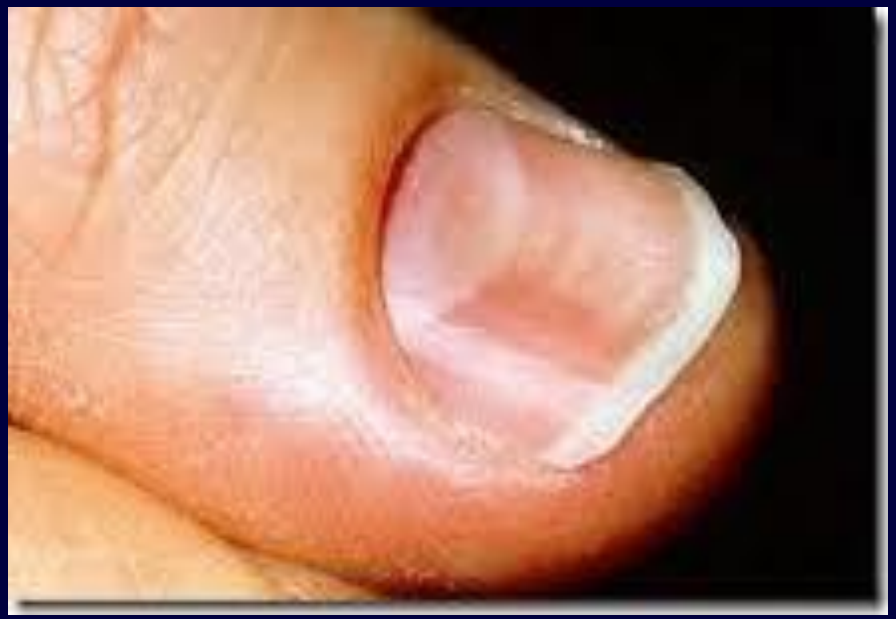
Specific signs according to cause:

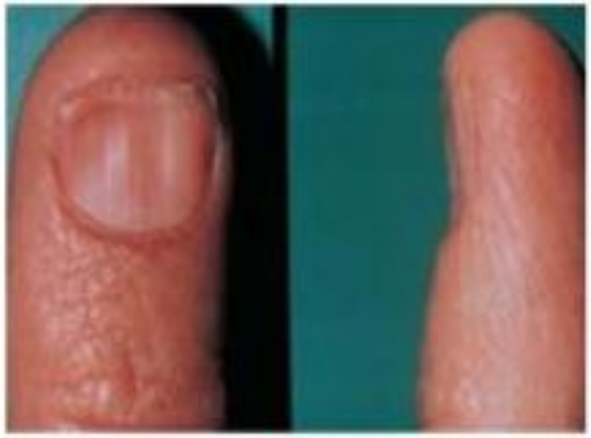
- Koilonychias (spoon nails) → Iron ↓
- Jaundice
  - Hemolytic
  - Megaloblastic
- Bone deformity & mongoloid facies → thalassemia
- Leg ulcer → sickle cell anemia.
- Purpura & infection → BM ↓ & infiltration.
- Beefy red tongue painful tongue → megaloblastic.
- Red glazed tongue → IDAand pernicious anemia.
- Pain & parasthesia → B12 ↓ (subacute combined degeneration).

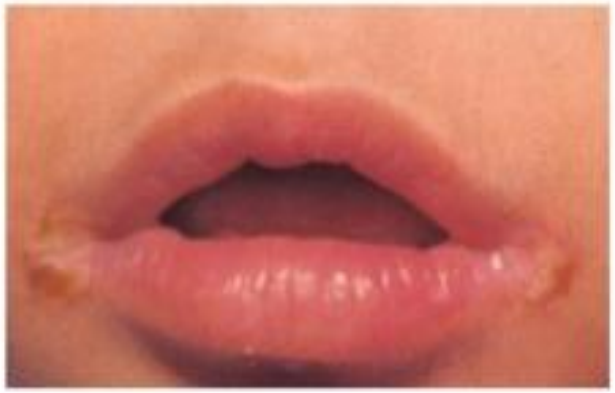
Signs of iron deficiency anemia

- Pallor

- Glossitis







Laboratory investigations

1) RBCs indices:

- Normocytic, microcytic, macrocytic

2) Reticulocytic count: (n 1-2%)

- ↑ : Hemolytic anemia, Hgic anemia, Anemia under treatment
- ↓ : Bone marrow ↓ or infiltration

3) WBCs & Platelets:

- Aplastic anemia
- Hypersplenism
- Myelofibrosis
- A leukemic leukemia
- BM infiltration (lymphoma, leukemia, carcinoma myelofibrosis)
- Megaloblastic anemia

4) Bone marrow ex:

- BMF
- Leukemia
- Infiltration
- Sideroblastic anemia.

Investigation according to morphology

I. Microcytic anemia:

A) Iron profile:

S. Iron (90 – 150 μg%)

S. ferrtin (20 – 250 ng)

TIBC (280 – 400 μg%)

In iron ↓ S. Iron & ferritin ↓

TIBC ↑

In Anemia of ch dse:

S. Iron ↓

TIBC ↓

S. ferretin N/↑

In thalassemia **S. iron, TIBC (N)**

May be ↑ S. iron & ferritin in hemochromatosis

In sideroblastic

S. Iron ↑ **S. ferritin ↑**

TIBC N **BM: ringed sideroblasts**

B) Hb electrophoresis:

In Thalassemia

II. Normocytic anemia:

- **Reticulocytes:**

  ↑ → **Hemolytic**

  → **Hgic**

  ↓ → **BM ↓**

- **BMA in Aplastic anemia:**

  ↓ cellularity and ↑ fatty spaces.

- **Investigations of hemolytic anemia:**

  ↑Serum bilirubin (indirect), ↓serum haptaglobin, reticulocytosis, BMA erythroid hyperplasia.

Investigations of hemolytic anemia:

Hereditary:

- HB electrophoresis: Hemoglobinopathies
- Sickling test for sickle anemia
- Osmotic fragility → spherocytosis
- Enzyme assay → GP6D

Acquired:

- Direct coomb's test → autoimmune hemolytic anemia
- Ham's test → PNH (hemolysis of RBCs at low PH serum).

III. Macrocytic:

MCV ↑ 95 fL

- **Exclude alcoholism & other causes of macrocytosis**
- **For megaloblastic anemia:**
  - Folic acid & B12 level
  - BMA: megaloblastic changes.
  - Schilling test: radioactive cobalt ^{57}Co absorption test
  - Gastric function test & gastric acidity
  - Therapeutic test: correction with B12 & folic acid.

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Don't go away?

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Case scenario

56 Y old male presented with pallor ,easy fatigability and CBC showed:

- **TLC: 5.6**
- **Hb: 8.7 gm/dl**
- **MCV: 66 fl**
- **MCH: 28 pg**
- **PLT: 515**

Q1: Other items needed in history?

- Loss of wt.
- Upper GIT symptoms: Appetite, heart burn,epigastric pain.
- Lower GIT symptoms: bleeding /rectum,piles, anal fissure, constipation and diarrhea.
- Dietition:

Findings: Loss of wt and appetite, Prolonged constipation for 2y

Q2: what is the first test to do?

S. Iron & ferritin

Findings: sferritin:8 ng/l

What is the expected Aetiolog?

Colonoscopy: huge coliflower mass in RT colon.

The hematopoietic stem cell is capable of :

- a-Replication
- b-Differentiation
- c-Replication and differentiation

- **The process of hematopoiesis under the control of:**
  1. **Growth hormone**
  2. **Hematopoietic growth factors**
  3. **Thyroid hormone**

Definition of anemia is:

1. Decrease hemoglobin percent below the normal for the age and the sex
2. Decrease red cell count only
3. Decrease the hematocrit value

Megaloblastic anaemia

1. Small erythrocyte
2. Due to vitamin B-12 deficiency
3. Presence of macrocytes
4. Caused by increase folate
5. Decrease in cell thickness

Which is the cause of microcytic, hypochromic anaemia

- Iron deficiency anaemia
- Lead poisoning
- Thalassaemia
- Pernicious anaemia
- Acute bleeding

- **Inherited or congenital forms of hemolytic anemia include all of the following except**

A. Red cell membrane abnormalities

B. Red cell enzyme abnormalities

C. Paroxysmal nocturnal hemoglobinuna

D. Hemoglobinopathies

Evans' syndrome refers to the combination of

A. Autoimmune hemolytic anemia and thrombotic thrombocytopenic purpura (TTP)

B. Autoimmune hemolytic anemia and idiopathic thrombocytopenic purpura (ITP)

C. Autoimmune hemolytic anemia and autoimmune neutropenia

D. TTP and ITP

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Thank you