Morphological Classification of Anemia

Anemia is strictly defined as a decrease in red blood cell (RBC) mass.

Causes of decrease
- Blood loss
- Increased destruction of RBCs (hemolysis)
- Decreased production of RBCs

I. Microcytic anemia

- Small RBCs, often hypochromic
- Low MCV (< 80 fL)

👉 Most common cause: Iron deficiency

A. Iron Deficiency Anemia

Key facts
- Most common nutritional deficiency worldwide
- Iron distribution:
- 80% in hemoglobin
- 20% in storage (ferritin & hemosiderin in liver, spleen, bone marrow, skeletal muscle)

Etiology of Iron Deficiency
- Chronic blood loss:
- GI bleeding (peptic ulcers, colon cancer, hemorrhoids)
- Female genital tract (menorrhagia, endometrial cancer) ♀
- Low intake / poor bioavailability (vegetarian diets)

- Increased demand:
- Pregnancy
- Infancy

- Malabsorption:
- Celiac disease
- Post-gastrectomy

Clinical Manifestations
- Fatigue
- Reduced ability to perform work
- Leg cramps on climbing stairs
- Cold intolerance
- Nail changes:
- Thinning
- Flattening
- Spoon-shaped (koilonychia)
- Pica

B. Anemia of chronic inflammation

Causes
- Chronic infections:
- Osteomyelitis
- Endocarditis
- Chronic immune diseases:
- Rheumatoid arthritis (RA)
- Neoplasms:
- Carcinoma
- Lymphoma

Pathogenesis
1. ↑ Hepcidin:
   - Blocks iron release (↓ ferroportin in macrophages & duodenum)
   - Caused by IL-6
2. ↓ Erythropoietin production by kidneys

II. Normocytic anemia

- Normal size RBCs (normocytic)
- Normal color (normochromic)

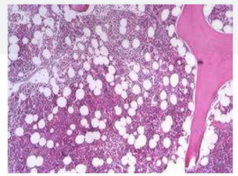
anemia with primary bone marrow involvement

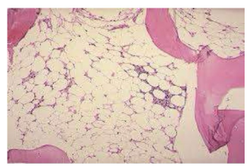
- Aplastic anemia
- Myelophthisic anemia.

Definition
- Bone marrow failure syndrome
- Peripheral pancytopenia
- Marrow hypoplasia

Cause
- Stem cell damage or marrow microenvironment defect
- 80% are acquired

Clinical Features
- Anemia
- Bleeding
- Fever / infections





anemia secondary to underlying disease.

Definition
- Bone marrow failure due to destruction of marrow cells and stroma

Mechanism
- Fibrosis or infiltration by:
- Non-hematopoietic cells
- Pathogens

👉 Leads to destruction of normal hematopoietic cells and supportive stroma

III. Macrocytic anemia

- RBCs larger than normal
- MCV > 100 fL

👉 Most common cause: Megaloblastic anemia

Non-Megaloblastic Macrocytic Anemia

Occurs without hypersegmented neutrophils

Causes
- Alcohol (RBC toxicity)
- Hereditary spherocytosis (↑ cell size يسبب volume regulation defect)
- Hypothyroidism
- Liver disease (lipid deposition in membrane)
- Reticulocytosis:
- Hemolysis
- Pregnancy
- Bone marrow disease

👉 Reticulocytes are larger than RBCs

Megaloblastic anemia

Definition
- Group of disorders with:
- Large cells
- Arrest in nuclear maturation

Pathophysiology
- Due to impaired DNA synthesis
- Also affects RNA & protein synthesis (less)

👉 Most affected cells:
- Blood cells
- Gastrointestinal cells

Causes
- Vitamin B12 deficiency
- Folate deficiency
- Medications
- HIV infection (direct interference with DNA synthesis)

Mechanism (Important)

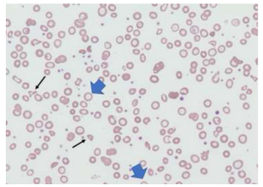
👉 When DNA synthesis is impaired:
- Nuclear maturation ↓ (delayed)
- Cytoplasmic maturation → normal

➡️ Result:
- Large cell with immature nucleus = megaloblast

Consequences
- Unbalanced cell growth
- Impaired cell division
- Intramedullary apoptosis → anemia
- Ineffective hematopoiesis in all 3 cell lines → pancytopenia

Laboratory Findings

- CBC:
- ↓ MCV
- ↓ MCHC
- Microcytic, hypochromic erythropoiesis
- ↓ Serum iron
- ↓ Ferritin
- Peripheral smear:
- Microcytic, hypochromic RBCs



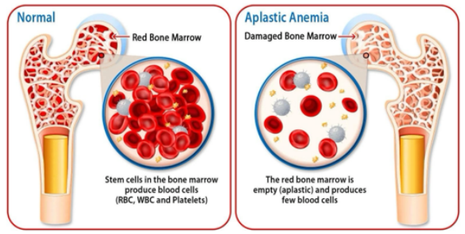


Table 1 Laboratory test of blood, stool and Samples

Laboratory test	Patient's results	Reference range*
CBC		
WBCs (10^3/ul)	8.3	4-11
RBCs (10^6/ul)	2.5	4.0-5.2
Hb (g/dl)	5	12-14
→ MCV (fl)	53	80-100
MCH (pg)	25.3	28-32
→ MCHC (g/dl)	24	32-36
Hct (%)	29	36-47
RDW (%)	17	11.5-14.5
Retic.(%)	0.3	0.5- 1.5%
Plt. ($\times 10^3$/l)	540	150-450
Blood film	Microcytosis with hypochromia, thrombocytosis, normal WBCs and tear drops	
Stool analysis		
Parasites	Negative	
Occult blood	Negative	
Sickling test	Negative	
Hemoglobin electrophoresis	Type A hemoglobin	
LFT	Normal	
KFT	Normal	
PT	Normal	
PC	Normal	
INR	Normal	
Electrolytes		
S. Na++(mmol/L)	132	135-145
S. K++(mmol/L)	3.2	3.5-5.5

Vitamin B12 (Cobalamin) Deficiency

Sources

- Meat
- Fish
- Dairy

❌ Not in vegetables & fruits

Storage

- Stored in liver
- Enough for 5–20 years

👉 Symptoms appear after long-term malabsorption

Absorption

- Needs Intrinsic Factor (IF)
- Absorbed in terminal ileum

Causes

- Pernicious anemia
- Gastrectomy
- Ileal resection
- Distal ileum disease (Crohn disease)
- Pancreatic insufficiency

Folate (Folic Acid) Deficiency

Cause

- Poor dietary intake
- Increased demand

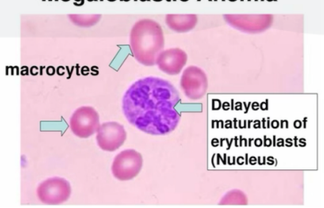
Risk factors

1. Poor diet (poverty, elderly)
2. Increased demand:
   - Pregnancy
   - Chronic hemolytic anemia
3. Malabsorption / metabolism defects:
   - Beans & legumes inhibit absorption
   - Drugs:
   - Phenytoin
   - Methotrexate
   - Malabsorptive disorders

سُورَةُ التَّوۡبَةِ

وَقُلِ ٱعۡمَلُواْ فَسَيَرَى ٱللَّهُ عَمَلَكُمۡ وَرَسُولُهُۥ وَٱلۡمُؤۡمِنُونَۖ وَسَتُرَدُّونَ إِلَىٰ عَٰلِمِ ٱلۡغَيۡبِ وَٱلشَّهَٰدَةِ فَيُنَبِّئُكُم بِمَا كُنتُمۡ تَعۡمَلُونَ ١٠٥

Megaloblastic Anemia



Morphology of Megaloblastic Anemia

Bone Marrow (BM)

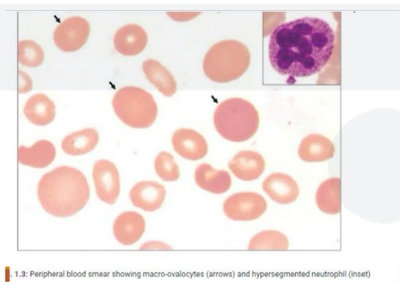
- Hypercellular
- Many megaloblastic erythroid & granulocytic precursors
- Megaloblasts:
- Large
- Fine nuclear chromatin (immature nucleus)

Peripheral Blood (PB)

- Hypersegmented neutrophils (≥ 5 lobes)

👉 appear before anemia

- Macroovalocytes (large, oval RBCs)



1.3: Peripheral blood smear showing macro-ovalocytes (arrows) and hypersegmented neutrophil (inset)

Clinical Manifestations

General anemia symptoms

- Loss of appetite
- Weight loss
- Nausea
- Constipation

Neurological symptoms (B12 only)

بسبب demyelination في: 👉

- Posterior columns
- Lateral columns

Symptoms

- Numbness
- Tingling
- Burning (hands/feet)
- Unsteady gait
- Loss of position sense (toes)

Physical Findings

- Glossitis (smooth tongue)
- Lemon-yellow skin (↑ indirect bilirubin بسبب intramedullary hemolysis)
- Hyperpigmentation (↑ melanin)

Investigations

- CBC
- RBC indices
- Peripheral blood smear
- Serum cobalamin
- Serum folate

Treatment

- Vitamin B12 + folate supplementation
- Parenteral route if malabsorption
- Treat underlying cause

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Done by : Raghad Mrayat

لَا حَوْلَ وَلَا قُوَّةَ إِلَّا بِاللَّهِ

"من كنوز الجنة"