

ANEMIA

Objectives

- Understand causes and classification of anemia
- To know the diagnostic approach to anemia
- Learn basic features of common causes of anemia

Definition

- Anemia is characterized by reductions in hemoglobin concentration, red-cell count, or packed-cell volume, and the subsequent impairment in meeting the oxygen demands of tissues.

ANEMIA is not a
disease but a
symptom/sign !!

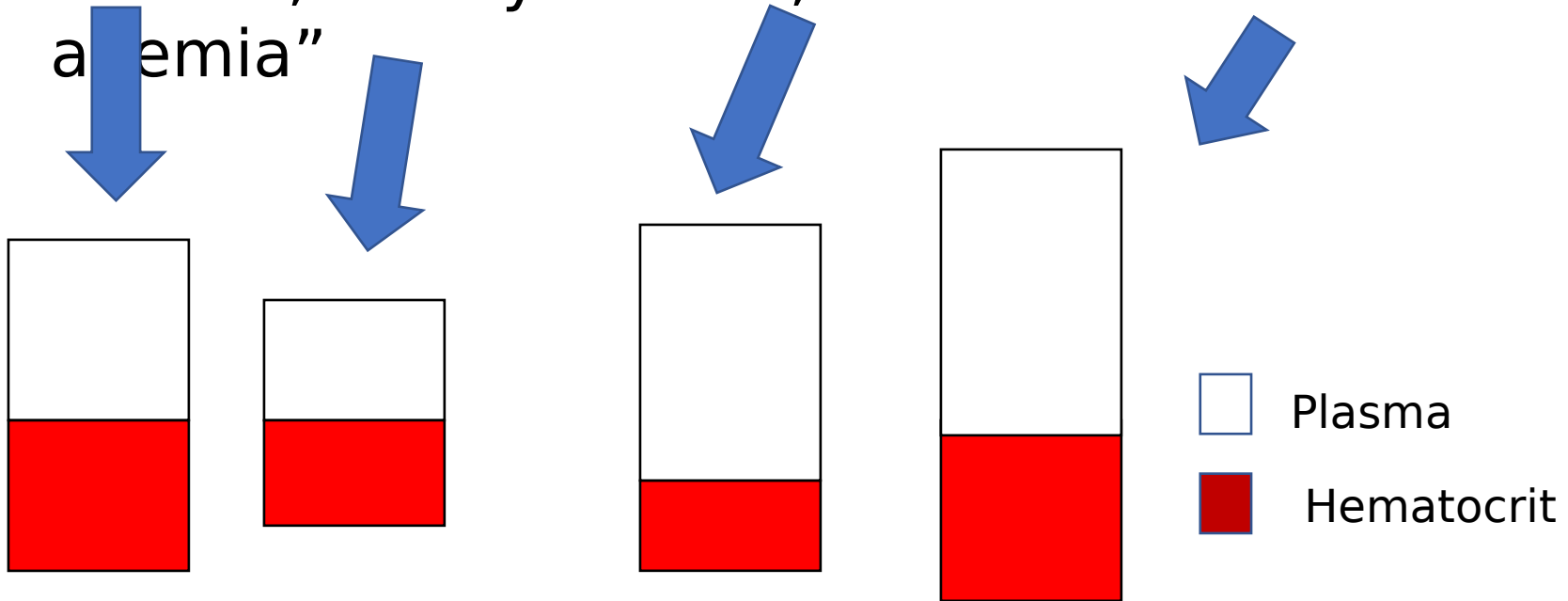
WHO Criteria

Thresholds of hemoglobin used to define anemia in different subpopulations, at sea level

	Hemoglobin concentration(g/dl)
Non-pregnant women(>15 years)	< 12
Pregnant women	<11
Men	< 13

“falsely low or normal Hgb/Hct”

- Normal, falsely normal, true anemia and “false anemia”



Factors affecting Hgb concentration

- Age
- Sex
- Racial background
- Pregnancy status in women
- Smoking
- Altitude

Causes/Classification

- **Pathophysiologic classification**

1. Decreased production/maturation of RBCs
2. Decreased RBC survival(bleeding/hemolysis)

- **Morphologic classification**

1. Normocytic
2. Microcytic
3. Macrocytic

Decreased production/maturation of RBCS

- Bone marrow infiltration- leukemia, lymphoma, multiple myeloma, myeloproliferative disorders ,secondary carcinoma
- Deficiency- Fe , folate, B 12
- Drugs
- infections
- EPO deficiency- CKD
- Hypothyroidism

Decreased RBC survival

- **Bleeding**- acute or chronic
- **Hemolysis**-different classifications
 - Hereditary or acquired
 - Extrinsic or intrinsic causes(extracorpuscular vs intracorpuscular defects)
 - Immune or non-immune mechanisms

Morphologic

- **Normocytic**

- post-hemorrhage
- Hemolytic anemia
- Bone marrow infiltration-eg. leukemia, lymphoma
- Anemia of CKD
- Drugs toxins e.g.. Cancer chemotherapy

- **Microcytic**

- Iron deficiency
- Thalassemia
- Chronic illness
- Sideroblastic anemia

- **Macrocytic**

- Folate deficiency
- Vitamin B 12 deficiency
- Drugs
- hypothyroidism

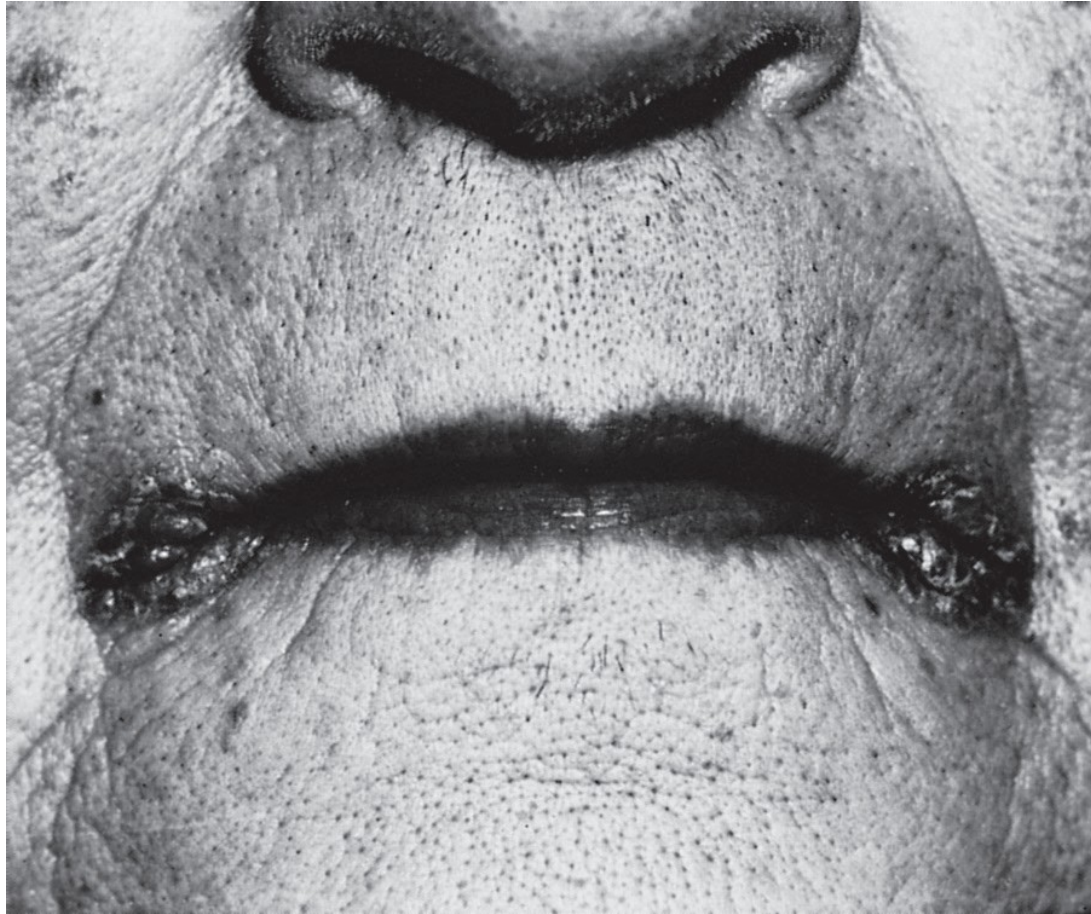
Clinical features

- **Symptoms**: depend on the severity, underlying cause and speed of onset
 - Acute blood loss-mainly symptoms of volume depletion/hypotension.
 - Insidious onset- fatigue, palpitations, SOB, angina, claudications, faintness, tinnitus, headache, vertigo ,cold sensitivity .If severe may have symptoms of CHF
 - Symptoms of underlying disease (eg. Bleeding)
- **Signs**: pallor(conjunctival, nail bed, palmar, tongue or generalized) , tachycardia, increased arterial pulsation, reversible cardiac enlargement. Signs of CHF
- Signs of specific cause- Fe deficiency(atrophic tongue,koilonychia; jaundice(hemolytic anemia) splenomegaly and lymphadenopathy(lymphoproliferative disorder) petechiae (platelet no/functional abnormality)

Atrophic tongue in iron deficiency anemia.



Cheilosis in iron deficiency.



Nail changes in iron deficiency anaemia (koilonychia).



Diagnostic approach/Laboratory tests

- **Complete blood count(CBC)**

- ✓WBC with differential
- ✓Hgb, Hct
- ✓Platelet count
- ✓Reticulocyte count

Calculate reticulocyte production index (RPI)= $\frac{RC}{[pt's\ Hgb\ or\ Hct / expected\ Hgb\ or\ Hct]} \times$
correction factor

(correction factor varies from 1-3 depending on degree of anemia)

- **RBC indices**

- ✓MCV(N=80-96 fl)
- ✓MCH(N=27-32 pg)
- ✓MCHC (N=32-36 g/dl)
- ✓RDW

.....

- **Peripheral blood smear**

- ✓ WBC- blast cells, nuclear segmentation
- ✓ RBC – size(Normocytic, microcytic, macrocytic)
 - variation in size (anisocytosis), variation in shape (poikilocytosis)
 - polychromasia

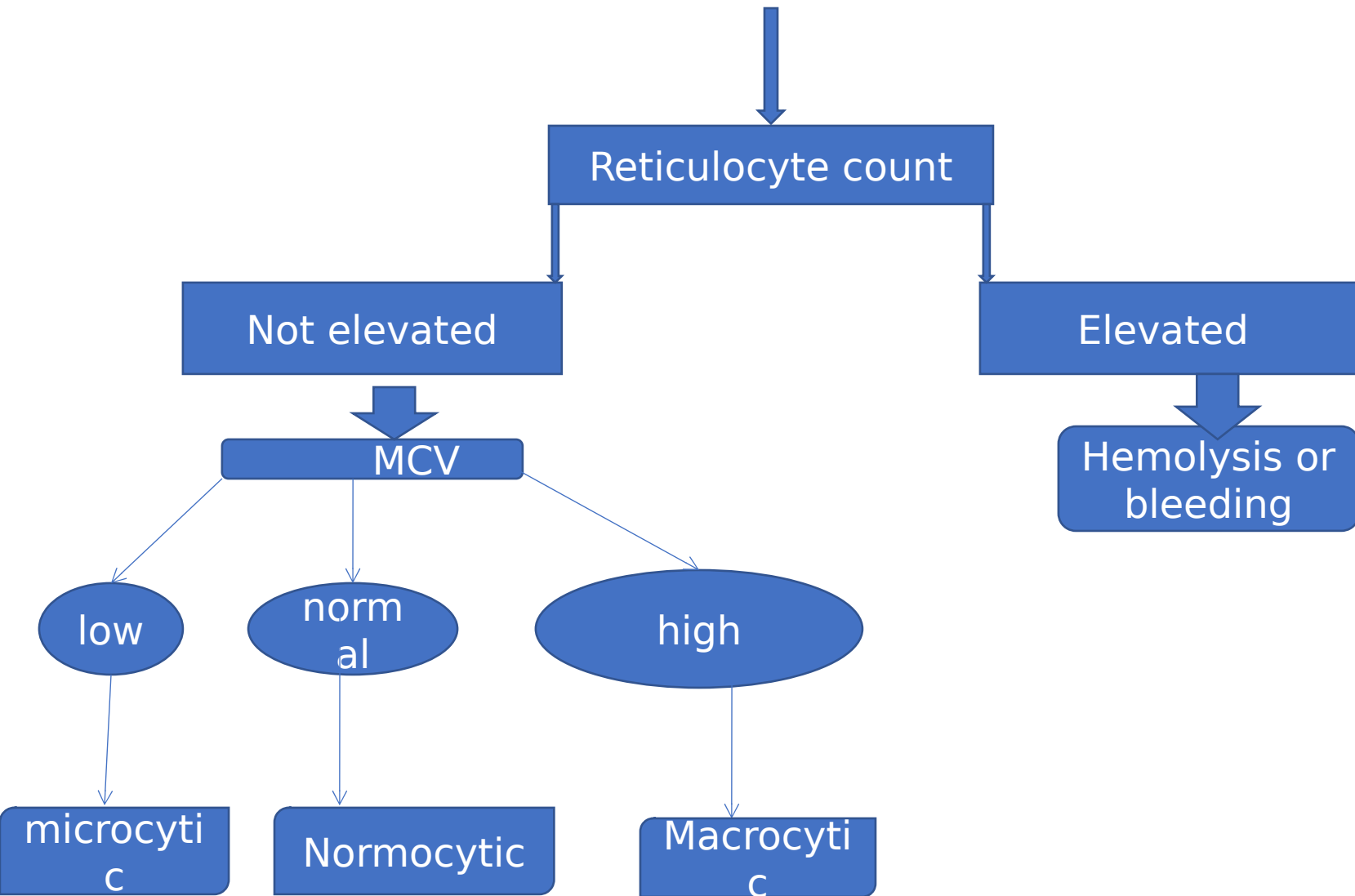
- **Iron supply studies-** serum iron, TIBC, serum ferritin

- **Bone marrow exam (aspirate or biopsy)**

- ✓ Aspirate- M/E ratio, cell morphology, iron stain
- ✓ Biopsy –cellularity and cell morphology

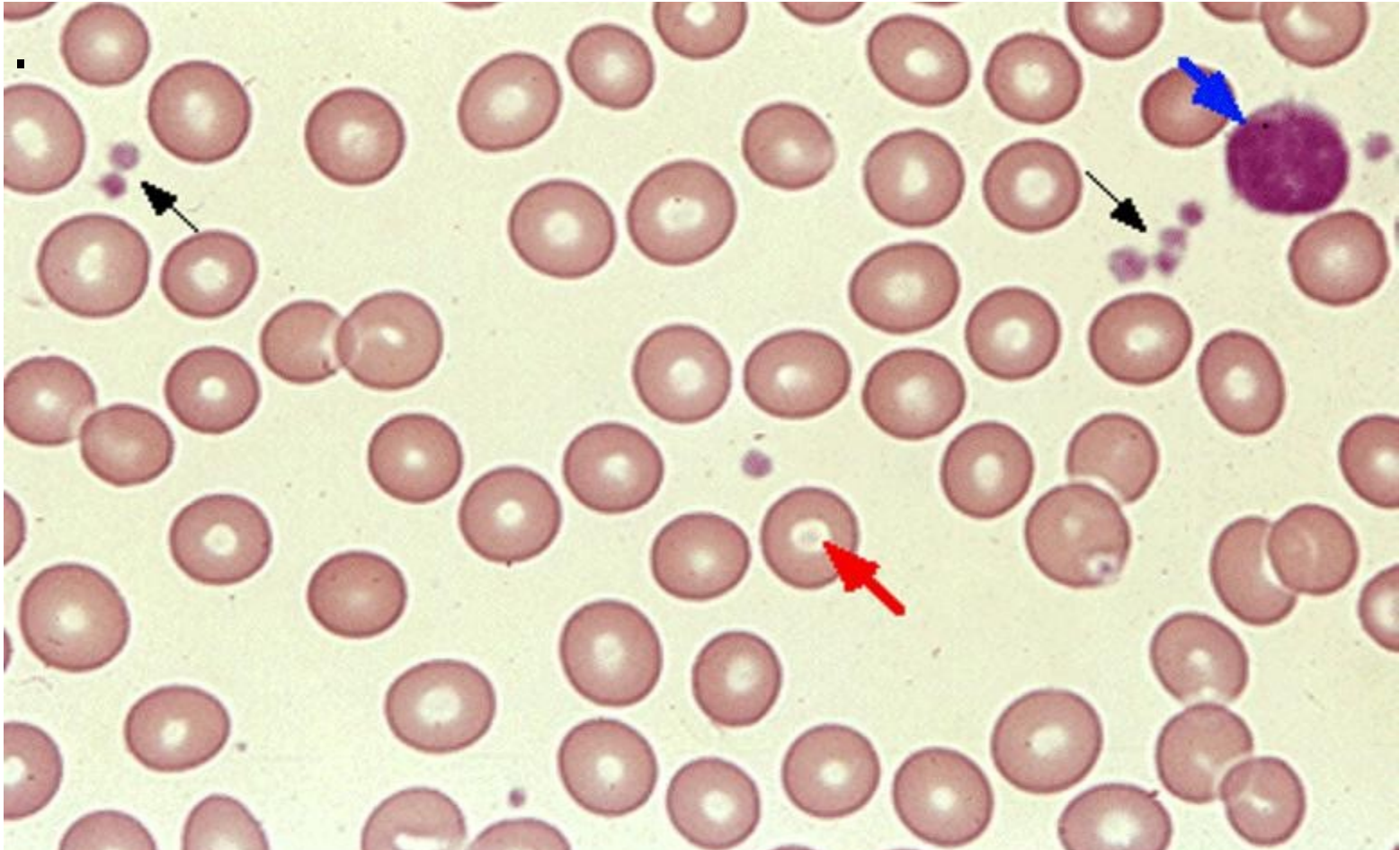
- **Other tests- (based on clinical indication) e.g.**
vitamin B 12 and folate levels, Coomb's test,
hemoglobin electrophoresis

Anemia

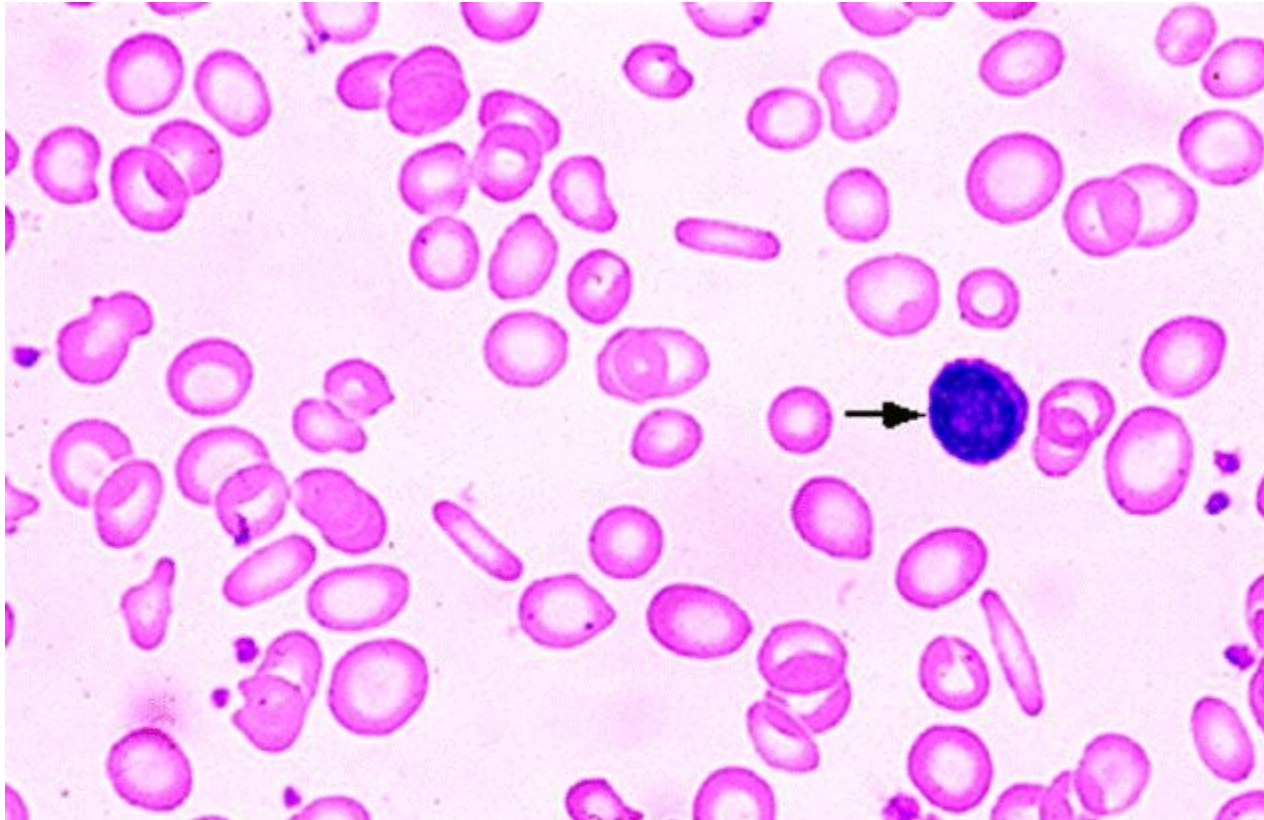


Peripheral blood smear in anemia

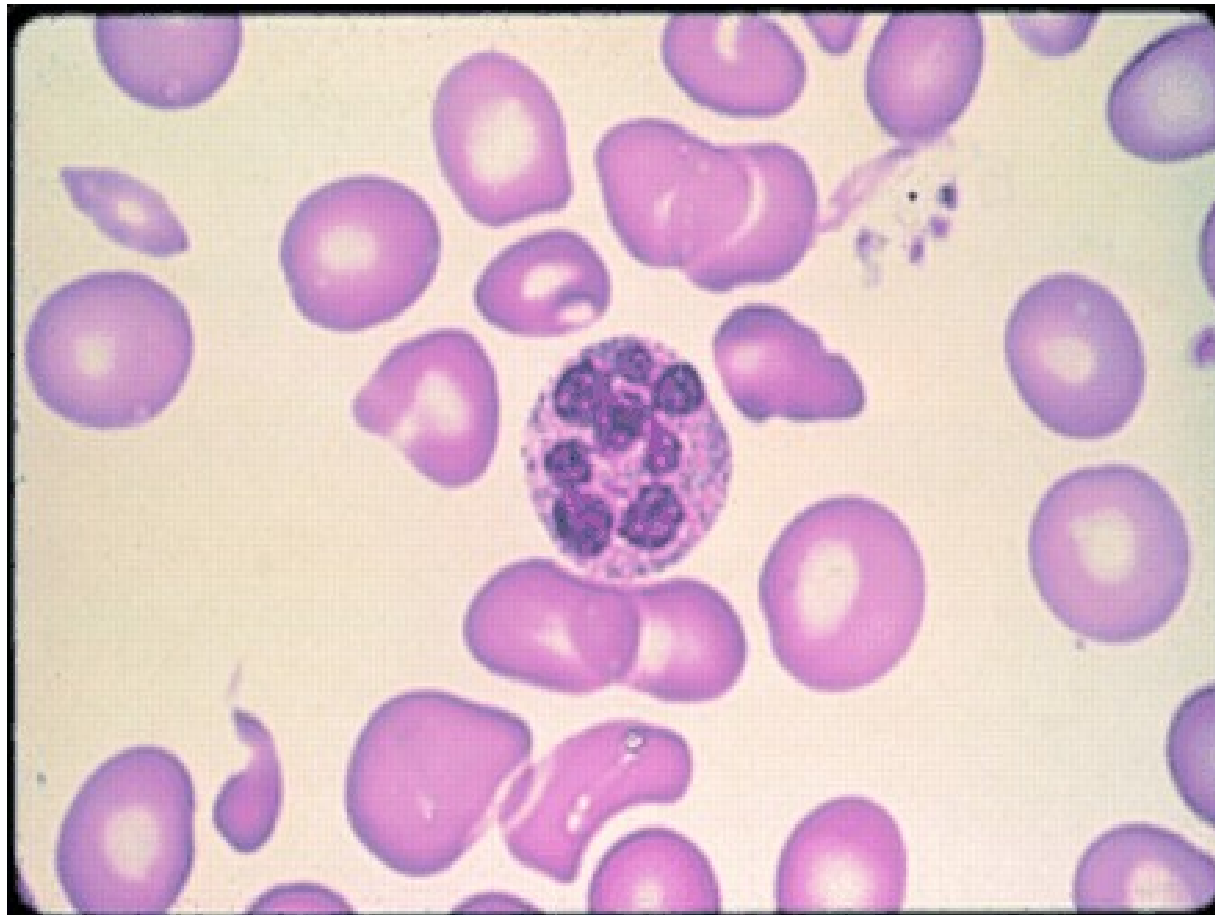
Normal peripheral blood smear



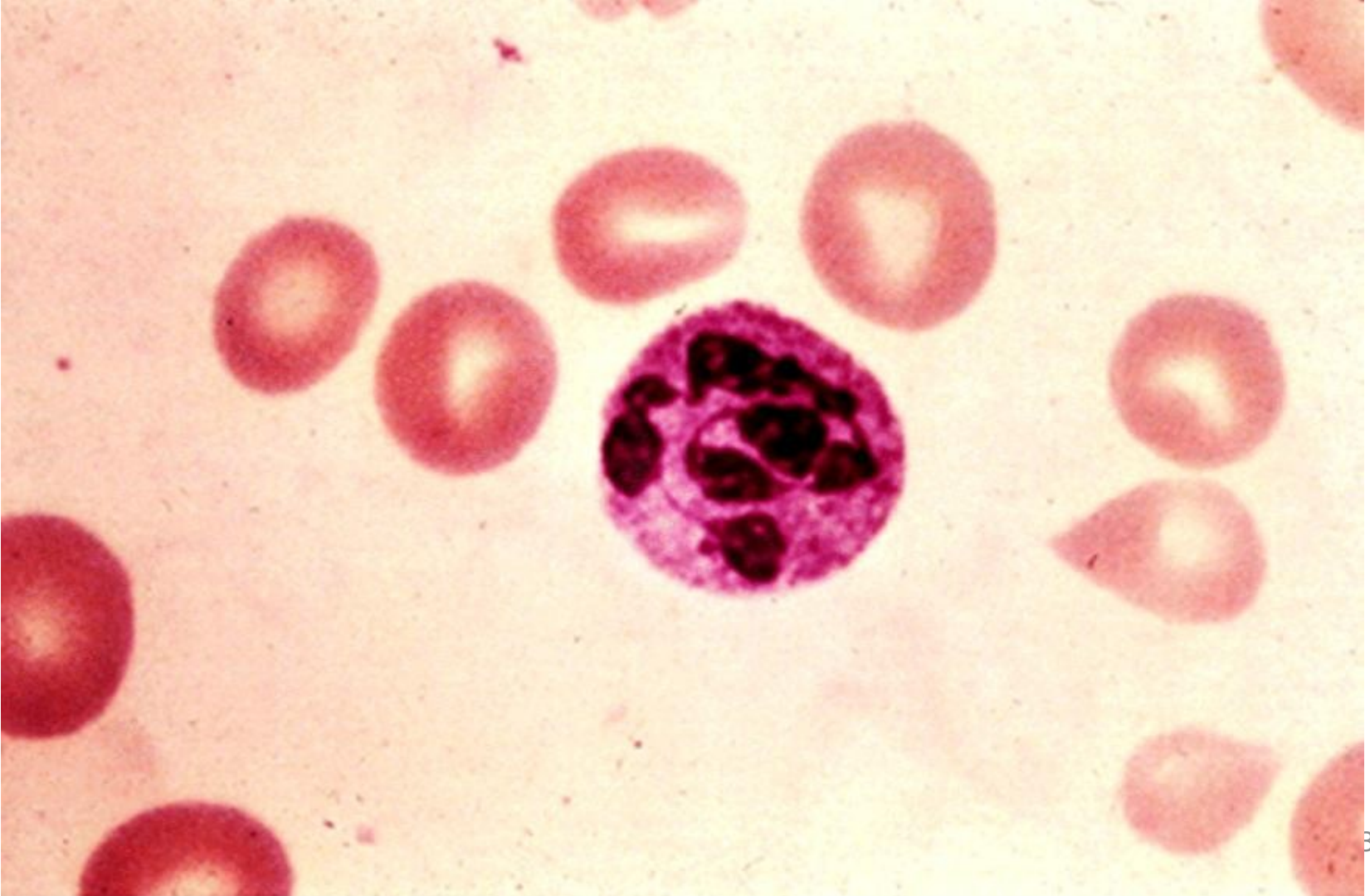
Iron deficiency anemia



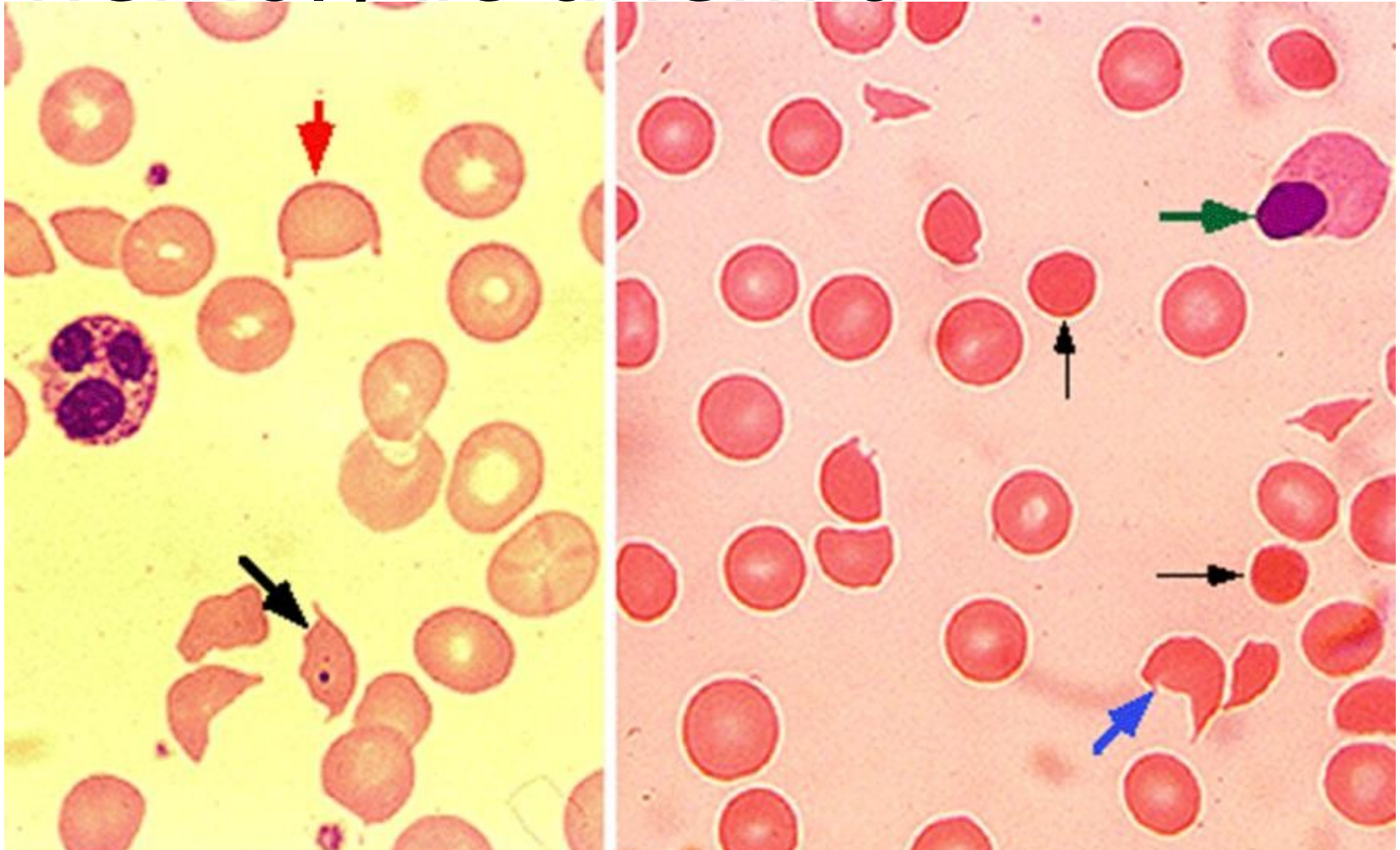
Macrocytosis



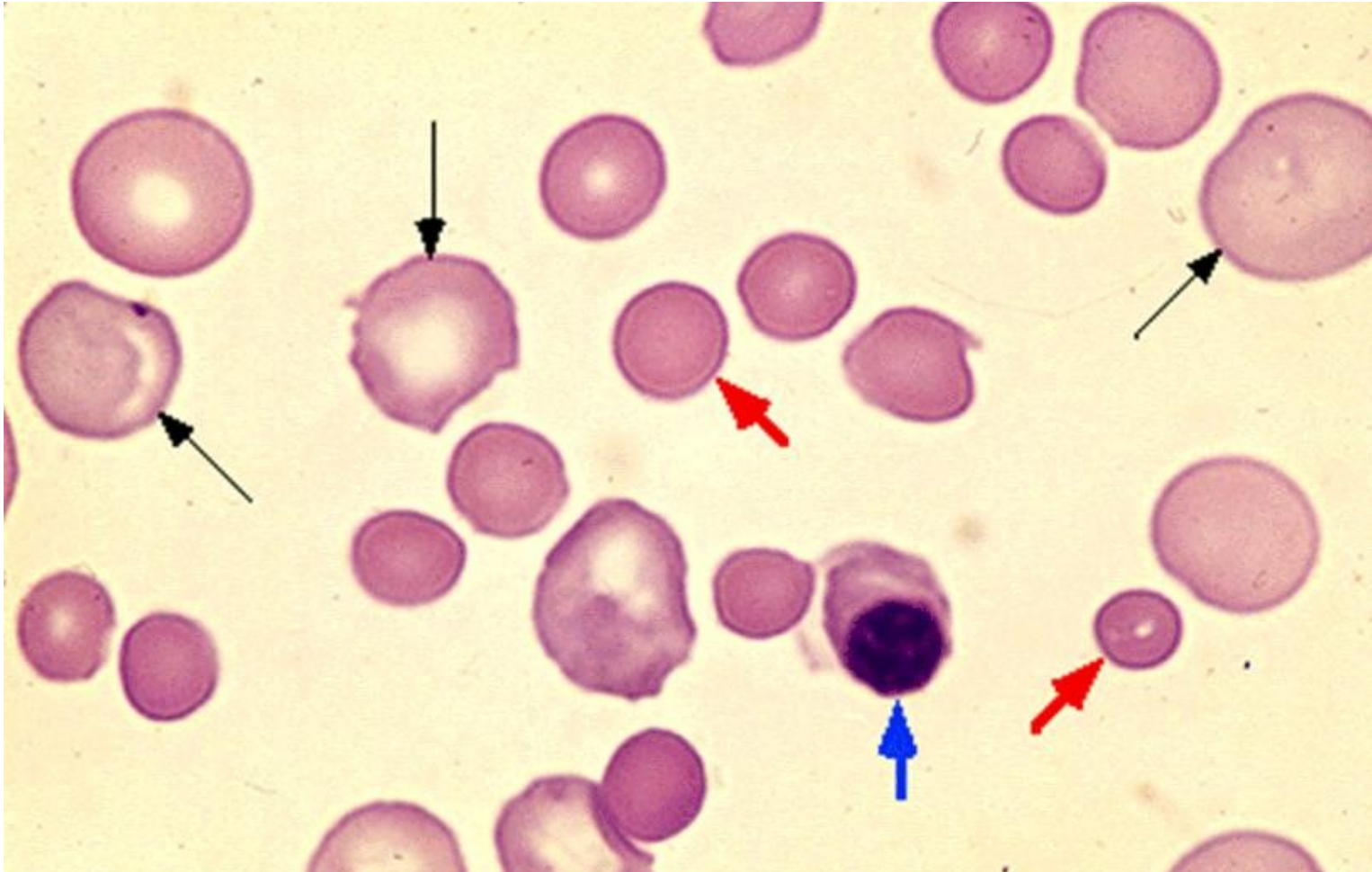
Hypersegmented neutrophil



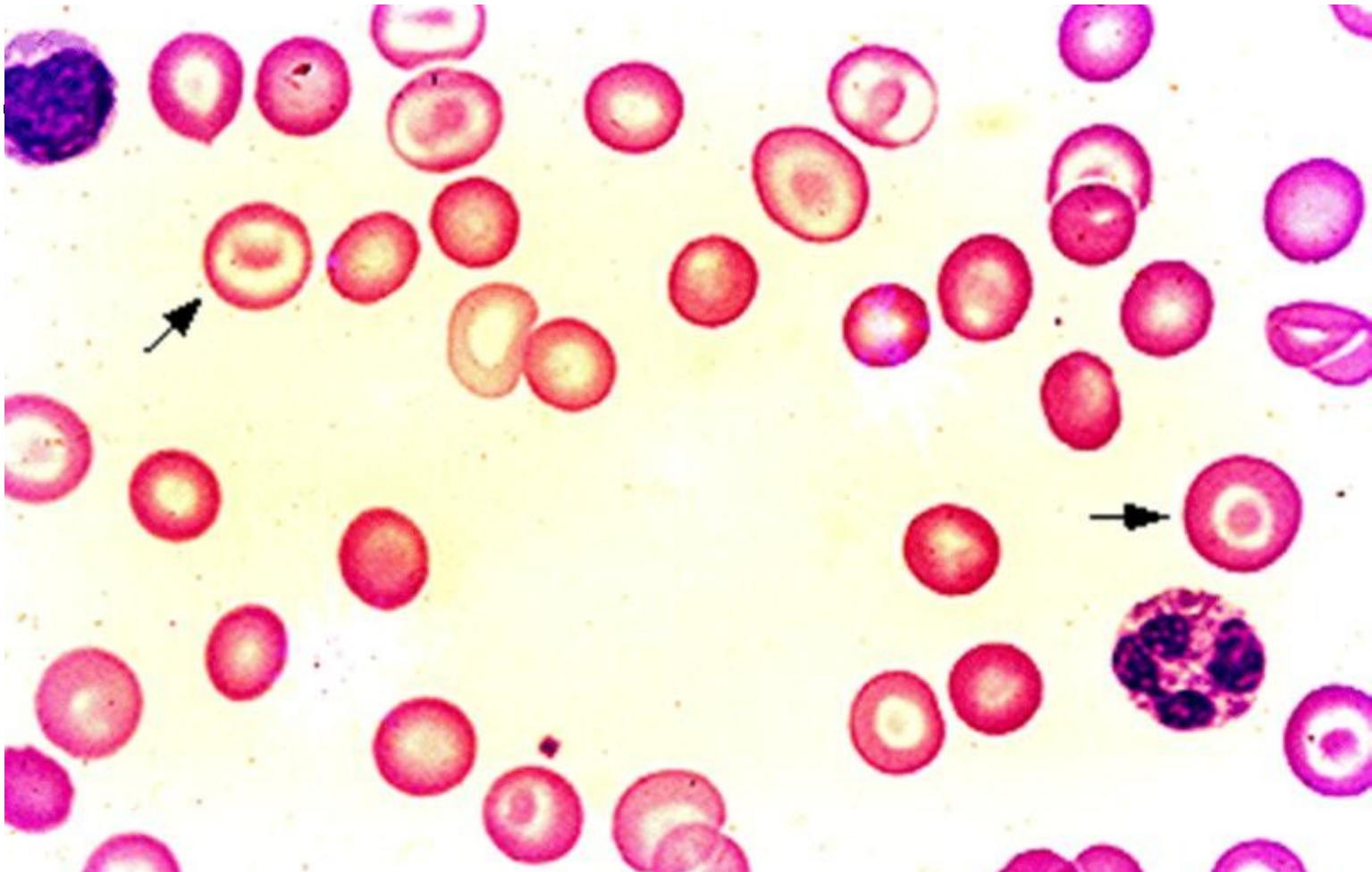
Microangiopathic hemolytic anemia



Autoimmune hemolytic anemia



Target cells



Iron deficiency anemia

- Most common cause of anemia world wide
- Causes
 - Blood loss: eg. GI, menstrual, hookworm infestation
 - Deficient diet
 - Increased demand(eg. Pregnancy, lactation)
 - Decreased absorption (eg. Post gastrectomy)

Stages of iron deficiency

- **Negative iron balance**

- ✓ Iron demand/loss > iron absorption
- ✓ Decreased serum ferritin and stainable iron in bone marrow
- ✓ Normal serum iron, TIBC, RBC protoporphyrin
- ✓ Normal RBC morphology and indices

- **Iron deficient erythropoiesis**

- ✓ low serum iron, increased TIBC, raised RBC protoporphyrin and absent bone marrow stainable iron

- **Iron deficiency anemia**

- Hypochromic microcytic anemia

Investigations

- Low hgb, hct
- Low RBC indices
- Low serum iron and ferritin
- Increased TIBC and RBC protoporphyrin
- Decreased bone marrow stainable iron
- Increased serum TRP (transferrin receptor protein)
- Investigations to find the cause (eg stool for O/P and occult blood, endoscopy, colonoscopy,

DDx of microcytic anemia

	Fe deficiency	Anemia of chronic illness	Thalassemia	Sideroblastic anemia
MCV	Reduced	Low normal or normal	Very low for degree of anemia	any
Serum Fe	Reduced	Reduced	Normal	Raised
Serum TIBC	Raised	Reduced	Normal	Normal
Serum ferritin	Reduced	Normal or raised	Normal	Raised
Serum TRP	Increased	Normal	Normal or raised	Normal or raised
Iron in marrow	Absent	Absent or reduced	present	Present

Treatment of iron

deficiency anemia

- Find and treat the underlying cause !!
- Iron to correct the anemia and replace stores, which can take 6 months!

Macrocytic anemias

- Increased MCV
- Peripheral film- macrocytes(macroovalocytes)
- **Causes/ classification**
 1. Megaloblastic anemia (megaloblastic marrow)
 - Vitamin B 12 deficiency
 - Folate deficiency
 2. Other cause of macrocytosis (non-megaloblastic marrow)
 - Alcohol
 - Liver disease
 - Hypothyroidism
 - Drugs
 - Myelodysplasia
 - Aplastic anemia

Common causes of vitamin B 12 deficiency

- Dietary- eg. Vegans
- Pernicious anemia
- Gastrectomy
- Ileal disease (resection, Crohn's disease)
- Blind loop syndromes
- Malabsorption syndromes

Common causes of folate deficiency

- Poor intake (old age, poverty, alcoholics)
- Increased requirement/ loss- pregnancy, hemolysis
- Malabsorption
- Drugs- e.g. Phenytoin, Methotrexate

Clinical features

- Symptoms and signs of anemia
- Symptoms and signs of underlying disorders
- Jaundice, increased bilirubin, increased LDH -reflect ineffective erythropoiesis (resulting from increased destruction of precursors)
- Leucopenia and thrombocytopenia can occur(i.e. pancytopenia)
- Hypersegmented neutrophils
- Peripheral neuropathy and subacute combined degeneration of spinal cord in vitamin B 12 deficiency
- Psychiatric disturbances

Other investigations

- ✓ LFT
- ✓ TFT
- ✓ Serum vitamin B 12
- ✓ Serum and RBC folate
- ✓ Vitamin B 12 absorption test—Schilling test
- ✓ Bone marrow
- ✓ Endoscopy +/- gastric biopsy
- ✓ Parietal and IF antibodies

Treatment

- Vitamin B 12 deficiency- Vitamin B12 injection (for life)
- Folate deficiency –oral folate for 4 months(continued if underlying cause can't be corrected)

Hemolytic anemias

➤ Hereditary or acquired

- Hereditary- eg. hemoglobinopathies, enzyme defects
- Acquired-eg. drugs ,infections,

➤ Extrinsic or intrinsic causes(extracorpuscular vs intracorpuscular defects)

- Intrinsic- membrane defects eg.spherocytosis, hemoglobinopathies eg.sickle cell, enzyme defects eg G6PD
- Extrinsic –autoimmune, microangiopathic, drugs/toxins

➤ Immune or non-immune hemolysis

Clinical features of hemolytic anemia

- **Symptoms** - of anemia
 - of underlying cause
 - red or dark brown
- **Signs**- of anemia (eg pallor),jaundice, splenomegaly may present, bossing of skull(congenital cases)
- **Lab-**
 - ✓ Hgb – normal to severely reduced
 - ✓ MCV, MCH- usually increased
 - ✓ Reticulocytes-increased
 - ✓ Bilirubin- increased(mostly unconjugated)
 - ✓ LDH- increased
 - ✓ Haptoglobin-reduced to absent
 - ✓ ?autoimmune- Coomb's test
 - ✓ ?malaria- blood film
 - ✓ ?hemoglobinopathy-Hb electrophoresis

Treatment

- Underlying cause
- May need iron and folic acid supplements if low

Summary

- Anemia is not a diagnosis by itself but **ALWAYS** signifies other underlying causes.
- Diagnosis of the underlying cause is important for proper management.
- Anemia is a commonly encountered clinical problem, the diagnosis of which is facilitated by understanding of pathophysiologic processes causing the anemia and the morphologic appearance of RBCs