MICROCYTIC AND MACROCYTIC ANEMIA

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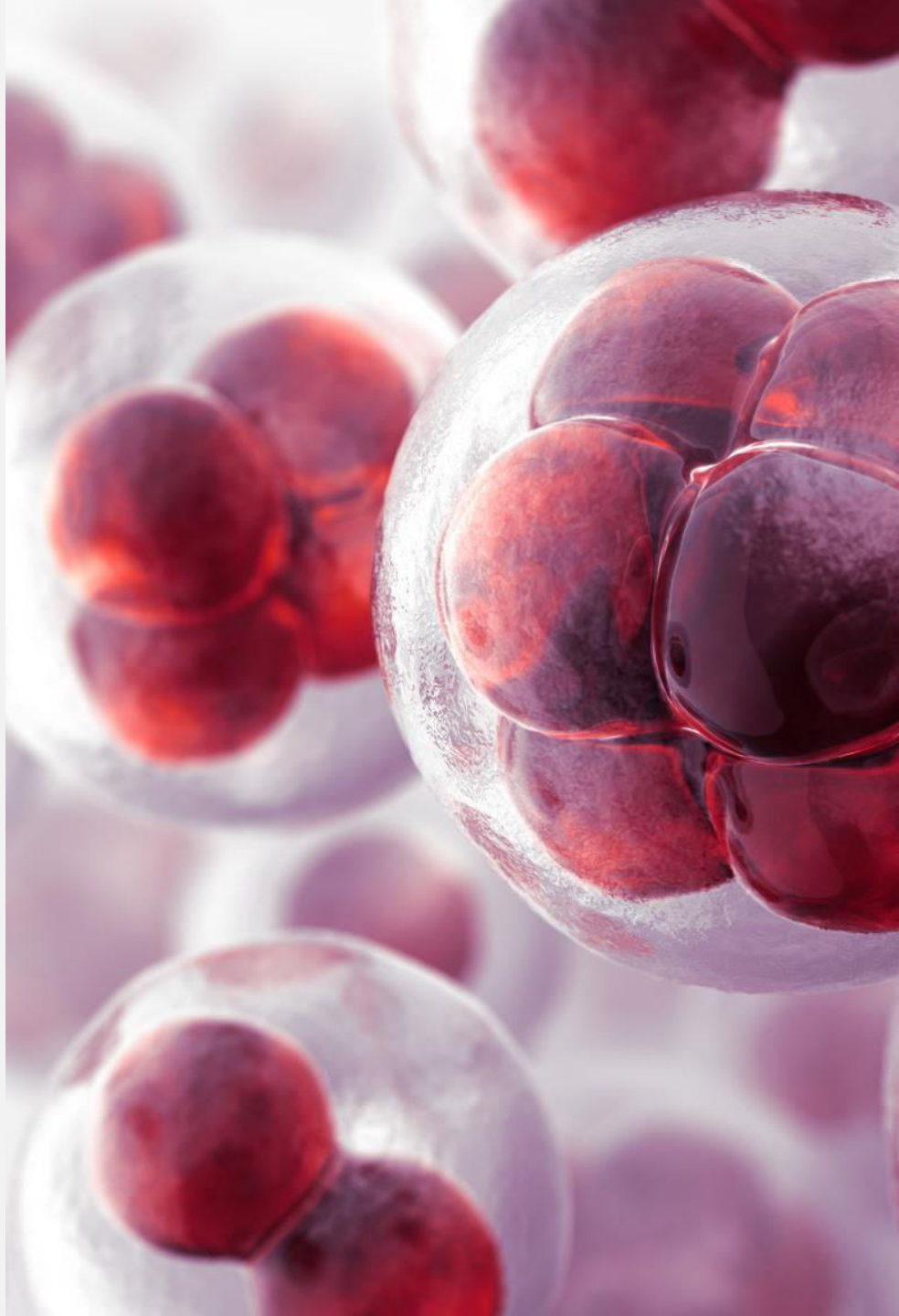
DEFINITION

- Anemia is a pathologic state resulting in an insufficient number of erythrocytes to deliver oxygen to organs and tissues. Anemia can arise from blood loss, erythrocyte underproduction, erythrocyte destruction (hemolysis), or a combination of these factors

  - Men: HGB < 13.5 or HCT < 41%
  - Women: HGB < 12 or HCT < 36%



QUICK HIT

- Symptoms from anemia are related to its severity and How rapidly it occurs. As well as to whether underlying organ or vascular disease is present
- Anemia should never be considered a final diagnosis: the cause must be identified. Recognizing the underlying cause leads to more focused treatment beyond transfusion to correct the anemia. As well as therapeutic opportunities linked to the specific cause.

CLASSIFICATION OF ANEMIA

- Anemias are most easily classified according to their **cell size**, **microcytic** anemia means low mean corpuscular volume (**MCV) < 80** , **macrocytic** anemia means elevated **MCV > 100**.

- **Low MCV anemias**:

1. iron deficiency anemia
2. thalassemia
3. sideroblastic anemia

4- lead poisoning.

- **High MCV anemias**:

Megaloblastic
• B12 deficiency
• Folate deficiency
• Drugs that impair DNA synthesis (methotrexate, sulfa, chemotherapy)
Non-megaloblastic
• Liver disease
• Alcoholism
• Reticulocytosis (see high reticulocyte, on left)
• Hypothyroidism
• Myelodysplasia.

CLINICAL FEATURES

History:

◦symptoms of anemia: fatigue, weakness, dyspnea, decreased exercise tolerance, palpitations, headache, dizziness, tinnitus, syncope, Orthostatic lightheadedness ,poor concentration ,vague abdominal discomfort .

◦acute vs.chronic:acute bleeding(hematemesis , oliguria , absent tears) + episodes of jaundice or dark urine during acute illnesses / episodes of anemia that is exacerbated during acute illnesses or with exposures to medications .

- diet : (alcohol, Malabsorption, malnutrition , anorexia nervosa)
- past medical : SLE , Cancer ,Chronic kidney disease , Rheumatologic conditions , Hypothyroidism ,Infections
- family history
- drug history : [NSAIDs],PPI, Ceftriaxone , Metformin , Methotrexate , Nitrous oxide.
- past surgical : Gastric surgery
- menstrual history: menorrhagia, menometrorrhagia, dysfunctional uterine bleeding
- rule out pancytopenia (recurrent infection, mucosal bleeding/easy bruising)

Physical examination:

The presentation may vary depending on the acuteness of onset, hematocrit levels, and the general health conditions of the patient (age, sex , pregnancy , cardiac conditions, and any other comorbidities) so Perform systematic examination :

Vital signs : BP,T,RR and HR.

- EYES= pallor in mucous membranes, palmar creases and conjunctiva +jaundice+ sunken eyes.
- MOUTH =Glossitis , dry mucous membranes , angular stomatitis
- NECK =enlargement of lymph nodes for evidence of infection or neoplasia , goiter.
- Hands = cyanosis , decreased capillary refill , dry skin ,Nail changes
- cardiac: tachycardia, orthostatic hypotension, systolic flow murmur, wide pulse pressure, signs of CHF.
- ABDOMEN=search for hepatomegaly and splenomegaly
- CNS = peripheral neuropathy +Impaired position and vibratory sense may be associated with B12 deficiency.
- Lower limbs = edema

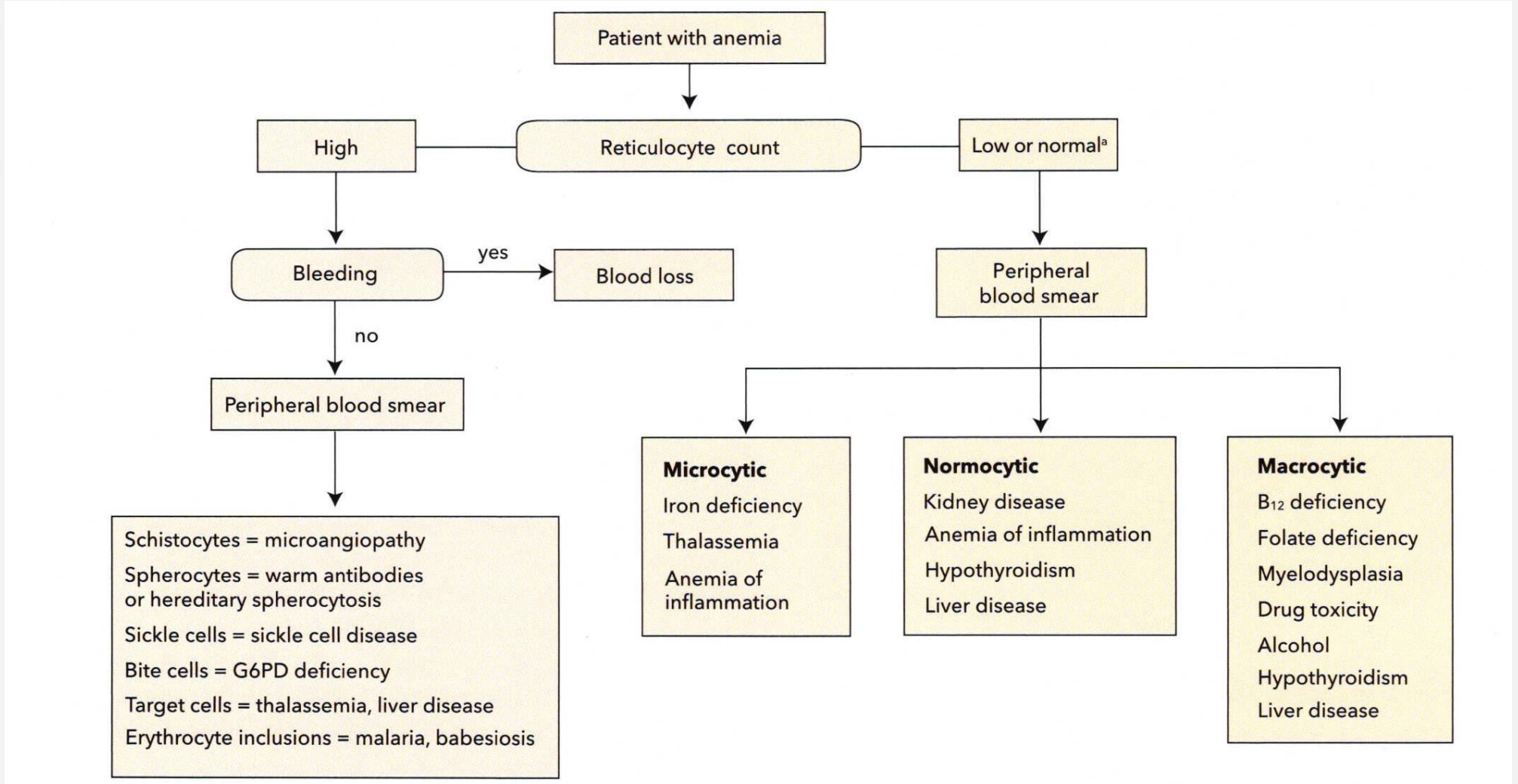
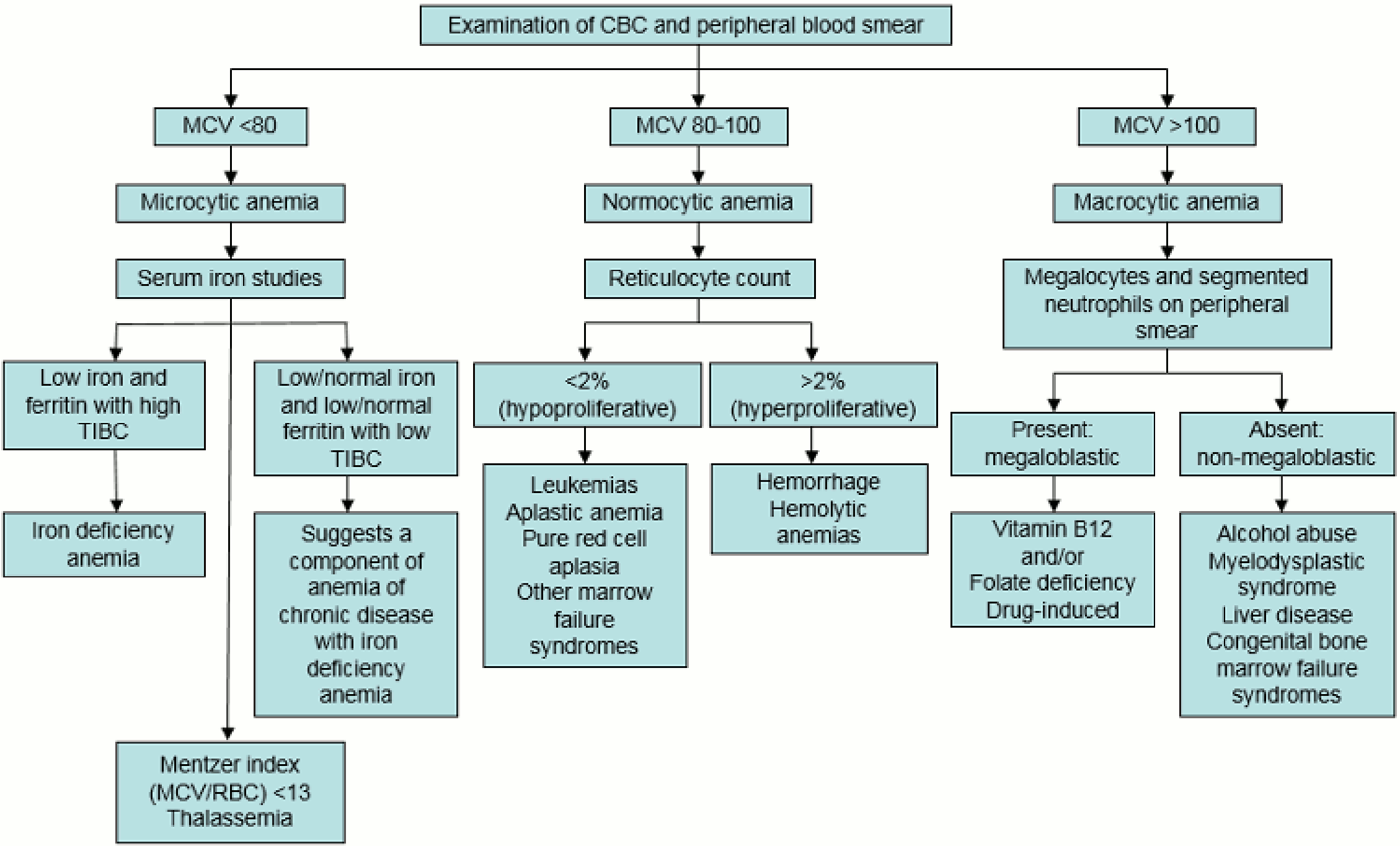
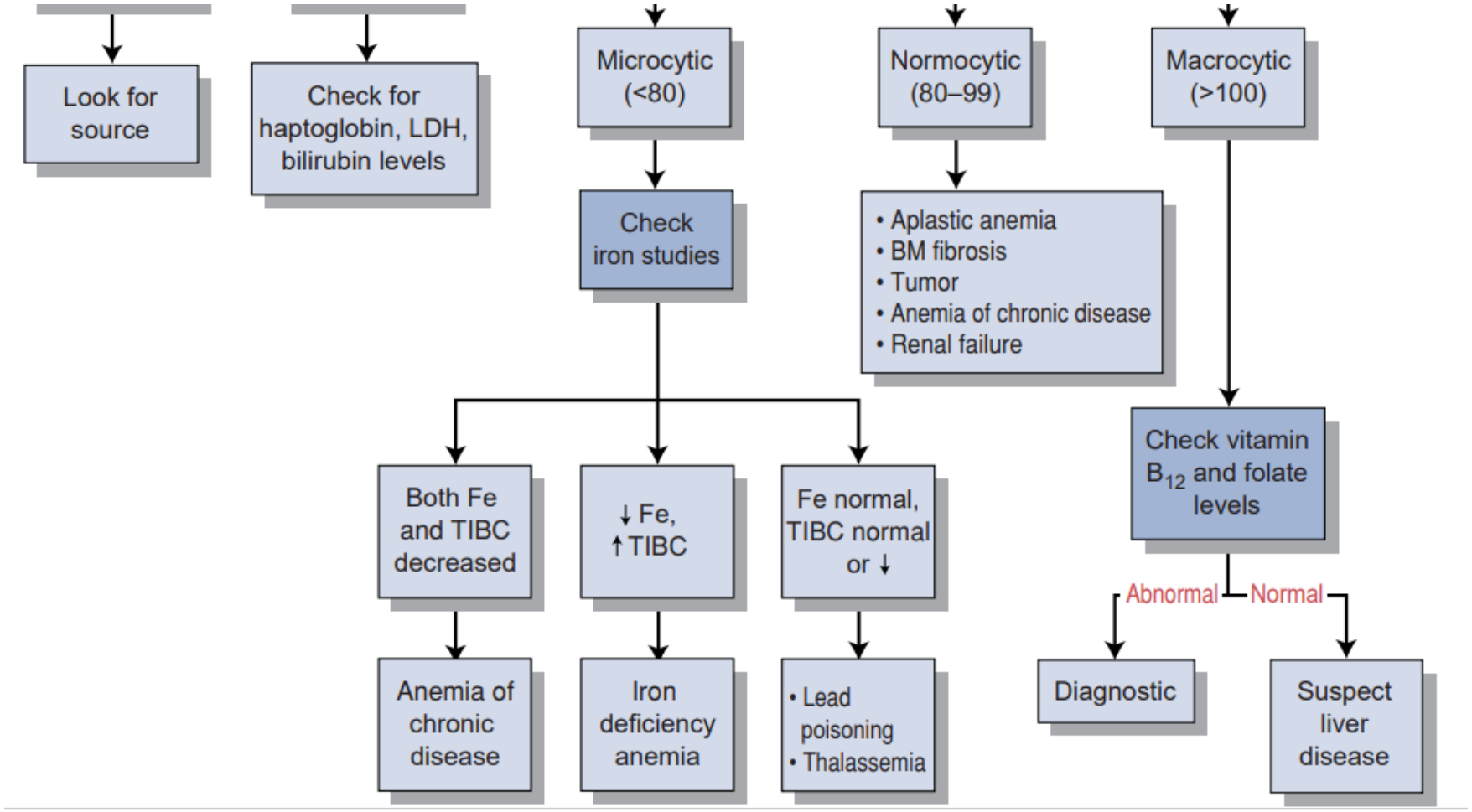


FIGURE 10. Diagnostic algorithm for the evaluation of a patient with anemia.


Examination of CBC and peripheral blood smear
MCV <80
MCV 80-100
MCV >100
Microcytic anemia
Normocytic anemia
Macrocytic anemia
Serum iron studies
Reticulocyte count
Megalocytes and segmented neutrophils on peripheral smear
Low iron and ferritin with high TIBC
Low/normal iron and low/normal ferritin with low TIBC
<2% (hypoproliferative)
>2% (hyperproliferative)
Present: megaloblastic
Absent: non-megaloblastic
Iron deficiency anemia
Suggests a component of anemia of chronic disease with iron deficiency anemia
Leukemias
Aplastic anemia
Pure red cell aplasia
Other marrow failure syndromes
Hemorrhage
Hemolytic anemias
Vitamin B12 and/or
Folate deficiency
Drug-induced
Alcohol abuse
Myelodysplastic syndrome
Liver disease
Congenital bone marrow failure syndromes
Mentzer index (MCV/RBC) <13
Thalassemia

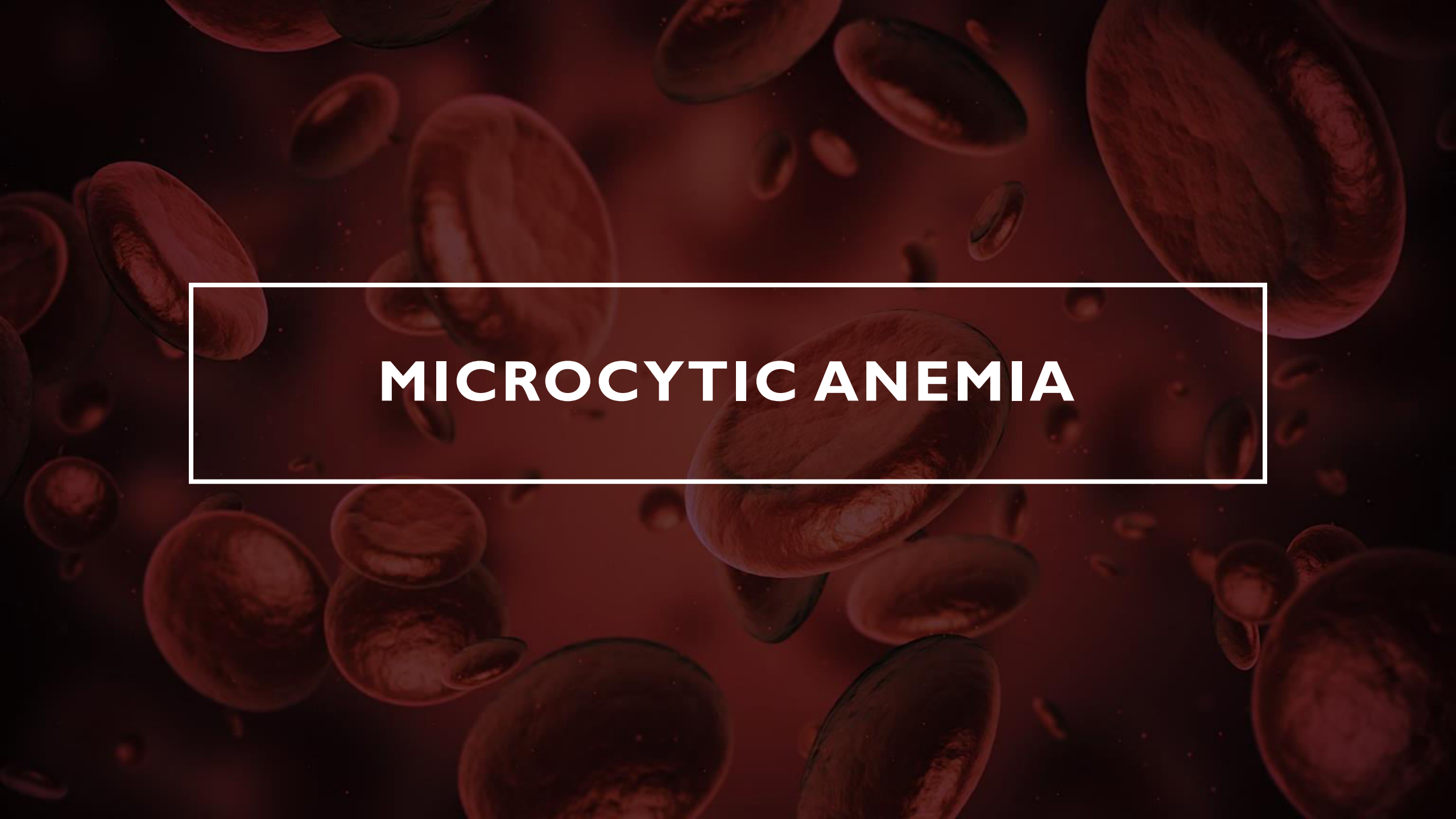

Look for source
Check for haptoglobin, LDH, bilirubin levels
Microcytic (<80)
Normocytic (80–99)
Macrocytic (>100)
Check iron studies
• Aplastic anemia
• BM fibrosis
• Tumor
• Anemia of chronic disease
• Renal failure
Both Fe and TIBC decreased
↓ Fe, ↑ TIBC
Fe normal, TIBC normal or ↓
Check vitamin B_{12} and folate levels
Abnormal
Normal
Anemia of chronic disease
Iron deficiency anemia
• Lead poisoning
• Thalassemia
Diagnostic
Suspect liver disease

RBC size/ MCV	Reticulocyte count	
	Low or normal*	**Increased**
Microcytic MCV <80 fL	▪ Iron deficiency (late) ▪ Anemia of chronic disease/inflammation ▪ Sideroblastic anemias	▪ Thalassemia ▪ Hemolysis¶
Macrocytic MCV >100 fL	▪ Vitamin B12 or folate deficiency ▪ Excess alcohol ▪ Myelodysplastic syndrome ▪ Liver disease ▪ Hypothyroidism ▪ HIV infection ▪ Medications that interfere with nuclear maturation (hydroxyurea, methotrexate, some chemotherapy agents)	▪ Hemolysis¶ ▪ Bone marrow recovery (eg, after infection, vitamin B12 or folate replacement, and/or iron replacement)

TREATMENT

Treatment can't be generalized.

blood transfusion is not recommended unless anemia is severe, then treat with packed red blood cells:
a. The Hb concentration is <7 g/dL, OR
b. The patient requires increased oxygen-carrying capacity (e.g., patients with coronary artery disease or some other cardiopulmonary disease) OR
c- patient symptomatic (hemodynamically unstable)



MICROCYTIC ANEMIA

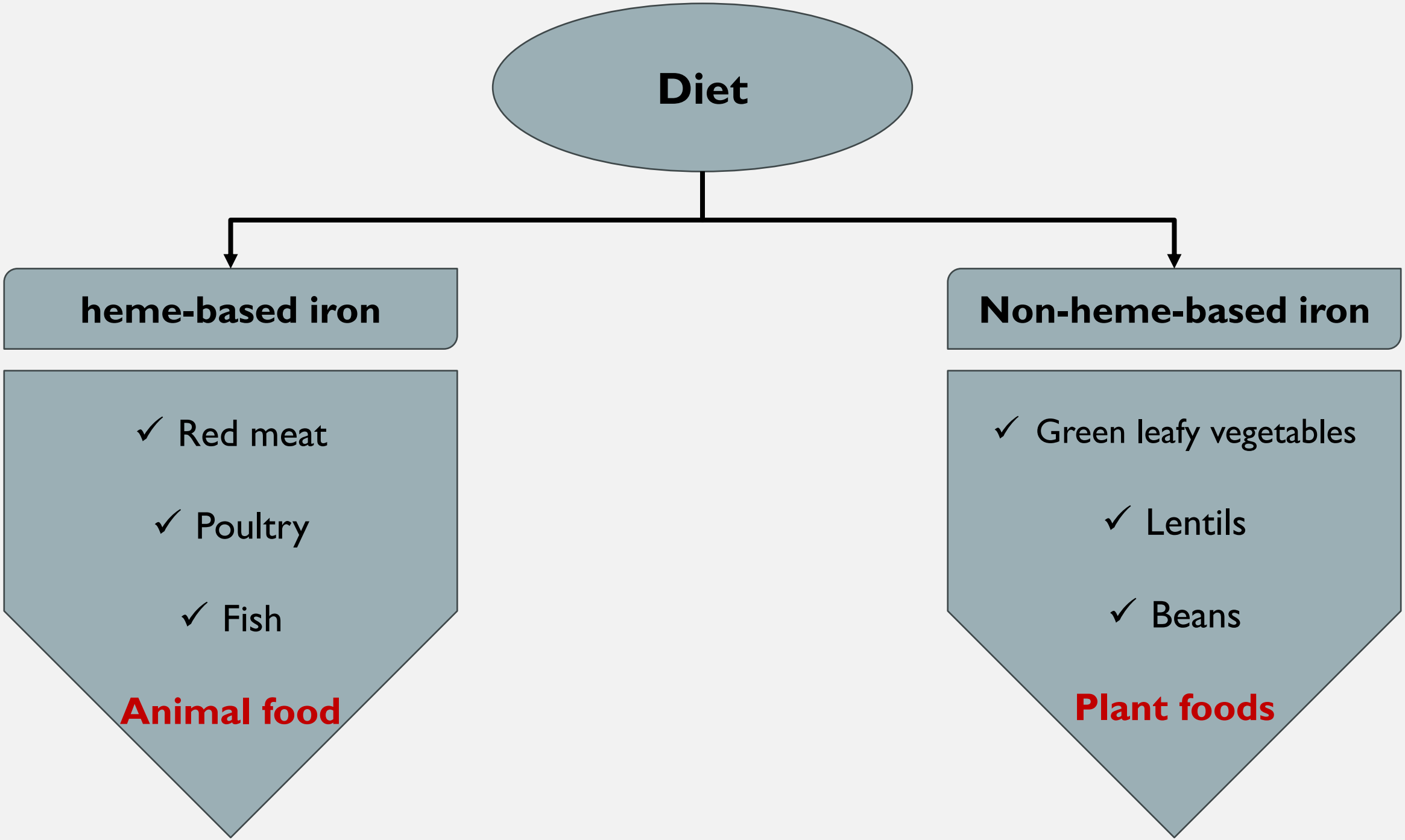
IRON DEFICIENCY ANEMIA

IRON DEFICIENCY ANEMIA

Most common cause of anemia worldwide

- Iron is essential for the **production of hemoglobin**, and a deficiency leads to impaired erythropoiesis and iron deficiency anemia (IDA).
- critical role in **oxygen delivery**
- **DNA synthesis**
- **cellular transport**

- **Hepcidin**, the key peptide involved in iron regulation, is produced in the liver and is a negative regulator of iron absorption.
  - ✓ production increases with inflammation
  - ✓ decreases in response to hypoxia, anemia, and iron deficiency.


Diet
heme-based iron
Non-heme-based iron
✓ Red meat
✓ Poultry
✓ Fish
Animal food
✓ Green leafy vegetables
✓ Lentils
✓ Beans
Plant foods

What about iron absorption and loss ? ? ?

- ✓ In a normal physiologic state, iron absorption = iron loss
- ✓ Dietary iron is absorbed from the gut (mainly the **duodenum**) into the blood stream via enterocytes
- ✓ adult male loses approximately **1 mg** of iron daily from GI mucosal turnover
- ✓ Female, during reproductive years, loses approximately **1.5 mg** of iron daily GI mucosal turnover and menstrual blood loss

Iron deficiency in adult mostly due to ? ?

- ✓ Iron deficiency in adults rarely occurs secondary to decreased oral intake but is more commonly **secondary to blood loss**
- ✓ For premenopausal Female, this is typically secondary to menstrual blood loss, but for male or postmenopausal Female, occult GI blood loss should be suspected

Causes of Iron Deficiency Anemia

Decreased intake

- ✓ Nutritional deficiency
- ✓ Decreased absorption
  - After gastric/duodenal surgery
  - Celiac disease (malabsorption)
  - H pylori infection
  - Autoimmune atrophic gastritis

Increased iron requirements

- ✓ Pregnancy
  (increased iron requirements 4-6 mg/day)
- ✓ lactation
- ✓ Infancy, childhood

Loss of iron

- ✓ Bleeding
  - Menstruation
  - GI bleeding
    (PUD, malignancies)
  - occult blood loss
- ✓ Intravascular hemolysis

HISTORY OF IDA

History of other GI symptoms that might suggest celiac disease, autoimmune gastritis, or H. pylori infection

History of blood loss → melena, hematemesis, and hematuria

History for females → Menstrual/pregnancy/lactation

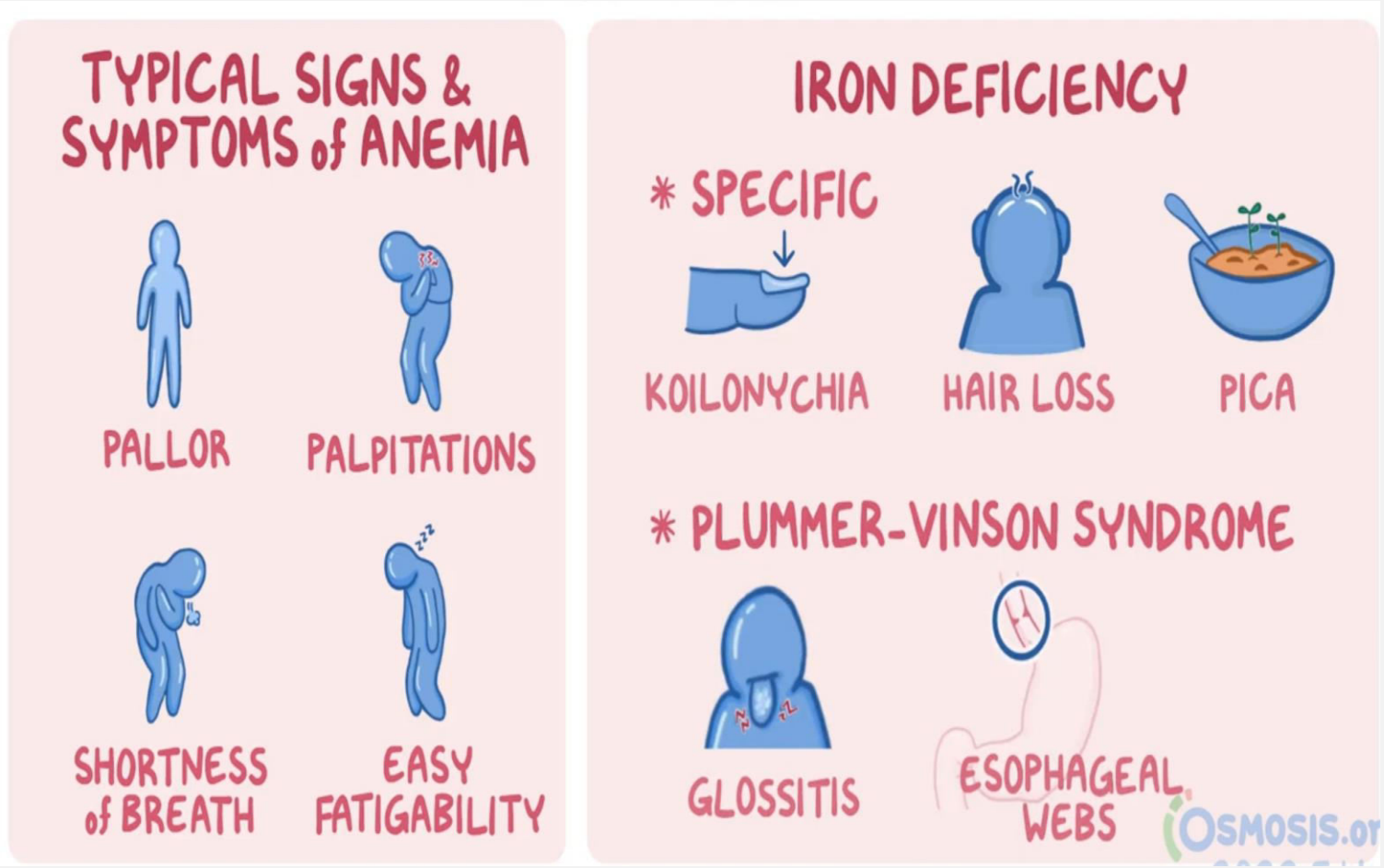
History of Medication

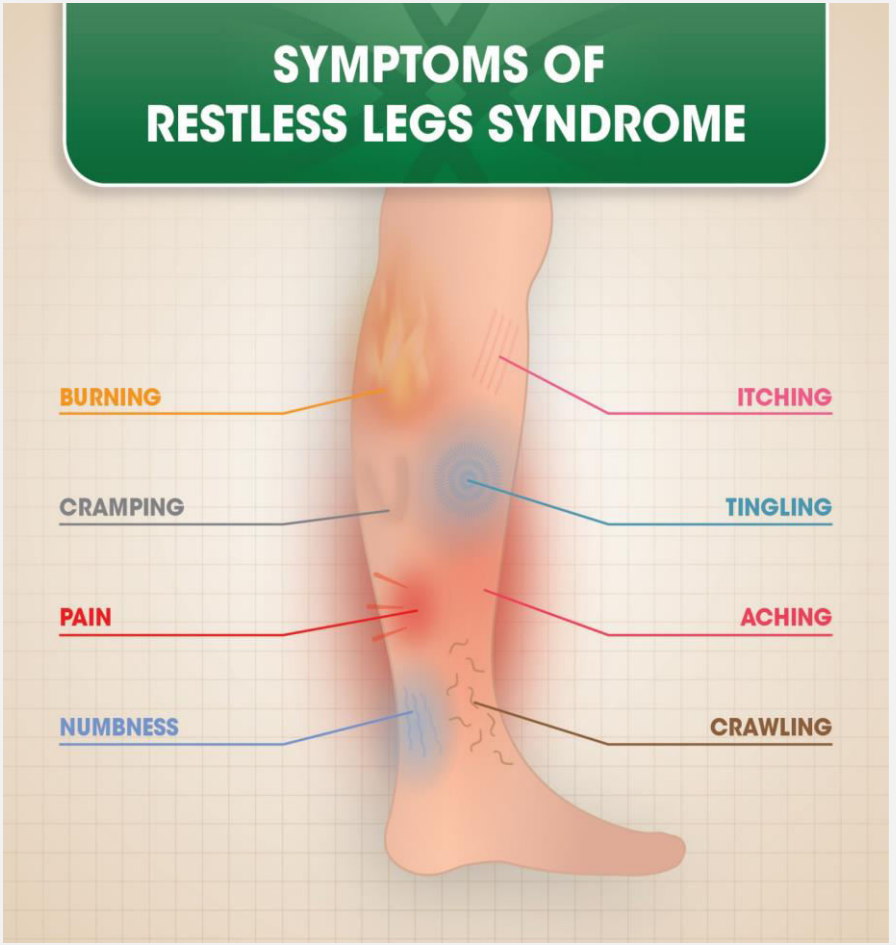
- ✓ NSAIDS or anticoagulants
- ✓ Multiple blood donation

Personal or family history of

- ✓ bleeding diathesis, including platelet disorders, von Willebrand disease, hereditary hemorrhagic telangiectasia
- ✓ celiac disease, colon cancer, or other GI disorders

CLINICAL FEATURES





DIAGNOSIS

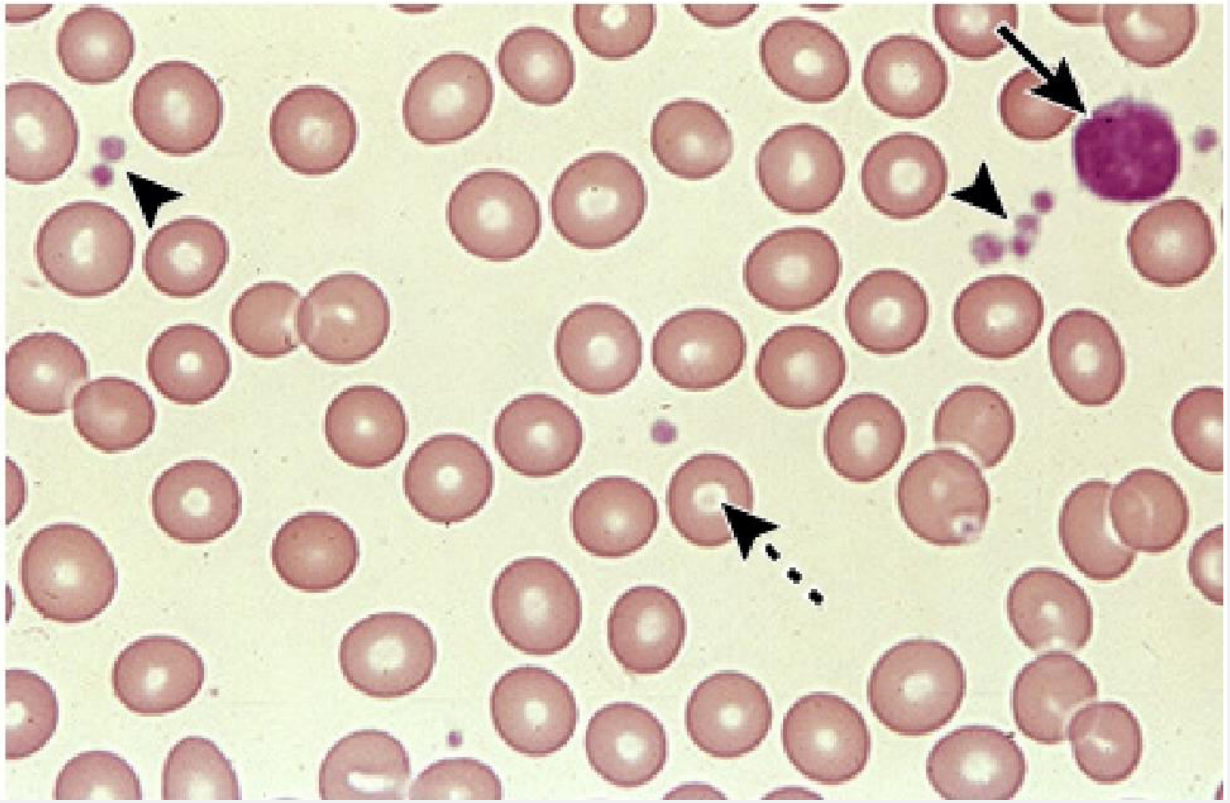
1. Peripheral blood smear:
   - CBC → Red cells are **micro**cytic (MCV < 80 mm3) **hypo**chromic (decreased MCHC), with a **low reticulocyte count, High RDW**
   - Blood Film → microcytosis and anisopoikilocytosis (variation in erythrocyte shape and size)

2. Iron studies:
- ↓ **serum iron**
- ↓ **serum ferritin**—most reliable test available
- ↑ **TIBC**
- **Increased TIBC/transferrin levels**

3. Bone marrow biopsy—the gold standard, but rarely performed.

4. If GI bleeding is suspected—guaiac stool test or colonoscopy

Normal peripheral blood smear



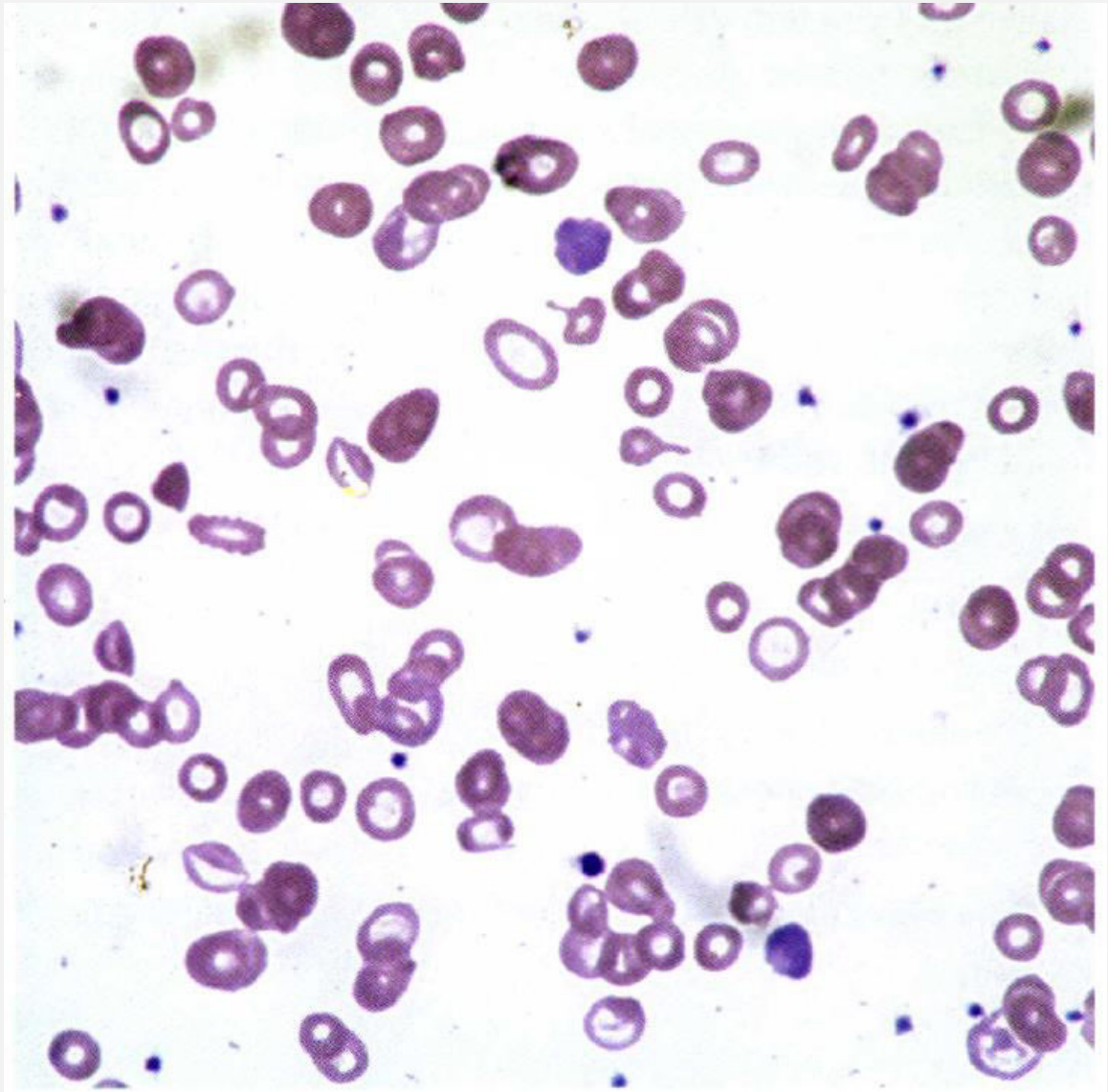


FIGURE 12. Hypochromia and microcytosis with anisopoikilocytosis (variation in erythrocyte shape and size) in a patient with iron deficiency.

TREATMENT

Severe and highly symptomatic: RBC transfusion

- ✓ Severely reduced hematocrit or myocardial ischemia

Oral iron

GI side effects very common (Constipation, diarrhea, epigastric pain, nausea/vomiting, Black, green or tarry stools)

Intravenous iron

- ✓ oral iron may not be adequate treatment
- ✓ Used when GI side effects prohibit oral replacement
- ✓ Or patients with malabsorption (celiac disease, inflammatory bowel disease)
- ✓ undergone resection of the stomach or small bowel
- ✓ Pregnancy (more rapid repletion of iron)

ORAL IRON THERAPY

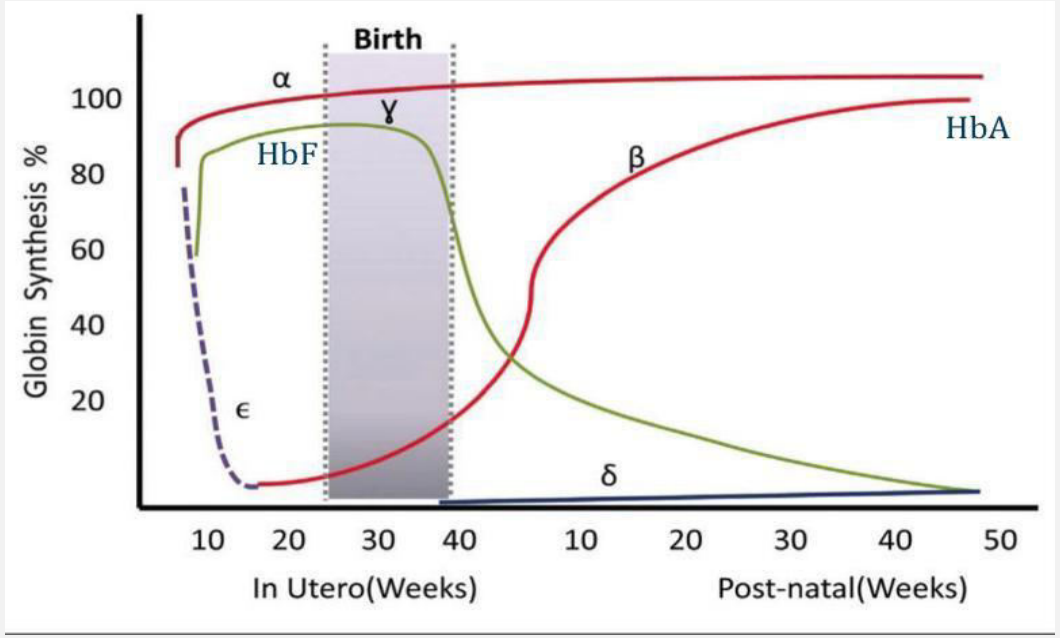
- Iron deficiency is typically managed with oral iron
- Oral **ferrous sulfate** is the least expensive preparation, Although oral **ferrous fumarate**, **ferrous gluconate**
- Oral absorption can be increased with supplemental **vitamin C**
- Frequent dosing (two or three times daily) of oral iron can lead to increased **hepcidin** production, which actually reduces iron absorption. For this reason, a **single daily or every-other-day dose** of oral iron sulfate may be the best replacement dose.
- **Hemoglobin levels** typically increase by approximately **1 g per week**.
- Oral iron replacement typically **lasts 3 to 6 months** after normalization of hemoglobin to replace **iron stores**

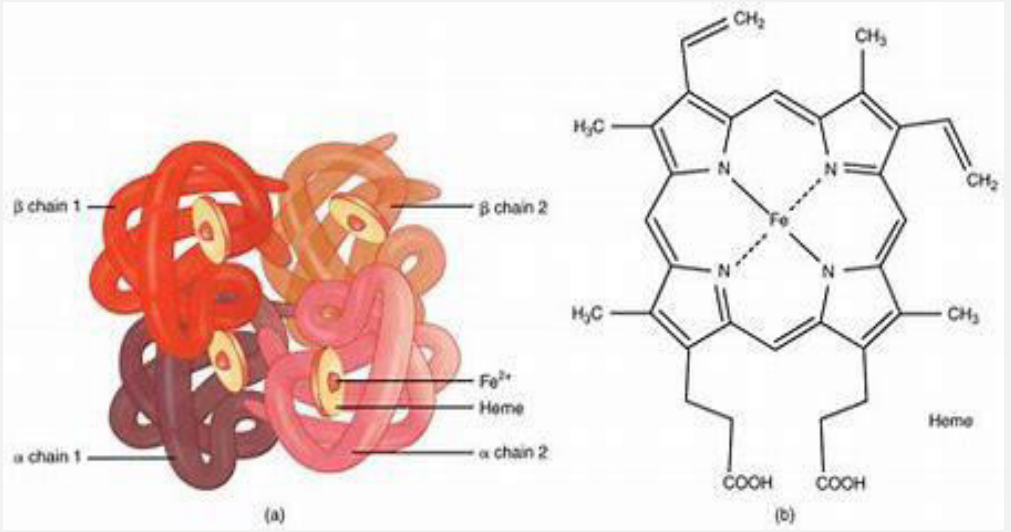
CAUSES FOR LACK OF RESPONSE TO ORAL IRON THERAPY

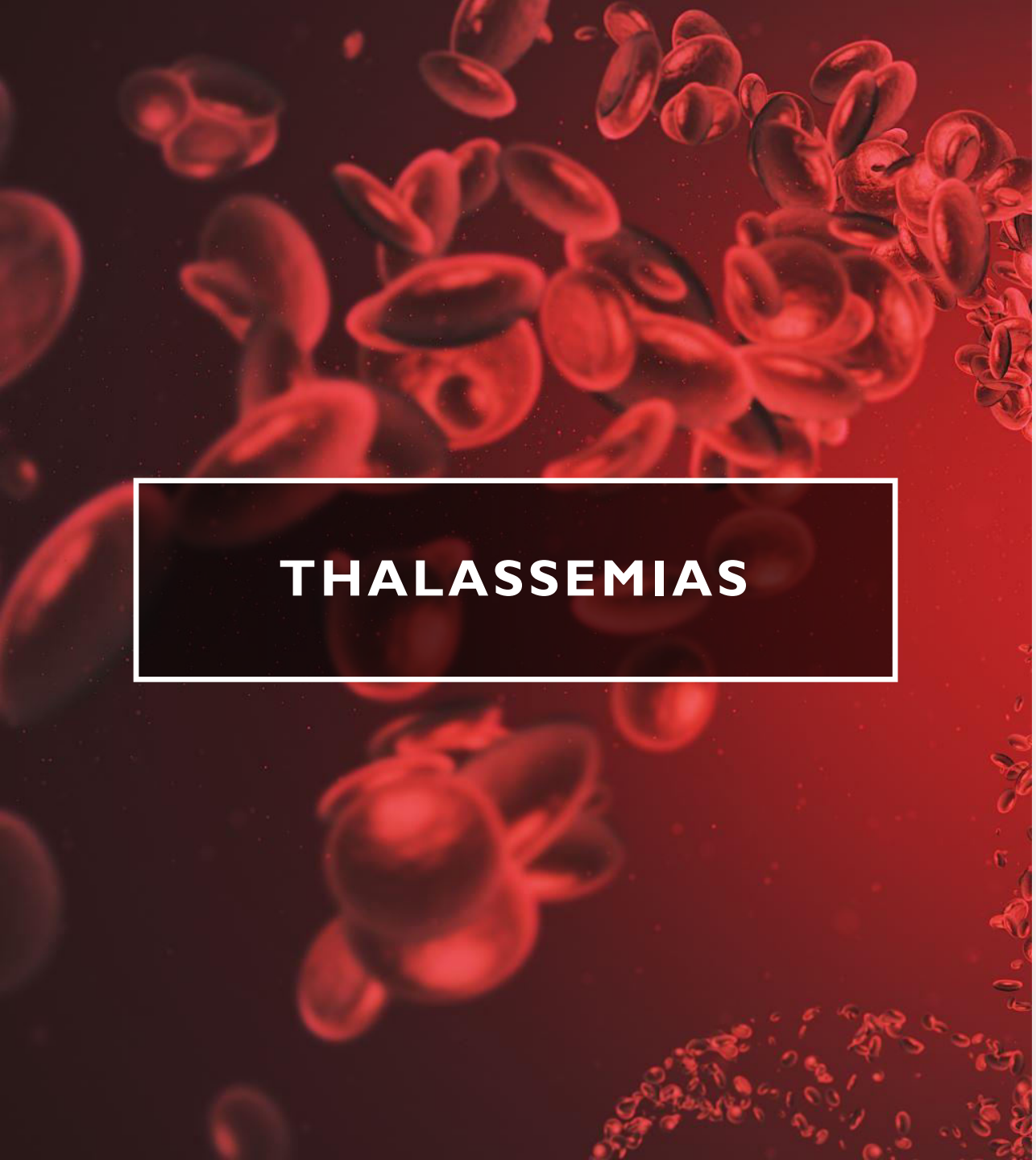
1. **Patient is not compliance**
2. **need in excess of iron dose ingested**
3. **Medication is being taken but is not being absorbed**
4. **A coexisting condition is interfering with bone marrow response to iron repletion**
   1. Infection
   2. Inflammatory disorder (eg, rheumatoid arthritis)
   3. Concomitant malignancy
   4. Coexisting folate and/or vitamin B12 deficiency
   5. Bone marrow suppression from another cause
5. **Continued blood loss**

GLOBIN CHAINS AND HEMOGLOBIN

- Hemoglobin is a tetramer with **2 α- and 2(β, δ ,or ɣ -globin chains).**
- Types of normal hemoglobin are **Hemoglobin A(2 α 2 β), Hemoglobin A2 (2 α 2 δ),and Hemoglobin F (2 α 2 ɣ).**
- These tetramers are covalently linked to **heme**, a complex of **ferrous iron and protoporphyrin.**



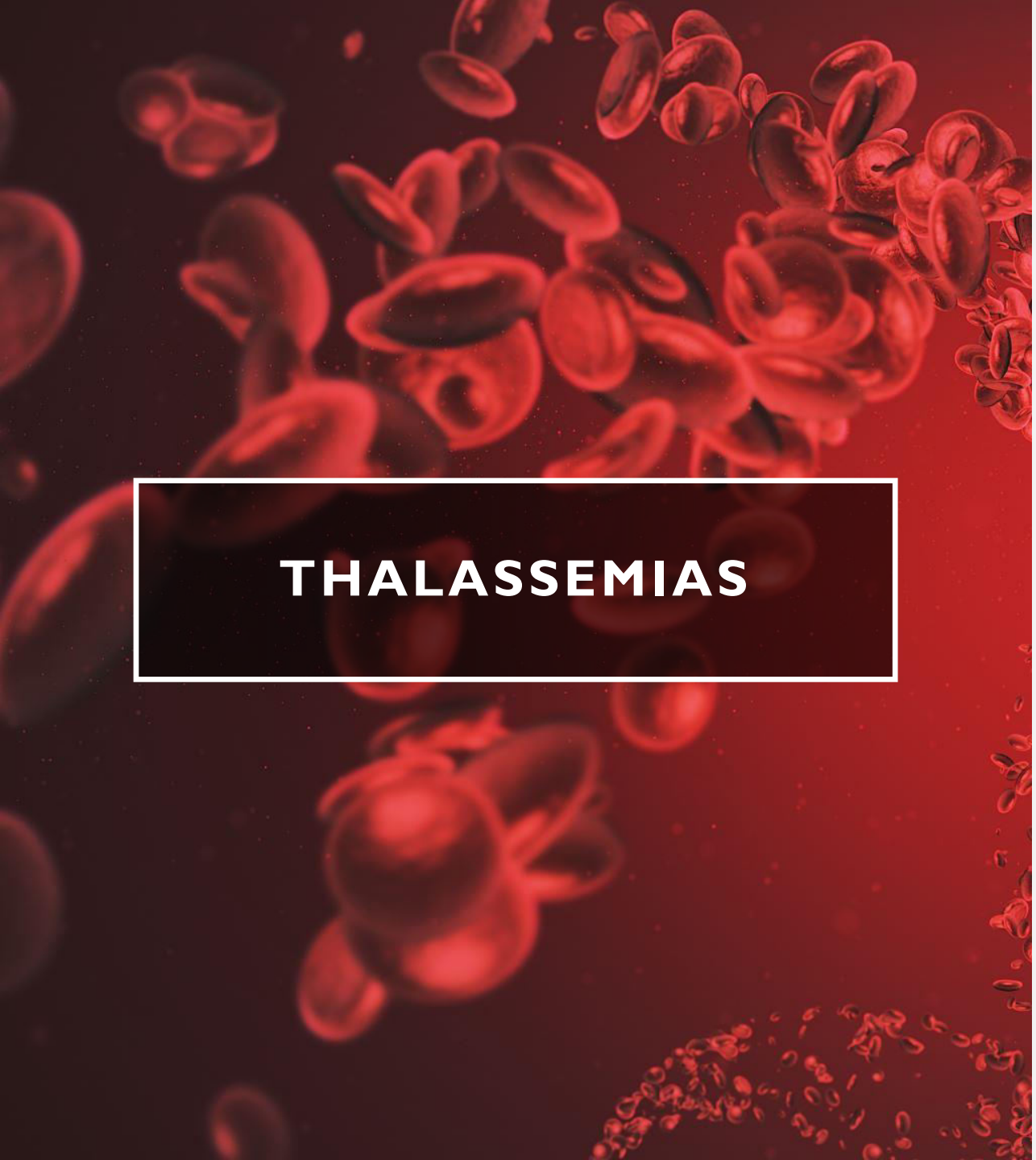




THALASSEMIAS

- Inherited disorders characterized by defect synthesis of **either the α- or β-globin chains of hemoglobin.**

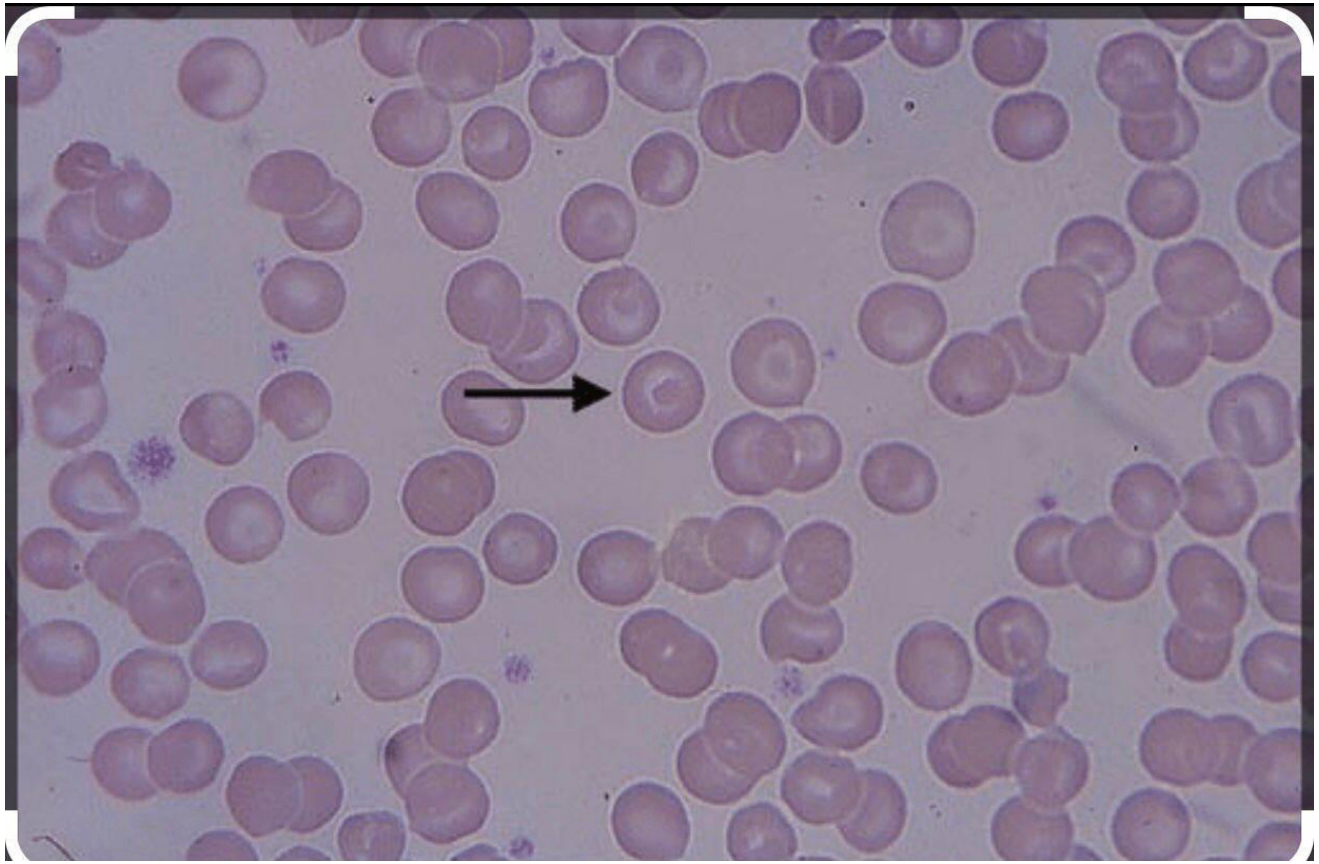
- The defective synthesis of globin chains in thalassemia leads to imbalanced globin chain production , leading to precipitation of globin chains within the red cell precursors and resulting in ineffective erythropoiesis



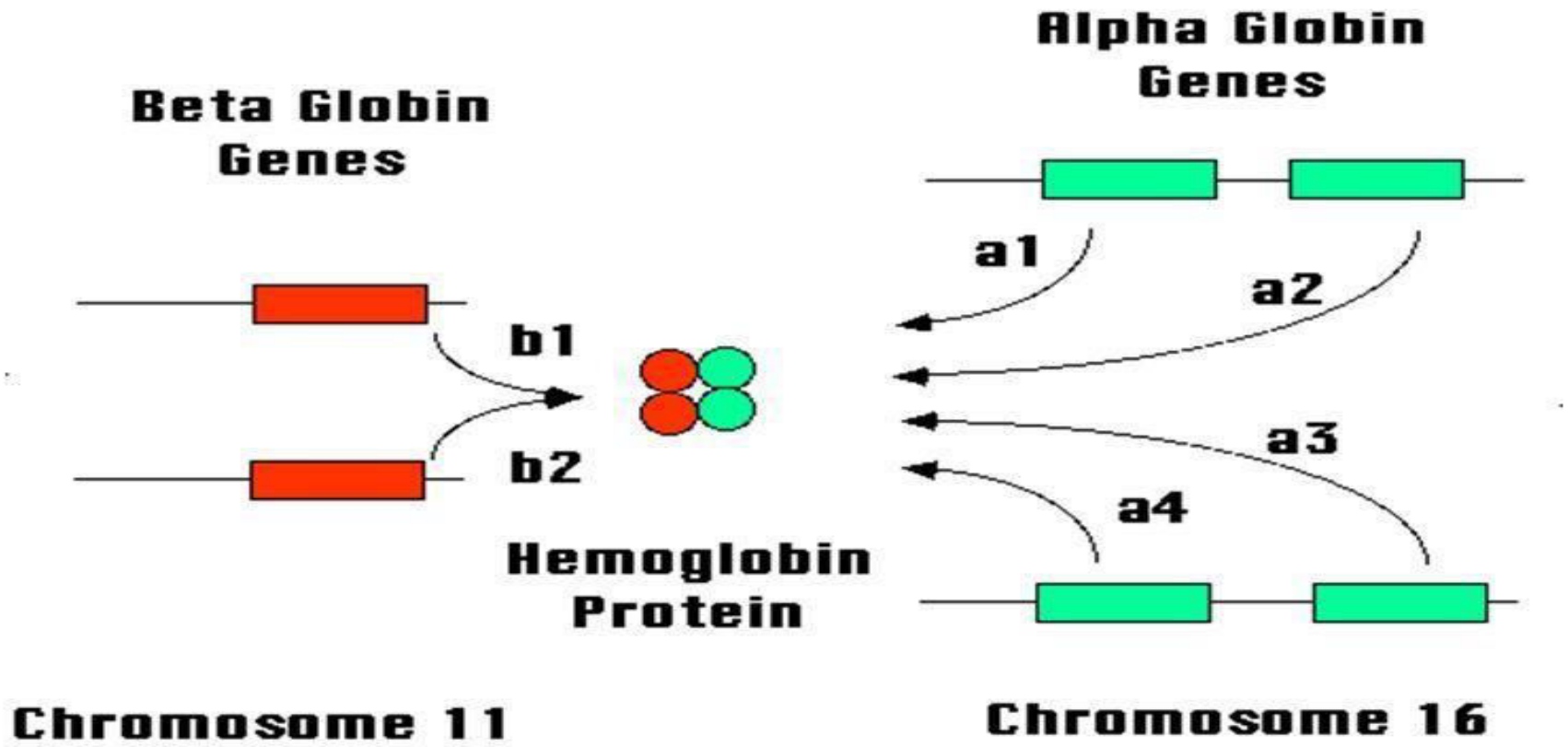
THALASSEMIAS

- Because of ineffective erythropoiesis, thalassemia can be associated with:
  - increased lactate dehydrogenase
  - increased unconjugated bilirubin
  - decreased haptoglobin levels

- In patients with thalassemia, the PBS typically shows microcytosis, nucleated erythrocltes, and target cells.
- The microcytic cells in thalassemia are uniform and the RDW is normal.



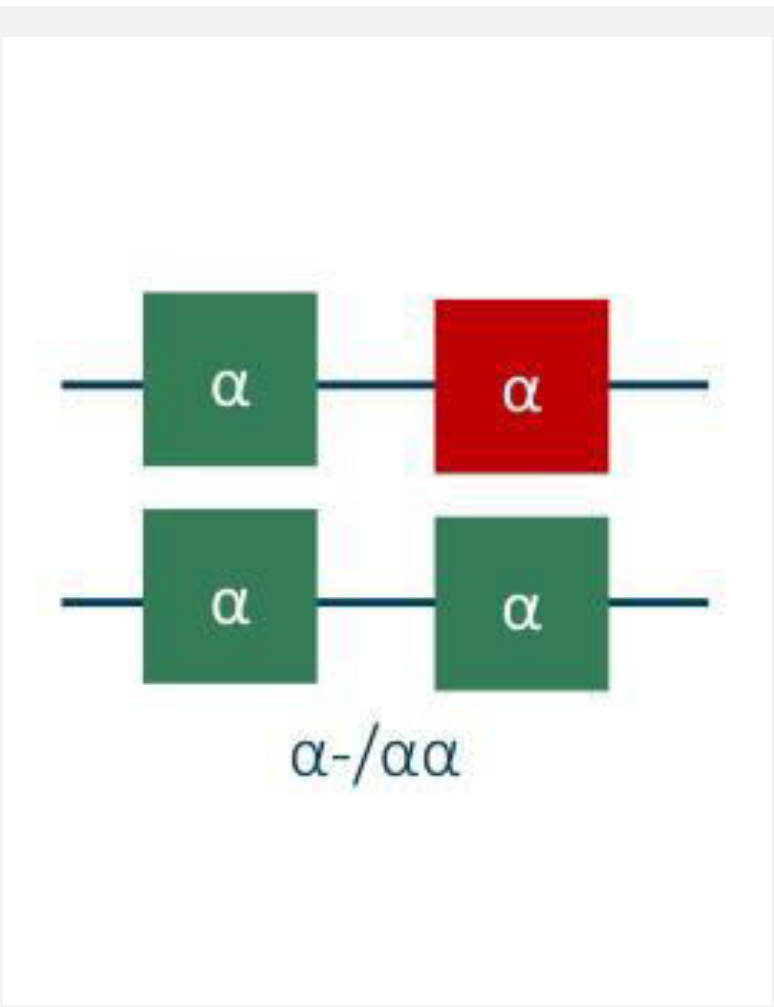
Genes responsible for synthesis of Hb molecule (α and β globin chains)



ALPHA - THALASSEMIA

ALPHA - THALASSEMIA

- The gene for α globin is duplicated on both chromosomes 16 (4 genes code for α chains 2 from each parent) .
- α-thalassemia is often caused by gene deletions, and this will lead to reduce production of α chains.
- The severity of phenotype increases with **the number of α -genes that are affected.**
- **This type is more common in individuals from Southeast Asian.**

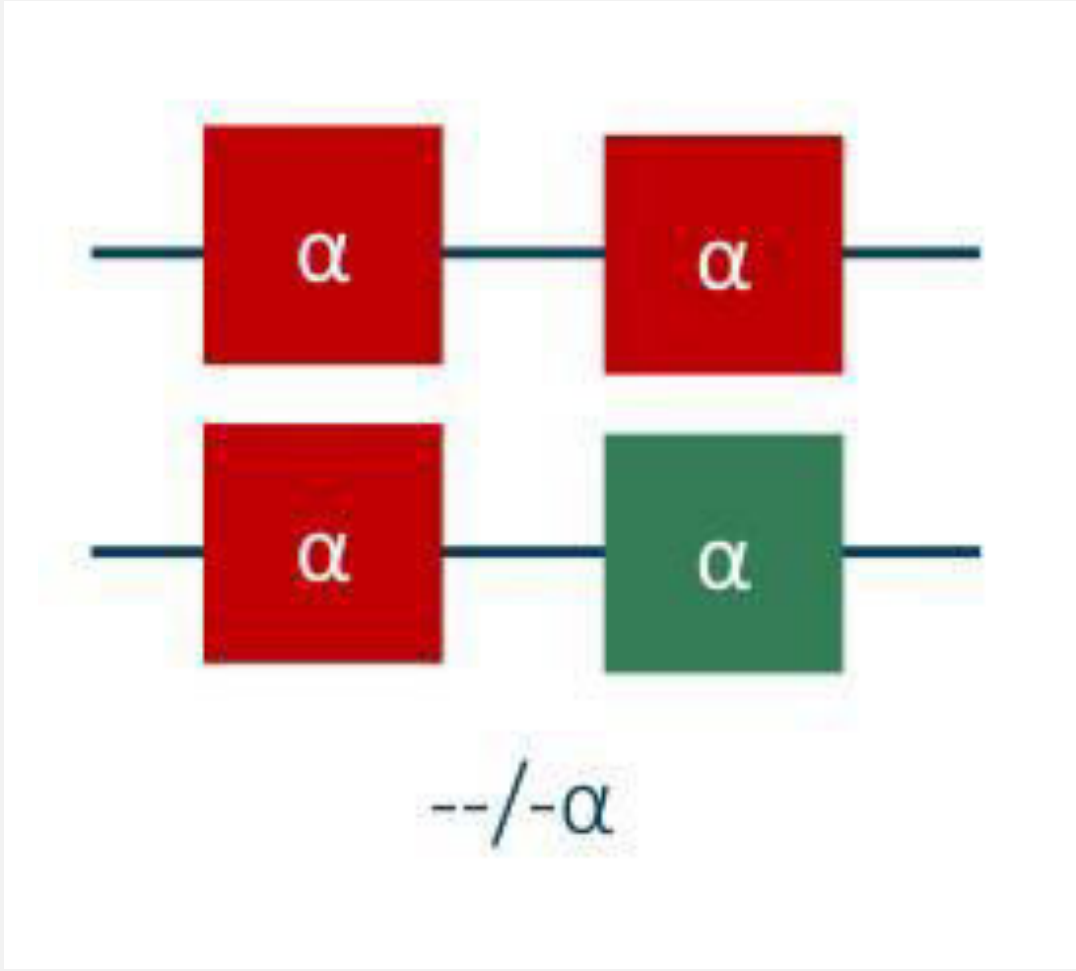


α Thalassemia Minima (silent carrier)

- Loss of a single α-chain gene.
- Asymptomatic
- Normal hemoglobin analysis , anemia is absent.
- No treatment necessary.

α-Thalassemia Minor (trait)

- Loss of two α-chain genes.
- Asymptomatic
- Low MCV/MCH/MCHC (mild microcytic hypochromic anemia).
- No treatment necessary
- characterized by a hemoglobin level approximately 10 g/dL with microcytosis.
- Diagnosis is usually achieved by excluding other causes of hypochromic microcytic anemia.
- hemoglobin electrophoresis results are normal.



α-Thalassemia Intermedia (Hb H disease)

- Loss of three α-chain genes.
- Excess **β** chains pair together to form Hb H (tetramers of **β** globin)
- Highly variable presentation (often symptomatic at birth).
- Microcytic hypochromic anemia (low MCV/MCH/MCHC)
- Approximately 70% of patients with Hb H disease develop complications associated with ineffective erythropoiesis ,extramedullary hematopoiesis, iron overload, hemolytic anemia, and splenomegaly.

Diagnosis

- Peripheral blood smear : Microcytic hypochromic anemia.

- Electrophoreses : Hb H , decreased HbA ,HbA2, HbF .

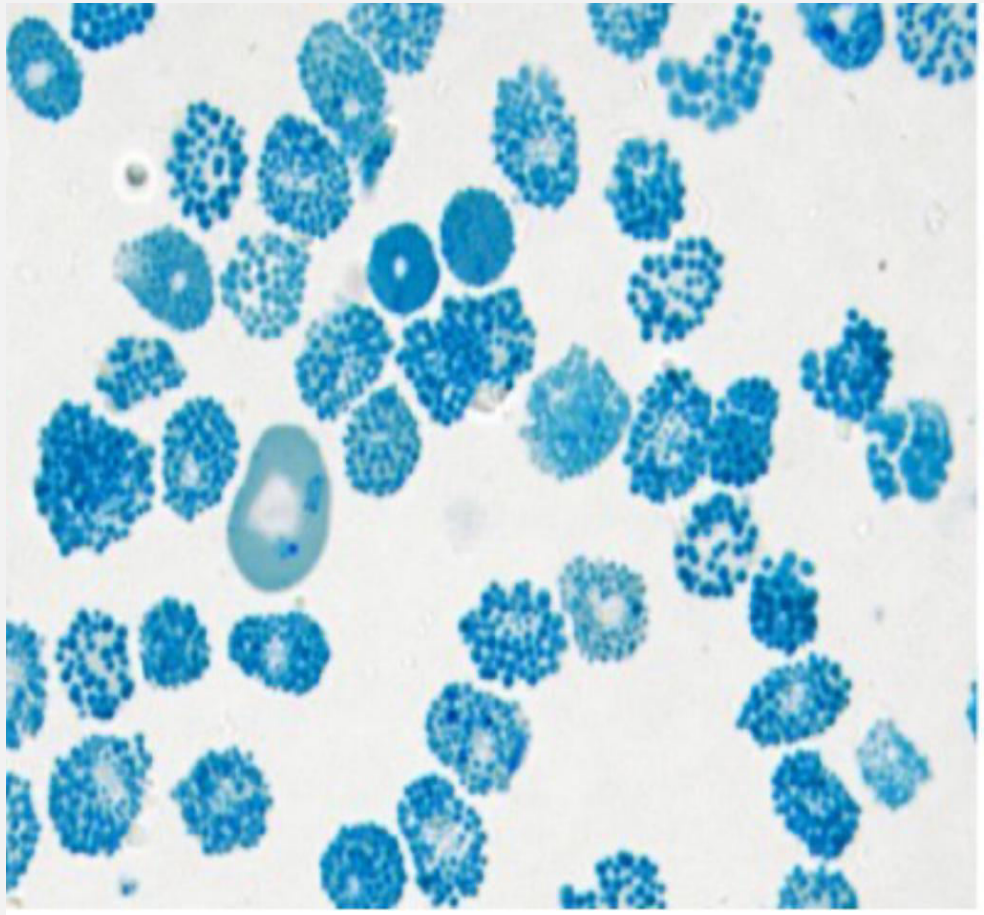
- DNA testing.

Treatment

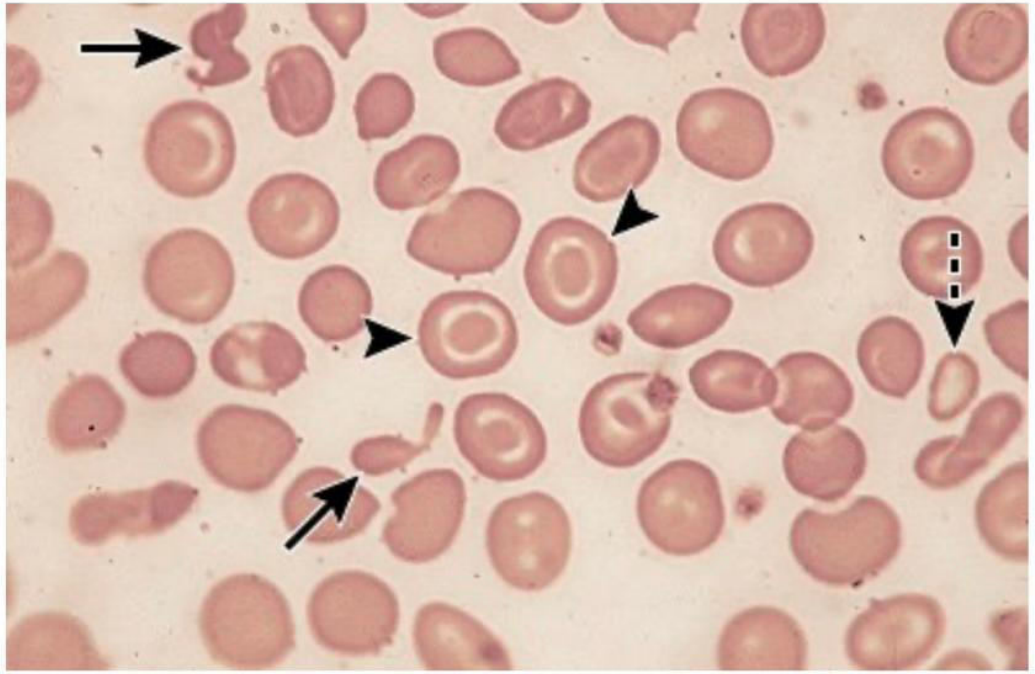
- Patients with **hemoglobin H disease** typically have hemoglobin concentrations of approximately **7 - 8 g/dl** and seldom rely on transfusion.

- Care should be taken to **avoid supplemental iron** because these patients absorb iron more efficiently and are at increased risk of iron overload and injury to the liver, heart, and other organs.

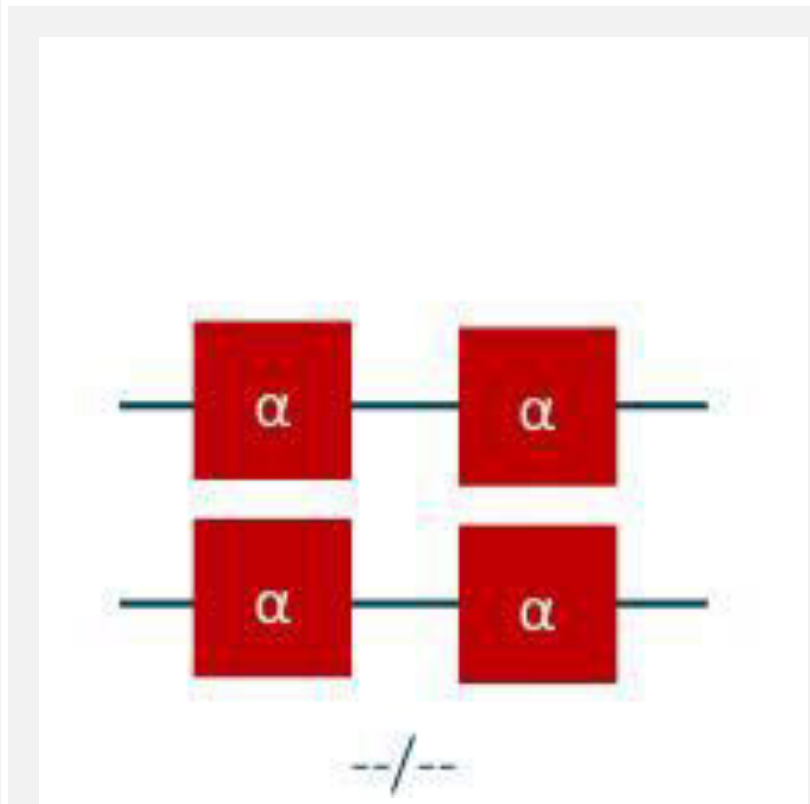
- Routine transfusions should also be avoided.



Hemoglobin H disease



Peripheral blood smear from a patient with hemoglobin H disease and an intact spleen. The smear shows target cells (arrowheads), microcytic red cells (dashed arrow), and red cell fragments (arrows).



α-Thalassemia major (Hemoglobin Barts)

- Loss of four α-chain genes.
- Hb Barts : form in utero , four gamma globin chains , and have such high oxygen affinity that they do not deliver any oxygen to the tissues, hydrops fetalis , and causing death in utero " unless in utero transfusion are administrated .

NUMBER OF α-GLOBIN GENES DELETED	DISEASE	CLINICAL OUTCOME
1 (α α/α –)	α-thalassemia minima	No anemia (silent carrier)
2 (α –/α –; *trans*) or (α α/– –; *cis*)	α-thalassemia minor	Mild microcytic, hypochromic anemia; *cis* deletion may worsen outcome for the carrier's offspring
3 (– –/– α)	Hemoglobin H disease (HbH); excess β-globin forms β_4	Moderate to severe microcytic hypochromic anemia
4 (– –/– –)	Hemoglobin Barts disease; no α-globin, excess γ-globin forms γ_4	Hydrops fetalis; incompatible with life

Phenotype	Hb A	Hb Barts	Hb H
Normal	97 – 98%	0	0
Silent Carrier	96 – 98%	0 – 2% (At birth)	0
α Thalassemia	85 – 95%	2 – 8% (At Birth)	< 2%
Hb H Disease	Dec	<10% (At birth)	5 – 40%
Hydrops Fetalis	0	70 – 80% (with 20% Hb Portland)	0 – 20%

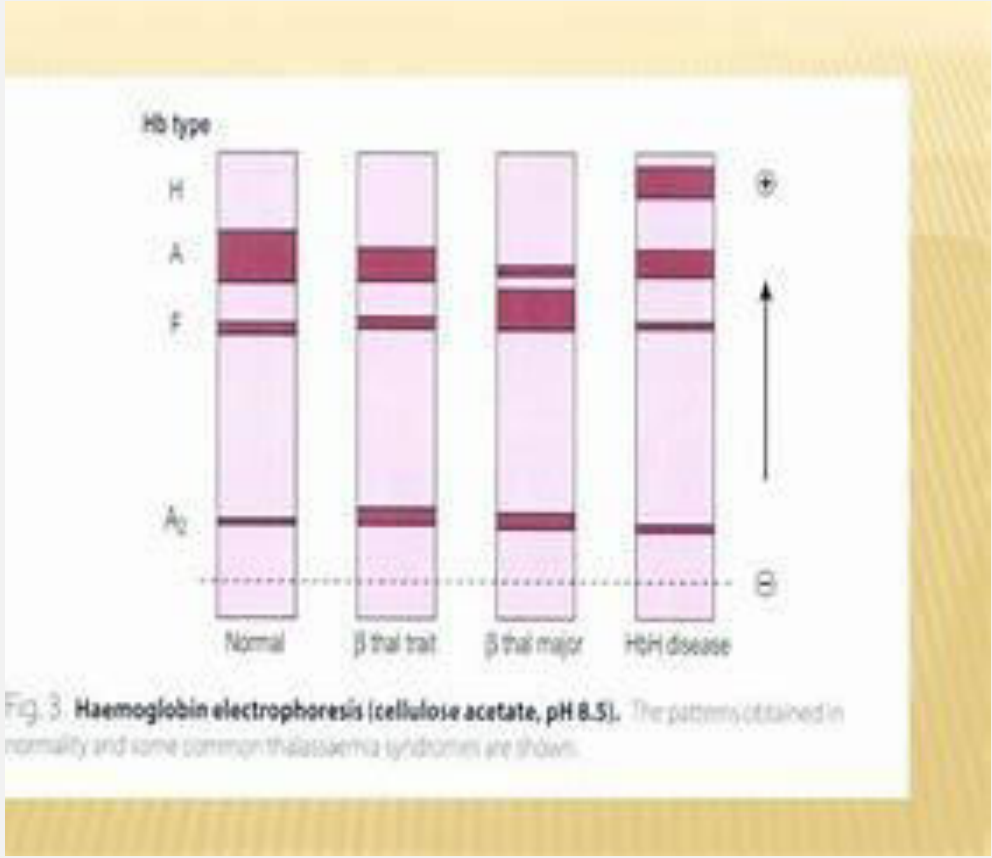
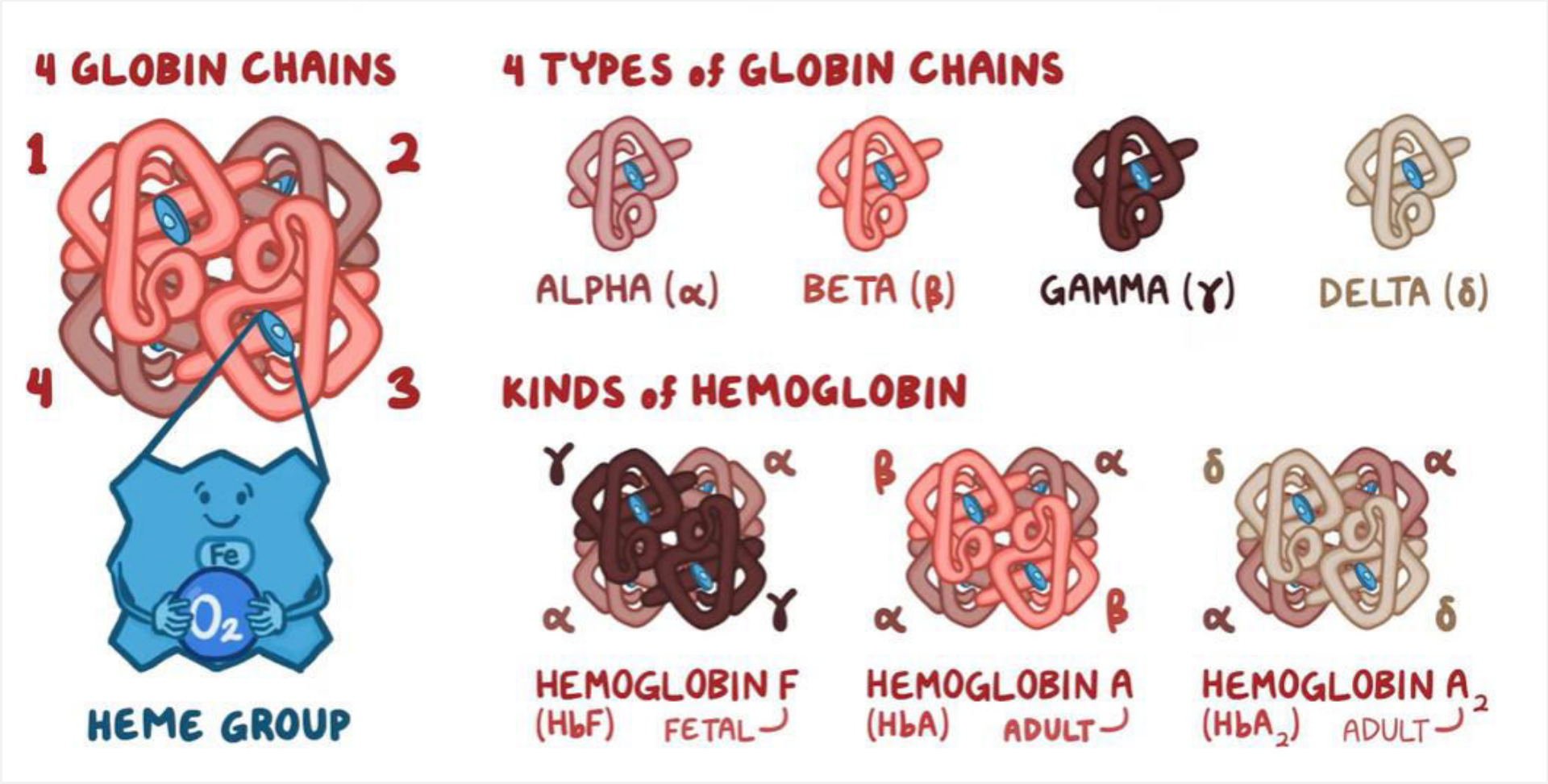


Fig. 3 **Haemoglobin electrophoresis (cellulose acetate, pH 8.5).** The patterns obtained in normality and some common thalassaemia syndromes are shown.

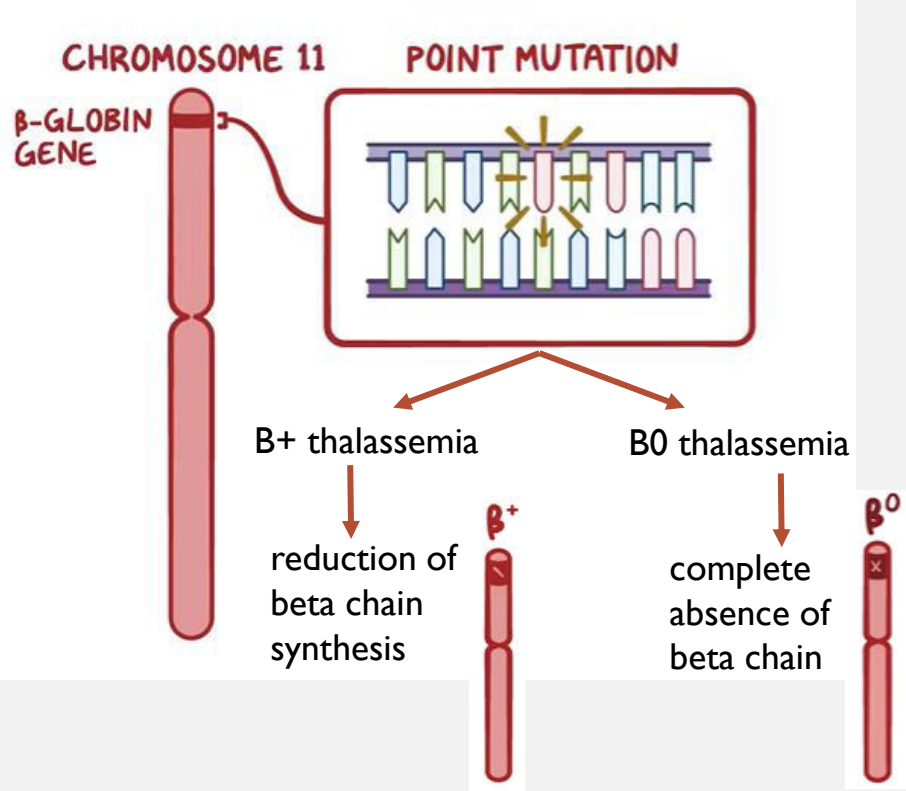
BETA - THALASSEMIA

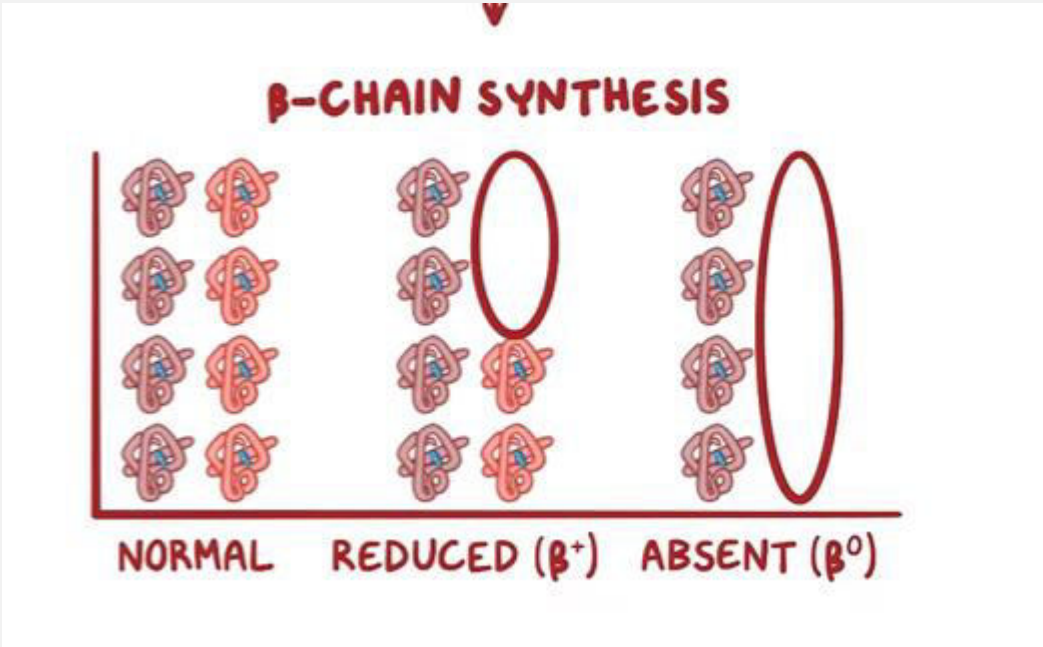
BETA - THALASSEMIAS



BETA - THALASSEMIAS

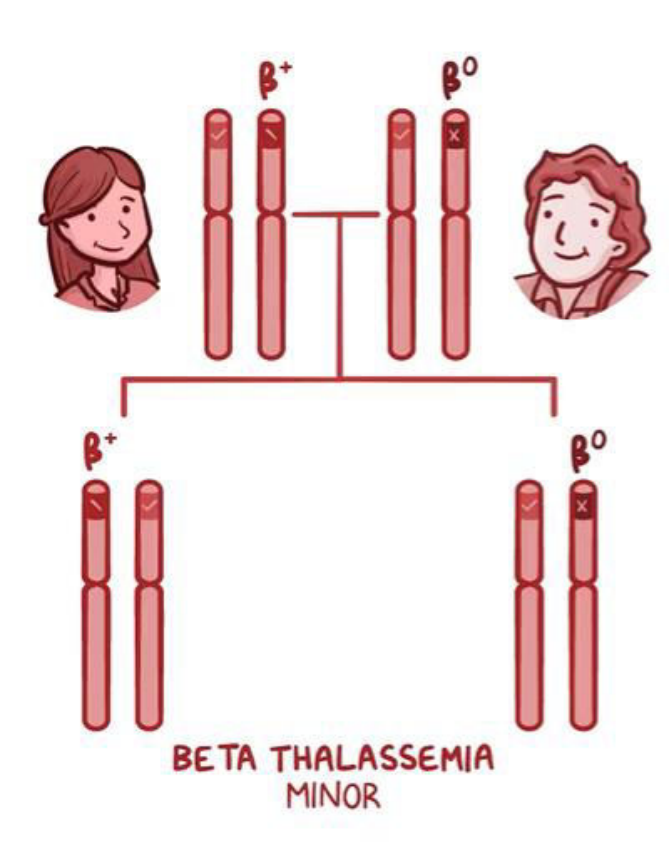
- **Autosomal recessive**.
- Mutation in β-globin gene on **chromosome 11.**
- β-chain production is deficient, but the synthesis of α-chains is unaffected

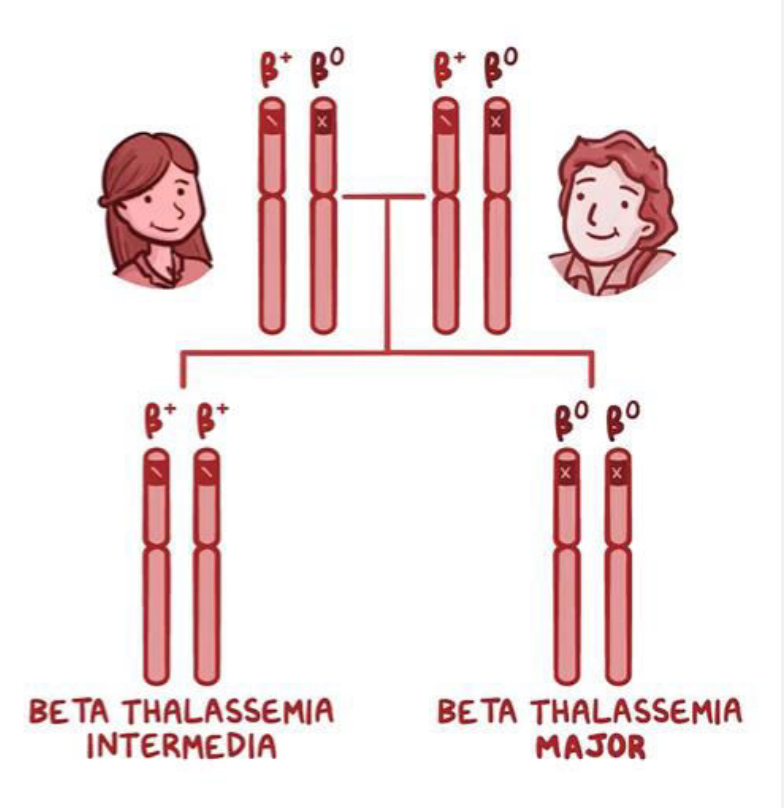




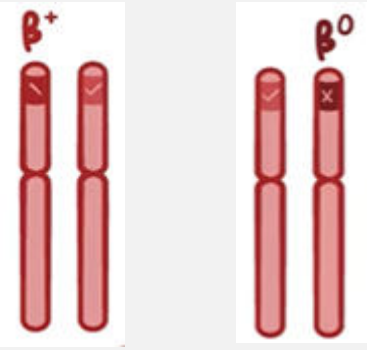
Beta Thalassemia

- Previously classified as minor, intermedia or major
- Now classified as **transfusion-dependent** or **transfusion-independent**





1. THALASSEMIA MINOR (HETEROZYGOUS B-CHAIN THALASSEMIA)



- Clinical features: usually **asymptomatic**.

- Diagnosis:

1. Hemoglobin level (10-12 mg/dl)
2. hemoglobin electrophoresis: **reduced HbA2 (> 3.5%)**
3. Peripheral blood smear: A **mild microcytic, hypochromic anemia**

- Treatment: usually not necessary (Patients **are not transfusion dependent**.)

2. THALASSEMIA INTERMEDIA

- Usually involves both β-globin genes
- Severity of anemia is **intermediate**
- Patients usually are **not transfusion dependent**

* May require **episodic transfusions** with stress
* Especially during infection or pregnancy

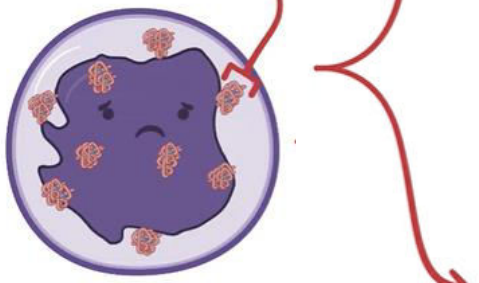
3. THALASSEMIA MAJOR (COOLEY ANEMIA; HOMOZYGOUS B-CHAIN THALASSEMIA)

Clinical features:

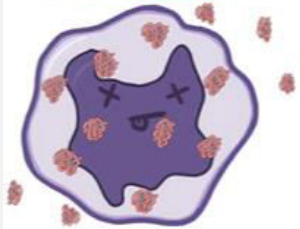
1. **Severe anemia (microcytic hypochromic**).
2. **Massive hepatosplenomegaly.**
3. Expansion of marrow space—can cause **distortion of bones.**
4. **Growth retardation** and **failure to thrive.**
5. If untreated (with blood transfusions), death occurs within the first few years of life secondary to progressive **CHF.**
6. Skull x-ray may show **"crew-cut" appearance.**

β-GLOBIN CHAIN DEFICIENCY

FREE α CHAINS
↓
INCLUSIONS



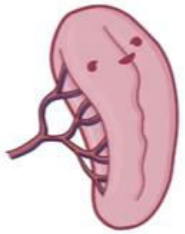
HEMOLYSIS



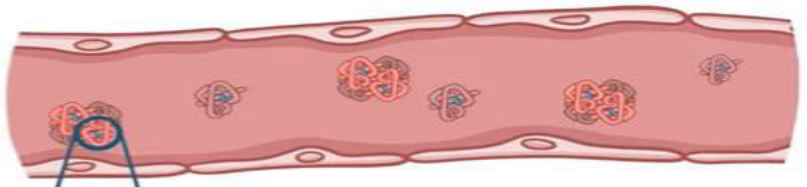
BONE MARROW

EXTRAVASCULAR HEMOLYSIS

SPLEEN



PLASMA



HEME → BILIRUBIN + IRON

BILIRUBIN → JAUNDICE

IRON → 2° HEMO-CHROMATOSIS

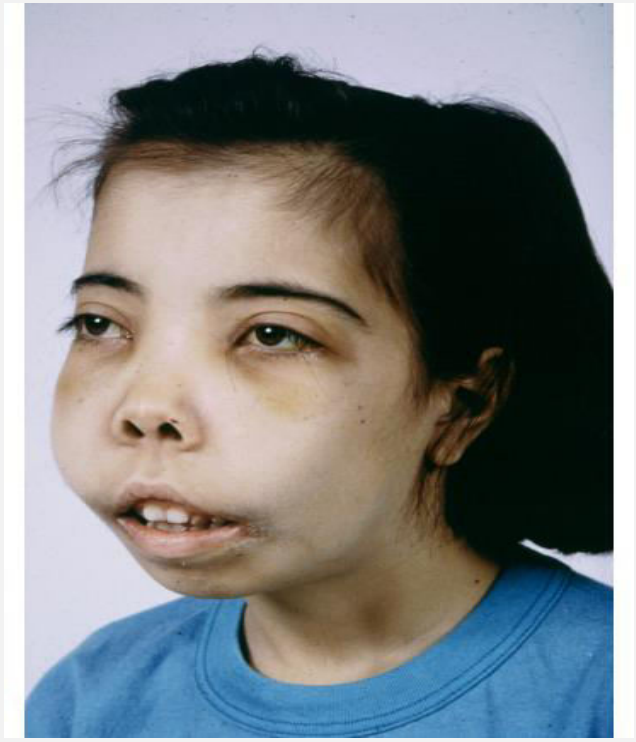
ANEMIA

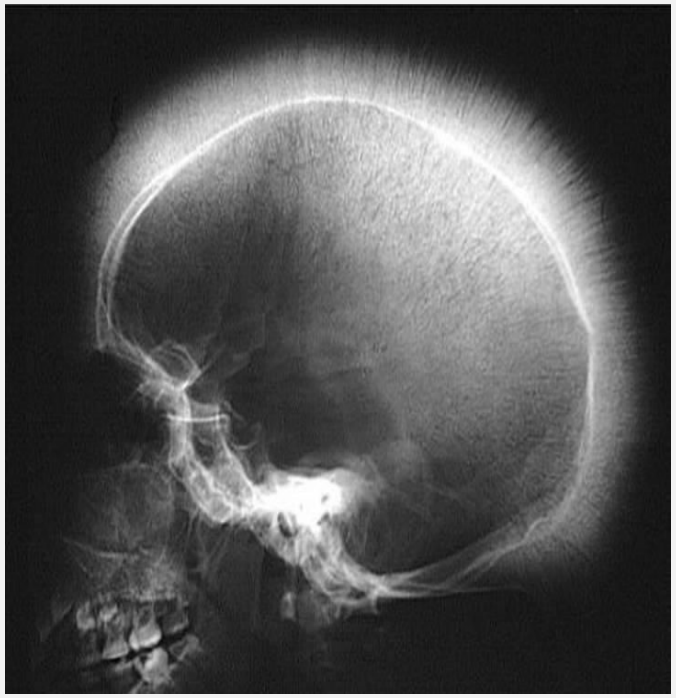
- PALLOR
- SHORTNESS of BREATH
- EASY FATIGABILITY

HEPATOSPLENOMEGALY

- JAUNDICE
- SWOLLEN ABDOMEN

GROWTH RETARDATION



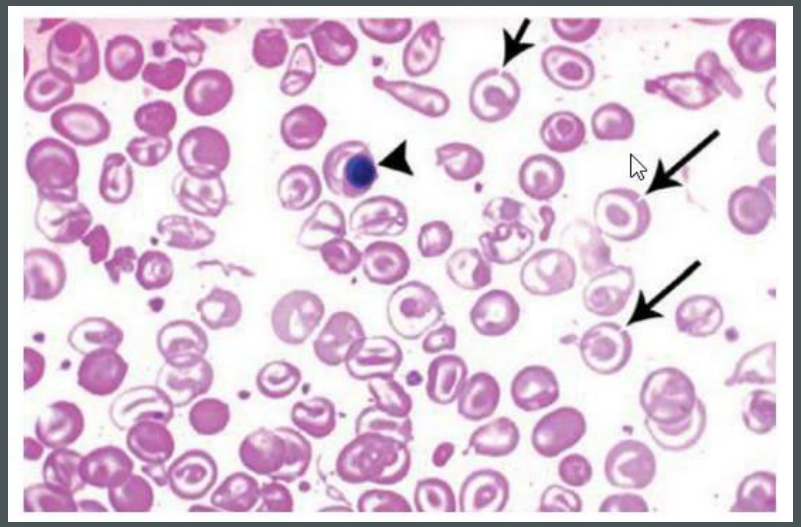


Thalassemic/chipmunk face

1. frontal bossing
2. maxillary hypertrophy
3. depression of nasal bridge
4. malocclusion of teeth

“crew-cut”/”Hair-on-end” appearance

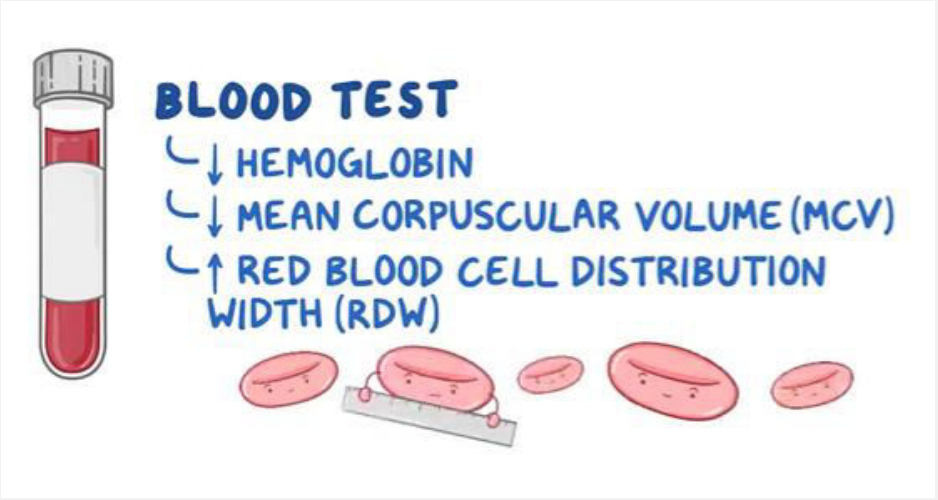
DIAGNOSIS

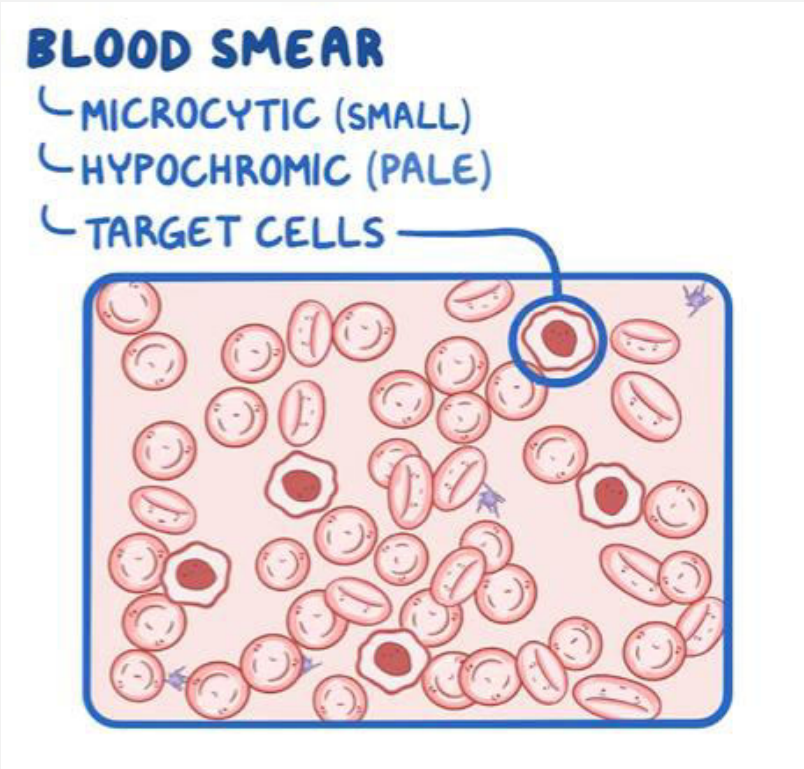


Blood smear: thalassemia.

Target cells (arrows)

circulating nucleated red blood cells (arrowhead).

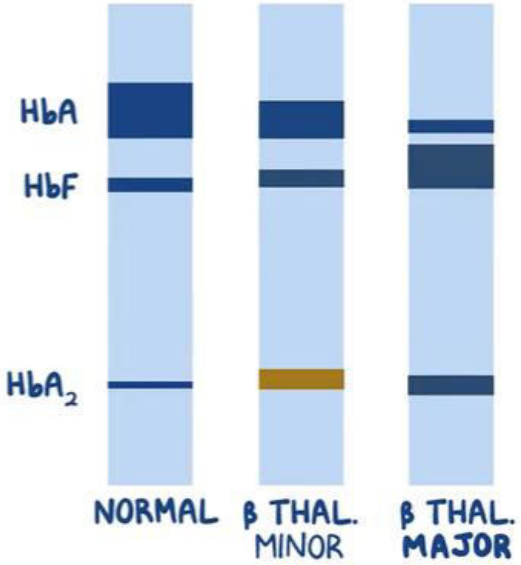




DIAGNOSIS

CONFIRMED:
HEMOGLOBIN ELECTROPHORESIS

- ↓ HbA
- ↑ HbF, HbA_2



- Iron studies:
  - Serum Ferritin: Normal/high
  - Serum Iron: Normal/high

TREATMENT

- **“Transfusion dependent”**
- frequent PRBC transfusions are required to sustain life.
- **Splenectomy**
- **Bone marrow transplantation**

- **Iron overload** sometimes develops in patients with transfusion-dependent thalassemia, and if untreated this can lead to **CHF** (symptoms of hemochromatosis). Therefore, these patients are often treated with chelating agents that eliminate excess iron:

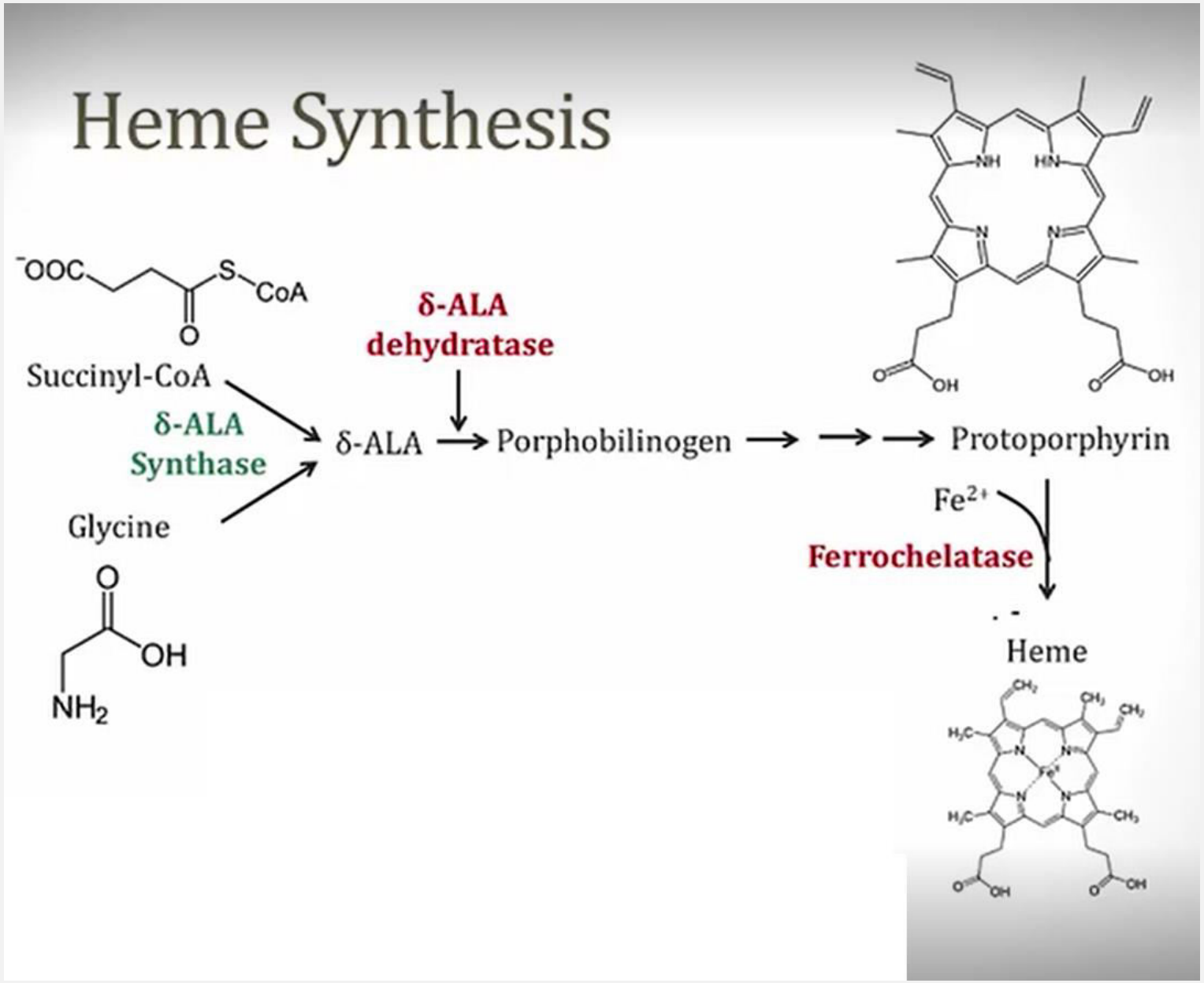
1. **Deferoxamine** (IV).
2. **Deferiprone** (Oral).

SIDROBLASTIC ANEMIA

SIDROBLASTIC ANEMIA

- Type of microcytic anemias that occur due to defective in protoporphyrin synthesis
- Hemoglobin = hem + globin
- Hem = ferretin + protoporphorin , so any decrease in protoporphorin will lead to decrease heme thus will decrease hemoglobin which will cause microcytic anemia .
- Mainly it's an abnormality in RBC iron metabolism

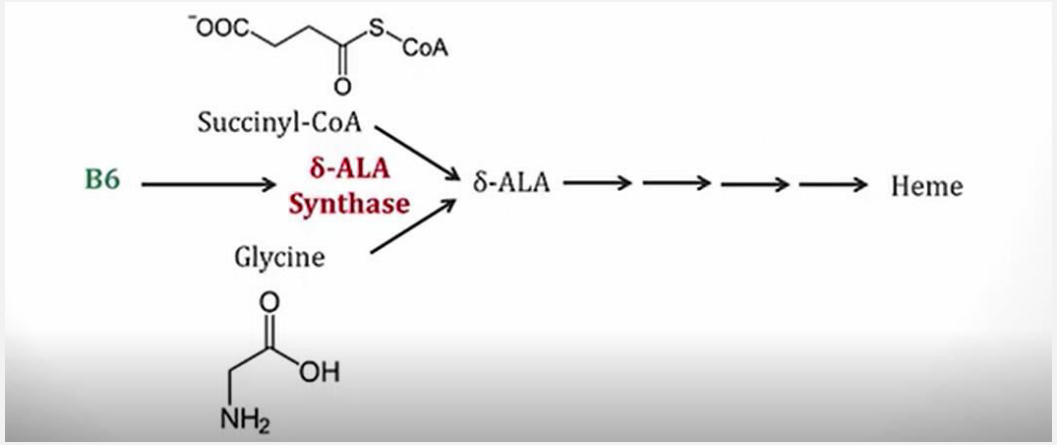
Heme Synthesis



CONT.

- It can be divided into :
- **Congenital :** mainly due to ALAS defect (the rate limiting step enzyme) → often responds to treatment with Vit B6
- **Acquired (reversible) :**

1. Exposure to **lead** which denature the enzyme (inhibit ALAD and FERROCHELATASE)
2. **Alcohol** (toxic to the mitochondria, hence it will damage the production of protoporphorin)
3. **Vitamin B6 deficiency** (cofactor and a rate limiting step for ALAS to function properly)
4. **Drugs** (isoniazid , chloramphenicol)
5. **Neoplastic disease** (Myelodysplastic syndromes).



CONT.

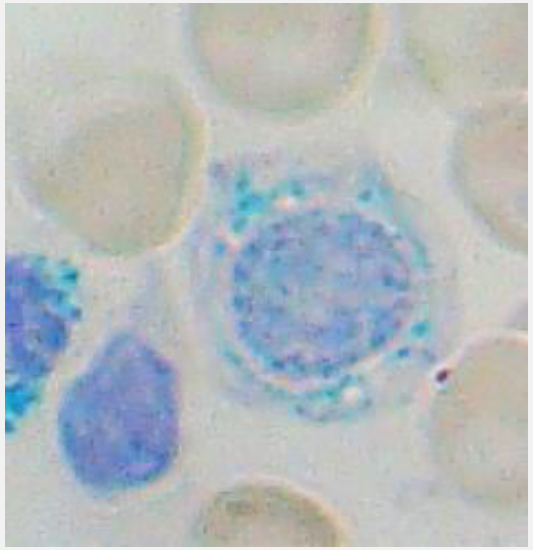
- **Clinical features** : general signs and symptoms of anemia.

- **Lab findings:**

➢ **Iron studies :** High iron, normal/low TIBC, high ferritin.

➢ **Bone marrow biopsy** : Ringed sideroblasts (with iron-laden, Prussian blue–stained mitochondria .

➢ **Peripheral blood smear**: Basophilic stippling of RBCs.



- **Treatment :**

➢ Remove the offending agent .

➢ Pyridoxine (B6, cofactor for δ-ALA synthase)

MACROCYTIC ANEMIA

Macrocytic

B_{12} deficiency

Folate deficiency

Myelodysplasia

Drug toxicity

Alcohol

Hypothyroidism

Liver disease

MEGALOBLASTIC ANEMIA

VITAMIN B12 DEFICIENCY

COBALAMIN (VITAMIN B12)

- is necessary for DNA synthesis. Humans cannot synthesize cobalamin but must consume it in their diet; it is found in animal meats, shellfish, and dairy products.

- **Causes of Cobalamin Deficiency :**

- **1- age-related gastric achlorhydria or the use of proton pump inhibitors.**

- **2- malabsorption**
- such as inflammatory bowel disease, pancreatic insufficiency, bacterial overgrowth,and metformin use.

- **3- Pernicious anemia**
- Characterized by autoimmune gastritis and intrinsic factor deficiency.

- **4- Dietary deficiency**
- is an uncommon cause of cobalamin deficienry because body stores are typically available for many years.

Symptoms of vit.b12 deficiency :

1- pallor and glossitis

"lemon-yellow" skin because of pallor and jaundice resulting from ineffective erythropoiesis.

2- neurologic symptoms

loss of vibratory sense, loss of proprioception, spastic ataxia, and other dorsal column symptoms.

3- psychiatric symptoms

(megaloblastic mania) : dementia, hallucinations, and frank psychosis.

4- symptoms of pancytopenia

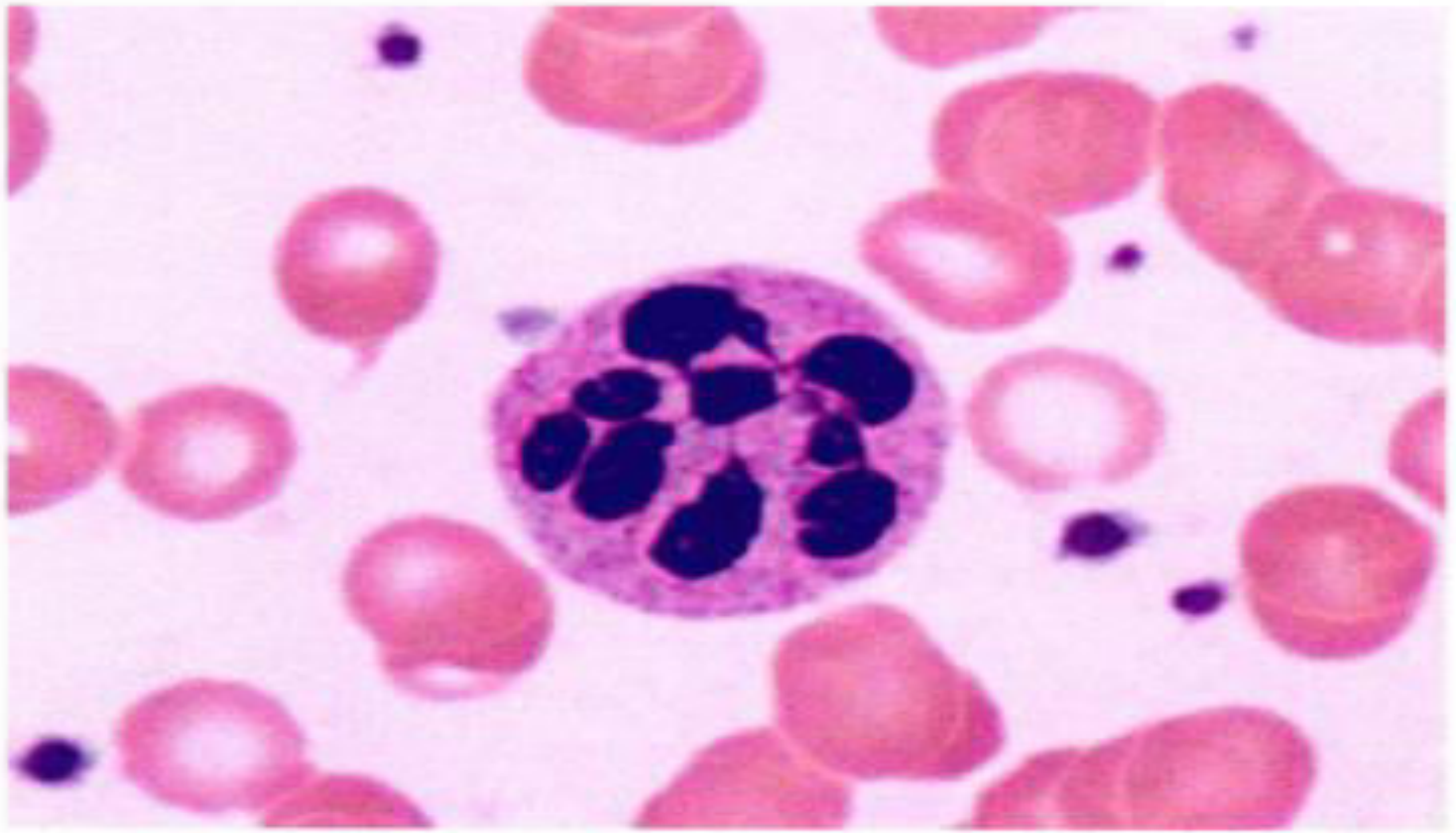


FIGURE 15. Hypersegmented polymorphonuclear (PMN) cell in a patient with pernicious anemia. The presence of hypersegmented PMNs becomes significant when they constitute greater than 5% of PMNs with five or more lobes or 1% with six or more lobes.

PBS shows oval macrocytes and hypersegmented neutrophils

Labs :

1- increased homocysteine and methylmalonic acid level.

(more sensitive)

2- vitamin B12 level lower than 300 pg/mL

Treatment : **oral cobalamin (1000-2000 pg/d)**

absorbed well even in patients with malabsorption.

Parenteral cobalamin is more expensive and more cumbersome to administer

When cobalamin is replaced, megaloblastic changes in the marrow improve within hours. Reticulocytosis appears in several days, and the hemoglobin level increases by approximately I g per week. If the response to cobalamin is inadequate, an alternative diagnosis, such as myelodysplasia, should be considered.

Neurologic changes may not be reversible with replacement.

Note : Folate supplementation in vitamin B12 deficiency can correct the anemia, but worsens neurologic symptoms.

FOLIC ACID DEFICIENCY

FOLATE DEFICIENCY

Folate is found in green leafy vegetables and most fruits.

Causes of folate Deficiency :

1- malnutrition (eg, alcoholics)

Folate is poorly stored, and deficiency can develop in weeks to months in patients with insufficient folate ingestion

2- malabsorption

gastric bypass and small bowel diseases such as celiac disease or inflammatory bowel disease

3-Drugs

such as triamterene, phenytoin, or methotrexate

4- rapid cell turnover

such as pregnancy, hemolysis, or desquamating skin disorders (psoriasis), have increased folate requirements

Labs :

Incresesd homocysteine, normal methylmalonic acid.

Serum folate measurement

if very low, helps establish the diagnosis; however, a normal level maybe unreliable because a single meal can normalize levels.

****

The PBS in folate deficiency **is identical** to that of cobalamin deficiency

No neurologic symptoms (vs B12 deficiency).

Treatment:

After cobalamin deficiency is excluded, patients with

folate deficiency should receive **oral folate, 1to 5 mg/d.**

OROTIC ACIDURIA

Orotic aciduria

Inability to convert orotic acid to UMP (de novo pyrimidine synthesis pathway) because of defect in UMP synthase.

Autosomal recessive

Presents in children as failure to thrive, developmental delay, and megaloblastic anemia refractory to folate and B12.

No hyperammonemia

(vs ornithine transcarboxylase deficiency—orotic acid with hyperammonemia)

Orotic acid in urine.

Treatment: uridine monophosphate or uridine triacetate to bypass mutated enzyme.

NON-MEGALOBLASTIC ANEMIA

NON-MEGALOBLASTIC ANEMIA

Macrocytic anemia in which DNA synthesis is normal.

RBC macrocytosis without hypersegmented neutrophils.

Causes: alcoholism, liver disease, diamond-Blackfan anemia

Diamond-Blackfan anemia

A congenital form of pure red cell aplasia.

Rapid-onset anemia within 1st year of life due to intrinsic defect in erythroid progenitor cells.

Short stature, craniofacial abnormalities, andupper extremity malformations (triphalangealthumbs) in up to 50% of cases.

THANK YOU

Resources

- UpToDate -

- MedStudy –

- 'MKSAPC' Medical Knowledge Self-Assessment Program@ 19th Hematology -

- OSMOSIS -