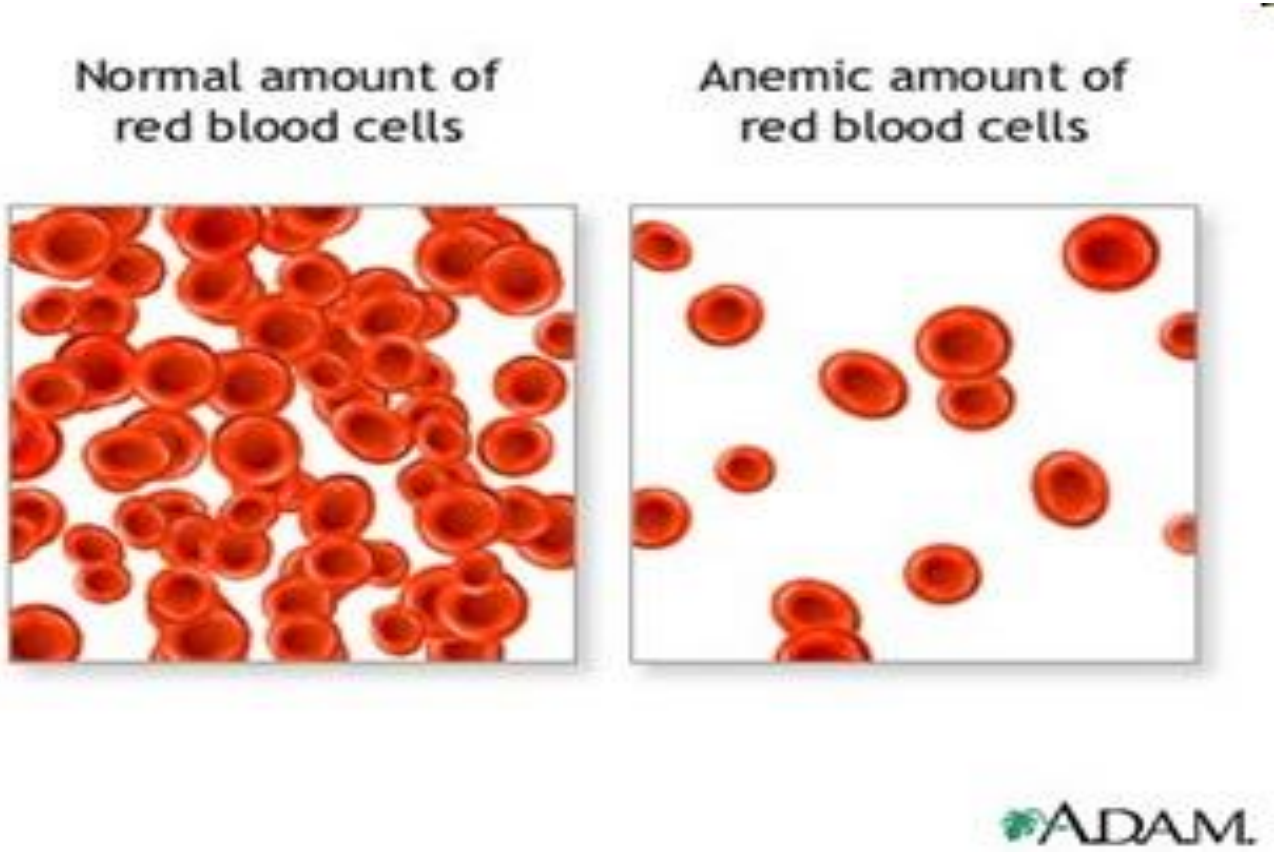
Anemia


Normal amount of red blood cells
Anemic amount of red blood cells
A.D.A.M.

What is anemia?

- Anemia is due to **deficiency of Hb** in blood due to lack of erythrocytes and/or their Hb content

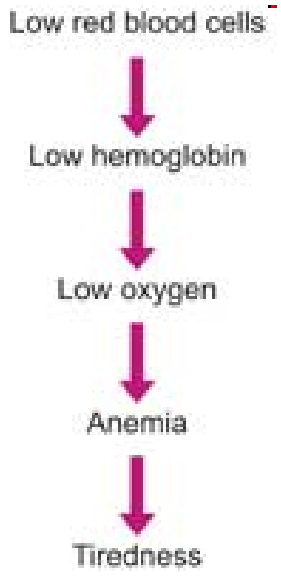
- Normal Hb concentration
  - Adult male =**14g/dl** (14-17)
  - Adult female not pregnant = **12g/dl** (12-14)
  - Adult female pregnant = **11g/dl** (11-12)

Symptoms of anaemia

The most common symptom of anaemia is tiredness.

Other signs and symptoms of anaemia include:

1. Weakness,
2. pale skin,
3. brittle nails,
4. Dizziness,
5. irritability.



Causes of anemia

- **Excess** blood loss due to bleeding

- **Under nutrition:** deficiencies of several vitamins and minerals like vitamins A, B2, B6, B12, C, iron, calcium and folic acid along with protein all of which can cause anaemia.

- **Pregnancy**

- **Others causes:** include worm infestation and chronic disease like AIDS, cancer or kidney disease, cancer treatment, and hereditary diseases

What is hemolytic anemia?

- Hemolytic anemia is a disorder in which the red blood cells are **destroyed prematurely**
- RBCs are destroyed **faster** than the bone marrow can produce them
- There are two types of hemolytic anemia: **Extrinsic** and **Intrinsic**

Types of hemolytic anemia

- **Extrinsic:**

Red blood cells are **produced healthy but are later destroyed** by becoming trapped in the spleen, destroyed by infection, or destroyed from drugs that can affect red blood cells.

Types of hemolytic anemia (cont.)

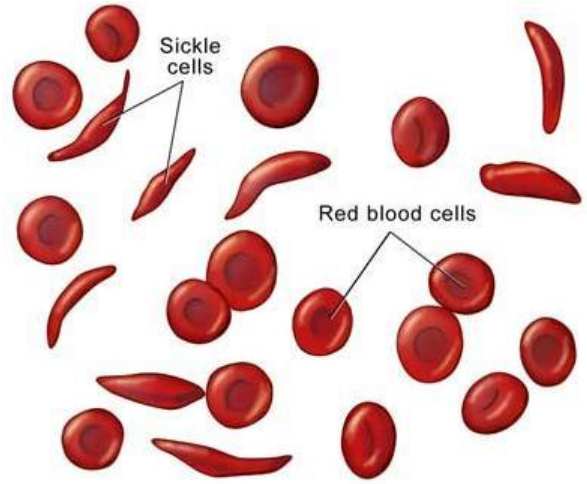
- **intrinsic:**
  - The destruction of the red blood cells due to a **defect within the red blood cells themselves**
  - Intrinsic hemolytic anemia is often **inherited**, such as sickle cell anemia and Glucose-6-Phosphate Dehydrogenase deficiency cells

Hemoglobinopathies

Family of disorders caused by production of :

- A structurally abnormal Hb
- Synthesis of insufficient quantities of normal Hb
- Rarely both together

What is Sickle Cell Anemia?

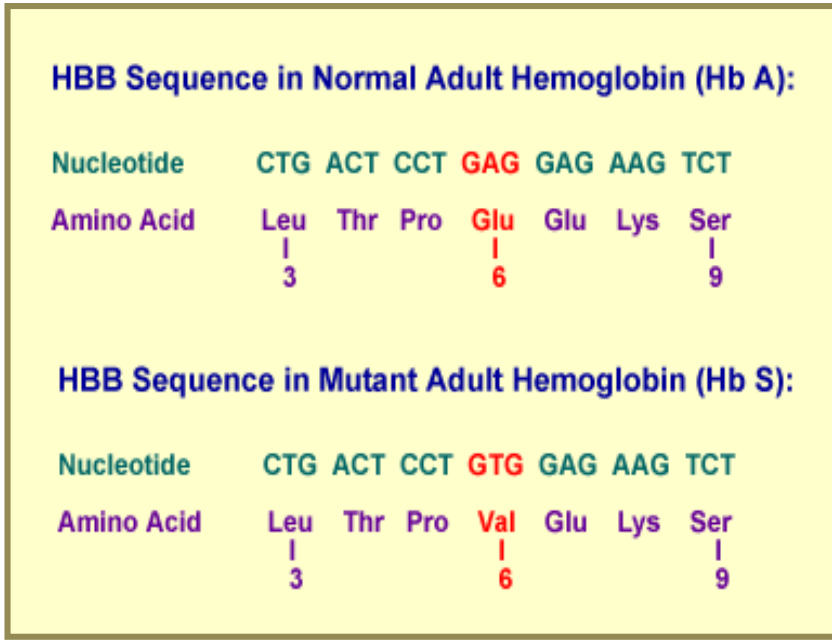


- Sickle Cell anemia is a **hereditary disease** which causes the body to make abnormally shapes red blood cells

- A normal red blood cell is shaped as a round donut while the abnormal red blood cell has a **“ C “ form** which causes complications because the blood cells are not able to reach certain parts of the body.

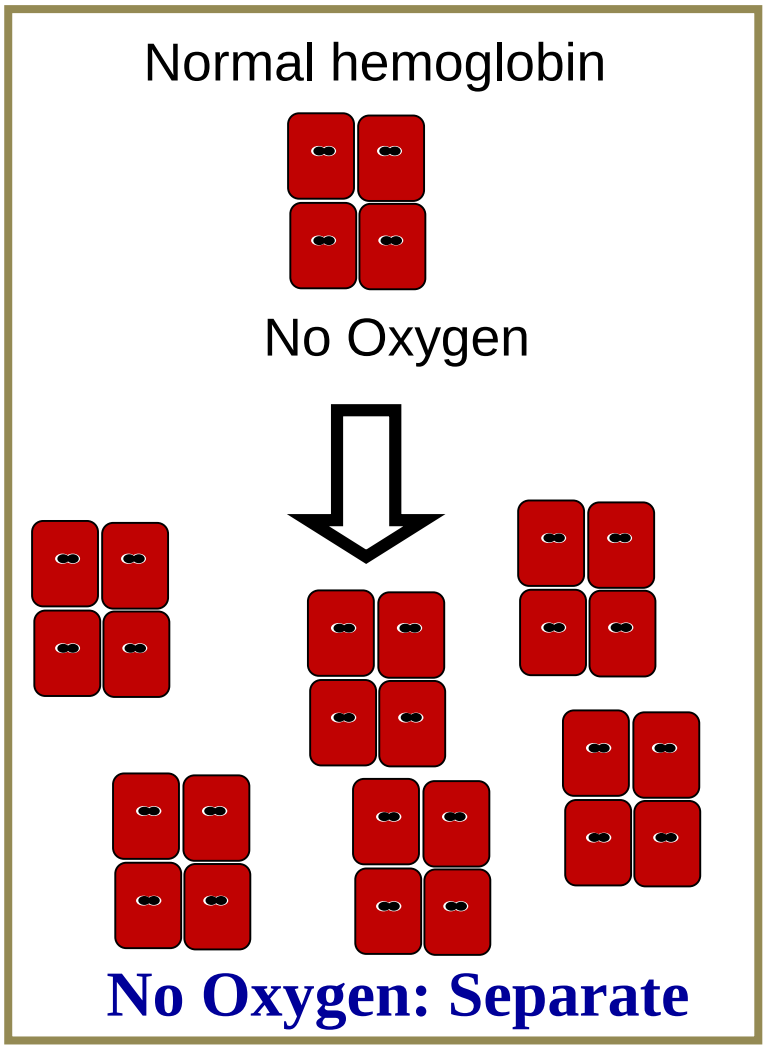
Sickle Cell Anemia

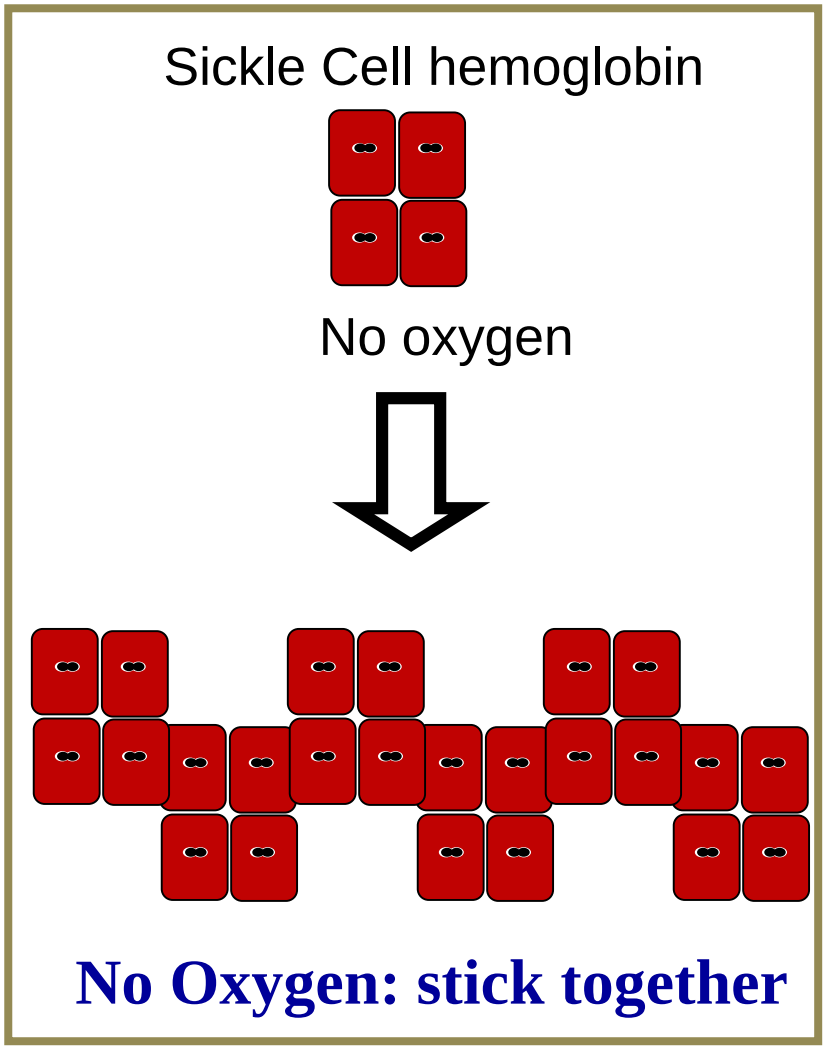
- The α chains in mutant Hb **(HbS)** are the same as in normal Hb **(HbA)**
- A point mutation in the **Hb β gene** is responsible for the sickling of RBCs seen in sickle cell anemia
- Substitution of non polar valine for a charged Glu.



Sickle Cell Hemoglobins Stick Together

Substitution of non polar valine for a charged Glu





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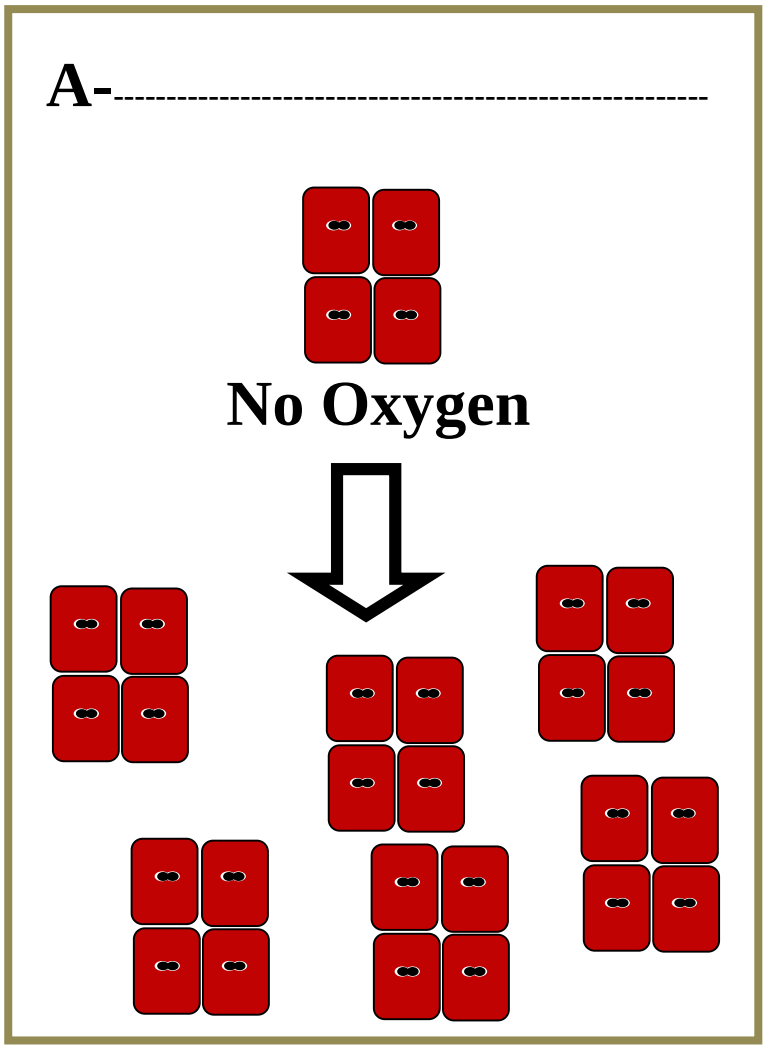
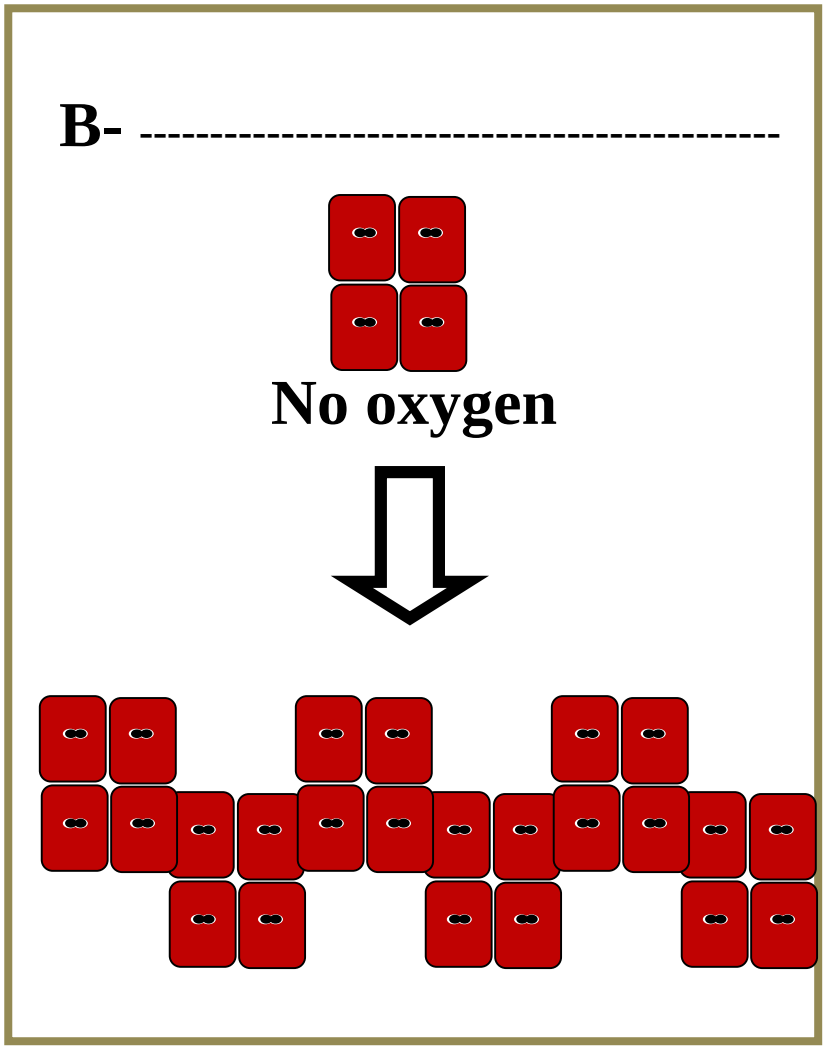
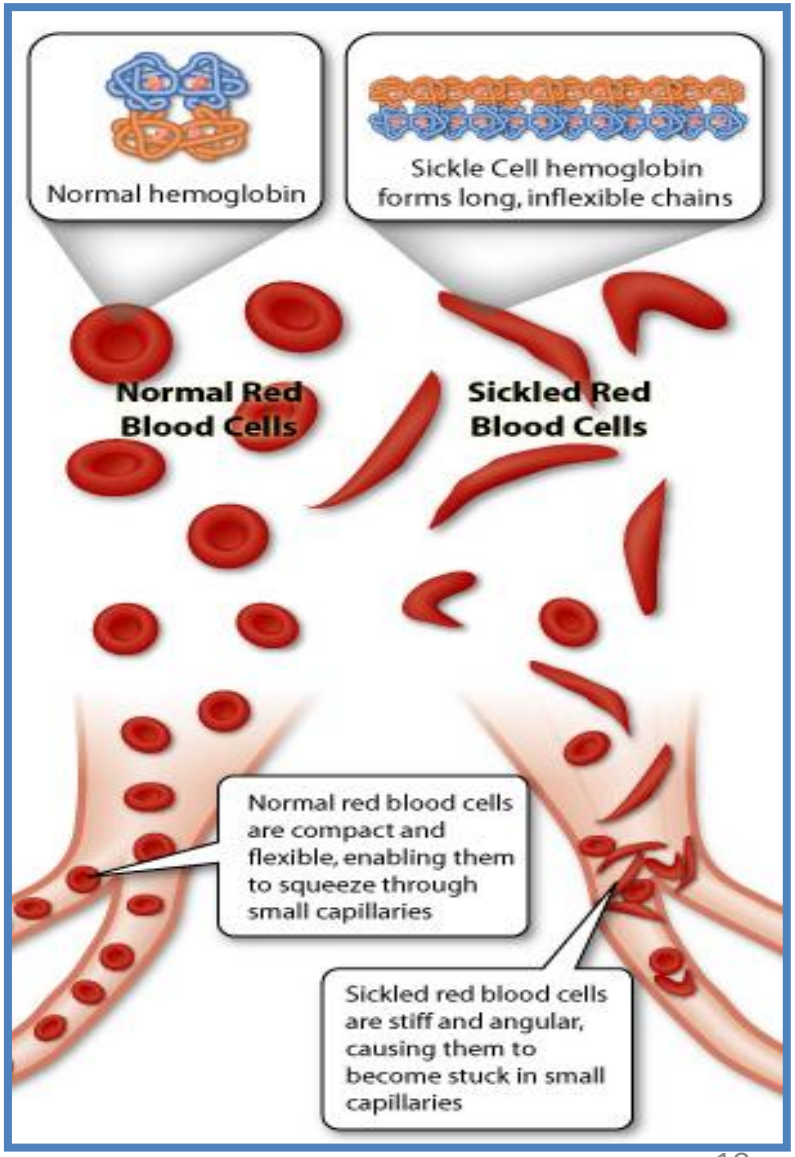




Red blood cells Going through Vessels

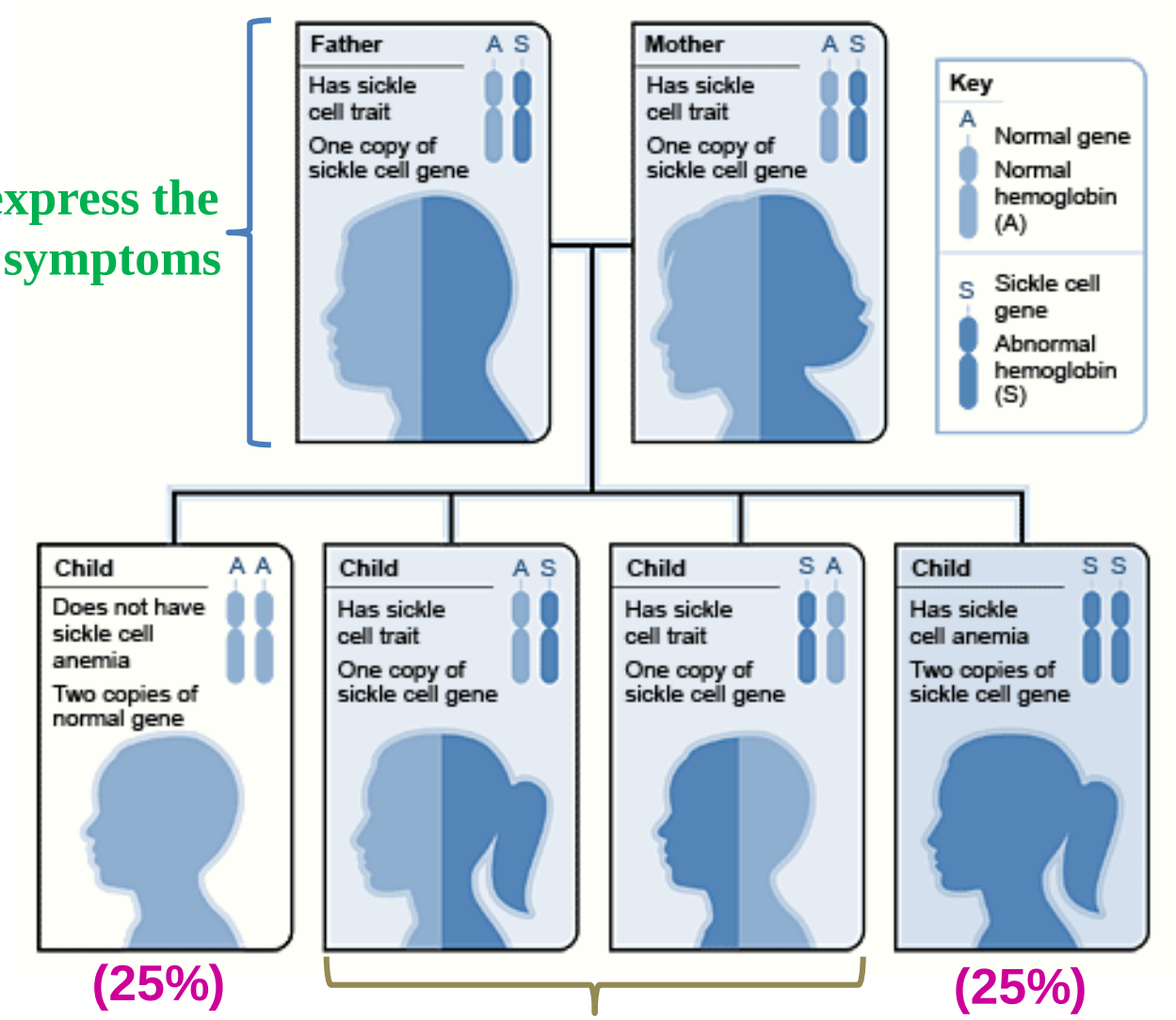
- Causes tissue anoxia (Interruption in O_2 supply)

- This blocking can produce micro vascular occlusions which can cause necrosis (death) of the tissue and pain.

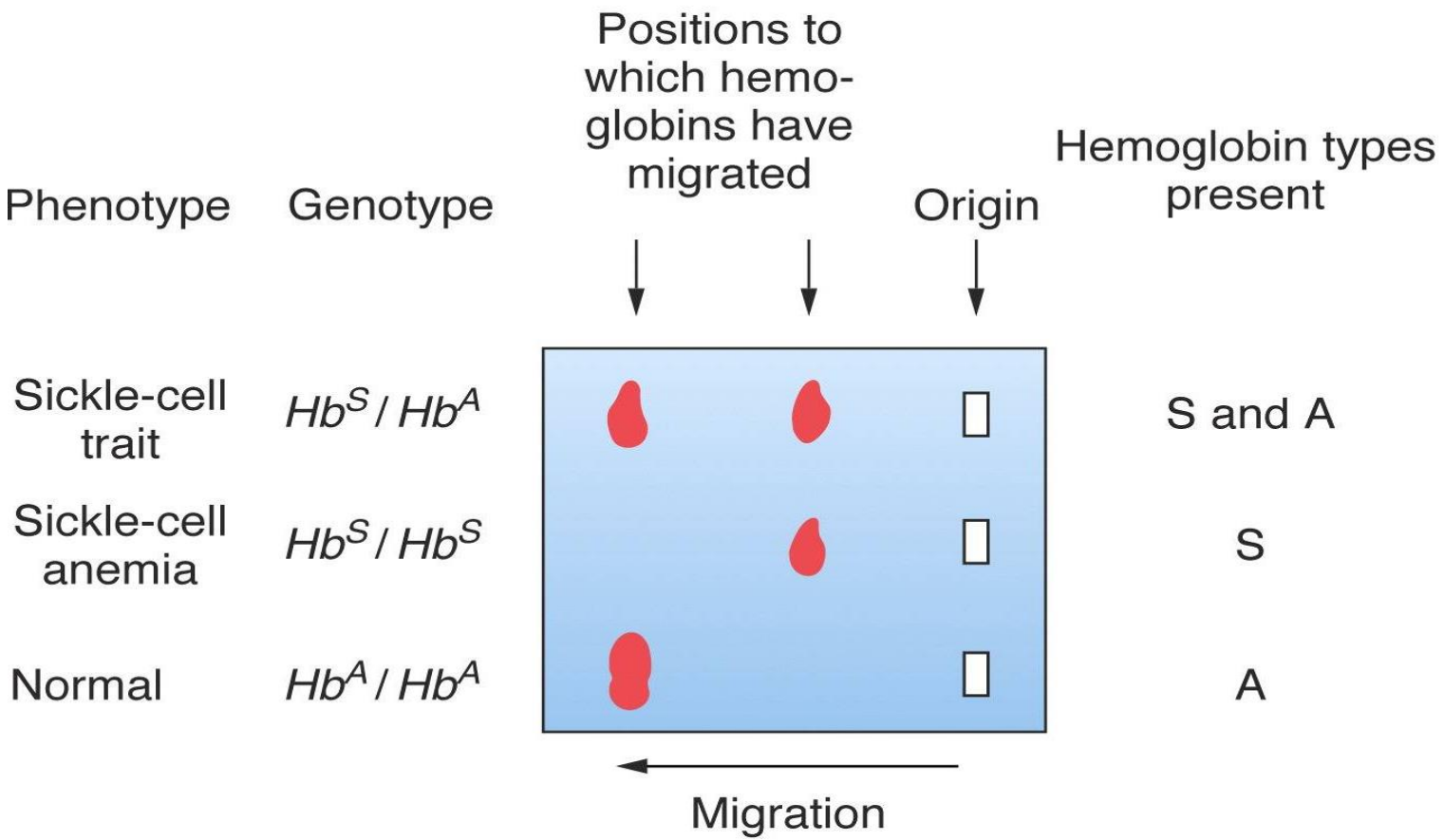


Sickle Cell Anemia is an autosomal recessive genetic disorder

Do not express the disease symptoms



- During electrophoresis, HbS moves slowly towards anode than HbA at alkaline pH

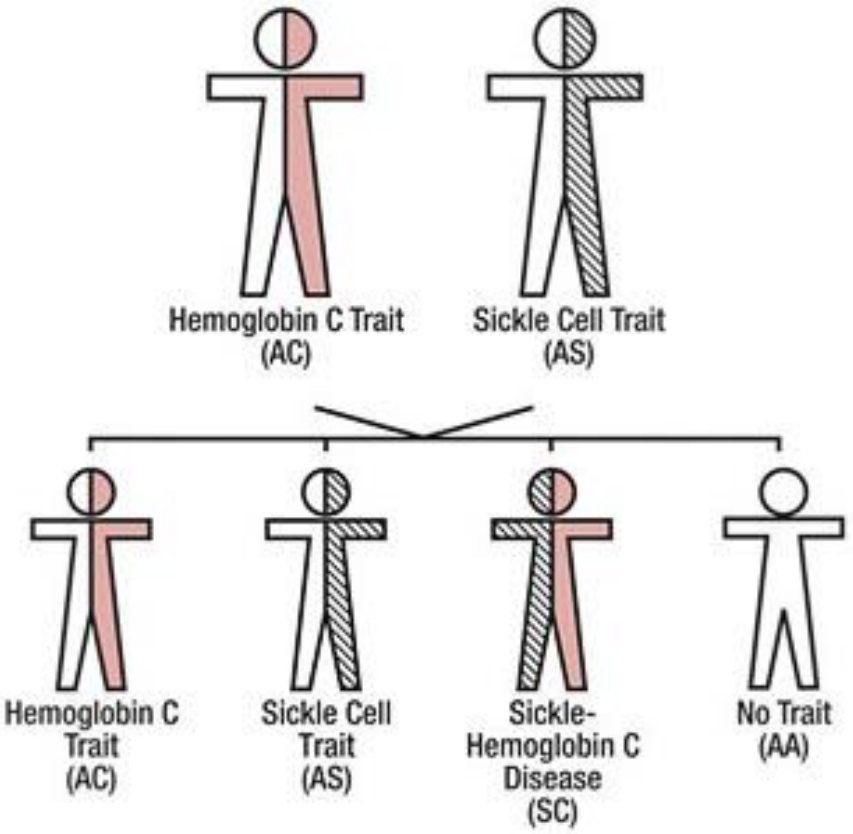


Hemoglobin C disease

- Lysine replaces glutamic acid at position 6 of the β globin gene.
- Mild chronic haemolytic anaemia

Haemoglobin SC disease

- Accounts for 25-50% of patients with SC disease
- Mixture of Sickle hemoglobin (Hb S) + (Hb C)



Thalassemia

- **Thalassemia** is inherited disorders characterized reduced or absent amounts of hemoglobin
- Two major types of thalassemia:
  1. **Alpha (α):** Caused by defect in rate of synthesis of alpha chains (**usually caused by gene deletion**)
  2. **Beta (β):** Caused by defect in rate of synthesis in beta chains (**usually caused by mutation**)

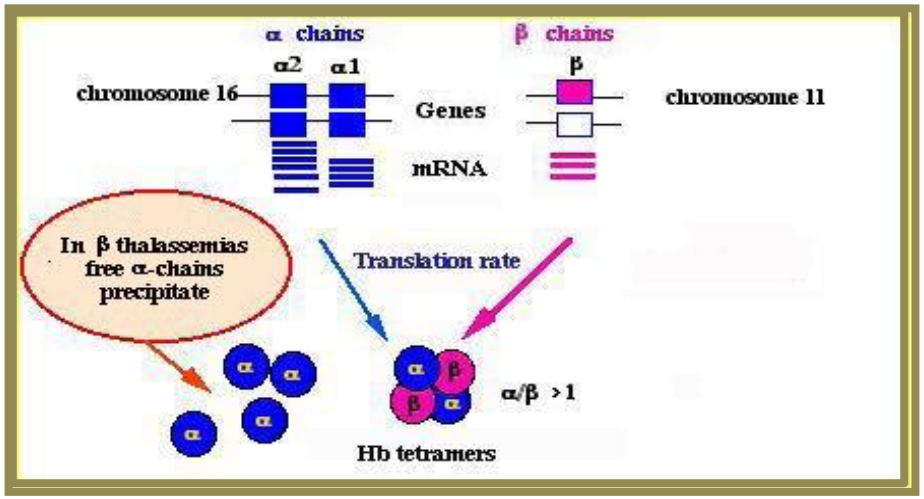
The structure of the normal and deleted α-globin structural genes in the various forms of α-thalassemia

- **Absence of 1 α gene (silent carrier)**: no symptoms, may be slightly anemia, does not require therapy
- **Absence of 2 α gene(α Thalassemia trait)**: no serious symptoms, except slight anemia
- **Absence of 3 α genes (Hb H disease)**: microcytic anemia (small RBC), splenomegaly
- **Absence of 4 α genes (Hydrops fetalis)**: most serious form, death before birth

Beta Thalassemia

- Usually caused by point mutations and short insertions or deletions limited to a few nucleotides.
- Two situations have clearly to be distinguished:
  1. **β^{o} thalassemia:** No β-globin chain is made
  2. **β^{+} thalassemia:** decreased β-globin chain is made

Disease results in an over-production of α-globin chains, which precipitate in the cells



There are 3 types of β-Thalassemia

Clinical Syndrome	Genotype	Hemoglobin (g/dl)
Minor (Trait)	β/β^{+} or β/β°	10-13
➢ Minor point mutation ➢ Minimal anemia ➢ No treatment indicated		
Intermediate	β^{+}/β^{+}	7-10
➢ Homozygous minor point mutation or more severe heterozygote ➢ Most often do not require chronic transfusions		
Major	β^{+}/β° or $\beta^{\circ}/\beta^{\circ}$	< 7
➢ Severe gene mutations ➢ Need careful observation and intensive treatment		

Iron deficiency anaemia

- Common world wide
- Common in pre-menopausal woman, infants, children, adolescents, & elderly
- Develops slowly

Iron deficiency anaemia (cont.)

- **Microcytic hypochromic anemia** (MCHC). Which causes by:

- Inadequate absorption of iron.
- Inadequate dietary intake of foods high in iron.
- Excess loss of iron due to bleeding, some parasites, menstrual loss and gastrointestinal bleeding.
- In pregnancy iron is taken from mother by growing fetus, so iron supplement must be taken by pregnant women.

Folic Acid Anaemia

- Folic Acid (also known as vitamin B9) Deficiency causes **megablastic anemia** (RBCs that are large and fewer in number)
- Deficiency can be due to:

1. Poor dietary intake
2. Malabsorption syndromes
3. Drugs that inhibit absorption
4. Alcohol abuse
5. Hemodialysis
6. Increased requirement (pregnancy)

Vitamin B12 deficiency anemia

- **Vitamin B12** is a water soluble vitamin with a key role in the normal functioning of the brain and nervous system, and for the formation of blood

➢ It is a type of megablastic anemia (large cell), dangerous, due:

- malabsorption of Vit B12 as a result of decreased gastric intrinsic factor IF which is needed for absorption of vit B12.
- Malnutrition or increase request as in pregnancy

Aplastic anemia

- Aplastic (hypoplastic) anaemia is defined as pancytopenia resulting from aplasia of the bone. It classified into primary (congenital or Aquired) or secondary types.

- It is due to destruction of the bone marrow , substantial reduction in the number of haemopoietic pluripotential stem cells, and a fault in the remaining stem cells or an immune reaction against them.

Causes of pancytopenia

Decreased bone marrow function

Aplasia

Acute leukaemia, myelodysplasia, myeloma

Infiltration with lymphoma, solid tumours, tuberculosis

Megaloblastic anaemia

Paroxysmal nocturnal haemoglobinuria

Myelofibrosis (rare)

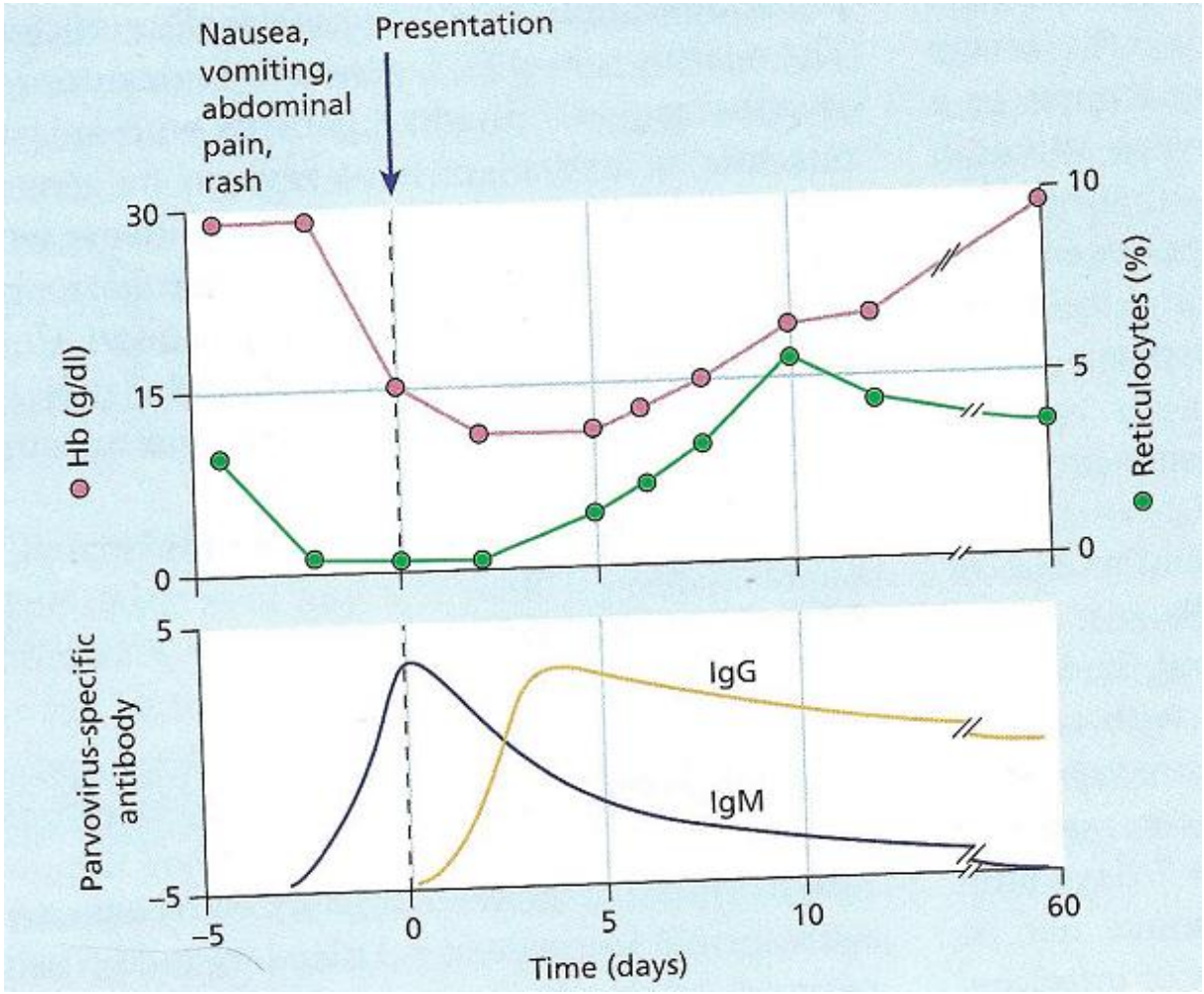
Haemophagocytic syndrome

Increased peripheral destruction

Splenomegaly

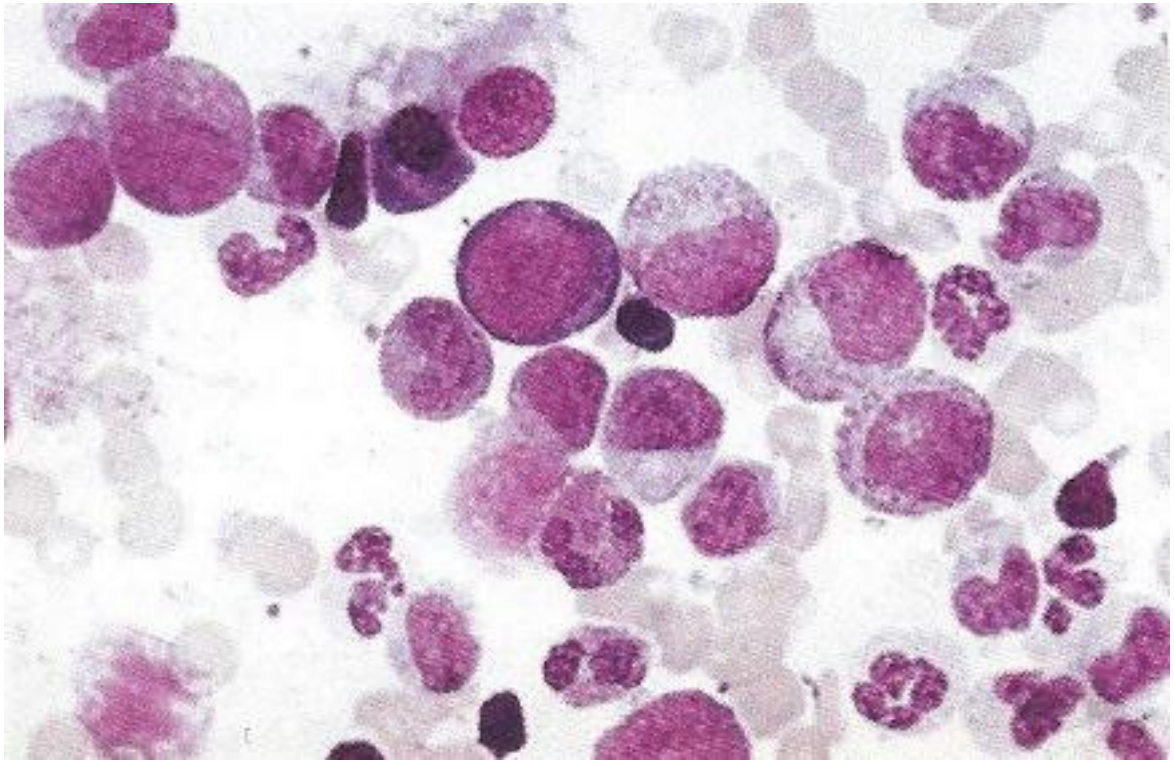
Causes of aplastic anaemia

Primary	Secondary
Congenital (Fanconi and non-Fanconi types)	**Ionizing radiations**: accidental exposure (radiotherapy, radioactive isotopes, nuclear power stations)
Idiopathic acquired	**Chemicals**: benzene and other organic solvents, TNT, insecticides, hair dyes, chlordane, DDT
	Drugs Those that regularly cause marrow depression (e.g. busulphan, cyclophosphamide, anthracyclines, nitrosoureas) Those that occasionally or rarely cause marrow depression (e.g. chloramphenicol, sulphonamides, gold and others)
	Infection: viral hepatitis (A or non-A, non-B)

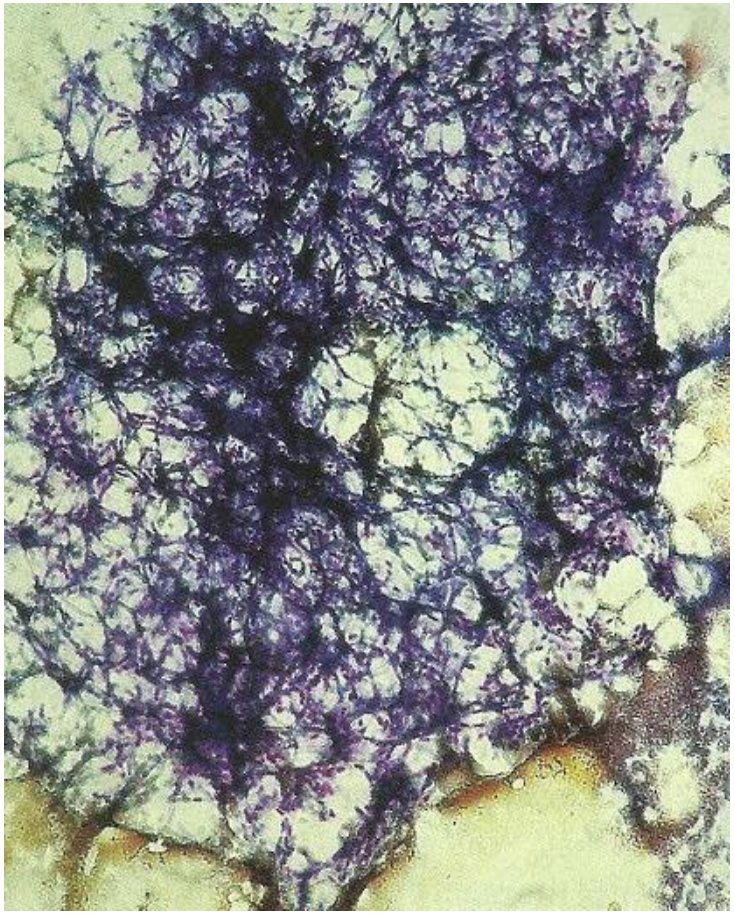


➢**Parvovirus infection: flow chart showing transient fall in haemoglobin and reticulocytes in a patient with hereditary spherocytosis.**

The bone marrow in primary red cell aplacia. There is selective loss of erythropoiesis.



A



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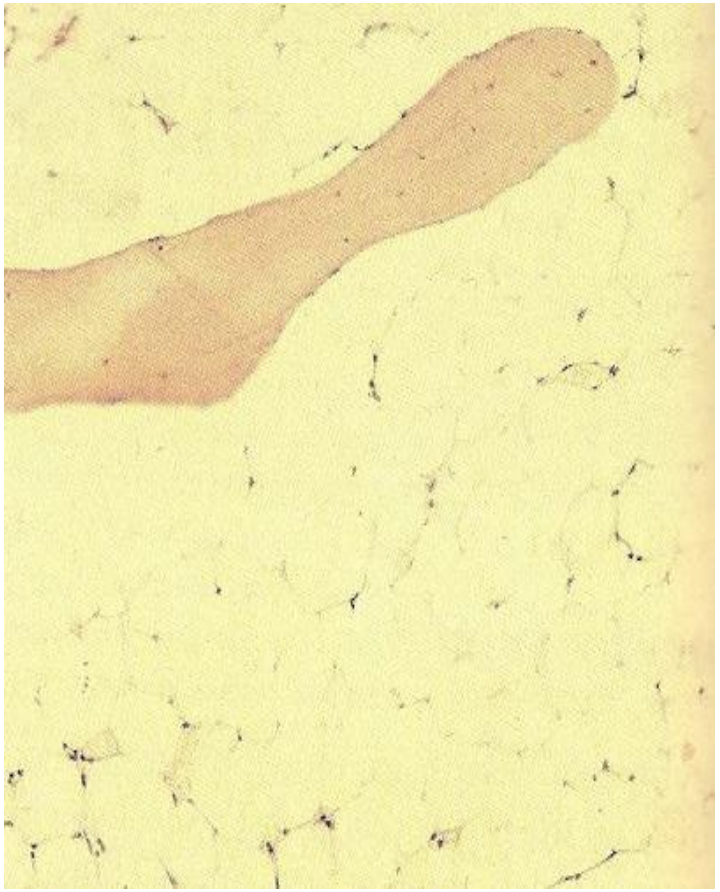
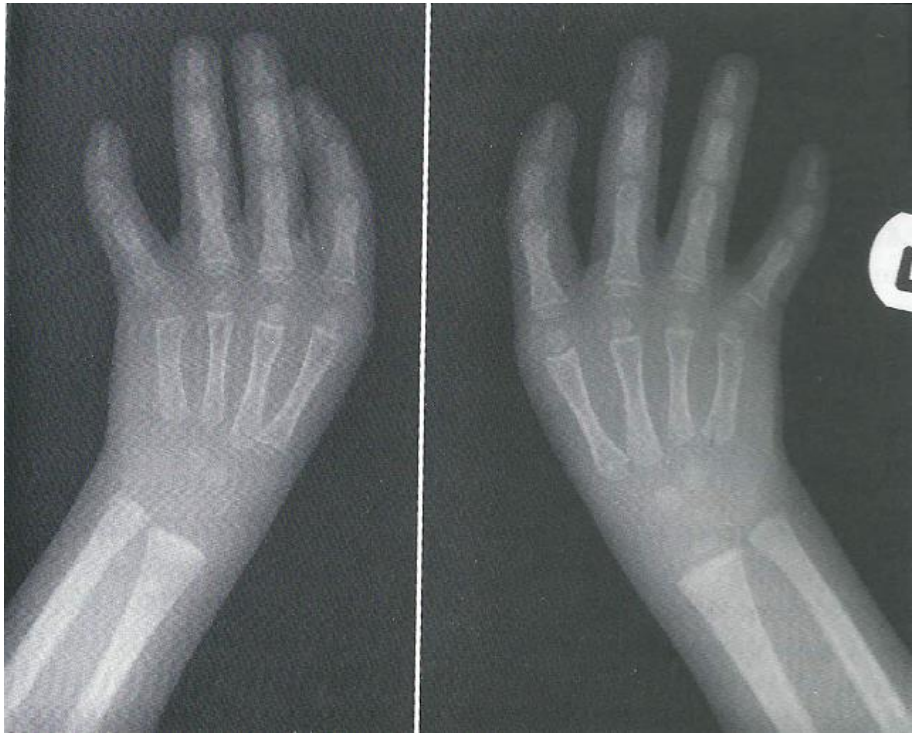


- Aplastic anemia: low power views of bone marrow show severe reduction of haemopoiieic cells with an increase in fat spaces.(A) Aspirated fragment. (B) Trephine biopsy.

Aplastic anemia and bone marrow failure



- **X-rays showing absent thumbs in a patient with Fanconi's anaemia(FA)**