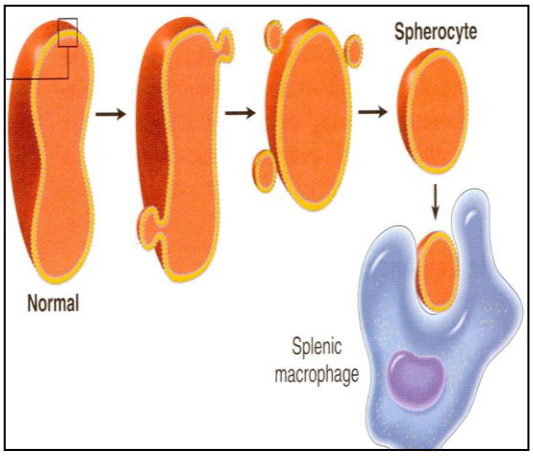
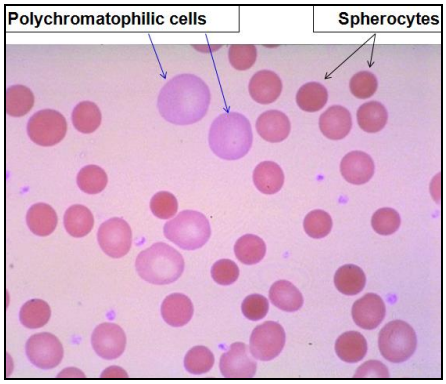
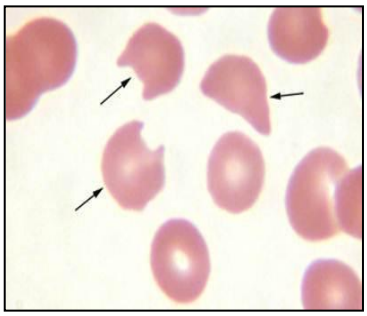
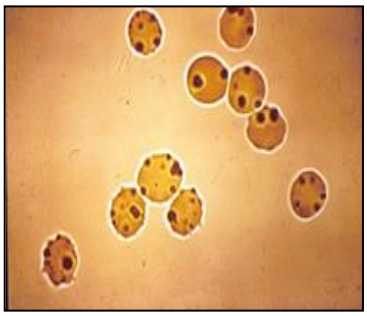
- **In hemolytic anemia**: there will be reduction in RBCs lifespan (less than the normal which is 120 days) and there will be early destruction of them either intravascular (hereditary) or extravascular (acquired).
- **Hereditary spherocytosis:**
  - It is an autosomal dominant disease which is a result of defect in the red cells membrane. This defect in turn results from abnormalities or deficiencies in the proteins of RBCs membrane (especially α&β spectrins and ankyrin).
  - Therefore, the phospholipid bilayer will lose its integrity resulting in the formation of microvesicles by the membrane which will be detached ---> reducing the surface area while volume is maintained.
  - The RBCs will lose their normal shape (biconcave) and become spherical in shape with fragile membranes.
  - As these RBCs move through the spleen they will rupture and get destructed leading to hemolytic anemia.
  - **Blood smear**: spherocytes with reduced diameter, dense, with no central pallor.



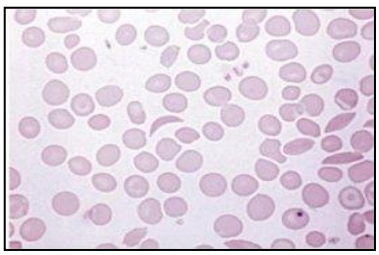


- **G6PD deficiency:**
  - G6PD enzyme reduces NADP to NADPH which keeps glutathione in its reduced form GSH. This helps in protecting RBCs from oxidative stress generated by free oxygen radical especially hydrogen peroxide.
  - Reduced enzyme acitivty will result in the oxidation of Hb and RBCs membrane forming Heinz bodies which will be removed by splenic macrophages resulting in blister or bite cells.
  - Deficiency of the enzyme is usually asymptomatic but acute hemolytic anemia event can be triggered by consuming fava beans, drugs (such as anti-malarial drugs) and infections.
  - It can produce neonatal jaundice in infants.
  - It is X-linked disease with males being more affected from carrier mothers. The most common variant of the disease is type B.





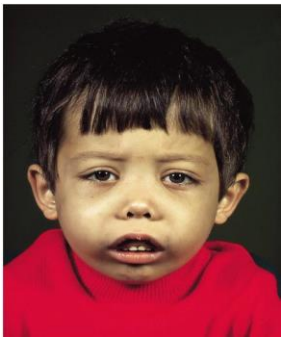
- **Pyruvate kinase deficiency (less common than G6PD):**
  - **Clinical picture**: chronic hemolysis (congenital non-spherocytic hemolytic anemia).
  - ATP deficiency ---> cation leak & less deformable RBC ---> abnormal RBC are sequestered in spleen.
- **Sickle cell disease:**
  - Characterized by the presence of the abnormal HbS which result from the point mutation in the 6th amino acid position of the β-chain (valine instead of glutamic acid).

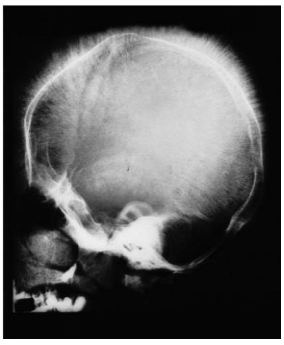


- When there is decreased oxygen tension, HbS polymerizes into long, rope-like fibers. These intracellular fibers of the HbS will distort the erythrocytes resulting in rigid erythrocytes that will occlude blood flow in the capillaries. Therefore, microinfarcts will produce tissue anoxia resulting in severe pain.
- At the beginning, the RBCs which are produced will be normal. When there is reduced oxygen tension, sickling will occur. Reversibly, RBCs can return to their normal conformation when oxygen is at normal level. With repeated sickling and unsickling permanent damage to the red cells will occur. They will get dehydrated and become sickle in shape with reduced lifespan (<20 days).
- **Clinical features:**
  - ✓ *Vaso-occlusive crises*: severe bone pain (hips, vertebra & shoulders), painful dactylitis leading to digits of varying lengths, autosplenectomy & stroke.
  - ✓ *Visceral sequestration crises*: acute sickle chest syndrome characterized by dyspnea, reduced arterial pO_2, chest pain & pulmonary infiltrate in x-ray. It is treated with analgesia, oxygen & exchange transfusion.
  - ✓ *Aplastic crises*: after infection with parvovirus of from folate deficiency. It is characterized by sudden fall in Hb and reticulocytes and treated with transfusion.
  - ✓ *Hemolytic crises*: increased rate of hemolysis and characterized by a fall in Hb but rise in reticulocytes.
  - ✓ *Other clinical features include*: leg ulcers, chronic damage to liver, pigment gallstones, kidneys papillary necrosis & osteomyelitis.
- **Treatment:**
  - ✓ *Prophylactic*: by avoiding dehydration, cold weather, anoxia & infections. Pneumococcal, hemophilus & meningococcal vaccines are given. Folic acid is also given to the patient.
  - ✓ *Crises is treated by*: rest, warmth, rehydration, analgesia (paracetamol, NSAIDs or opiates), antibiotics if infection is present & hydroxyuria to increase HbF levels.
- **Notes**: homozygous (HbSS) – doubly heterozygous (HbSC & HbSβthal) – carrier state: offers protection against malaria.

- **Thalassemia:**

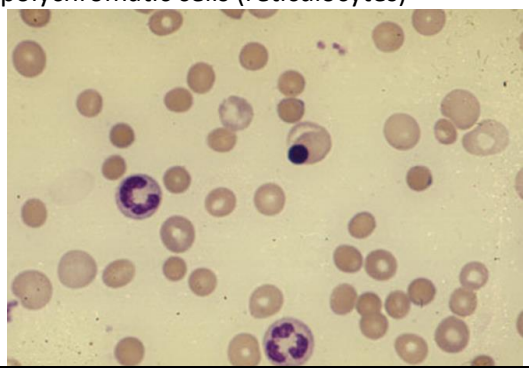
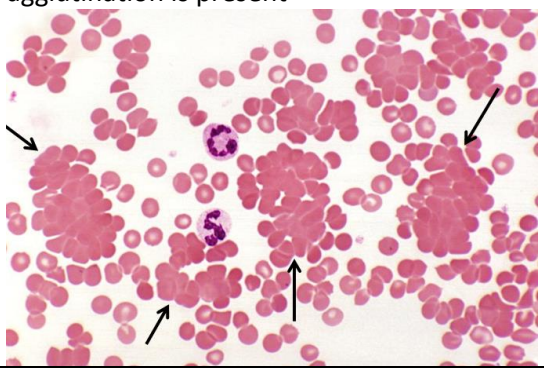
- **β-thalassemia**: there will be ↓β-globin chain synthesis which will result in excess α-globin chains that will bind to cell membrane resulting in membrane damage. Therefore, there will premature death of erythroblasts in the bone marrow (ineffective erythropoiesis).
  Notes:
  - ✓ Clinicalfeature of β-thalassemia major: thalassemia facies, hair-on-end appearance on the x-ray of the skull, hepatosplenomegaly, increased susceptibility to infection & osteoporosis.
  - ✓ Treatment for β-thalassemia major includes: regular blood transfusion – iron chelation therapy – regular folic acid if the diet is poor – allogenic stem cell transplantation offers prospect of permanent cure!
  - ✓ β-thalassemia minor is usually asymptomatic and characterized by hypochromic microcytic red cell but with high red cell count.
  - ✓ β-thalassemia trait + HbE trait = transfusion-dependent thalassemia major, β-thalassemia trait + HbS trait = clinical picture of sickle cell disease rather than thalassemia, β-thalassemia trait + HbD trait = hypochromic microcytic anemia with variant severity.



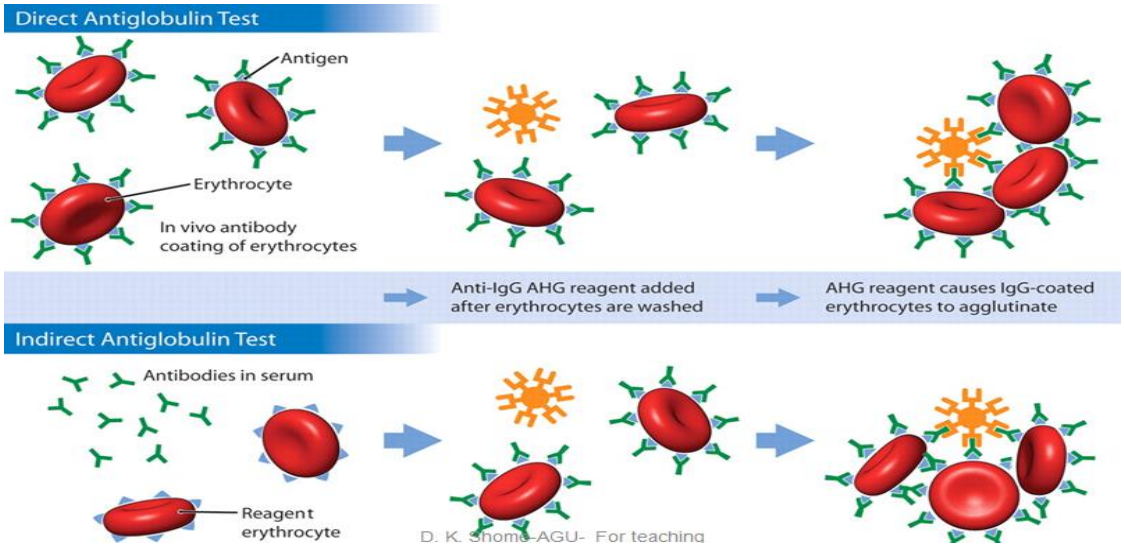


- **α-thalassemia**: there will be ↓α-globin chain synthesis which will result in excess γ-chains in infants (Hb Barts: 4γ) and β-chains in adults (HbH: 4β). HbH is not stable leading to premature death of circulating erythroblasts in the spleen.

- **Immune-mediated hemolytic anemia:**
  - The body is producing antibodies against its own red blood cells.

Warm antibody	Cold antibody
Reactive at 37 C	Reactive at 4 C
Antibody is: IgG ± complement	**Antibody is**: IgM
Idiopathic in 60% of cases or secondary to SLE	Acute form associated with infection & chronic form associated with lymphoma
Blood smear: spherocytes with polychromatic cells (reticulocytes) 	**Blood smear**: less spherocytes but red cell agglutination is present 
Lab tests: extravascular hemolytic anemia, positive Coomb's test for IgG	**Lab tests**: extra & intravascular hemolytic anemia with positive Coomb's test for complement only
Clinical features: hemolytic anemia with varying severity, splenomegaly	**Clinical features**: chronic hemolytic anemia aggravated by cold, mild jaundice, splenomegaly, acrocyanosis
Treatment: corticosteroids, if fails ---> splenectomy, if fails ---> immunosuppression. Folic acid is given in severe cases and transfusion when there is severe anemia with symptoms.	**Treatment**: keeping the patient warm

  - **Coomb's test:**



- **Microangiopathic hemolytic anemia (TTP):**
  - **Pathogenesis**: formation of platelet-fibrin thrombi due to increased activation of platelets and coagulation. The RBCs are physically damaged as these small blood vessels leading to fragmentation (schistocytes).