Hematology

Practical

432 ***Hematology*** *Team*

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Color Index: Female notes are in Green. Male notes are in Blue. Red is important. Orange is explanation.

Practical Haemaglobinopathy

Introduction to Haemoglobin Variants:

Hemoglobin variants are mutant forms of hemoglobin, caused by genetical variation. Some well-known hemoglobin variants such as Hb S are responsible for sickle cell anemia which is one of the **hemoglobinopathies**. And some are undetectable non-pathological variats. Some normal hemoglobin types are; Hemoglobin A (Hb A) which constitute 95-98% of hemoglobin found in adults, Hemoglobin A2 (Hb A2), which consitiute 2-3% of hemoglobin found in adults, and Hemoglobin F (Hb F) which is the fetal Hb.

Effects of Haemoglobin variants:

Variant	Clinical and haematological abnormalities
HbS	Recurrent painful crises (in adults) and chronic haemolytic anaemia; both related to sickling of red cells on deoxygenation*
HbC	Chronic haemolytic anaemia due to reduced red cell deformability on deoxygenation, * deoxygenated HbC is less soluble than deoxygenated HbA.
Hb Köln, Hb Hammersmith	Spontaneous or drug-induced haemolytic anaemia due to instability of the Hb and consequent intracellular precipitation.
HbM Boston, HbM Saskatoon	Cyanosis due to congenital methaemoglobinaemia as a consequence of a substitution near or in the haem pocket.
Hb Chesapeake	Hereditary polycythaemia due to increased O_2 affinity.
Hb Constant Spring, Hb Lepore, HbE	Thalassaemia-like syndrome due to decreased rate of synthesis of normal chains.
Hb Indianapolis	Thalassaemia-like syndrome due to marked instability of Hb

* Only in homozygotes

All of these have similar features (hemolytic anemia – target cells – spleenomegaly – trait usually asymptomatic or mild symptomatic – if the disease combined with another abnormal Hb, the patient will present with sever hemolytic anemia).

Abnormal Haemoglobin Variants:

1- Hb C:

- Is due to replacement of **Glutamic acid** in **position 6** of the beta chain by **Lysine** ($\alpha_2\beta_2$ 6-GLU → LYS).
- About 7-22% of people of West Africa ar hetrozygotes especially Nigeria and North Ghana.
- Homozygotes are rare and have mild to moderate hemolytic anaemia with many thick target RBCs in the blood film and mild to moderate splenomegaly.
- The chronic hemolytic anaemia is due to reduced red cell deformability on deoxygenation.
- Deoxygenated HbC is less soluble than deoxygenated HbA.
- Double heterozygotes with sickle Hb S/C give moderate to sever anaemia with symptoms of sickle cell disease.

2- Hb D Punjab:

- Is due to replacement of **Glutamic acid** in **position 121** of the beta chain by **Glutamine** ($\alpha_2\beta_2$ 121-GLU → GLN).
- Prevalent in Indian and Pakistani in every 100 persons about 1 trait (1% of the population).
- Trait are usually health.
- Homozygous D/D have mild to moderate anaemia.
- Combined double heterozygotes Hb S/D can give rise to moderate to a severe anaemia and symptoms of sickle cell disease.

3- Hb E:

- Is due to replacement of **Glutamic acid** in **position 26** of the beta chain by **Lysine** ($\alpha_2\beta_2$ 26-GLU → LYS) is one of the most common beta-chain variants.
- It is very prevalent in South East Asia (50%) of the population are heterozygotes. (Philbin, Taiwan and Indonesia)
- Patients who are homozygous generally have mild haemolytic anaemia, microcytic hypochromic red cells and mild enlargement of the spleen.
- Carriers are symptomless unless they have combined other mutations such as the one for alpha thalassemia, or beta-thalassemia trait.

4- Hb O Arab:

- Is due to replacement of **Glutamic acid** in **position 121** of the beta chain by **Lysine** ($\alpha_2\beta_2$-121 GLU → LYS)
- Heterozygotes are not symptomatic.
- Double heterozygous with sickle S/O are clinically severe.
- Hb O- Arab enhance the polymerization of HbS.

5-Hb S:

- Is due to replacement of **Glutamic acid** in **position 6** of the beta chain by **Valine** ($\alpha_2\beta_2$ 6-GLU → Val).
- There's two sickle cell traits one is homozygous sickle cell anemia (ss) and they other is double heterozgous sickle cell with Thalassemia's or Hb-C diseases.
- Hb-S under low oxygen tension form a an intracellualr rod-shpd polymer which affect the erythrocyte deformarion unableing them to squeeze in microcirculatory vessels(local hypoxia).
- Is highly prevalent in sub-saharan and equatorial africa with lesser but significant prevalence in the middle east,india and mediterrianian regions.

High Oxygen affinity Haemoglobins: Extra Info

Hb Chesapeake:

- (α_2-92 ARG → LEU β_2)
- Carriers are without clinical symptoms.
- Homozygous of erythrocytosis (polychemia) due to increased O2 affinity.
- The patients have no splenomegaly. (except for patient's with concomitant β-thalassemia).
- They have normal WBC, and normal platelets.
- High Hb, High RBCs count and high haematocrit. (HCT).

Unstable Haemoglobins Extra Info

Hb Köln ($\alpha_2\beta_2$-98 VAL → MET)
Hb Hammersmith ($\alpha_2\beta_2$ 42 PHE → SER)
Hb Hasharon (α_2-47 ASP → HIS β_2)

- These abnormal haemoglobin cause haemolysis in the newborn (congenital non-spherocytic haemolytic anaemia).
- Heinz body hemolytic anaemia with sensitivity to oxidant drugs, such as sulfonamides.
- Reticulocytosis out of proportion to the level of Hb.
- Increased formation of methemoglobin.
- Spontaneous or drug induced haemolytic anaemia due to instability of the haemoglobin and consequent intracellular precipitation.
- Thalassaemia – like peripheral blood picture.

Clinically: The patient have anemia, jaundice, splenomegaly / hepatomegaly and gall stones.

Low Oxygen affinity Haemoglobins:

Extra Info

More than 50 variants with reduced oxygen affinity have been identified.
Hb Kansas ($\alpha_2\beta_2$ 102 ASN → THR)
Hb Aukland ($\alpha_2\beta_2$ 25 GLY → ASP)
Rare as homozygotes.
Patients have anaemia and congenital cynosis due to reduced oxygen affinity.

Congenital methaemoglobinaemia

Extra Info

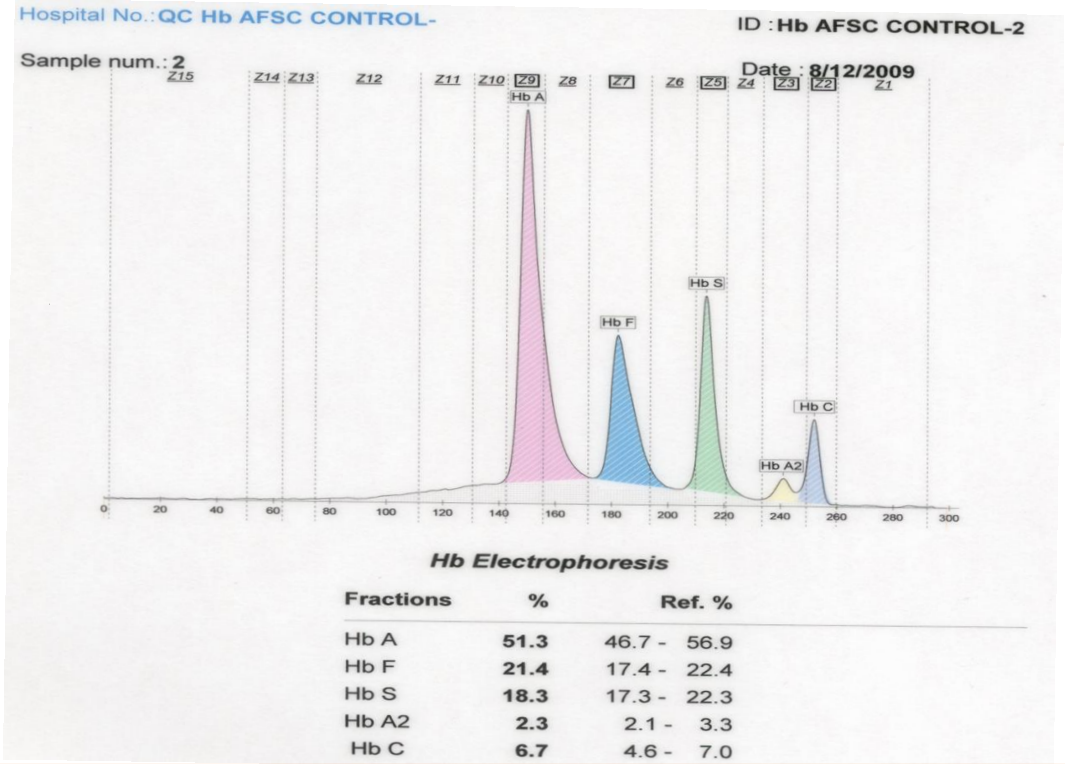
Hb M Boston (α2 58 HIS → TYR - β_2)
Hb M Saskatoon ($\alpha_2\beta_2$-63 HIS → TYR)
Hb M Hyde park ($\alpha_2\beta_2$-92 HIS → TYR)
Hb M IWATE (α_2-87 HIS → TYR-β_2)

Cynosis in homozygotes due to congenital methaemoglobinaemia as a consequences of substitution of amino acids near or in the haem pocket.

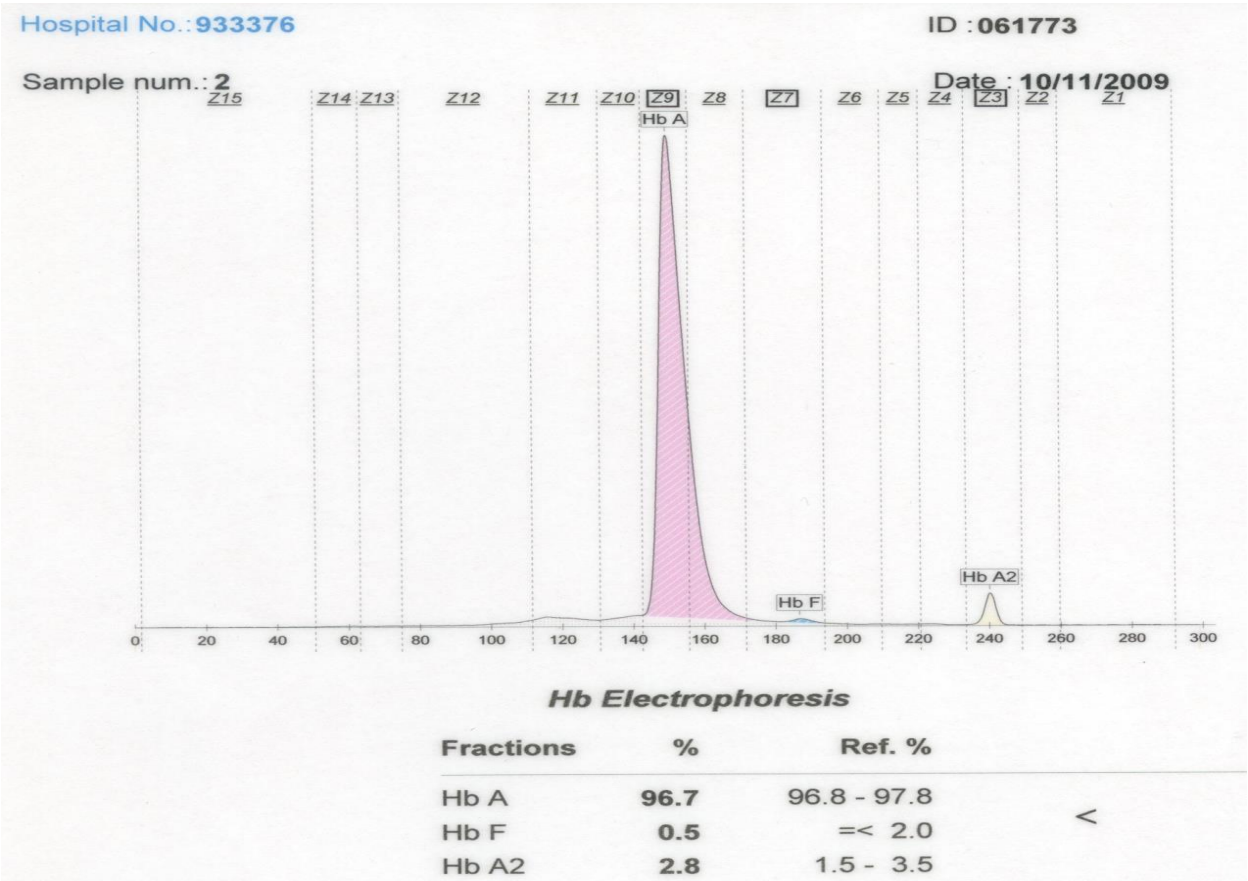
Hb Indianapolis

- (α2-β2 112 CYS → ARG)
- Is a rare and slightly unstable beta-globin variant.
- Carriers are clinically normal with only mild reticulocytosis.
- Homozygons have haemolytic anaemia and renal failure in severe cases.
- Thalassaemia-like syndrome due to marked instability of the Hb.

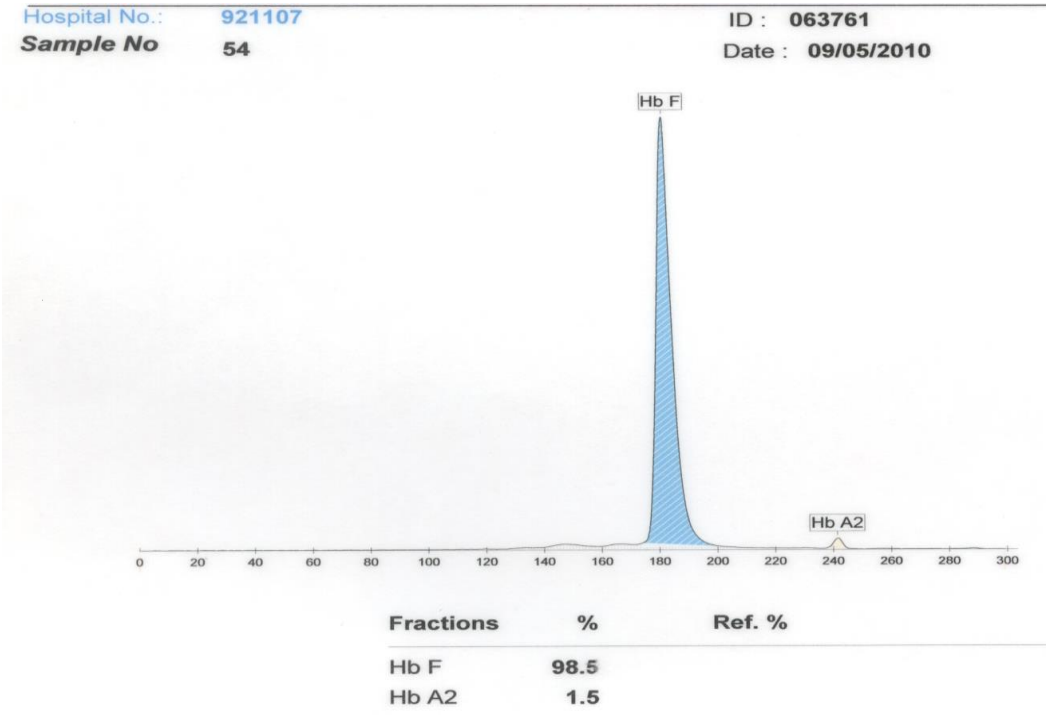
	Normal Range	Note
Hb A	95-97%	
Hb A2	2.5-3.5%	<1.5 = α-thalassemia >3.5 = β-thalassemia
Hb F	0.5-1.5%	
Hb S	Normally not present	<45 = Trait >45 = Sever



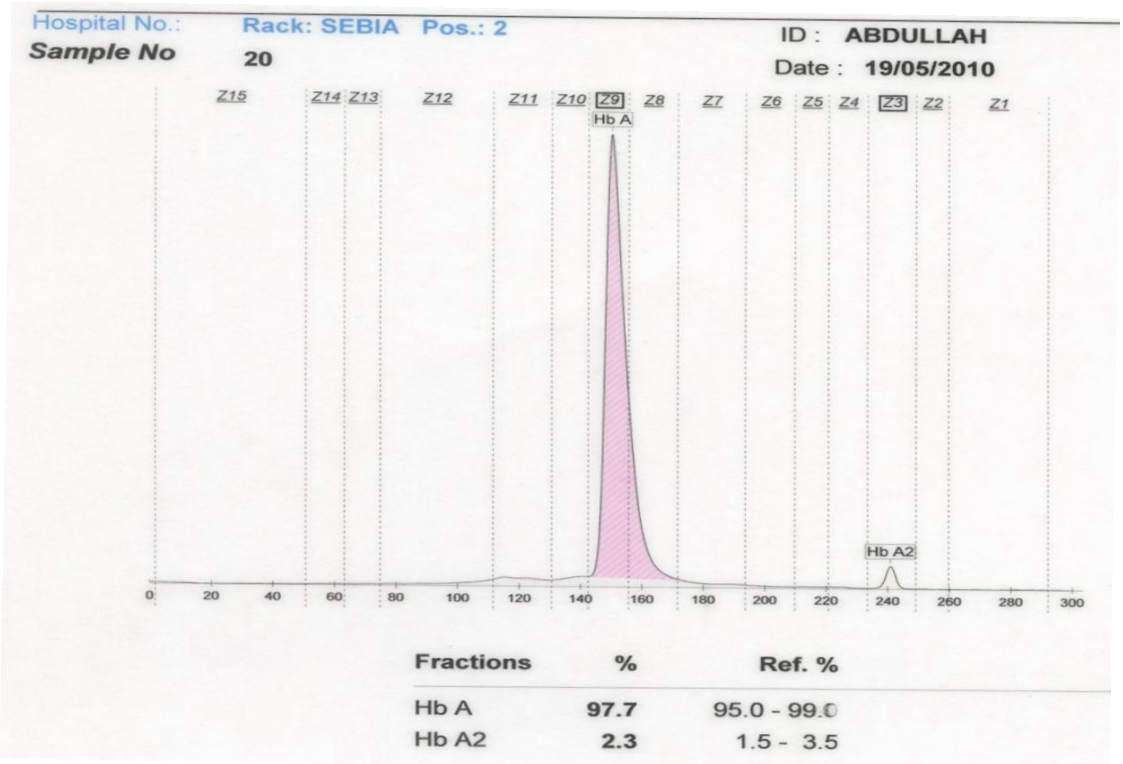
This is a control electrophoresis in which we have mixed different types of Hbs.



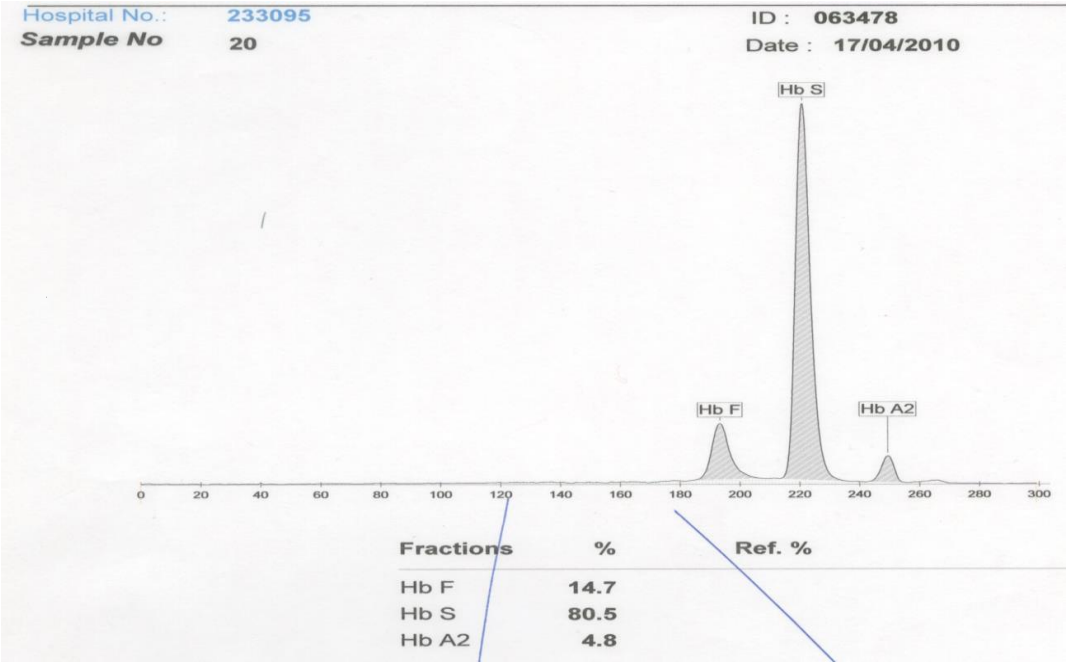
Hb F	Normal
Hb A	Normal
Hb A2	Normal
Dx	Normal



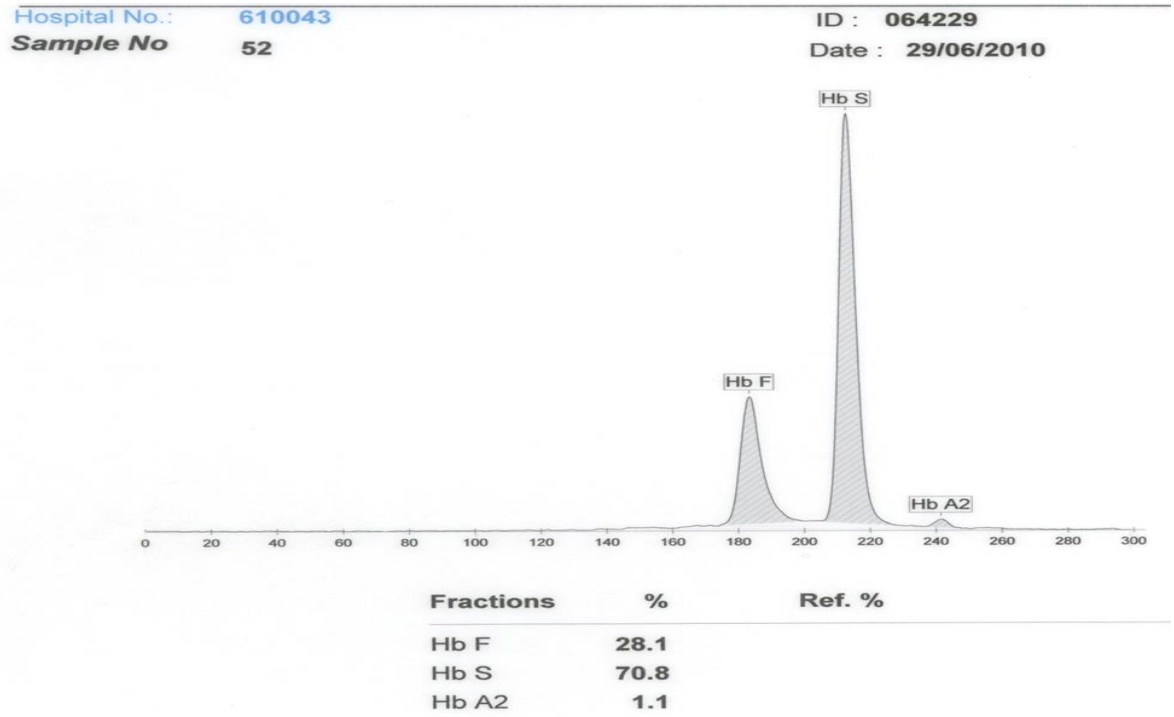
Hb F	Highly increased
Hb A	Absent
Hb A2	Normal
Dx	Fetal Hb F or an abnormal hereditary persistence of fetal hemoglobin (HPFH).



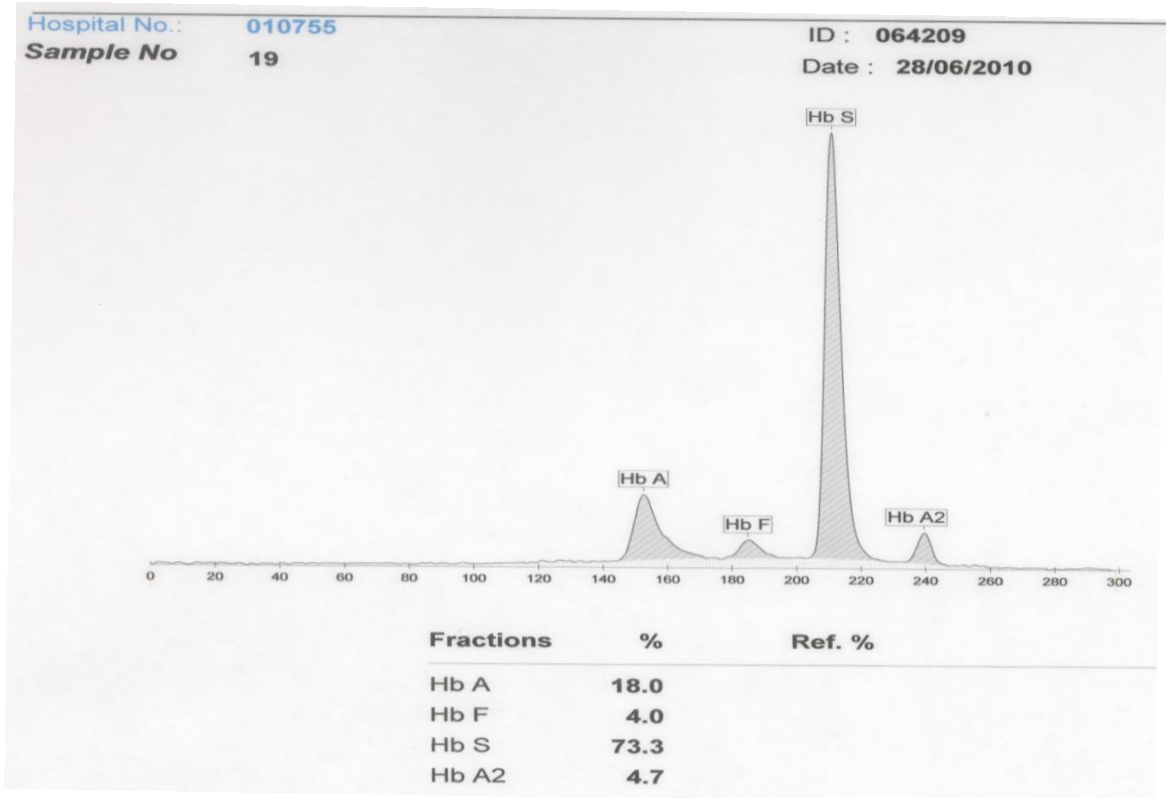
Hb F	Absent, sometimes undetectable.
Hb A	Normal
Hb A2	Normal
Dx	Normal

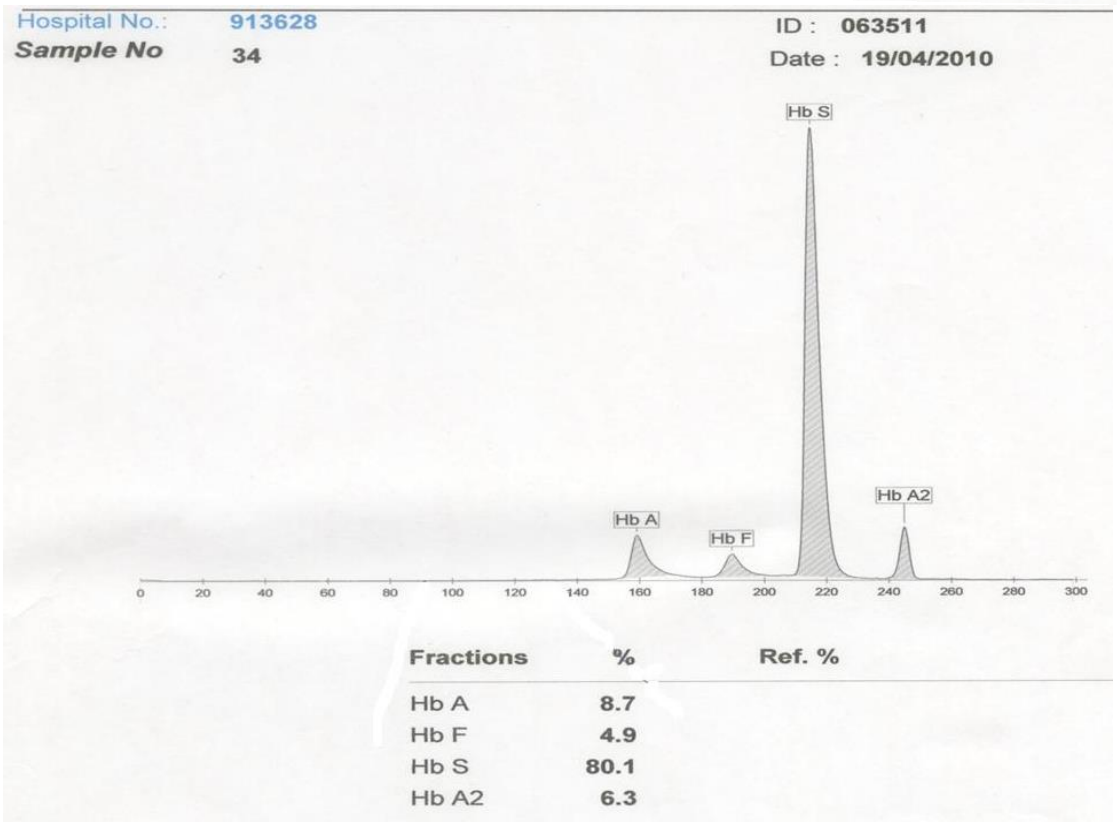


Hb F	Increased (Decreasing severity)
Hb A	Absent
Hb S	Increased
Hb A2	Increased
Dx	Sickle cell anemia with β-thalassemia and increased Hb f

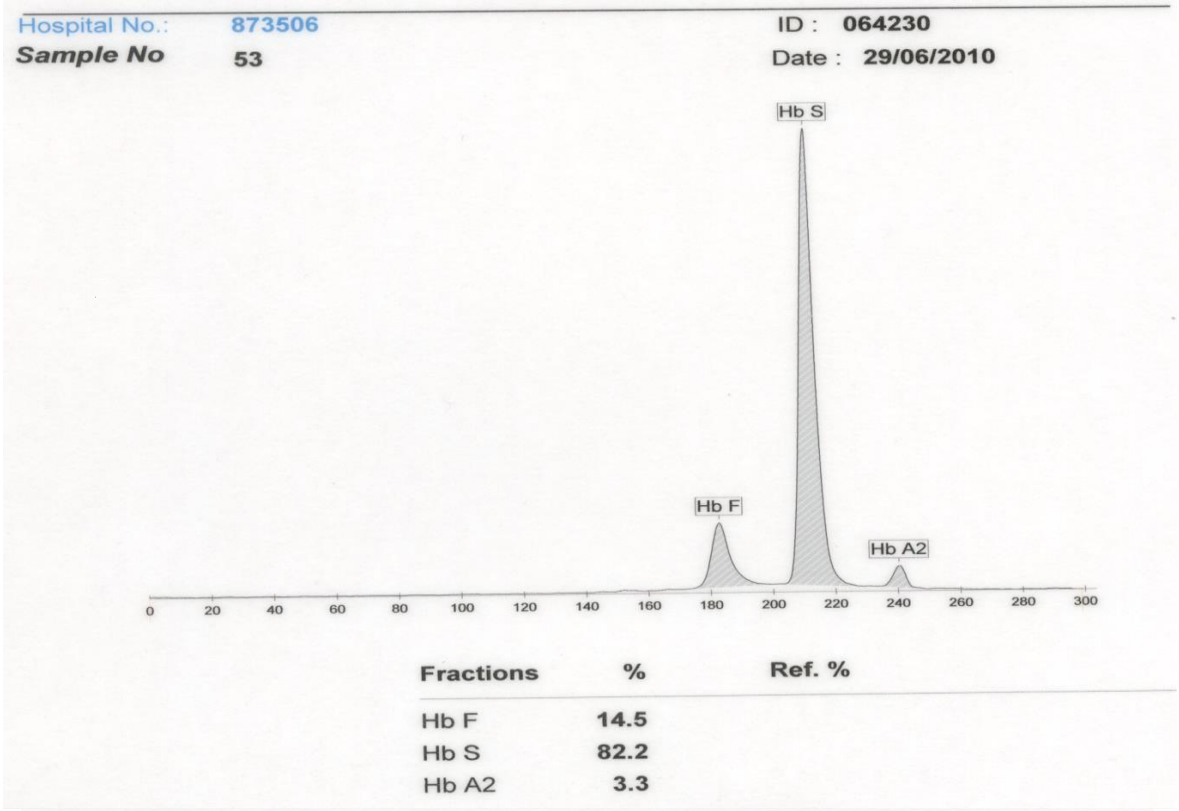


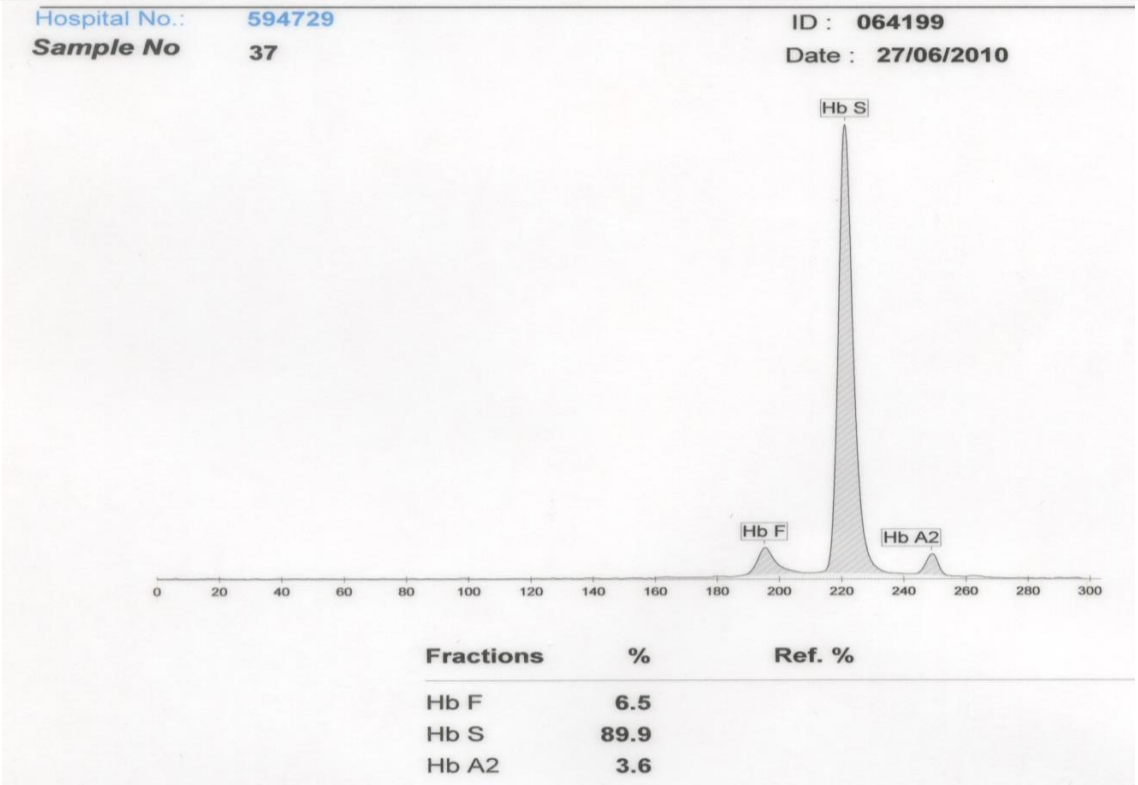
Hb A	Absent
Hb F	Increased (>15% mild form of anemia)
Hb S	Increased
Hb A2	Decreased
Dx	Sickle cell anemia with α-thalassemia and increased Hb F.





Hb A	Decreased, post-transfusion
Hb F	Little increase (in severe cases, <15%)
Hb S	Present
Hb A2	Increased
Dx	Post-transfusion Sickle cell anemia with β-Thalassemia and increased Hb-F.



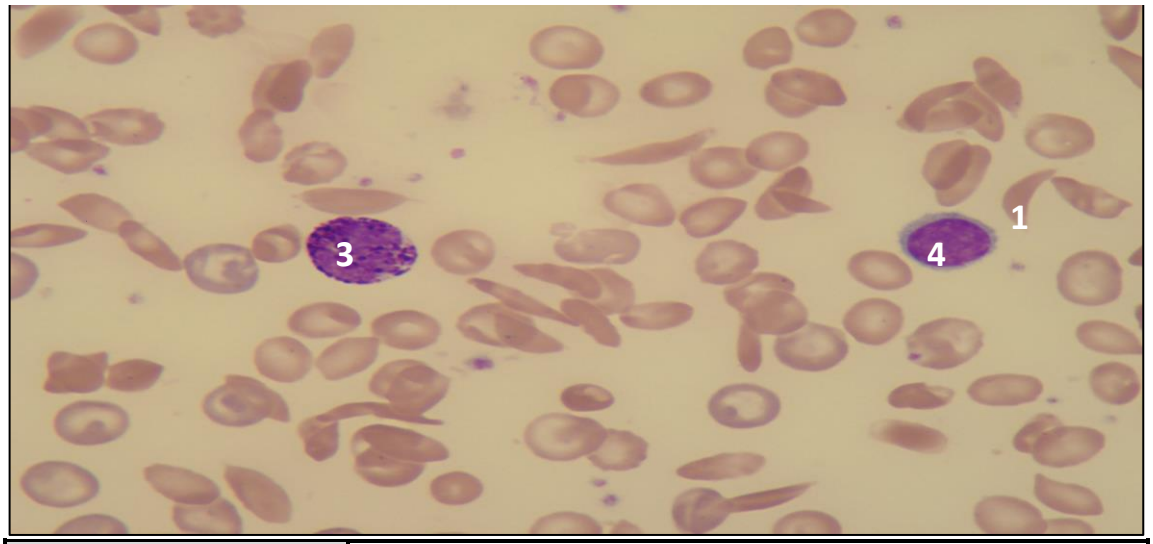


Hb F	Increased.
Hb S	Increased.
Hb A2	Normal.*
Dx	Sickle cells anemia with increased Hb F

*3.6 is considered relatively normal.

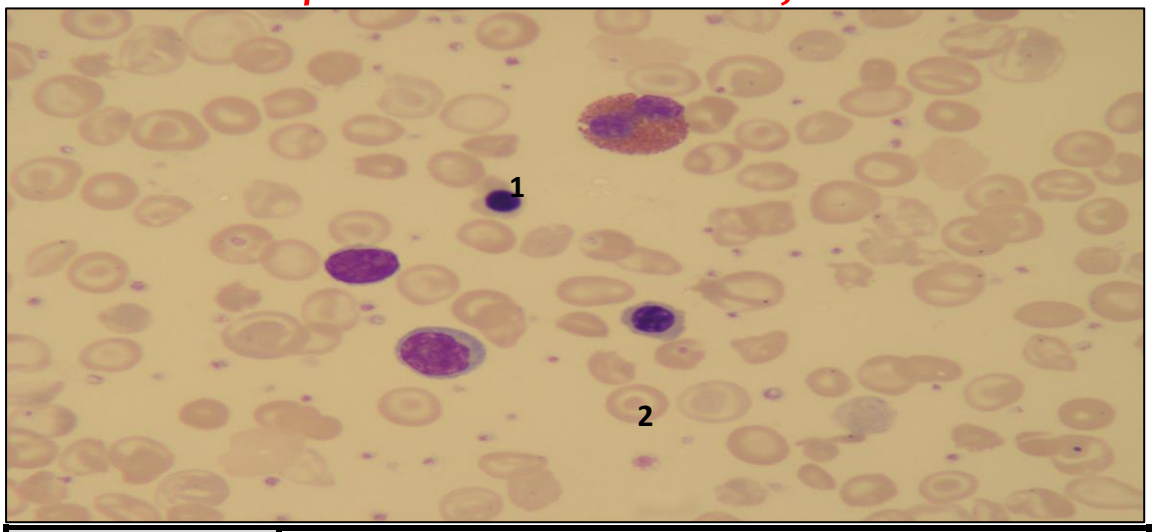
After Hb electrophoresis we do DNA analysis and family studies for further investigation (very important)

Sickle cell anemia



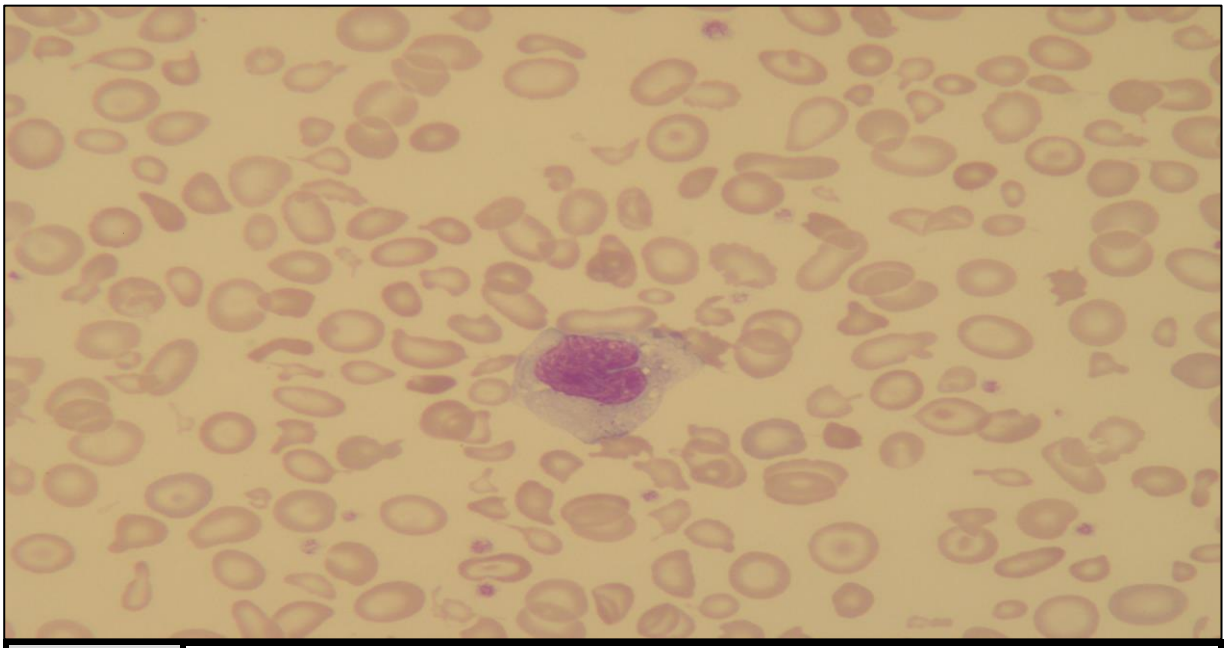
TEST	Blood film
Findings	1-Sickled RBC's. 2-Target cells. 3-Basophil. 4-lymphocyte.
Investigations	Hb electrophoresis.
Dx	Sickle cell anemia.

β-Thalassaemia Major



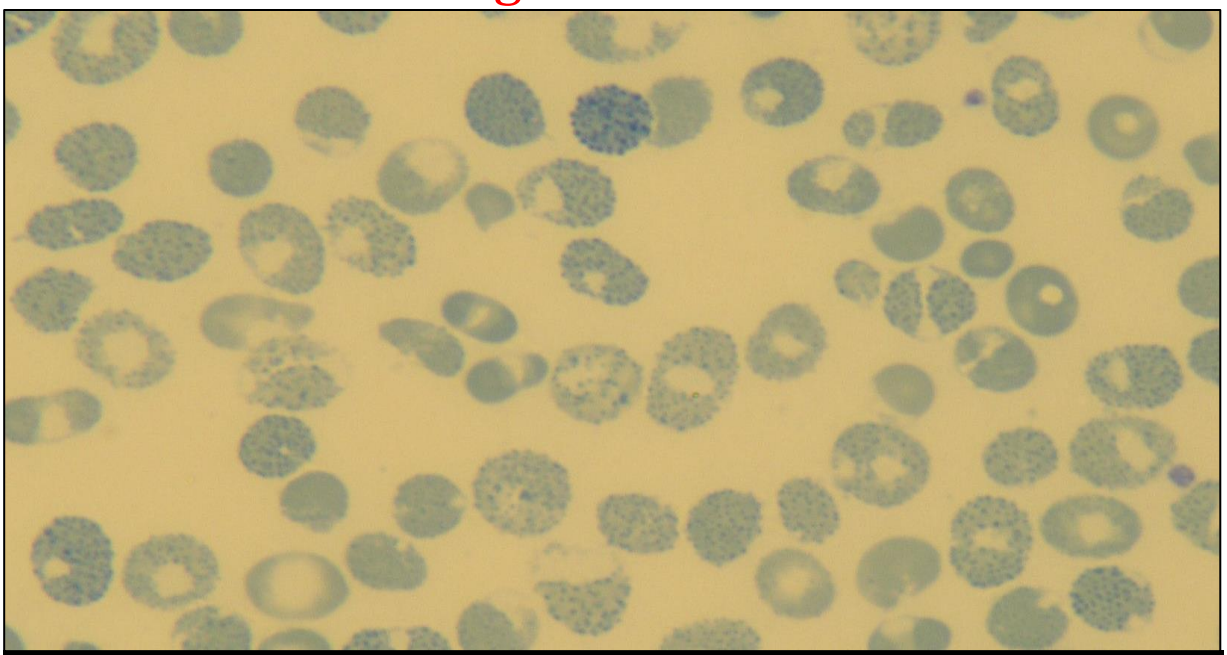
TEST	Blood film
Findings	1-Erythroid precursor(immature RBC's or Nucleated RBC(NRBC)) 2-Target cell (codocyte) 4-Anisocytosis. (unequal sized RBC's) 5- poikilocytosis .
Investigations	Hb Electrophoresis, Genetic studies.
Dx	Beta thalassemia major

α-Thalassaemia



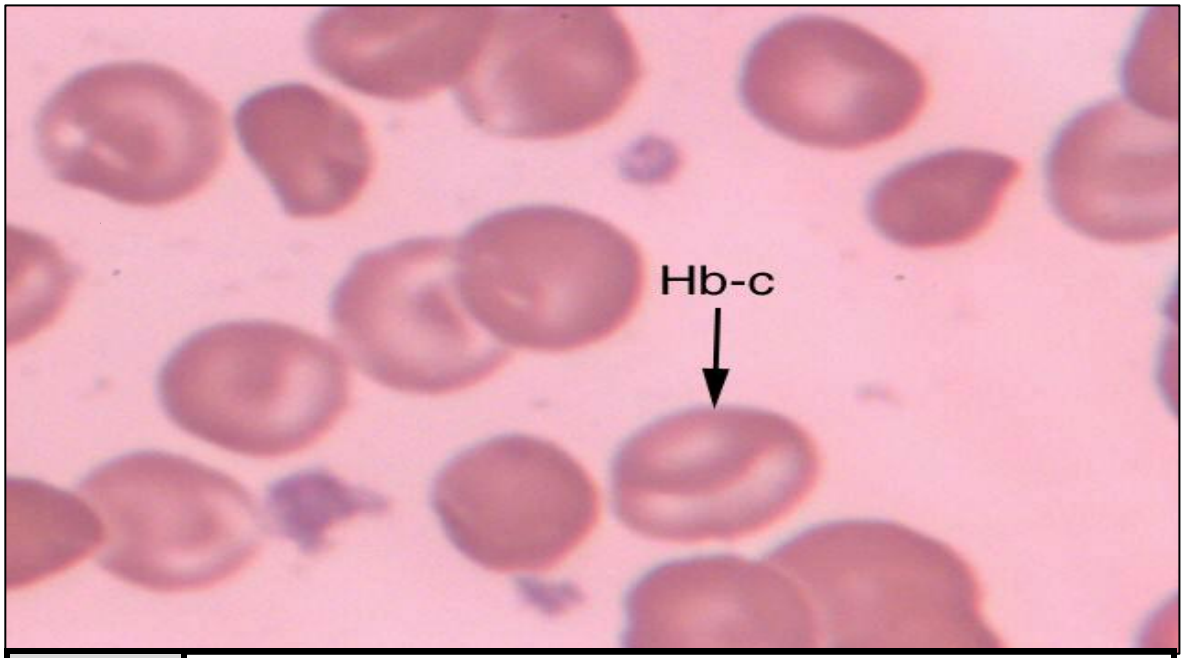
Test	Blood film
Findings	Target cell Hypochromic/microcytic
Inv.	Hb electrophoresis
Dx	Alpha thalassemia (no erythriod)

Haemoglobin H Disease



Test	Blood film
Findings	Golf ball appearance.
Inv.	Hb electrophoresis
Dx	Hb H thalassemia (alpha thalassemia)

Haemoglobin C Disease



Test	Blood film
Findings	Crystals within RBC's Target cells Hypochromic/microcytic
Inv.	Hb electrophoresis
Dx	Hb C disease

Gel electrophoresis (old test used before Hb electrophoresis)

Hematology Team Leaders:

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432 Haematology Team

*Good Luck ^_^*

اللهم إني استودعك ما قرأت و ما حفظت و ما تعلمت فرده عليَ عند حاجتي إليه انك على كل شيء قدير

If there is any mistake or feedback please contact us: 432PathologyTeam@gmail.com