Hemoglobinopathies – Part 1

They are disorders affecting the structure , function , or production of the Hb , and these conditions are usually inherited .
The Hb consists of haem (core iron) and globin (2 alpha and 2 non alpha chains) .

Adult Hb :

- 90% Hb A ..... 2 alpha and 2 beta .
- 1-3.5 % Hb A2..... 2 alpha and 2 delta .
- 0.5-2 % Hb F ..... 2 alpha and 2 gamma .

Types of Haemoglobinopathies

1- Qualitative abnormalities .
2- Quantitative abnormalties .

Qualitative abnormalities :

There is an alteration in the amino acid structure of the polypeptide chains of the globin fraction of the Hb . The best example is Hb S , fuond in Sickle – cell anaemia .

Quantitative abnrmalities :

In these abnormalities (the thalassaemias) , the amino sequence is normal but polypeptide chain production is impaired or absent

In these conditions the ratio of alpha to non – alpha chain production is disturbed . In alpha thalassae-Mia excess beta chains are present , whilst in beta – thalassaemia excess alpha chains are present .

Sickle ceil anaemia

Sickle cell disease results from a single glutamic acid to valine substitution at position 6 of the beta – globine polypeptide chain
It's inherited as an autosomal recessive trait .
Homozygotes only produce abnormal beta chains that make Hb S (termed SS) , and this results in the clinical syndrome of sickle – cell disease .
Heterozygotes produce a mixture of normal and abnormal beta chains that make normal Hb A and Hb S (termed AS) , and this results in the clinically a symptomatic sickle trait .
When HbS is deoxygenated , the molecules of Hb polymerise to form pseudocrystalline structures known as ' tactoids ' .These distort the red cell membrane and produce characteristic sickle shaped cells .

Clinical manifestations of SCA :

Start at 3-6 months of age .

- Vasoocclusion :

Intermittent episodes of vasoocclusion in connective and musculoskeletal structures produce painful ischemia manifested by acute pain and tenderness , fever , tachycardia , and anxiety .
These recurrent episodes , called ***painful crises*** , are the most common clinical manifestation .
Pain can develop almost anywhere in the body mostly in the extremities , chest , abdomen and back and may last from a few hrs to 2 weeks .
Painful crises are commonly precipitated by infections , dehydration , rapid changes in temperat-Ure and pregnancy , however , patients often have no obvious precipitating cause for an acute painful crises in practice .

- Acute chest syndrome

It is characterized by chest pain , tachypnoea , fever , cough , hypoxaemia , and Chest infiltrates .
It's life threatening condition .

It can mimic pneumonia , pulmonary embolism , bone marrow infarction and embolism , myocardial ischaemia , or lung infarction .
Pulmonary infarction and pneumonia are the most frequent underlying or concomittant conditions in patients with this syndrome .

Repeated pulmonary crises lead to pulmonary H.T and corpulmonale , an increasingly common causes of death as patients survive furthur into adult life .

APLASTIC CRISIS

- Very low Hb .
- Low reticulocyte count .
- Transient suppression of the B.M activity .
- Caused by an infection with parvovirus B19 .
- Some patients may go on to develop B.M necrosis , with a leukoerythroblastic picture .

SEQUESTRATION CRISIS

Thrombosis of the venous outflow from an organ causes loss of function and acute painful enlargement . In children the spleen is the most common site . Massive splenic enlargement may result in severe anaemia and circulatory collapse and death . Recurrent sickling in the spleen in childhood results in infarction and adults may have no functional spleen .

Thus the spleen is frequently lost within the first 18-36 months of life , causing susceptibility to infection , particularly by pneumococci .

- Neurological events

- Acute large – vessel occlusions can occur in children causing stroke . These are rarely occur in adults .
- Adults may suffer haemorrhagic stroke as a result of an aneurysmal dilatation of proliferative vessels that form in response to repeated micro-occlusion in the cerebral vessels .

- **Jaundice .**
- **Moderate to severe anaemia .**

To be continued ,,,