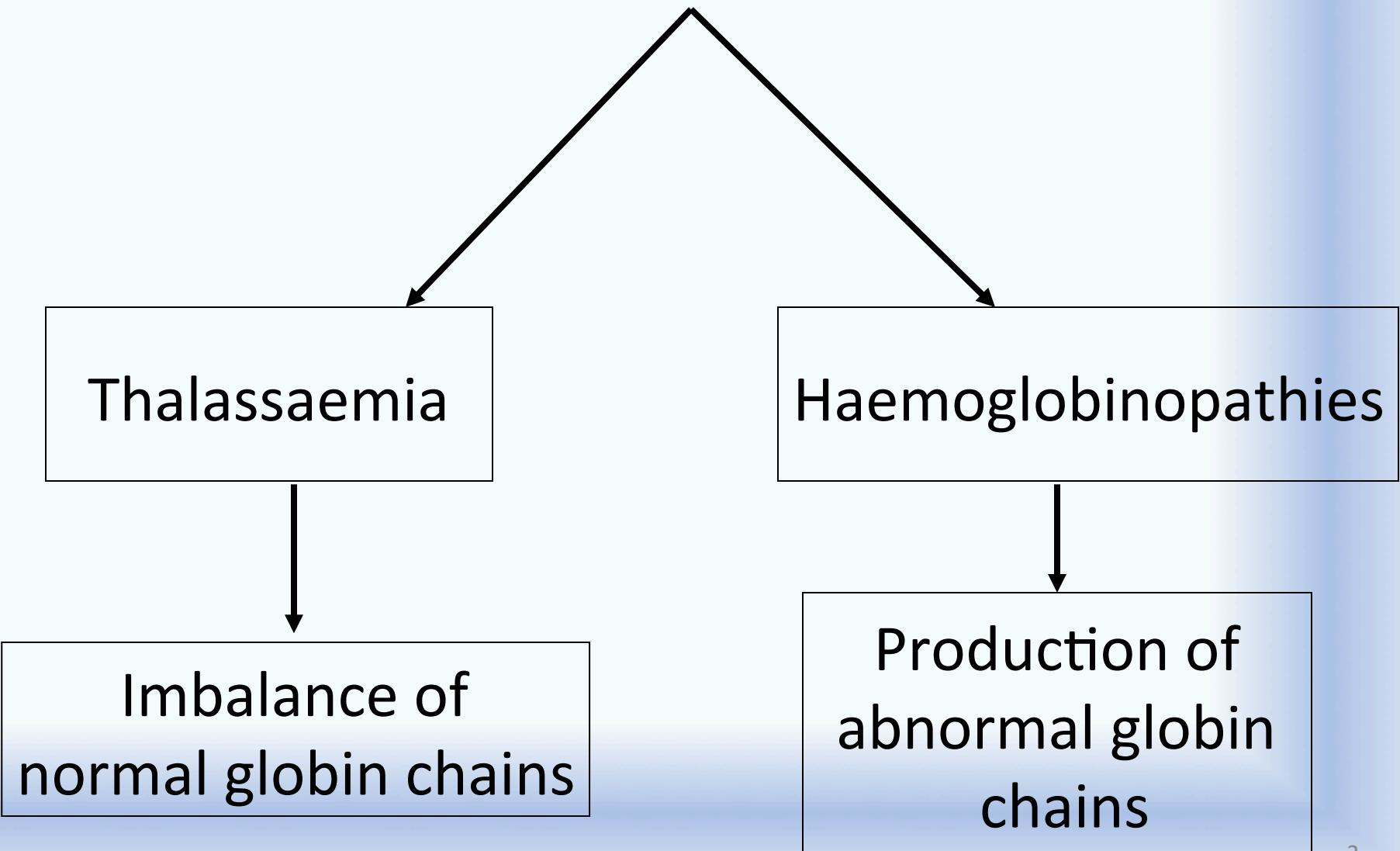


Sickle cell anaemia

Dr Senani Williams

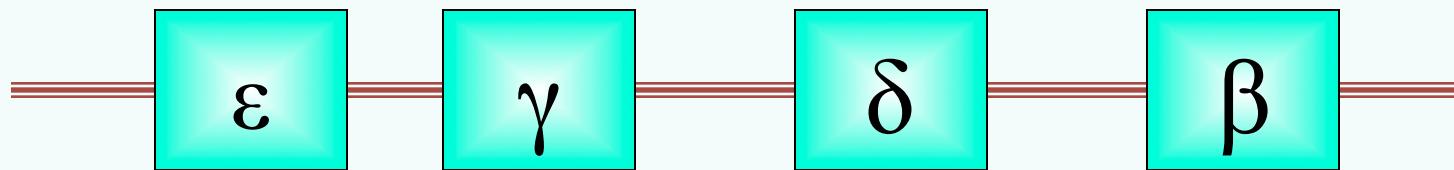
Haemoglobin defects



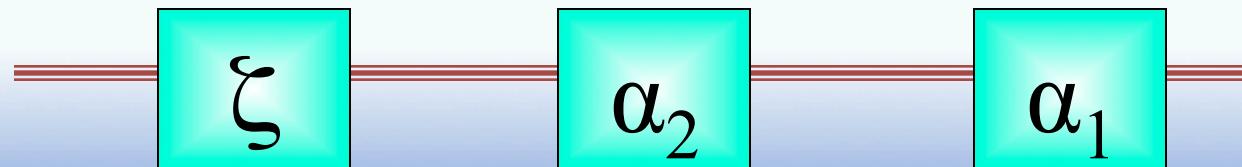
Hb synthesis

Globin genes are located on 2 chromosomes

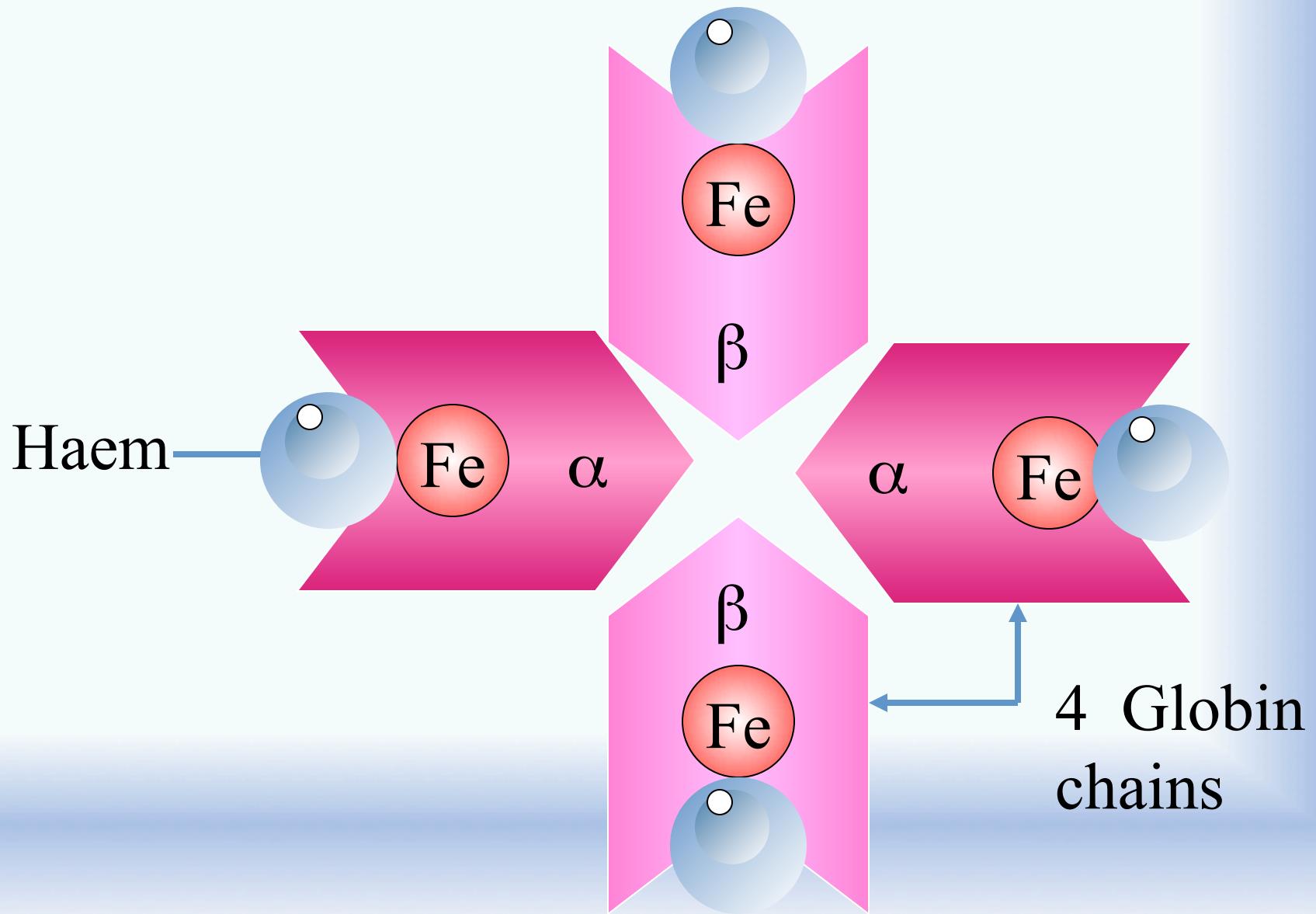
Chromosome 11



Chromosome 16



Haemoglobin



Inheritance

Unaffected carrier father



Unaffected carrier mother



LEGEND



RECESSIVE
GENE

DOMINANT
GENE

Unaffected child



Unaffected carrier child



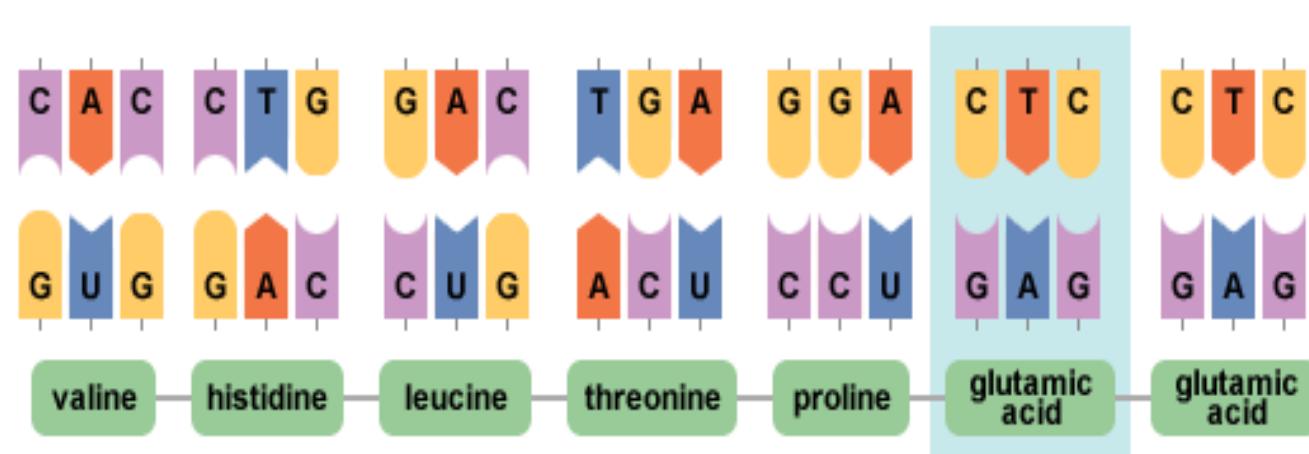
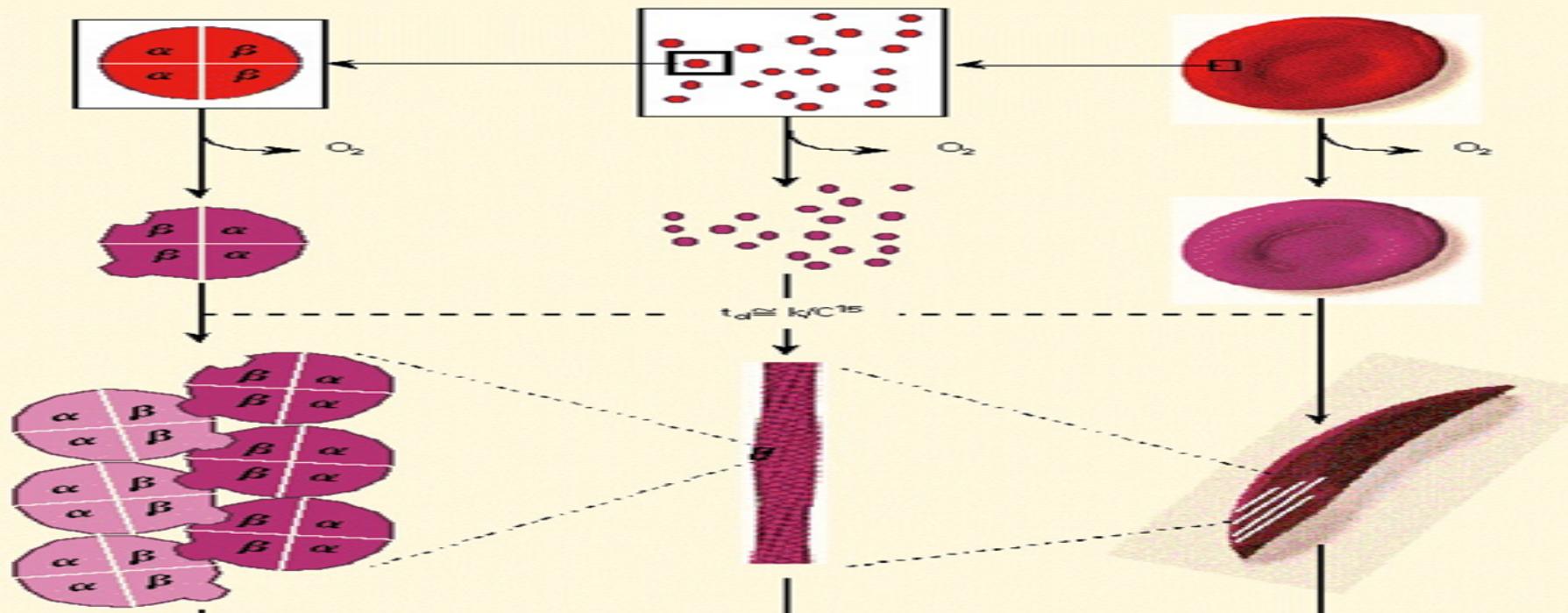
Unaffected carrier child



Affected child

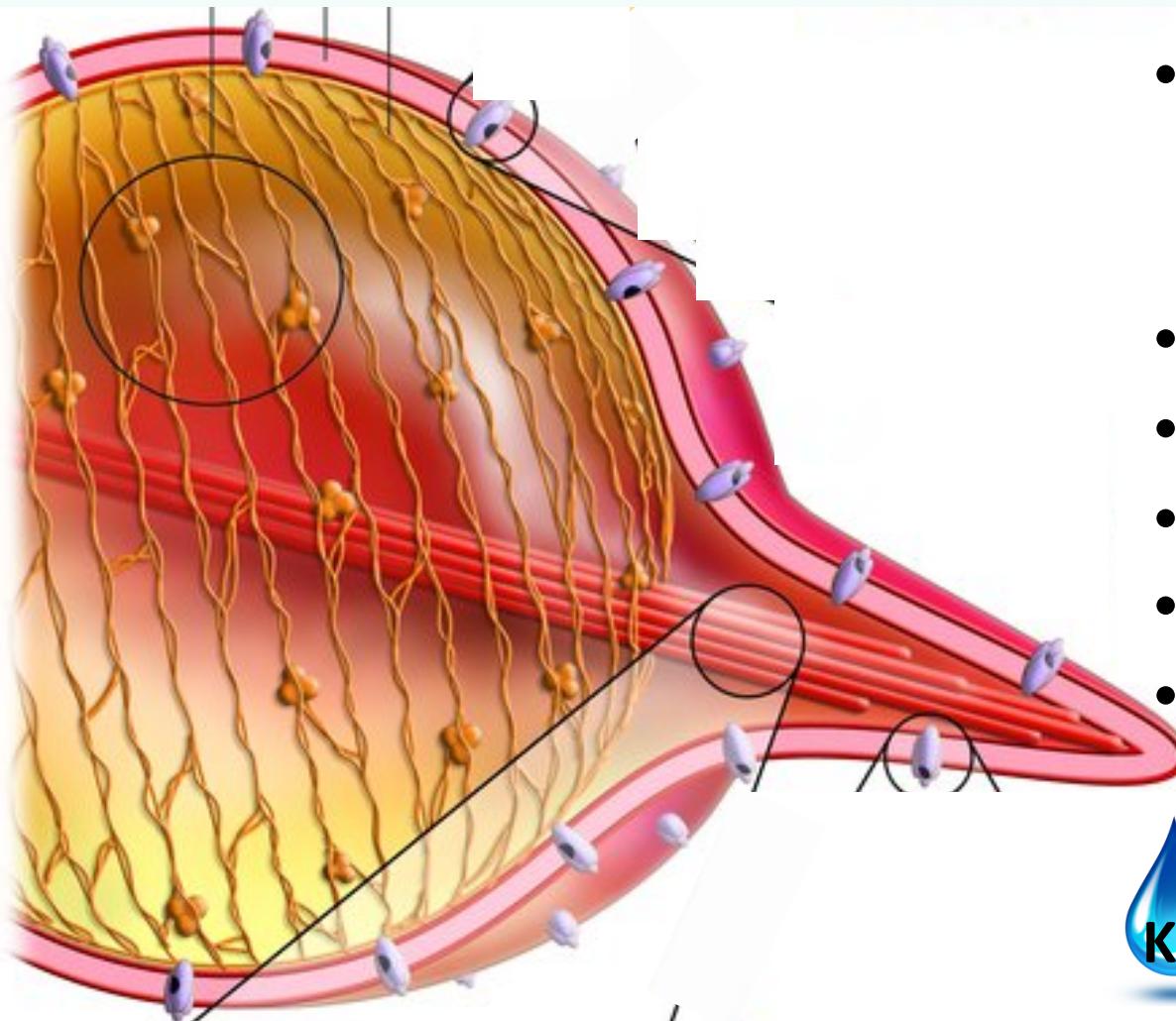


Pathogenesis of Sickling



6th position

Sickle cells



- Deoxygenated HbS molecules polymerize.
- ↓ Flexibility
- ↑ Rigidity
- Initially reversible
- Cellular dehydration,
- Via $K^+ - Ca^{2+}$ Gados Channel



Sickle cell anaemia



**Normal red
blood cell**

**Formation of sickled red
blood cell**

**Sickled red
blood cell**

Pathogenesis

- Reduced red cell survival
- Obstruction of microcirculation
- Tissue infarction

Precipitating factors

- Infection
- Dehydration
- Cold
- Acidosis
- Hypoxia
- VCAM on endothelial cells

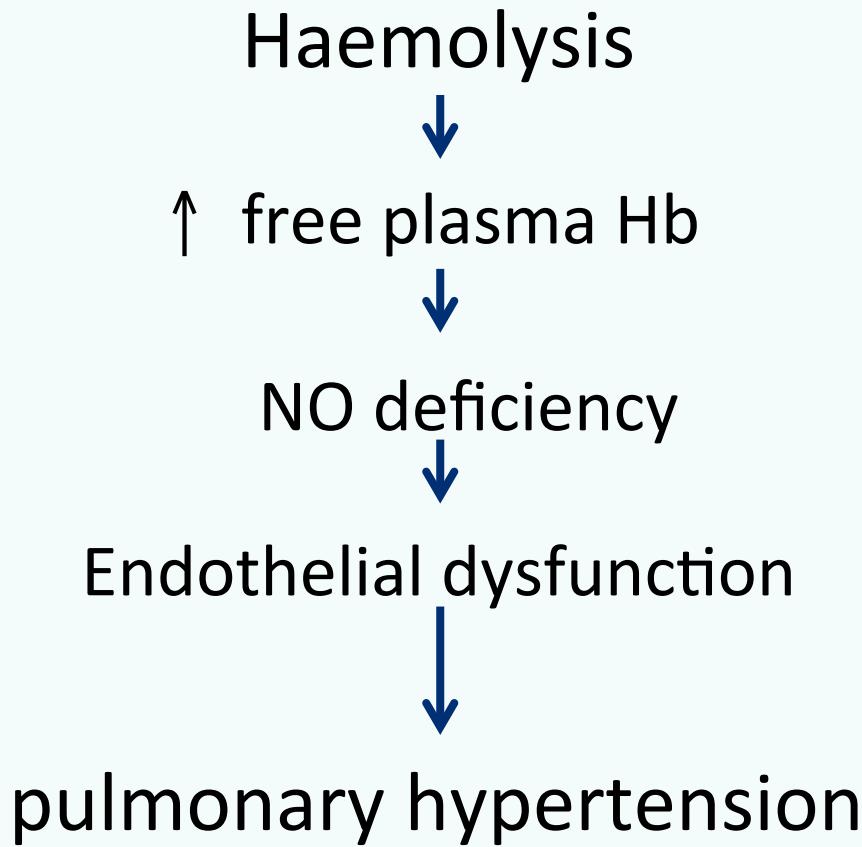
3 Clinical syndromes

- Homozygous HbSS - the most severe disease
- Combined heterozygosity (HbSC) for HbS and C intermediate symptoms
- Heterozygous HbAS (sickle cell trait) have no symptoms

Clinical features

- Vaso-occlusive crises
- Dactylitis
- Painful crises
- Acute chest syndrome – caused by
- Infection - Chlamydia and mycoplasma, Strept. pneumoniae.
- Fat embolism from necrotic bone marrow
- Pulmonary infarction due to sequestration
- Presentation gradual or very rapid, leading to death in a few hours

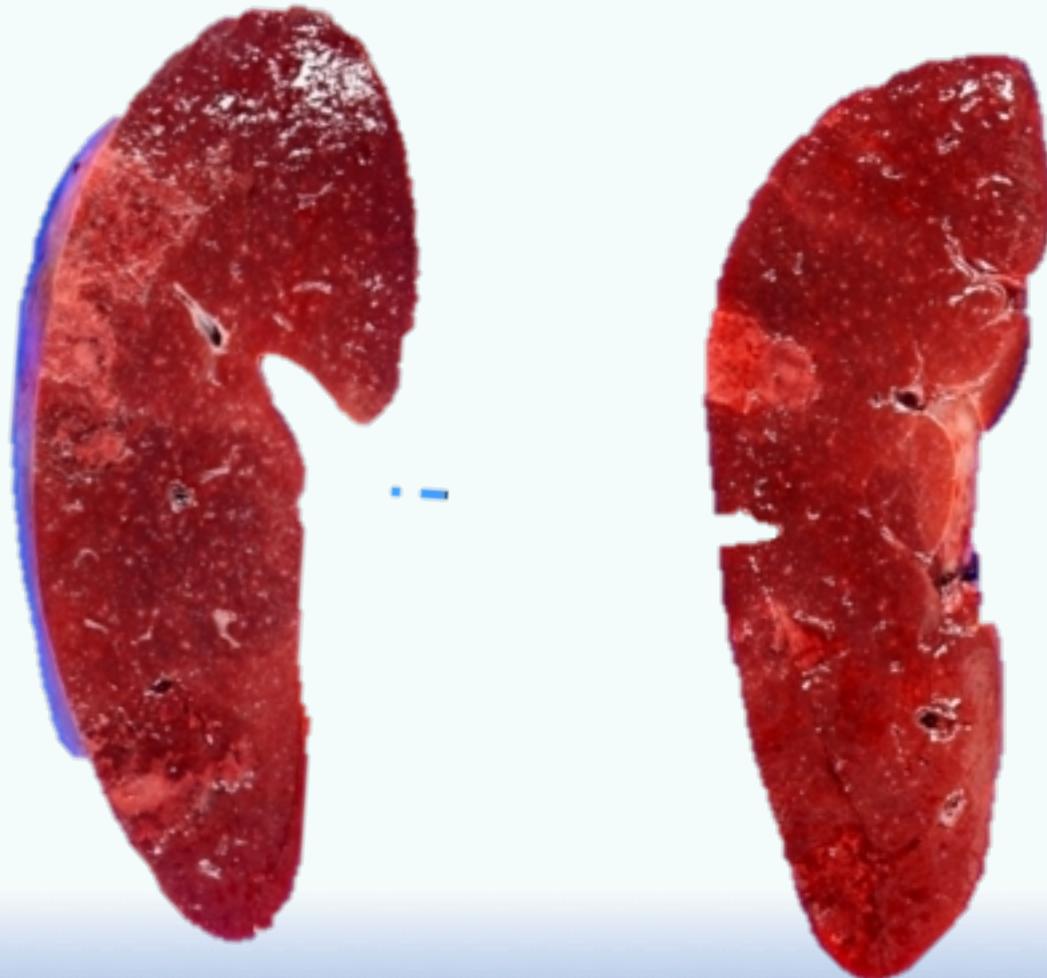
Pulmonary hypertension



Splenic sequestration

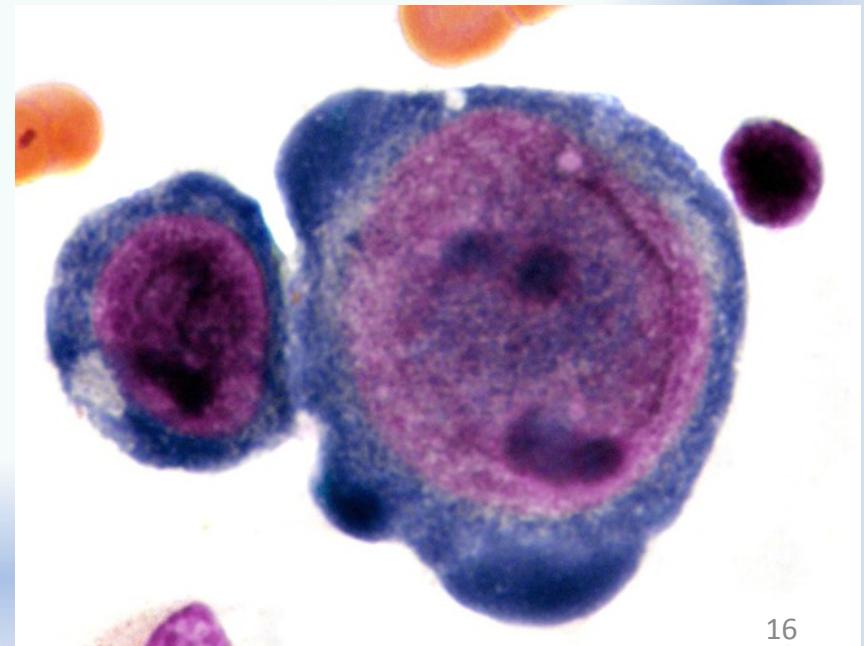
- Vaso-occlusion produces acute painful enlargement of the spleen.
- Splenic pooling of red cells
- Hypovolaemia
- Circulatory collapse and death.
- Occurs in childhood before multiple infarctions
- Leads to a fibrotic non- functioning spleen

Splenic Infarcts



Aplastic crises

- Following erythro- virus B19 infection
- Invades proliferating erythroid progenitors.
- Rapid fall in haemoglobin
- No reticulocytes



Long term Problems

- Children are short
- Below normal weight
- Delayed sexual maturation
- Chronic infarcts - Avascular necrosis of hips
Shoulders
- Compression of vertebrae
- Shortening of bones in the hands and feet
- Osteomyelitis by *Staphylococcus aureus*, *Staph. pneumoniae* and *salmonella*



Dactylitis



Hand-foot syndrome in patient aged 14 months with homozygous sickle cell disease

From: Davies SC, Oni L. BMJ. 1997;315:656-660

Eye

- Background retinopathy
- Proliferative retinopathy
- Vitreous haemorrhages
- Retinal detachments
- Yearly eye checks

Complications

- Leg ulcers
- Cardiomegaly
- Arrhythmias
- Iron overload cardiomyopathy
- Myocardial infarctions due to thrombotic episodes not secondary to atheroma.



Pregnancy

- Impaired placental blood flow
- Spontaneous abortion
- Intrauterine growth retardation
- Pre- eclampsia
- Fetal death.
- Painful episodes
- Infections
- Severe anaemia

Neurological complications

- Transient ischaemic attack
- Fits
- Cerebral infarction
- Cerebral haemorrhage
- Coma
- Strokes in 11% under 20 years
- Obstruction of distal intracranial internal carotid artery or a proximal middle cerebral artery
- Abnormal blood-flow velocity indicative of arterial stenosis

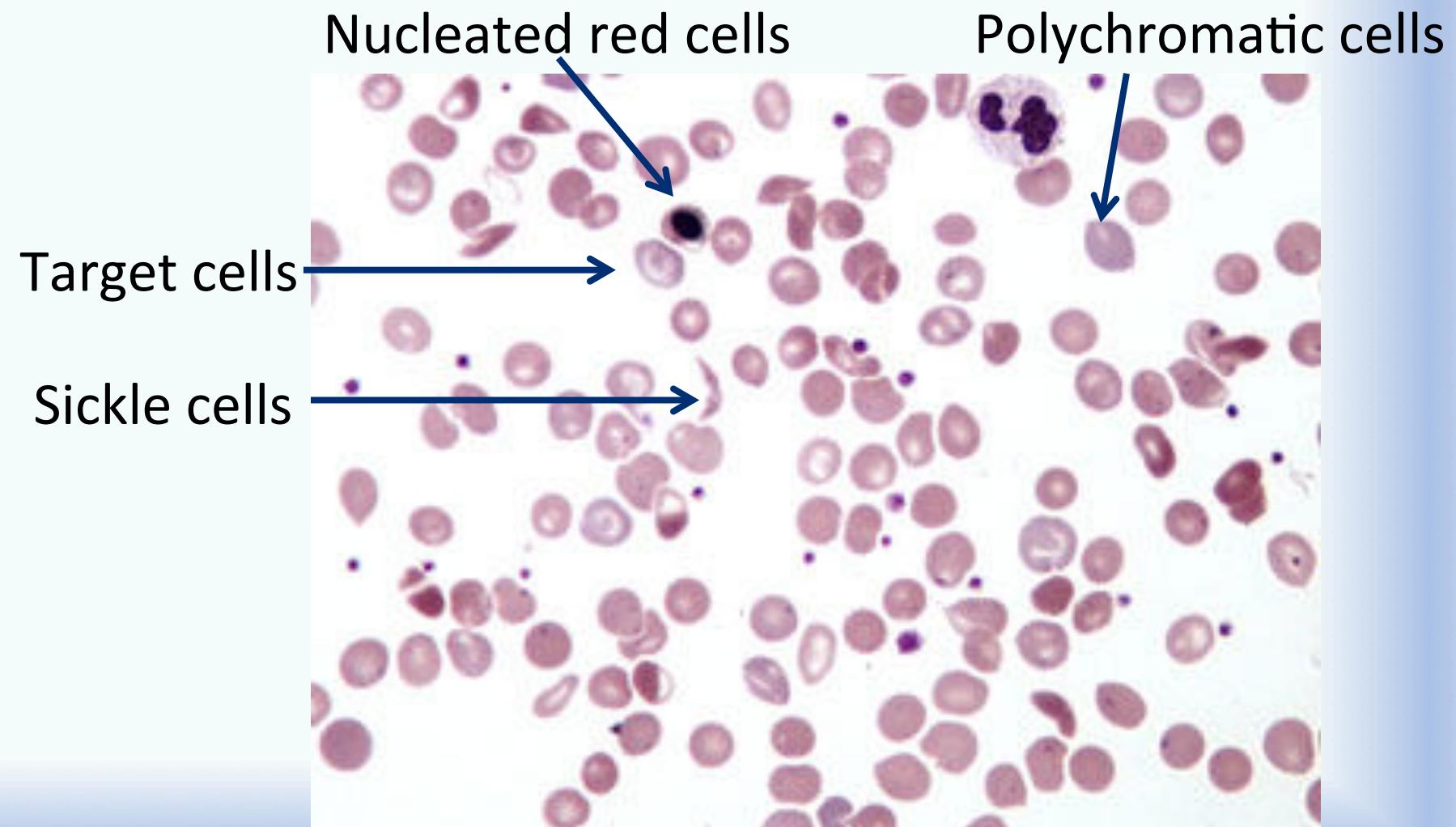
Prevention

- Transfusion to suppress erythropoiesis 90% of strokes in children could be prevented.
- Cholelithiasis - Pigment stones
- Chronic hepatomegaly and liver dysfunction
- Chronic tubulointerstitial nephritis occurs
- Priapism may result in impotence
- α -adrenergic blocking drugs
- Analgesia
- Hydration.

Investigations

- Hb 6–8 g/dL
- Reticulocyte count (10–20%).

Sickle cell blood film

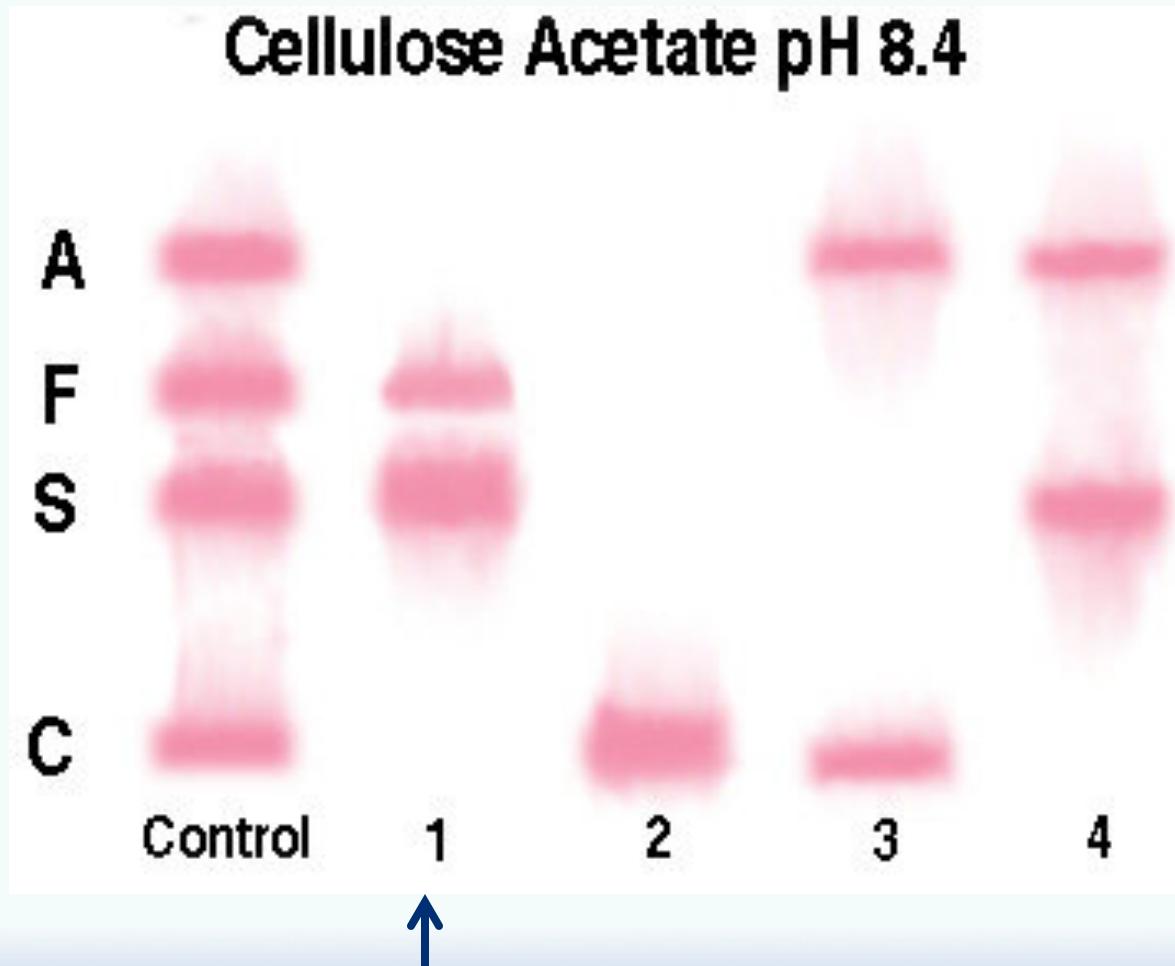


Sickling test

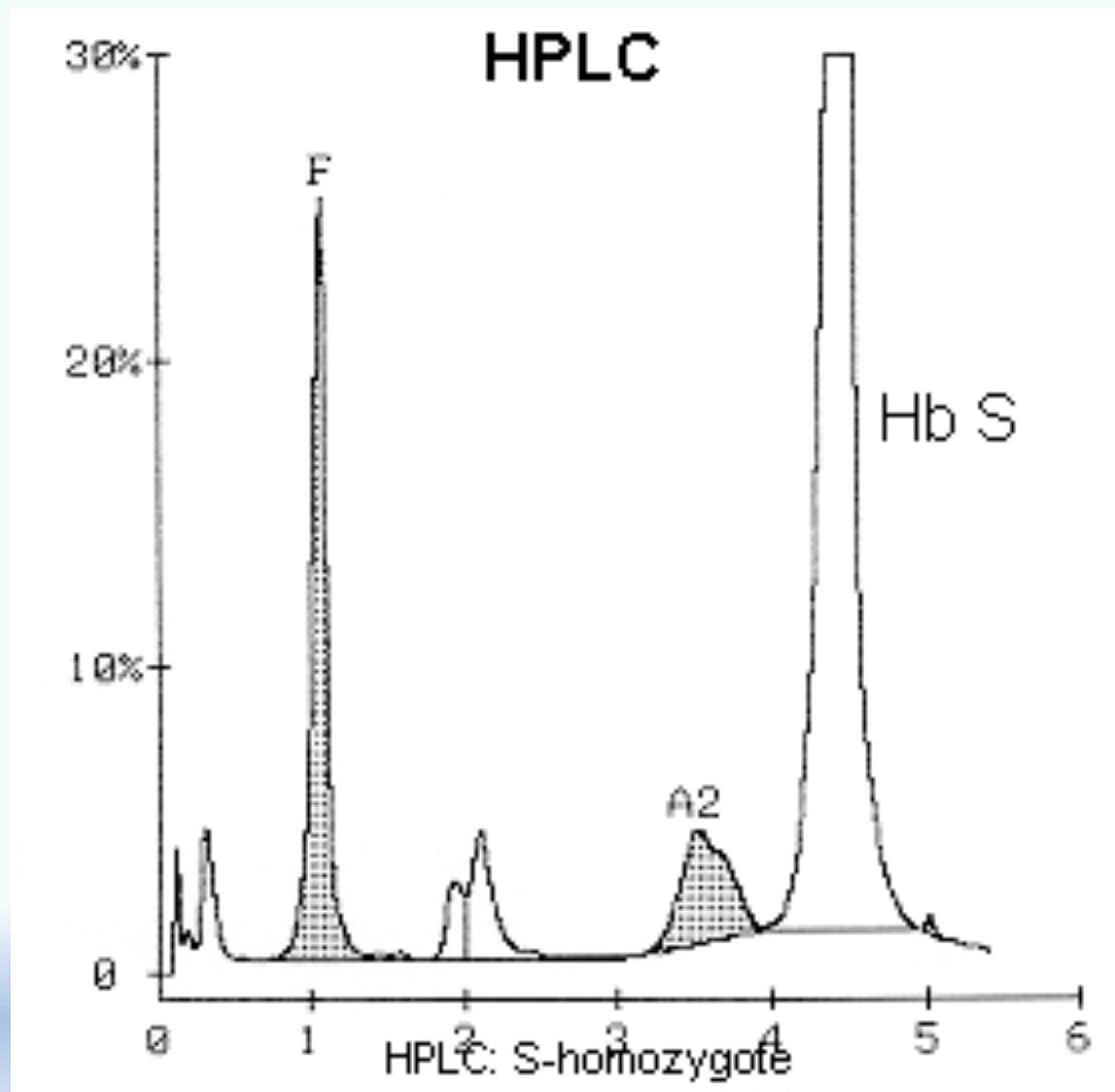


Negative Positive

Hb electrophoresis at alkaline pH



Sickle disease



Management

- Precipitating factors should be avoided or treated quickly.
- Pain relief - opioids - Morphine is the DOC
- High-flow O₂
- Antibiotics - Prophylaxis is with penicillin 500 mg daily
- Vaccination with polyvalent pneumococcal and Haemophilus influenzae type b vaccine
- Exchange transfusion to reduce HbS to <20%
- Ventilation (CPAP)
- Folic acid

Management

- Acute fall in Hb due to
- Splenic sequestration – acute painful enlargement of the spleen
- Bone marrow aplasia
- Drug induced haemolysis
- Acute infection
- Further haemolysis due to drugs, acute infection or associated G6PD deficiency
- Liver sequestration

Transfusions

- Patients with steady state anaemia, having minor surgery or painful episodes without complications should not be transfused.
- Transfusions if heart failure
- TIAs
- Strokes
- Acute chest syndrome
- Acute splenic sequestration
- Aplastic crises
- Before elective operations and during pregnancy, transfusions to reduce HbS <20%

Exchange transfusions

- Severe or recurrent crises,
- Before emergency surgery.
- Transfusion and splenectomy life- saving for young children with splenic sequestration.
- A full blood crossmatching compatibility screen
- Hydroxycarbamide (hydroxyurea) increases HbF concentrations.
- Reduce the episodes of pain, the acute chest syndrome, and the need for blood transfusions.

Management

- Inhaled nitric oxide for painful crises in sickle cell anaemia
- Stem cell transplantation
- Children and adolescents < 16 years with severe complications (strokes, recurrent chest syndrome or refractory pain) and have an HLA-matched donor are candidates for transplantation.

Counselling

- Multidisciplinary team
- Drug and birth control
- Some patients with HbSS die in the first few years of life

HbAS (sickle cell trait)

- No symptoms unless extreme circumstances cause anoxia,
- Flying in non-pressurized aircraft.
- Gives some protection against Pl falciparum
- Blood count and film of sickle cell trait are normal.
- diagnosis is by a positive sickle test or by Hb electrophoresis