
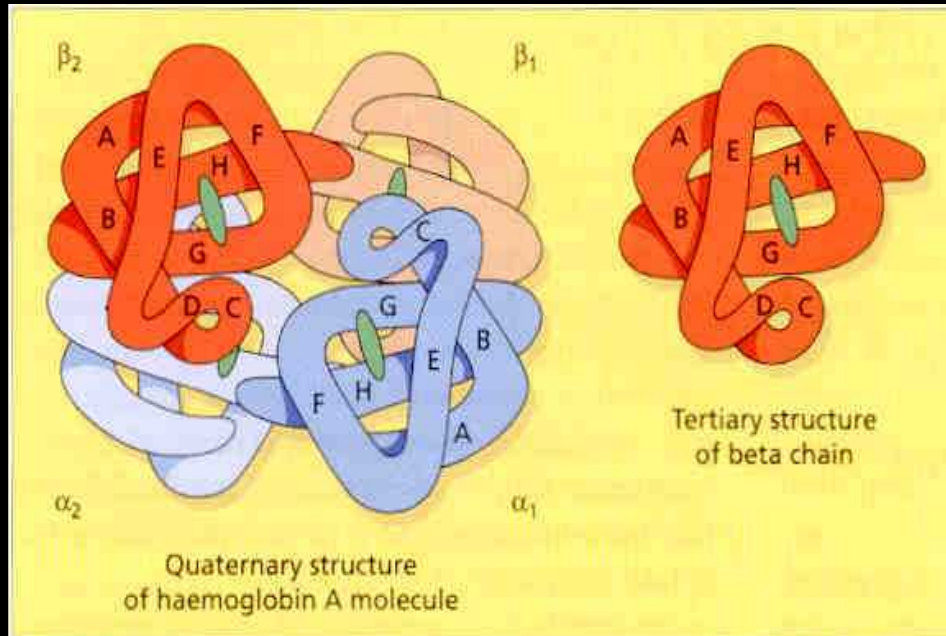


Sickle Cell Disease

Corrina Mc Mahon
Dept of Haematology, OLHSC/SJH

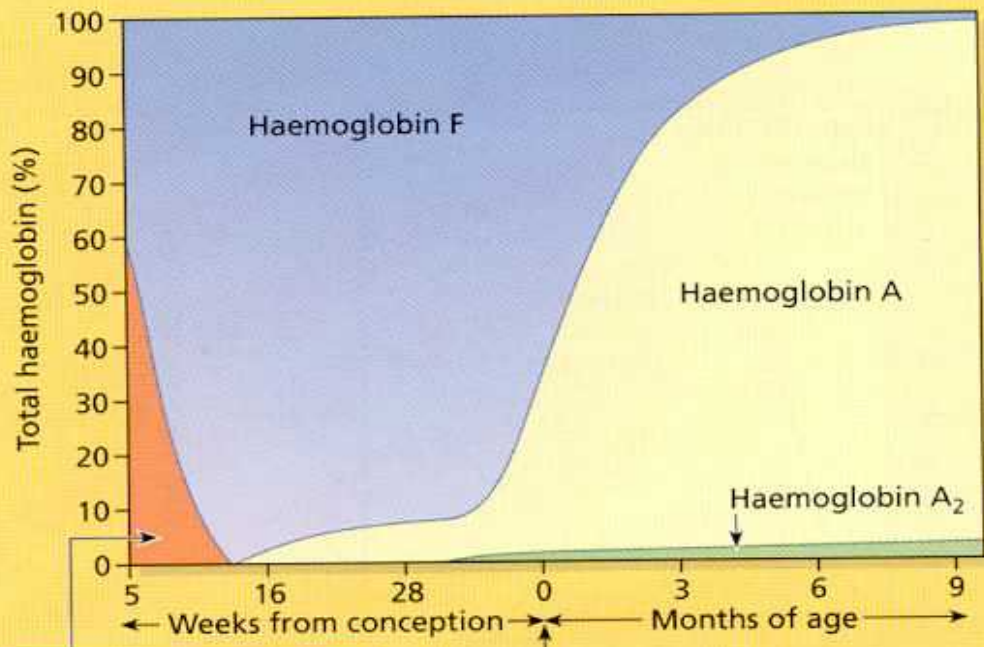


The Haemoglobin Molecule



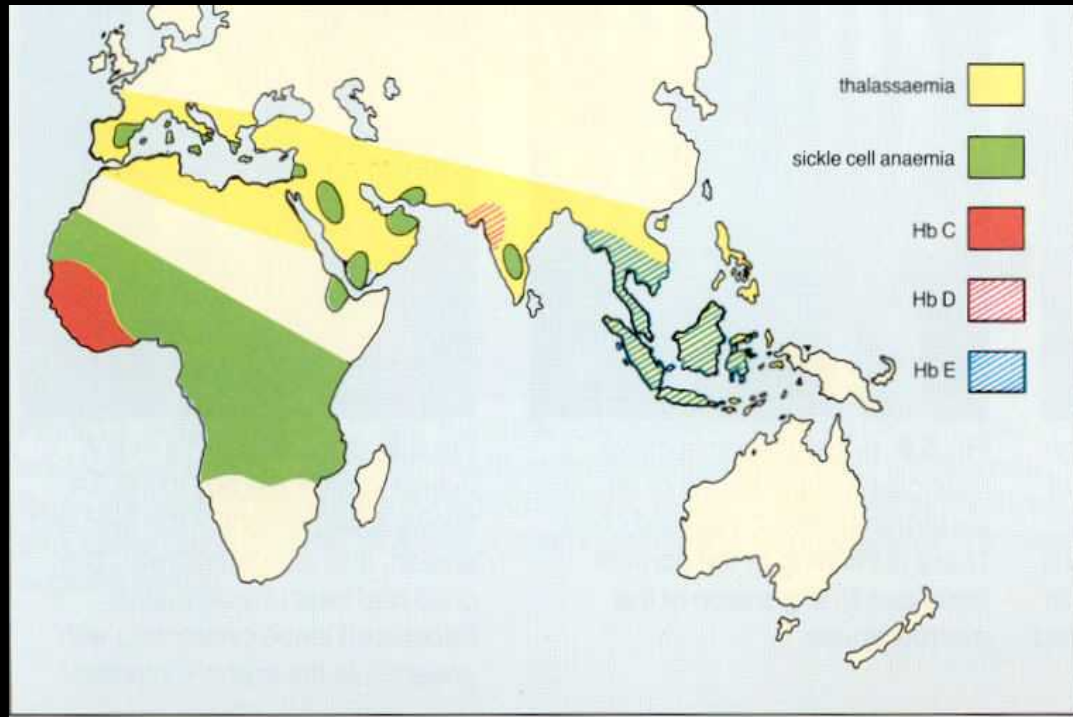
Types of Hb

Haemoglobin	Globin Chains	Normally present
HbA	$\alpha_2 \beta_2$	Major Hb >3mo 98%
HbA ₂	$\alpha_2 \delta_2$	Minor Hb adult life – 2.5%
HbF	$\alpha_2 \gamma_2$	Major Hb in fetal life & early neonatal period



Haemoglobins
Gower 1, Gower 2,
Portland 1 and Portland 2

Where does it occur?

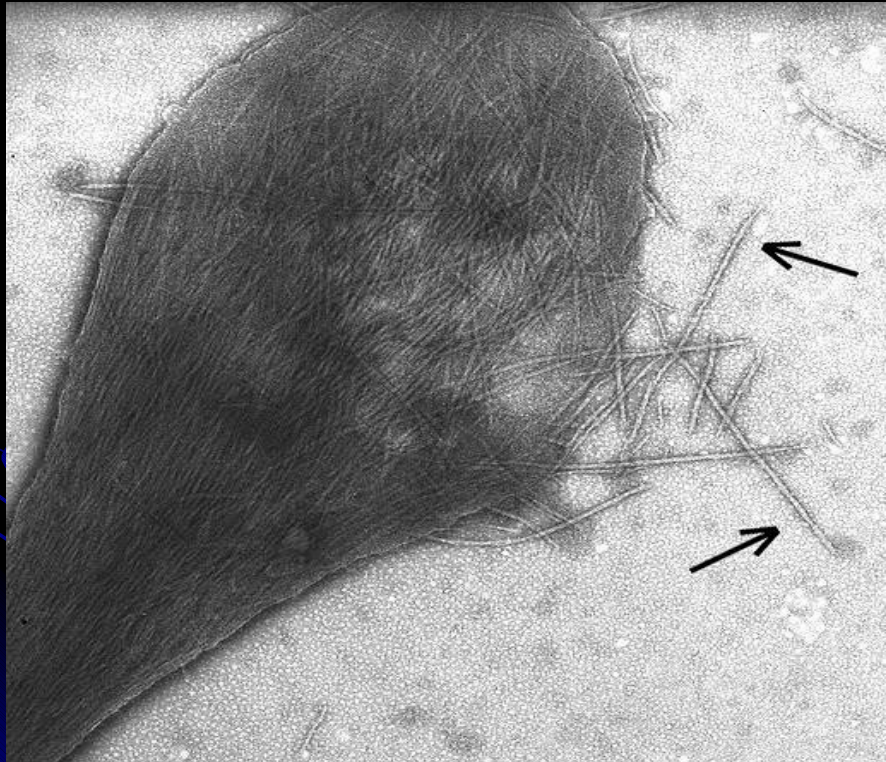


Sickle Cell Anaemia

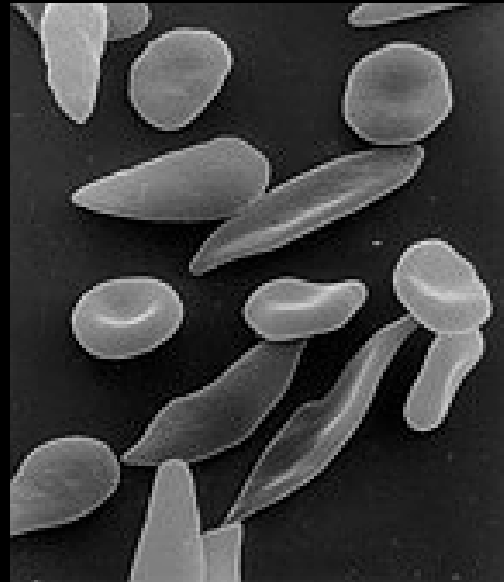
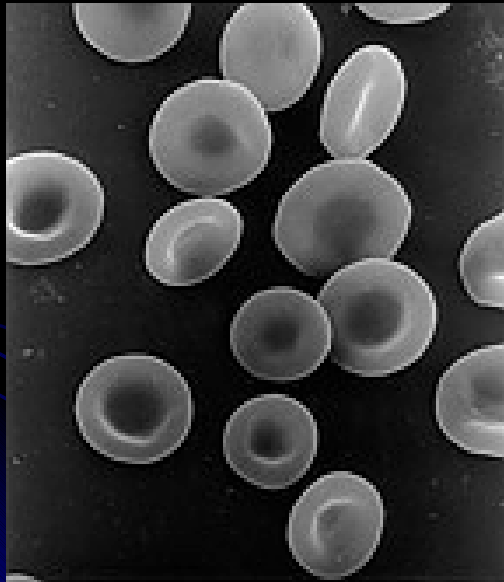


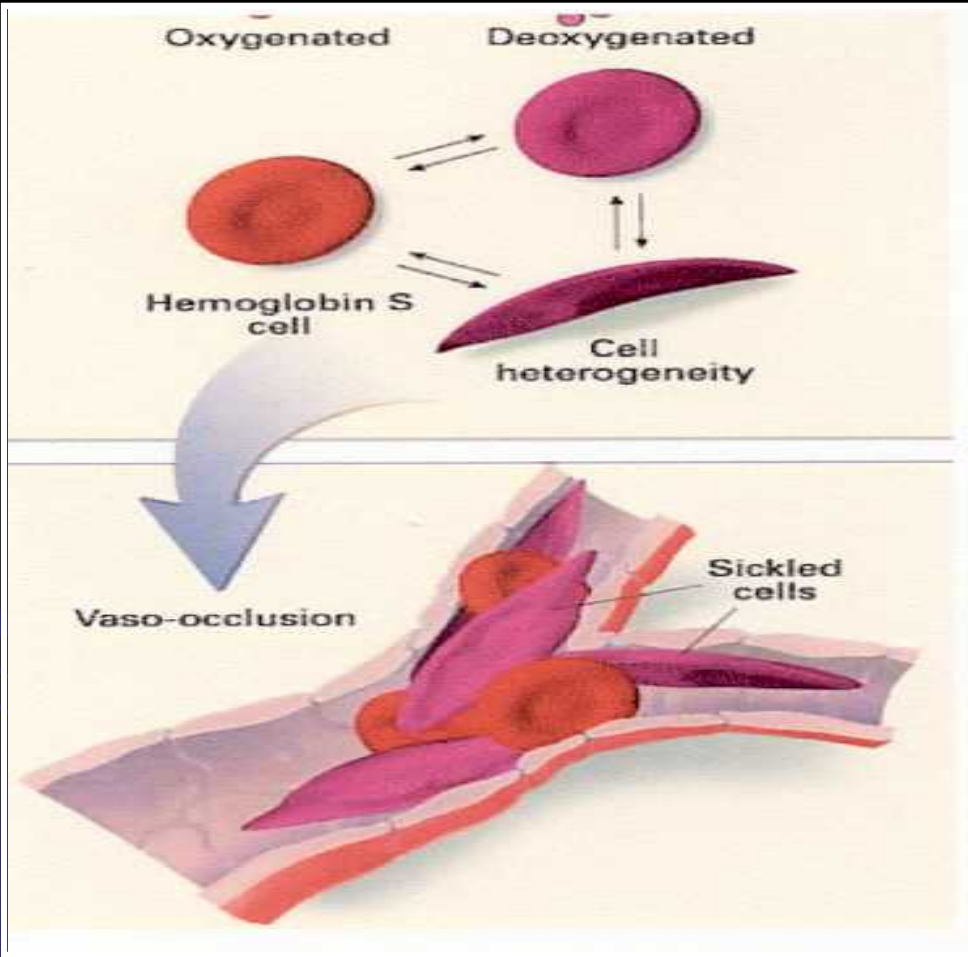
- | Valine for glutamine substitution at position 6 β -globin chain
- | Sickling; Abnormal adherence of RBC to endothelium \rightarrow Hb polymerisation \rightarrow elongated filaments \rightarrow semi-solid gel
- | Reversible sickling/irreversible changes
- | \uparrow HbS - \uparrow Sickling
- | \uparrow HbF/HbA - \downarrow sickling

Scanning electron microscopy



Scanning electron microscopy





Factors precipitating RBC sickling

Deoxygenation

Dehydration

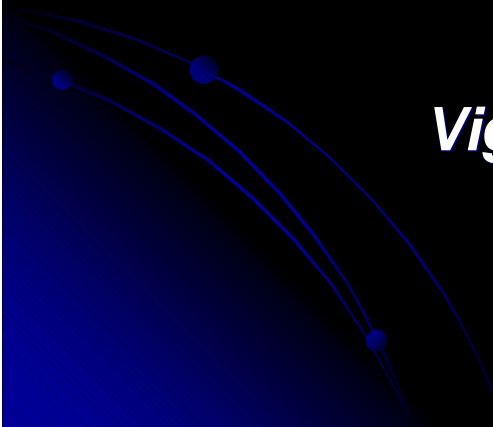
Infection

Acidosis

Cold

Vigorous exercise

Menstruation



SCD

The Statistics!

- | In Africa – 20% children die < 5 yrs of overwhelming sepsis
- | In Nigeria – many people with SCD die < 21yrs
- | In America – life expectancy for males 42yrs, females 48yr
- | Long term morbidity:
 - | Bone and joint damage
 - | Renal failure
 - | Loss of vision
 - | Restrictive lung disease
 - | Hemiparesis/hemiplegia
 - | Opiate addiction

Anaemia

I Haemolysis

- I Chronic
- I Acute infection
- I G6PD deficiency
- I RC Antibodies

I Aplasia

- I Parvovirus B19
- I Folate deficiency

I Chronic disease



Vaso-occlusion

| **Dactylitis**

- | Children <5yrs
- | Fever/leucocytosis
- | Cortical thinning after 2-3 weeks

| **Bone & joint infarction**

- | Children >2yrs; commonest 15 yrs

| **Abdominal events**

- | Splenic, gallbladder or mesenteric event
- | Acute abdomen

| **Priapism**

Life threatening events young children

I **Pneumococcal Sepsis**

- I Cause of - mortality in children <5 yrs

I **Splenic sequestration**

- I Infection
- I Mortality in <2yrs
- I Abd pain , pallor, shock, splenomegaly
- I Recurrent

Life threatening events – older children

I Chest syndrome

- I Commonest cause of mortality >2yrs
- I Pneumonia
- I ↓O₂ sats/tachypnoea
- I May follow a recent crisis

I Cerebrovascular Event

- I Children – thrombotic, Adults – haemorrhagic
- I Altered consciousness/sensations/ paralysis

Sickle cell Disease in Adolescence

- | Pubertal delay - 2.5 years
- | Chronic leg ulcers} **Poor school attendance**
- | Stuttering Priapism}
- | Enuresis
- | ↑ Painful Crisis
- | Avascular necrosis of femoral head

Sickle cell Disease in Adulthood

The survivors!

I **The Improvements**

- I ↓ Painful crisis; rare after 30 years
- I ↓ Leg ulcers
- I ↓ Infection
- I IHD & Hypertension less likely

I **The problems**

- I Renal failure
- I Pulmonary fibrosis
- I Intramural ventricular fibrosis → Heart failure
- I Stroke – Haemorrhagic (Subarachnoid or Intracerebral)
- I Pregnancy!

Complications of pregnancy in SCD

I **Bone Pain**

- I ↑ in 3rd trimester & post partum (x2-5)

I **Acute Chest Syndrome**

- I 33% patients; possible fat embolism from preceding bone crisis

I **Pre-eclampsia**

- I 14% pregnancies

I **Urinary Tract Infections**

- I 30%. Monthly MSU; if +ve antibiotics for duration

I **Pulmonary embolism**

Outcome of Pregnancy


I Maternal Mortality

- I Late booking/poor antenatal care
- I VTE
- I Pre-eclampsia

I Foetal Outcome

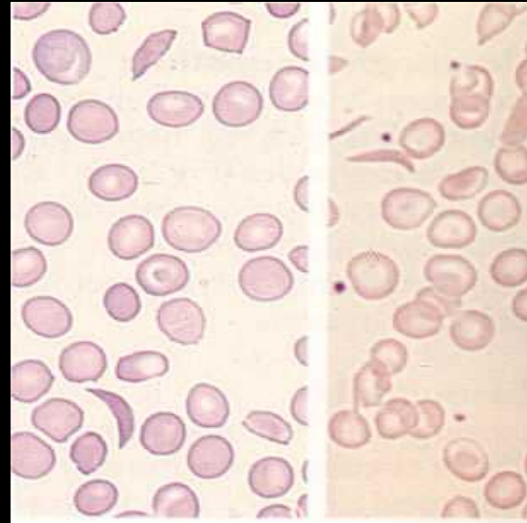
- I Spontaneous abortion – 10-15%
- I perinatal mortality - 10%
- I IUGR (30-40%)
- I Prematurity
- I Low apgar scores @ 1 & 5 minutes

Sickle Cell Disease and the Laboratory

- | Diagnosis
 - | Baseline Hb; WCC; Reticulocytes
 - | Red cell Phenotyping
 - | G6PD Screening
 - | Monitoring of treatment
 - | Monitoring of HbF levels
- 

How to test for SCD

- | FBC & film
- | Reticulocytes
- | Bilirubin/LDH
- | Sickledex
- | Hb electrophoresis

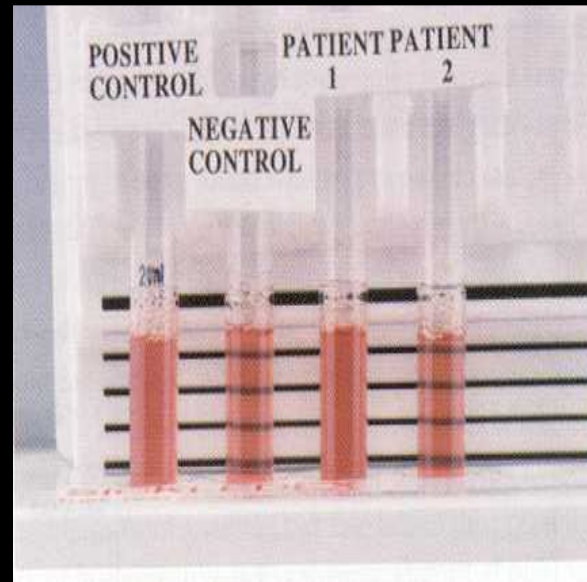


Sickledex

- | Blood is deoxygenated
- | HbS is insoluble & causes turbidity

But

- | Does not distinguish AS from SS
- | Inaccurate
 - | <6mo (↓HbS)
 - | post transfusion
 - | ↓Hb
 - | ↑wcc
 - | Hyperproteinaemia
 - | Hyperlipidaemia



Hb Electrophoresis



HPLC

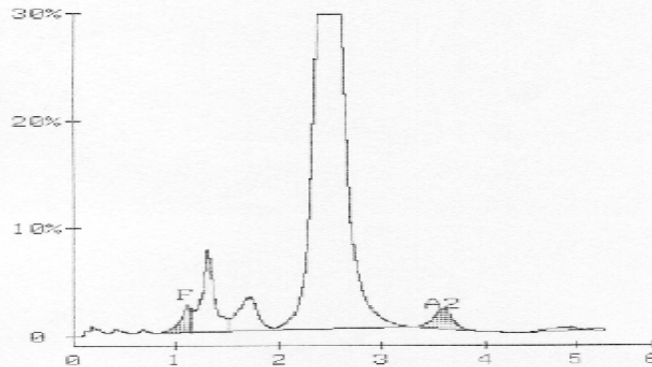
XXXX Data Thal Short 00495-0 XXXX
DATE:01/05/22 TIME:17:01:14

TECH ID# 0
VIAL# 10
SAMPLE ID# 00000000000000000000000000000000

ANALYTE ID	%	TIME	AREA
F	1.8	1.11	27816
FV100	0.7	1.01	99638
FV100	4.4	1.70	66248
A2	83.7	2.48	1250155
A2	2.6	3.58	35899
C-WINDOW	8.7	4.95	10684

TOTAL AREA 1480632

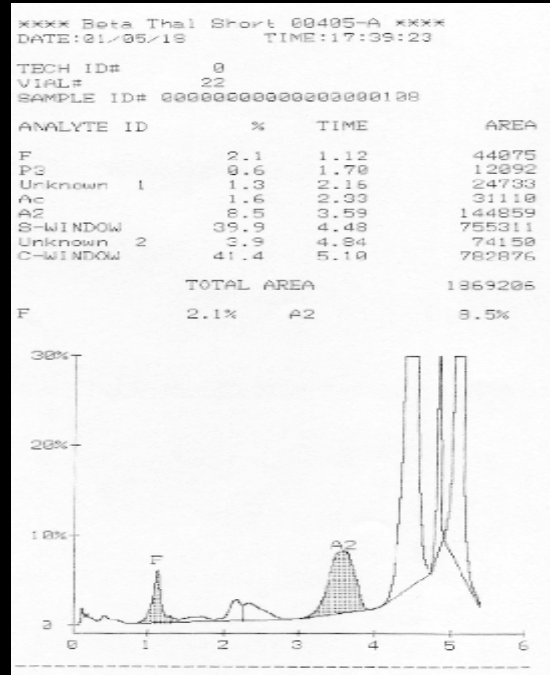
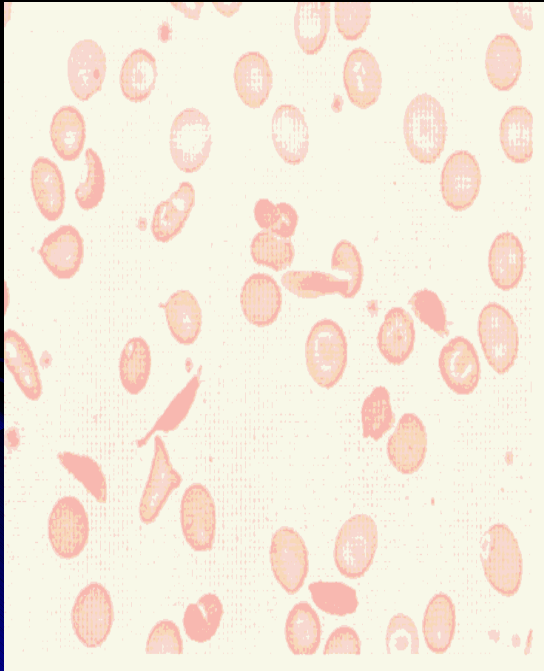
F 1.8% A2 2.6%



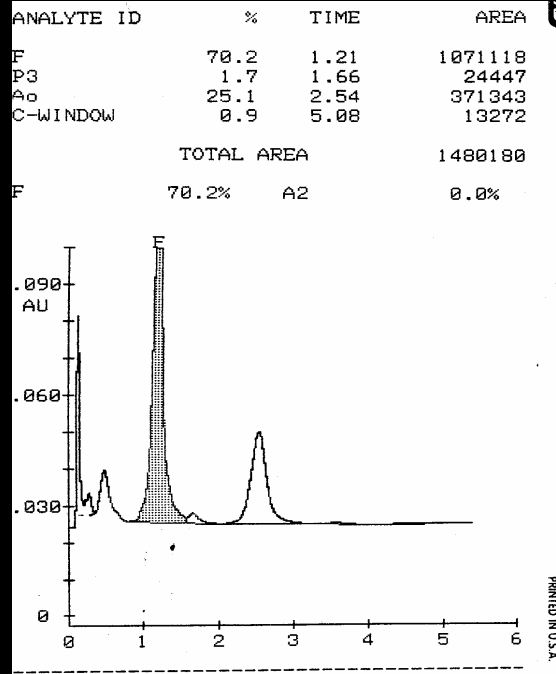
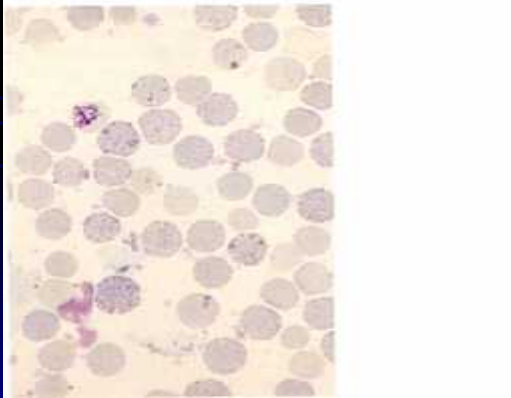
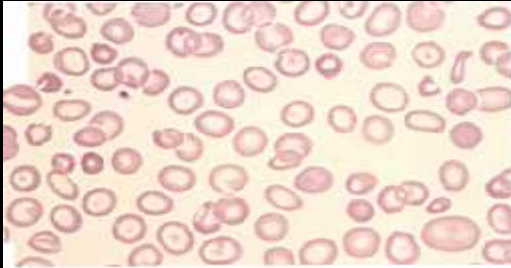
WALSH DATA

BIORAD

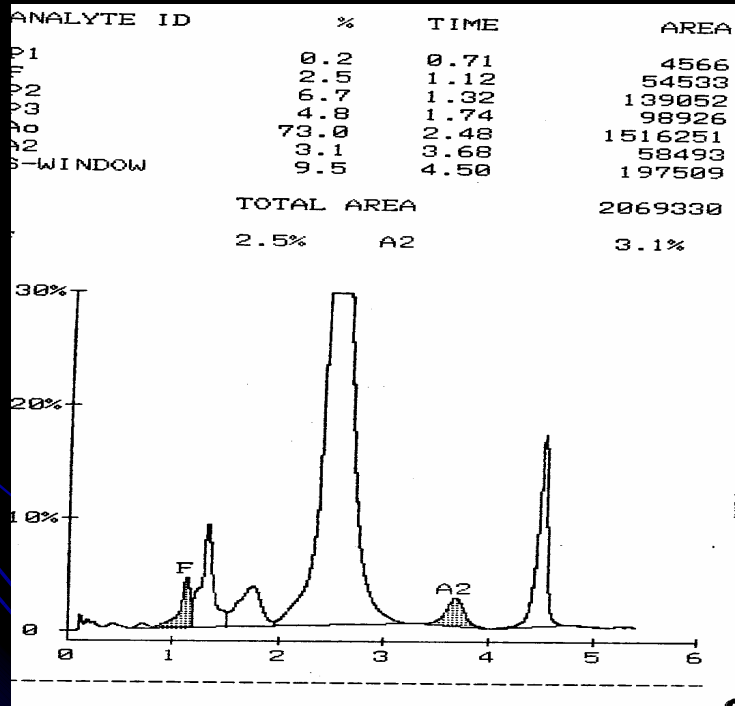
3 yr old Nigerian child; occasional back pain; Hb 10.5g/dl



Well African child; Hb 11.5 g/dl; MCV 60; MCH 28;
ferritin 80



4 year old african boy; history of ill health; recent medical interventions; now very well



What to do with a Positive result?

AS

- | Sickle cell trait
- | Almost benign
- | Deep sea diving
- | High altitudes
- | Major exertion

SS/SC

- | Sickle cell diseases
- | Penicillin
- | Folic acid
- | Vaccination
 - | Pneumococcal
 - | Influenza
 - | Hepatitis A & B
- | Life style advice

Specific Management strategies

- | Chronic transfusion programmes
- | Hydroxyurea
- | Bone Marrow transplantation

