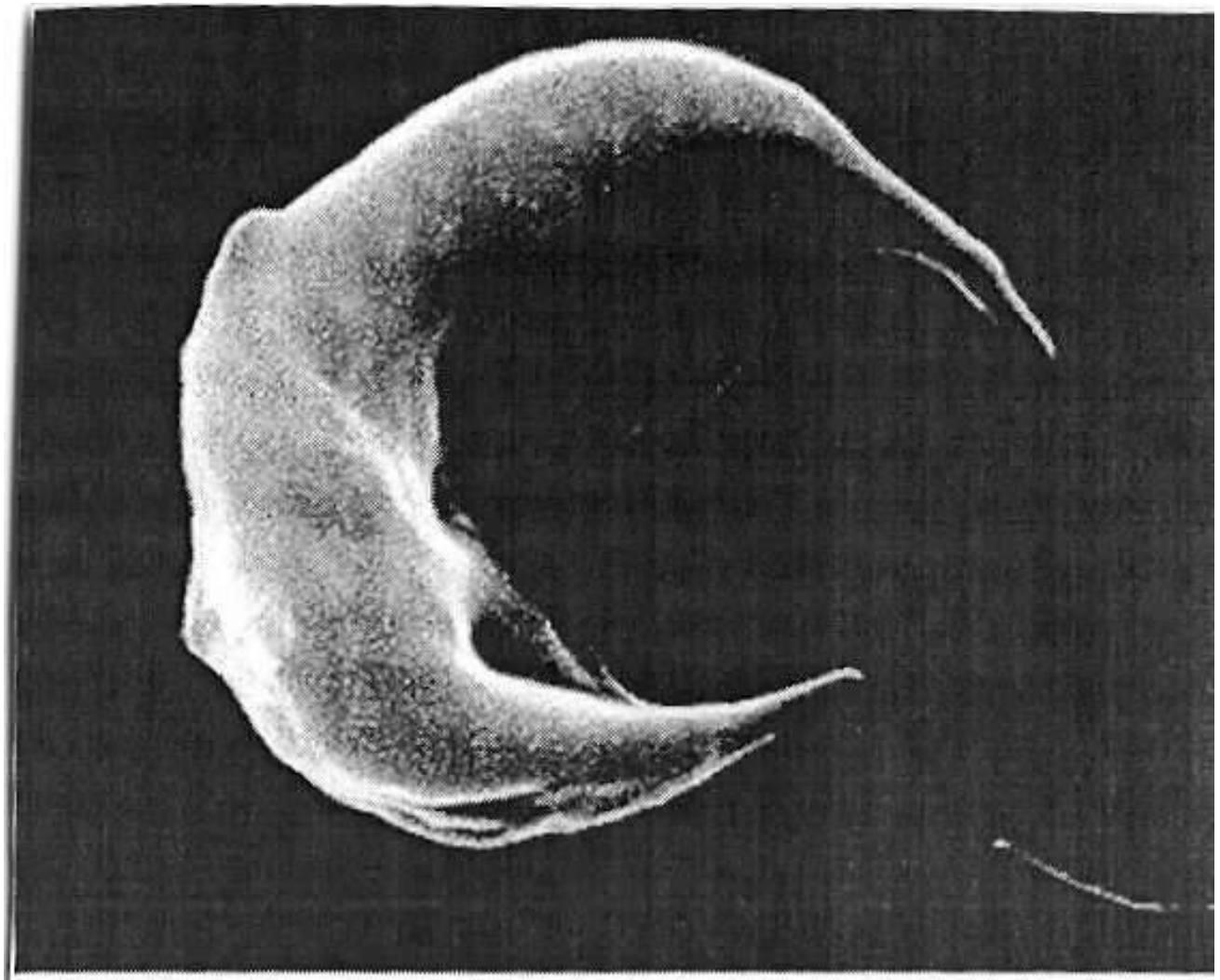
Sickle Cell Disease and impact on the society

Professor Z.A.Jeremiah Ph.D, FRCPath (London)
Professor of Haematology and Blood Transfusion Science
Niger Delta University, Wilberforce Island



Sickle cell Scanning electron micrograph of a single red blood cell from a patient with sickle cell disease, illustrating the classical "sickle" shape. Courtesy of RL

Outline

- What is sickle cell disease?
- How is it formed?
- Epidemiology
- Manifestations
- Laboratory findings
- Impact on the Society
- The future

What is it?

- Sickle cell disease is one form of hemoglobinopathy- a structural abnormality in hemoglobin molecule
- Substitution of glutamic acid by valine at the 6^{th} position
  - Negatively charged amino acid replaced by neutral amino acid

What is it?

- Hgb S maintains normal function in oxygenated state
- In de-oxygenated state- induced change in configuration allows valine to interact irregularly
- Formation of highly ordered polymers
- Polymers aggregate to rigid rods
- Spiny brittle RBCs
- Within vessels, thrombosis/obstruction

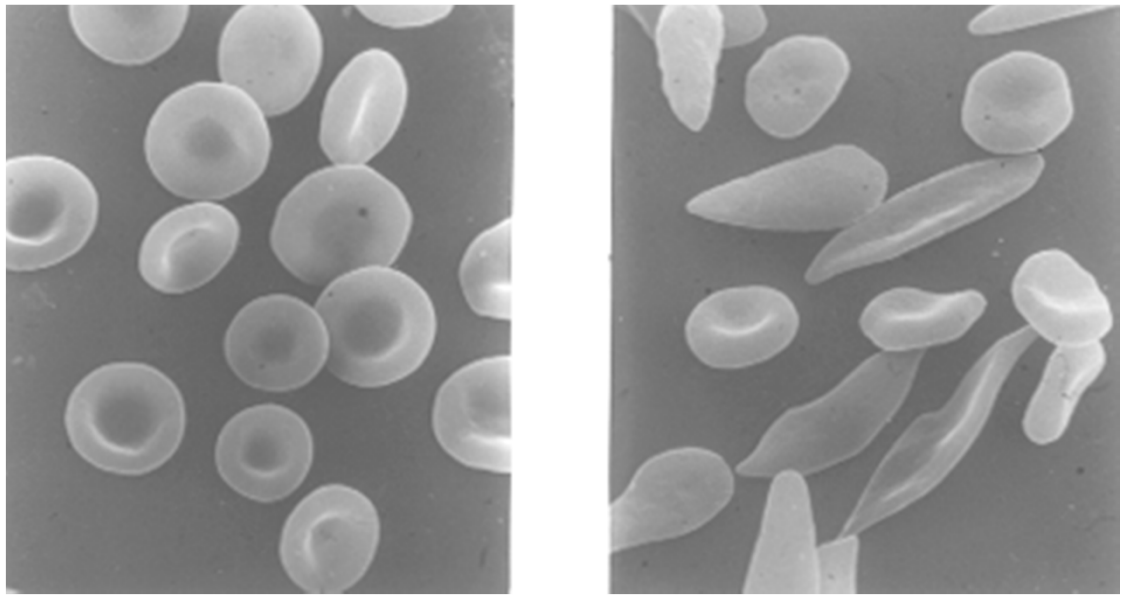
How it is formed?

- Sickle cell shape results in decrease cell deformability.
- Changes also occur in red cell membrane structure and function, disordered cell volume control and increase adherence to vascular endothelium.
- Vaso-occlusive phenomena and hemolysis are the clinical hallmarks of Sickle Cell Disease (SCD)

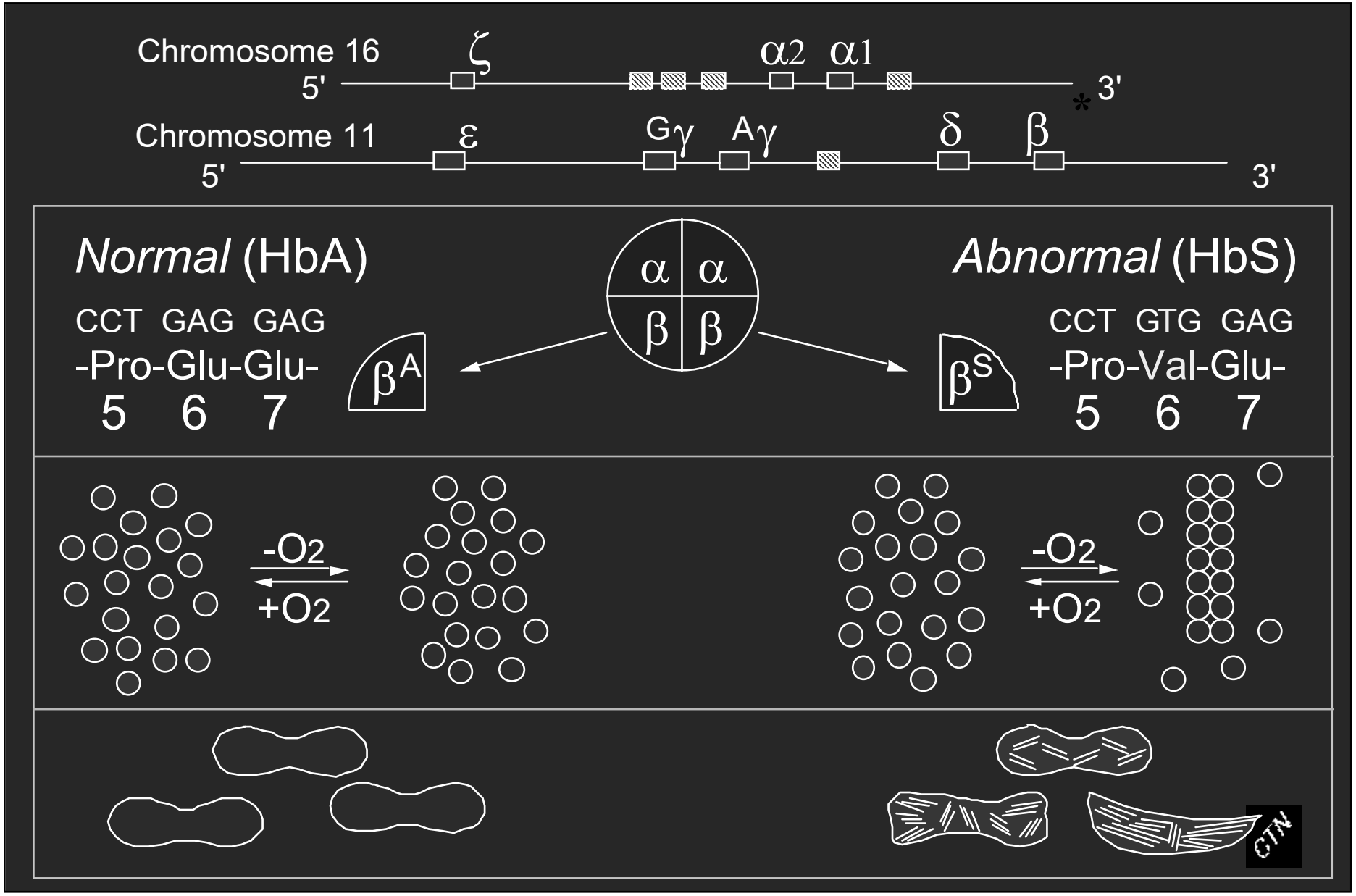
Red Blood Cells from Sickle Cell Anemia

- **Deoxygenation of SS erythrocytes leads to intracellular hemoglobin polymerization, loss of deformability and changes in cell morphology.**

OXY-STATE ⟷ **DEOXY-STATE**



Sickle Cell Mutation



Epidemiology

- About 5% of the world's population carries genes responsible for haemoglobinopathies.
- Each year about 300 000 infants are born with major haemoglobin disorders – including more than 200 000 cases of sickle-cell anaemia in Africa.

Epidemiology

- Globally, there are more carriers (i.e. healthy people who have inherited only one mutant gene from one parent) of thalassaemia than of sickle-cell anaemia, but the high frequency of the sickle-cell gene in certain areas leads to a high rate of affected newborns.

Epidemiology

- In broad terms, the prevalence of the sickle-cell trait (healthy carriers who have inherited the mutant gene from only one parent) ranges between 10% and 40% across equatorial Africa and decreases to between 1% and 2% on the north African coast and <1% in South Africa.

Epidemiology

- In west African countries such as Ghana and Nigeria, the frequency of the trait is 15% to 30% whereas in Uganda it shows marked tribal variations, reaching 45% among the Baamba tribe in the west of the country.

Epidemiology

- Frequencies of the carrier state determine the prevalence of sickle-cell anaemia at birth. For example, in Nigeria, by far the most populous country in the subregion, 24% of the population are carriers of the mutant gene and the prevalence of sickle-cell anaemia is about 20 per 1000 births. This means that in Nigeria alone, about 150 000 children are born annually with sickle-cell anaemia.

Manifestations

- Generally, no symptoms are seen in the 1st 6 moths of life due to circulating fetal hemoglobin
- Dactylitis (aka hand-foot syndrome)
  - Painful, symmetric swelling of hands and feet
  - Due to ischemic necrosis of small bones of hands and feet
  - ? Due to rapidly expanding bone marrow, choking of blood supply

Manifestations

- Acute pain episodes
  - Young children- extremities
  - Older patients- head, chest, abdomen, back
  - Recurrence of pain tends to occur in same sites within a particular individual
  - Exacerbated by fever, hypoxia, acidosis- promote deoxygenation of Hgb S

Manifestations

- Infarctions
  - Bone/bone marrow
    - Osteomyelitis- concern of salmonella infection
  - Autosplenectomy
    - Increased susceptibility to encapsulated organisms
      - Esp. pneumococcus & *H. influenzae*
      - Associated with reduction in serum opsonins
  - Pulmonary infarcts
    - Pneumonitis
    - Fat emboli

Manifestations

- Infarcts
  - Stroke
  - Kidney
    - Impaired renal function
    - Hyposthenuria
- Priapism
- Avascular necrosis

Manifestations

- Acute Chest Syndrome
  - Fever
  - Tachypnea
  - Chest pain
  - Hypoxia
  - Hypotension
  - X-ray findings

Manifestations

- Splenic seqestration
  - Large amounts of blood pools in spleen
    - Splenic enlargement
    - Criculatory collapse
  - Reason unknown
  - May follow febrile illness
- Aplastic episodes- may follow infection with parvovirus B 19

Manifestations

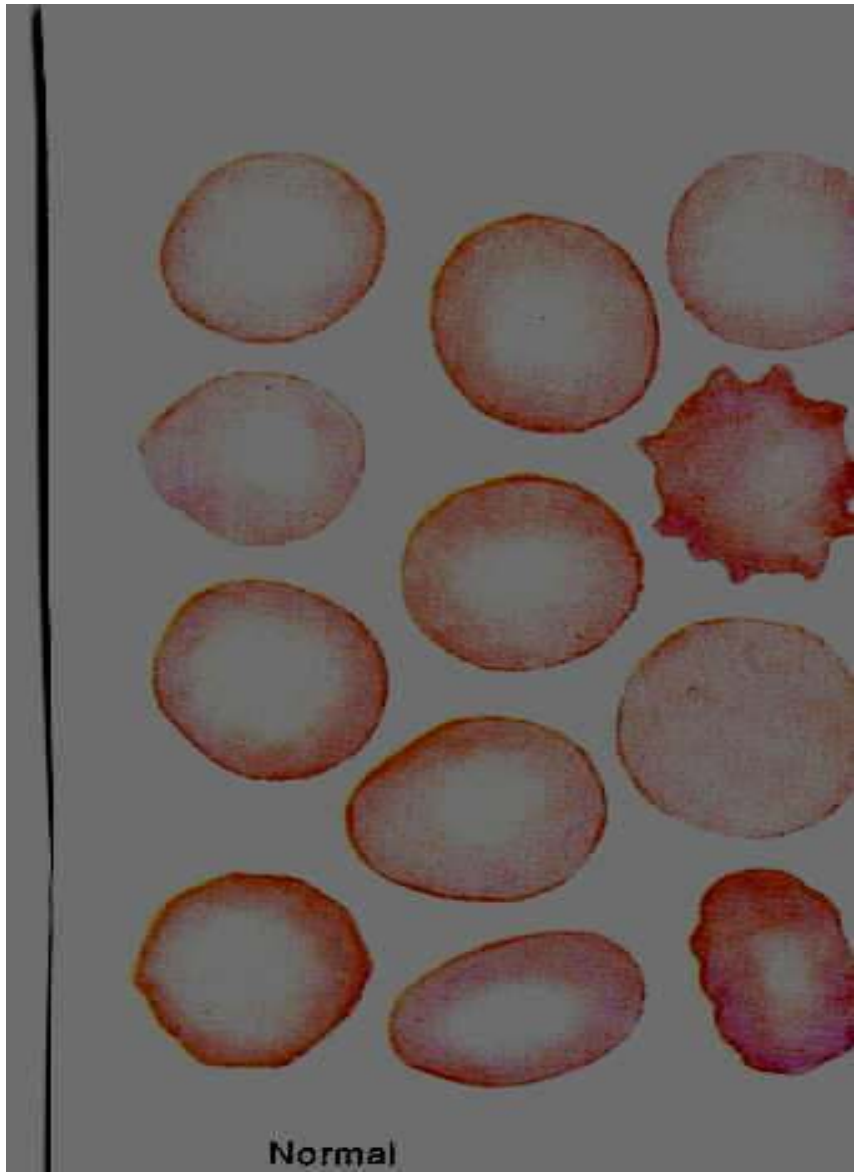
- Cardiomegaly
- Gallstones
- Body habitus
  - Underweight
  - Delayed puberty

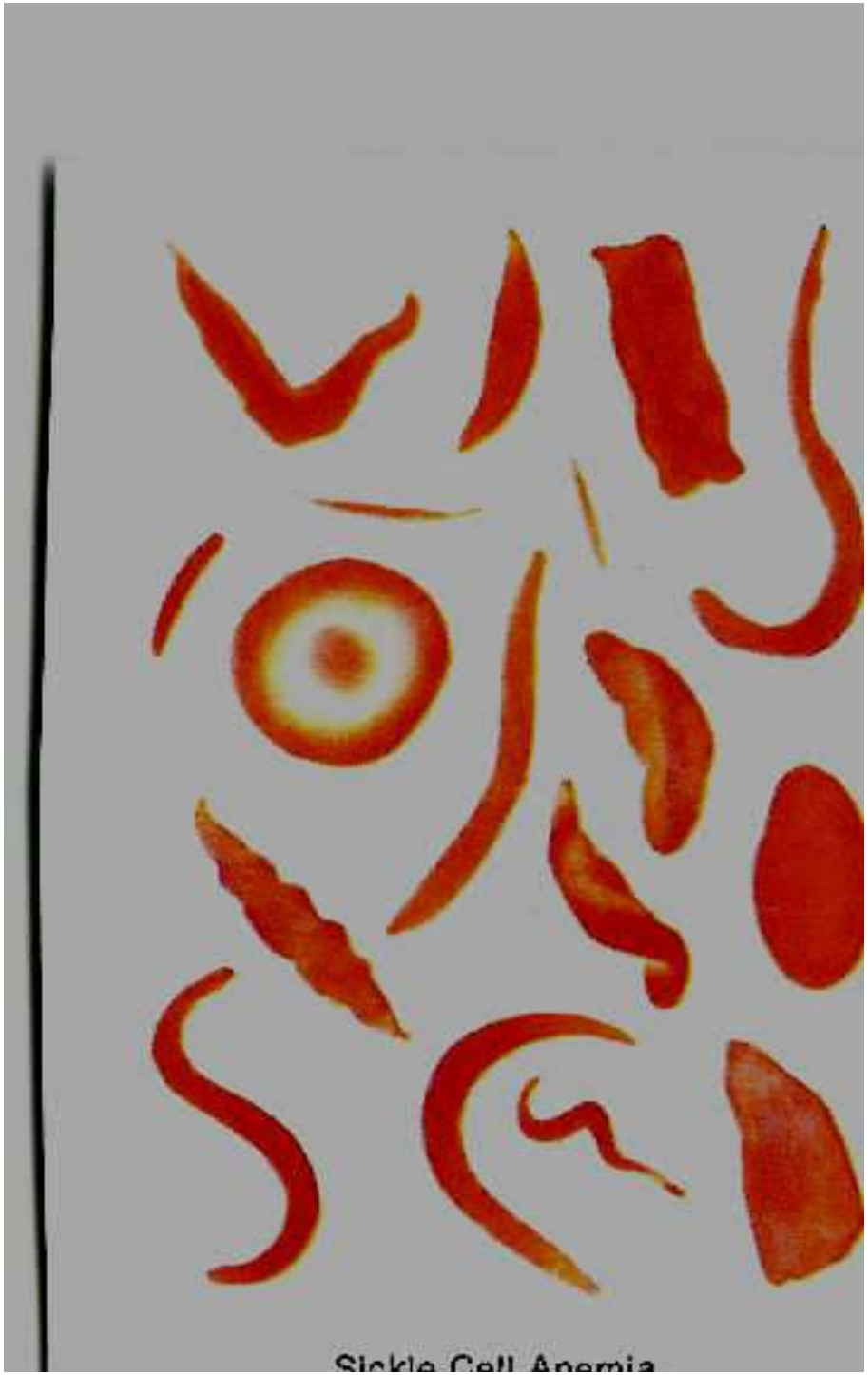
Manifestations

- Laboratory
  - Normocytic anemia- Hgb 5-9 mg/dL
  - Peripheral smear
    - Target cells
    - Poikilocytes
    - Sickled cells
    - Howell Jolly bodies
  - Leukocytosis with neutrophil predominance
  - Thrombocytosis
  - X-ray- expanded marrow spaces, osteoporosis

Laboratory findings

- Moderate anemia
- Reticulocytosis 3-15%
- High MCV
- Unconjugated hyperbilirubinemia
- Elevetaed LDH
- Low haptoglobin
- Folate & iron deficit
- Peripheral smear shows sickle cells
- Polychromasia
- Howell-jolly bodies
- Elevated WBC
- Elevated Platelets
- Low than after 18 yrs high creatinine


Normal


Sickle Cell Anemia

Impact of SCD on Society

- impact on human health may be assessed against the yardsticks of infant and under-five mortality. As not all deaths occur in the first year of life, the most valid measure is under-five deaths. An increasing proportion of affected children now survive past five years of age but remain at risk of premature death.

Impact of SCD

- When health impact is measured by under-five mortality, sickle-cell anaemia contributes the equivalent of 5% of underfive deaths on the African continent, more than 9% of such deaths in west Africa, and up to 16% of under-five deaths in individual west African countries.

Economic and Social impact

- In the United States of America median survival was estimated in 1994 to be 42 years for men and 48 years for women, whereas comparable figures for Jamaica published in 2001 suggested 53 years for men and 58.5 years for women. Data for sub saharan Africa not known

The future

- Gene therapy
- Increase expression of Hb F
- RNA repair
- Hematopoietic cell transplantation