Hematology

- Histology
- **Biochemistry**
- Pathology
- Pharmacology
- Physiology
- Microbiology
  - Handout
  - **Slide** 5b
  - Sheet

- Dr. name : Dr Nayef karadsheh
- lecture number :
- Done BY :

By: Anas Abu Shehab

Sickle Cell Anemia — sickle cell disease

- most common disorder caused by Hb variant
  homozygous recessive disorder
  1 in 500 newborn infants is affected

- Heterozygotes — sickle cell trait
  one of ten American black

- electrophoresis at alkaline pH

- $\alpha_2^A \beta_2^{6\,Glu \to Val}$

- Formation of aggregates + fibers

- Extent of sickling is increased by increasing proportion of deoxy HbS
  - decreased O_2 tension by high altitude or flying in non-pressurized plane
  - increased CO_2 conc.
  - decreased pH
  - increased 2,3-BPG

- selective advantage against malaria — parasite plasmodium falciparum

Hemoglobin C disease (HbC) $\alpha_2^A \beta_2^{6\,Glu \to Lys}$

HbCS disease — No sickling, HbC crystals, mild anemia

double Heterozygote

Characteristic Features of Sickle Cell Anemia

- Sickled cells lose water – becomes fragile → life span 17d instead of 120 → Anemia

- More serious – small blood capillaries in different organs become blocked by long abnormally shaped red cell → anoxia, causing pain → death of cells

- People with sickle cell trait live normal if they avoid vigorous excercise, high altitude, anaesthesia, air travel in unpressurised plane

- People with sickle cell trait have incred resistance to malaria, specifically plasmodium falciparum

Management

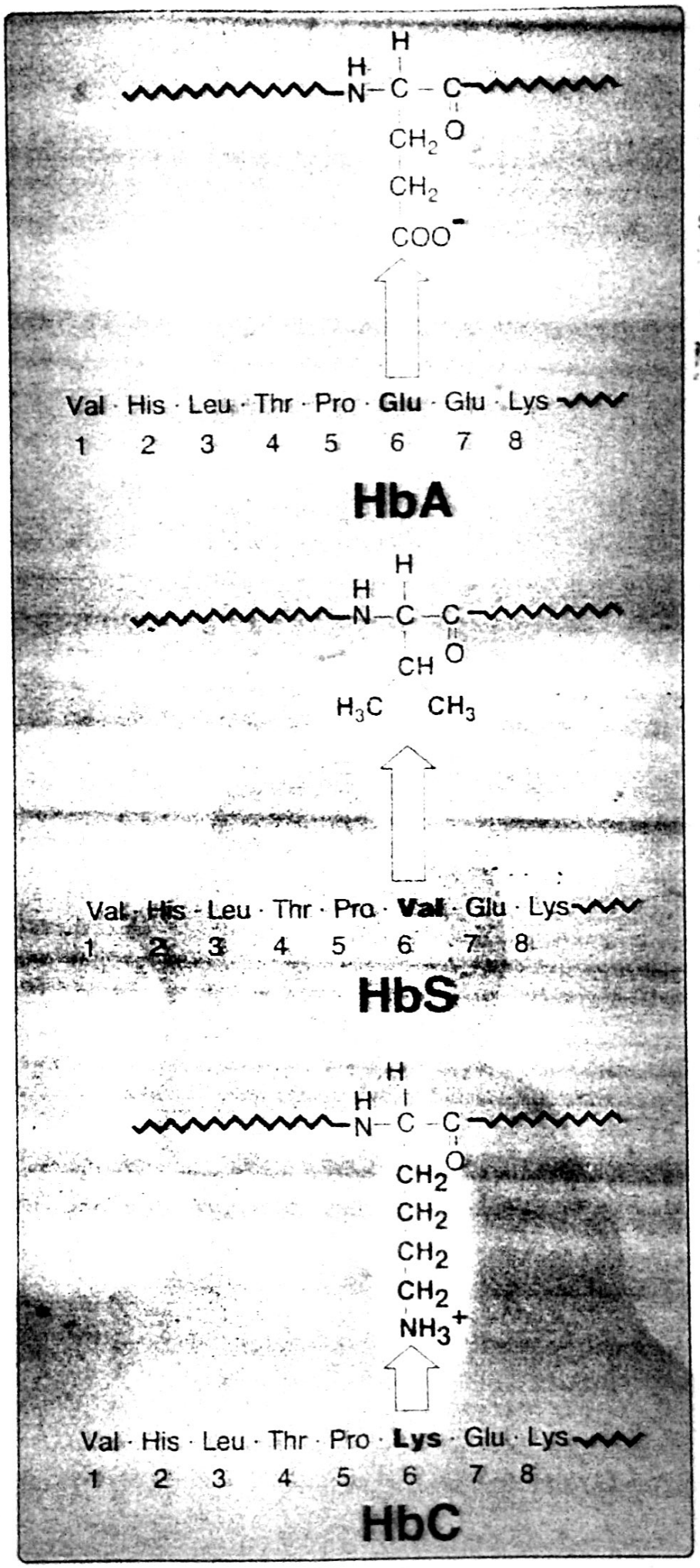
Hydration, analgesics, antibiotic, Intermittent transfusion.

Hydroxyurea → ↑ HbF

HbC : mild chronic anemia, no infarctive crisis, no sp. therapy required

Hb SC disease : double or compound heterozygote

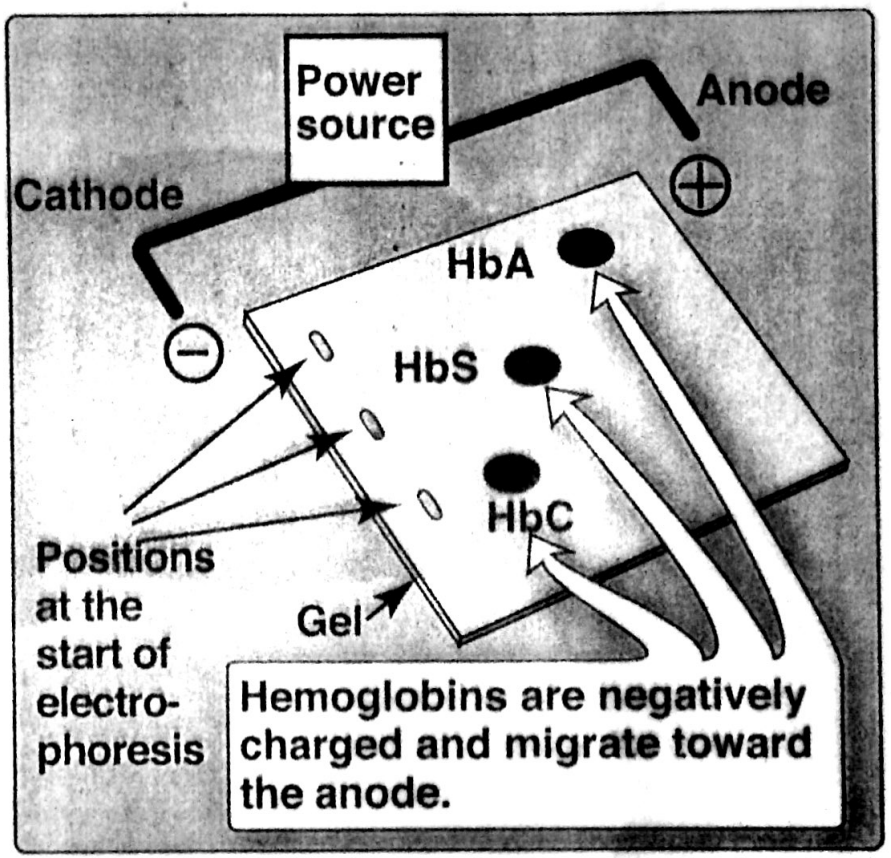
milder anemia than HbS, Painful crisis are less frequent



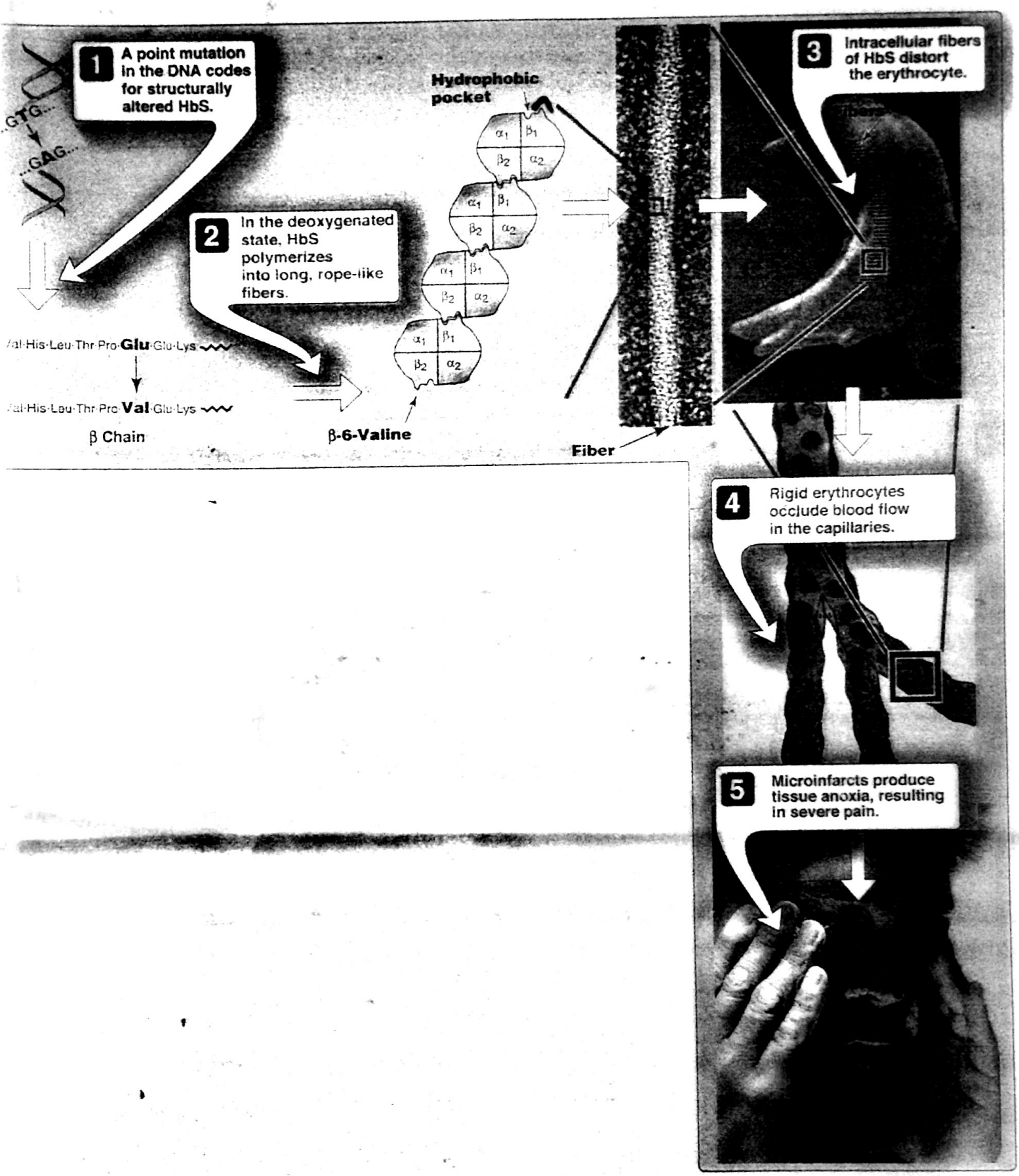
Copyright © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins

Amino acid substitution in HbS and HbC

Gel electrophoresis of Hemoglobins HbA, HbS, HbC



Copyright © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins


1 A point mutation in the DNA codes for structurally altered HbS.
GTG...
...GAG...
2 In the deoxygenated state, HbS polymerizes into long, rope-like fibers.
Val·His·Leu·Thr·Pro·Glu·Glu·Lys
Val·His·Leu·Thr·Pro·Val·Glu·Lys
β Chain
Hydrophobic pocket
α1 β1 β2 α2
β-6-Valine
Fiber
3 Intracellular fibers of HbS distort the erythrocyte.
4 Rigid erythrocytes occlude blood flow in the capillaries.
5 Microinfarcts produce tissue anoxia, resulting in severe pain.

Polymerization of Deoxy HbS

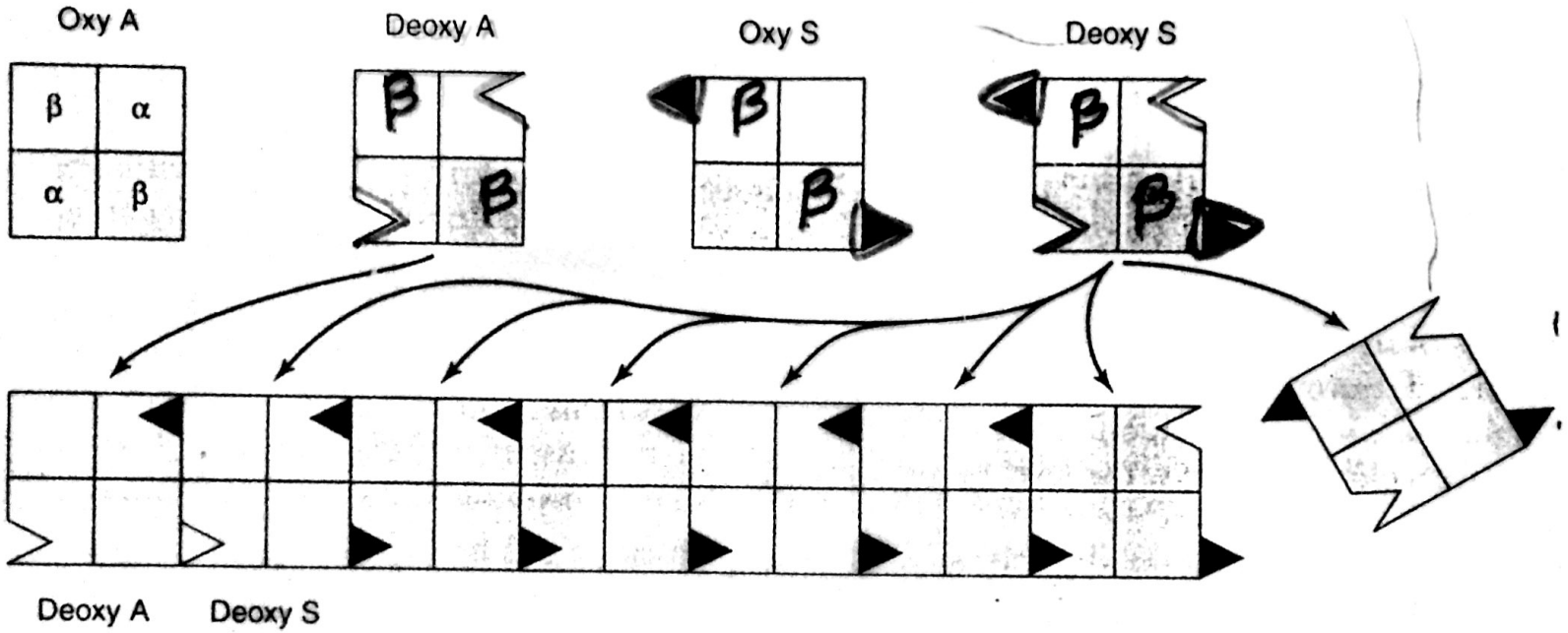
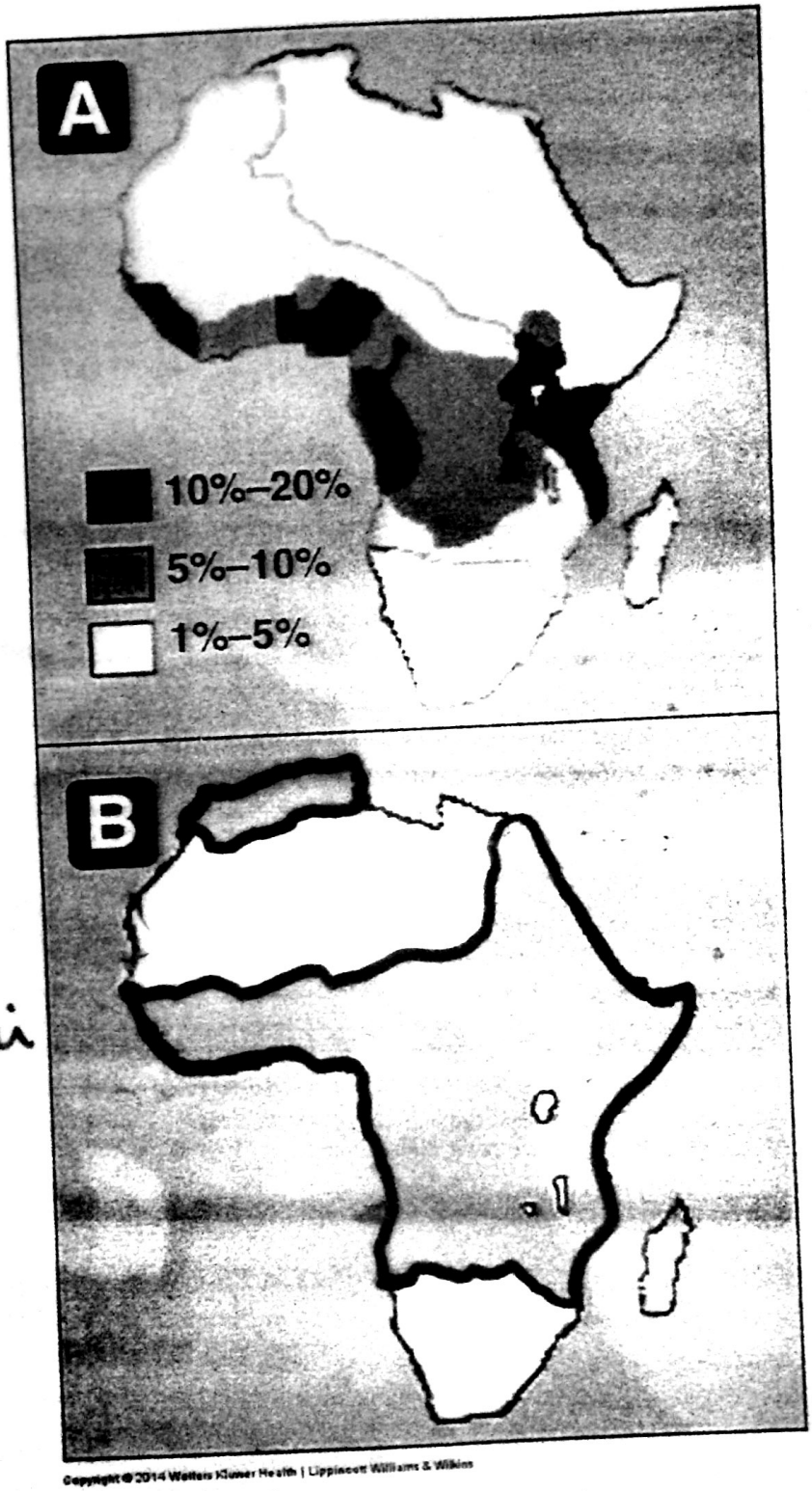


Figure 6–11. Representation of the sticky patch (▲) on hemoglobin S and its "receptor" (△) on deoxyhemoglobin A and deoxyhemoglobin S. The complementary surfaces allow deoxyhemoglobin S to polymerize into a fibrous structure, but the presence of deoxyhemoglobin A will terminate the polymerization by failing to provide sticky patches. (Modified and reproduced, with permission, from Stryer L: *Biochemistry*, 4th ed. Freeman, 1995. Copyright © 1995 W. H. Freeman and Company.)

Sickle Cell disease



Malaria in Africa

Copyright © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins