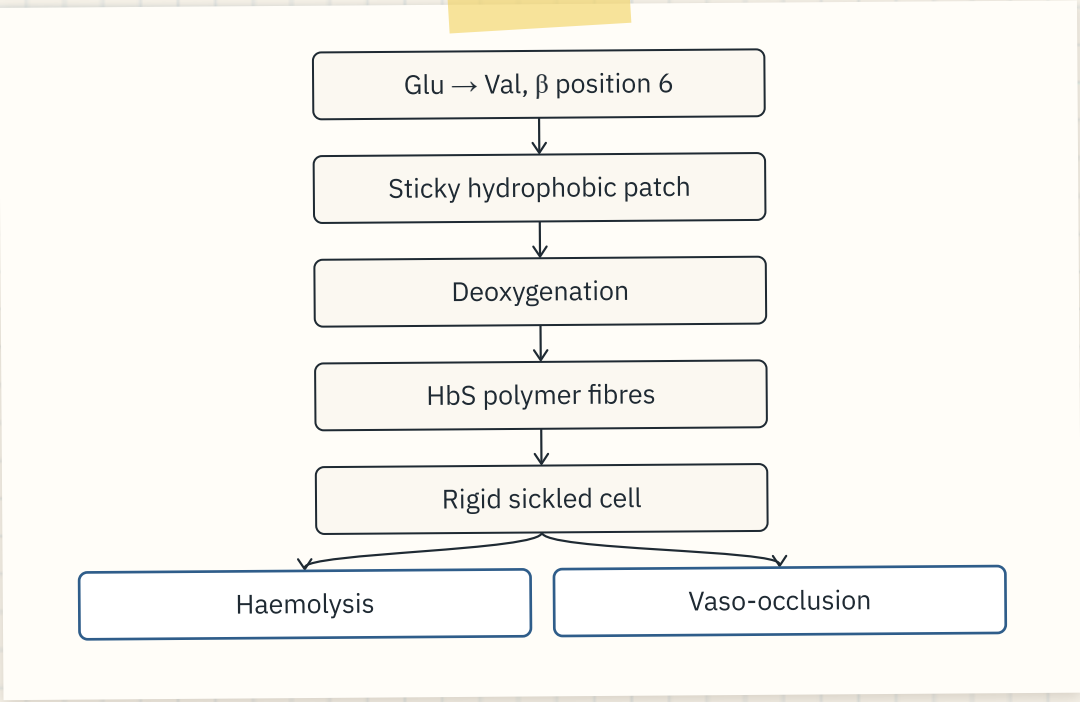
Sickle cell disease in one chain

From valine patch to haemolysis and blockage



Step by step

1. Glu → Val at β position 6 (GAG → GTG): sticky patch.
2. Deoxygenation: HbS polymerises into stiff fibres.
3. Cell sickles and stiffens; repeated cycles damage the membrane.
4. Haemolysis and vaso-occlusion follow; the spleen fails early.

Effect	Factors
More polymer	Hypoxia; acidosis; high CO_2; fever; more 2,3-BPG
More polymer	Higher HbS concentration; dehydration; ion-channel water loss
Less polymer	Fetal haemoglobin (raised by hydroxyurea)
Damage 1	Haemolysis: lifespan 120 days → 10–30 days
Damage 2	Vaso-occlusion: bone marrow infarcts, pain crises
Damage 3	Functional asplenia: encapsulated organisms

Promoters, protectors and the three kinds of damage

The chain

Valine patch → deoxygenation → polymer → rigid cell → haemolysis + blockage

Exam traps

- A newborn is protected because fetal haemoglobin has no β chains and blocks polymerisation; symptoms start as HbF falls.
- Dehydration raises HbS concentration and promotes sickling.
- Hydroxyurea helps by raising fetal haemoglobin.

Sickle cell disease pathophysiology: HbS to vaso-occlusion

Video, written lesson, practice question and sources: medservatory.com/usmle-step-1/haematology-oncology/sickle-cell-disease-pathophysiology

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