Sickle Cell Anemia (Mechanism)

Sickle cell anemia is a autosomal recessive hereditary blood disorder leading to abnormal and sickle-shaped red blood cells. These lead to many severe complications in patients. This disease is characterized as an intrinsic, normocytic hemolytic anemia, as the hemolysis seen with this disorder is due to an a defect in the RBCs themselves. It is caused by a point mutation in the β-chain of hemoglobin, replacing glutamic acid (hydrophilic) with valine (hydrophobic), leading to defective hemoglobin tetramers (HbS) being formed. These hemoglobin S which are formed have a tendency to sickle and deform in cases of low O₂ tension or dehydration. This repeated sickling decrease the cell's elasticity and cause cell rigidity, leading to small vessel occlusion and ischemia, and eventually hemolysis. Patients who are heterozygotes for HbS (meaning there is only one defective allele) are more resistant to malarial infection and show less severe symptoms if infected. Due to the presence of HbF (fetal hemoglobin), which does not include β-chains, but rather γ-chains, newborns are typically asymptomatic. Symptoms occur at 6-9 months of age as HbF production decreases and HbS is created as adult hemoglobin.



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Intrinsic Normocytic Hemolytic Anemia

N-Triscuits on Normal-sized-cells and Hemolysing-RBCs from Anemone

This disorder can be described as an intrinsic normocytic hemolytic anemia, meaning that this is a disease where blood cells are abnormally broken down and the defect is due to the red blood cell itself. In the case of sickle-cell disease, there is abnormal hemoglobin production, leading to abnormally shaped cells.

Point Mutation

Pointy Mutant

Sickle cell disorder is caused by a single point mutation in the β-globin chain of hemoglobin, causing glutamic acid to be replaced by valine. HbS (hemoglobin S) is formed from two normal α-chains binding with two mutant β-chains. Patients can be heterozygous (one abnormal allele of hemoglobin beta gene) or homozygous (more severe, because of both abnormal alleles).

Autosomal Recessive

Recessive-chocolate

Sickle-cell conditions have an autosomal recessive pattern of inheritance. The types of hemoglobin a person makes in the red blood cells depend on what hemoglobin genes are inherited from her or his parents. If one parent has sickle-cell anaemia (SS) and the other has sickle-cell trait then there is a 50% chance of a child having sickle-cell disease and a 50% chance of a child having sickle-cell trait. When both parents have sickle-cell trait a child has a 25% chance of sickle-cell disease, 25% will not carry any sickle cell alleles, and 50% will have the heterozygous condition.

African American

African American

8% of African Americans carry HbS trait (heterozygotes, who have 1 abnormal hemoglobin beta allele).

Dehydration or Decreased O2

Empty-canteen and Down-arrrow O₂-tank

In sickle-cell disease, low O₂ tension or dehydration leads to red blood cell sickling and repeated episodes of sickling damage the cell membrane and decrease the cell's elasticity. These cells cannot return to normal shape when normal O₂ tension is restored. Thus, these rigid blood cells are unable to deform as they pass through narrow capillaries, leading to vessel occlusion and ischaemia.

Newborns Asymptomatic

Baby with Thumbs-up

Due to the presence of HbF (fetal hemoglobin), which does not include β-chains, but rather γ-chains, newborns are typically asymptomatic. Symptoms occur at 6-9 months of age as HbF production decreases and HbS is created as adult hemoglobin.

Heterozygote Malarial Resistance

Hat-arrow-Z-Goat with Resistance-bandana and Malaria-mullet-mosquito

Patients who are heterozygotes for HbS, or those with sickle-cell trait, only have 1 abnormal β-hemoglobin allele. Thus, they produce both HbS and normal hemoglobin. Patients display more resistance to falciparum malarial infections and show less severe symptoms.

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