NEED TO KNOW #1
Hemoglobin and Red Blood Cell Abnormalities in Sickle-Cell Disease

Each year, about one in 625 African American children is born with sickle-cell disease. This disease is caused by a mutation in the gene that codes for **hemoglobin**, the protein that carries oxygen in red blood cells. The mutation changes the amino acid, glutamic acid into valine, which changes the shape of hemoglobin. When the oxygen supply in the blood is low, these abnormal hemoglobin molecules clump together. Normal hemoglobin molecules remain separate. Figure 1 shows normal hemoglobin on the left, and sickle hemoglobin on the right.

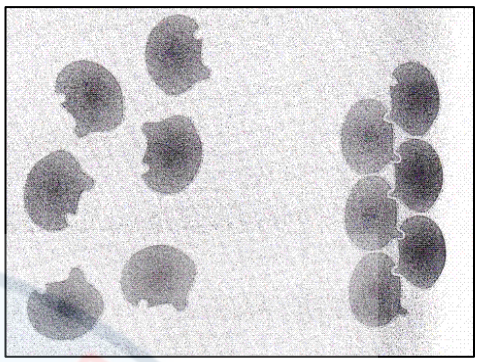

Figure 1

In a person with sickle-cell disease, the clumping of the hemoglobin molecules at low oxygen levels causes the red blood cells to become long and rigid like a *sickle* instead of remaining round and flexible (see Figure 2).

Figure 2

That change in cell shape causes a variety of problem in the body. For example, as cells become sickled, they block small blood vessels (Figure 3). This causes pain and damage to the areas that do not receive an adequate blood supply. The long-term effect of repeated blockages may permanently damage a person's organs, like the heart, kidneys, and brain. However, with good medical care, however, many people with sickle-cell disease can live reasonably normal lives.

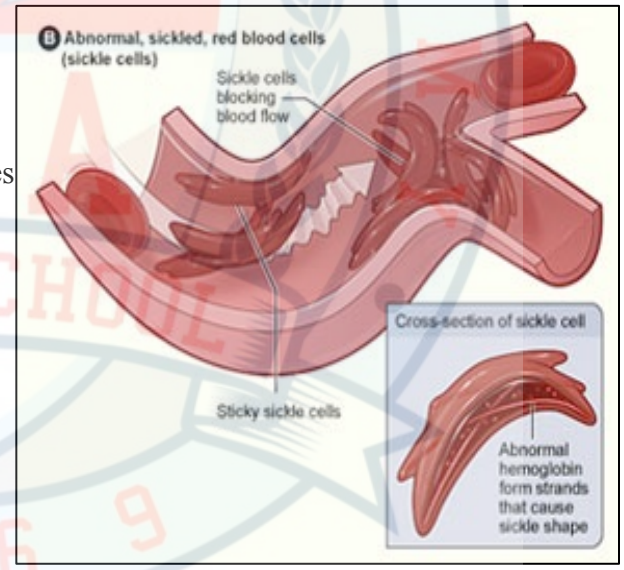


Figure 3

In a strange twist, it can actually be advantageous to have sickle cell disease. Individuals with sickle cell actually have immunity to malaria. Malaria is caused by a parasite that is transmitted to humans by mosquitos. When a person get bitten by a mosquito, the malaria parasite infects and destroys red blood cells, which can result in chills, fever, vomiting, and severe headaches. However, the parasite cannot infect individuals with sickle cell, or carriers of the sickle cell allele, so these individuals do not get sick from malaria.

NEED TO KNOW #2
Examining the DNA Sequence of Hemoglobin

Sickle-cell disease is associated with the genotype $Hb^sHb^s$. People who have this condition have two abnormal genes, one inherited from each parent. Individuals without sickle cell can have the genotypes $Hb^NHb^s$ or $Hb^NHb^N$

Below are the sections of the DNA sequences of a normal hemoglobin gene and the mutated gene that causes sickle cell disease.

Normal Gene DNA Sequence
...CAC GTG GAC TCA GGA GAA CTC...
Mutated Gene DNA Sequence
...CAC GTG GAC TCA GGA GTA CTC...

| First Letter | Second Letter | | | | Third Letter |
|---|---|---|---|---|---|
| | U | C | A | G | |
| U | phenylalanine | serine | tyrosine | cysteine | U |
| | phenylalanine | serine | tyrosine | cysteine | C |
| | leucine | serine | stop | stop | A |
| | leucine | serine | stop | tryptophan | G |
| C | leucine | proline | histidine | arginine | U |
| | leucine | proline | histidine | arginine | C |
| | leucine | proline | glutamine | arginine | A |
| | leucine | proline | glutamine | arginine | G |
| A | isoleucine | threonine | asparagine | serine | U |
| | isoleucine | threonine | asparagine | serine | C |
| | isoleucine | threonine | lysine | arginine | A |
| | (start) methionine | threonine | lysine | arginine | G |
| G | valine | alanine | aspartate | glycine | U |
| | valine | alanine | aspartate | glycine | C |
| | valine | alanine | glutamate | glycine | A |
| | valine | alanine | glutamate | glycine | G |