Why do we still have sickle cell trait?

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Abstract

Malaria is a potentially fatal disease that is especially common in Africa and tropical regions. Sickle cell trait is a genetic mutation in hemoglobin that is over-represented in parts of Africa, where malaria is endemic. Individuals who inherit two copies of the recessive sickle cell gene, i.e. individuals who are homozygous for the sickle cell gene, develop sickle cell disease. Individuals who are heterozygous, i.e. carry only one copy of the recessive sickle cell gene, are carriers and exhibit relative protection from the effects of malaria. This protection from malaria helps explain why the mutation is still present in the human population.

Malaria

Malaria is a disease caused by a parasite typically spread through infected mosquitos, although in rare cases it can also be spread through exposure to blood that is already infected with the malaria parasite. When the malaria parasites enter a person's body, they infect the liver and multiply. After the parasites mature, they start to infect red blood cells, at which point people start to show malaria symptoms. In the red blood cells, the parasites multiply, destroying the cell. Daughter parasites are released, which then enter other red blood cells and continues the cycle. (cdc.gov, 3/26/2021) . Recent research has found, that the malaria parasite also hijacks the cell's actin and uses it to transport adhesins to the cell surface, making the red blood cells sticky, which can lead to blockage in blood circulation and other malaria complications. (nature.com, 3/27/2021)

Malaria is typically found in warm and wet climates, since mosquitos and parasites survive best under these conditions. Although malaria in the U.S has been eliminated, other than imported cases, it still remains an issue in other parts of the world, such as sub-Saharan Africa and other parts of Africa, as well as south Asia, parts of east Asia, and parts of south America. In 2019, there was an estimated 229 million cases and 409,000 deaths from malaria worldwide. (cdc.gov, 3/26/2021)

Sickle Cell

Sickle cell disease is caused by one amino acid mutation in the beta chain of the hemoglobin protein. Red blood cells that have normal hemoglobin are usually round, smooth, and circulate unobstructed through blood vessels. People with sickle cell disease have the mutated gene and abnormal hemoglobin (hemoglobin S or HbS), which causes their red blood cells to be hard and c-shaped, or sickle shaped. The sickle cells' shape means that they don't circulate through blood vessels well, and can block blood flow, which can lead to complications such as strokes and pain episodes, as well as causing damage to organs such as the kidneys, spleen, and liver. The sickled red blood cells are also destroyed quickly, which causes anemia. People with sickle cell disease have a shorter life expectancy than the general population, with a national median life expectancy of 42-47 years. (hematology.org, 3/28/2021)

The gene for sickle cell is recessive gene, so in order for an individual to have sickle cell disease, they need to inherit two copies of the mutated gene. If an individual inherits only one copy of HbS (mutated hemoglobin) and one copy of HbA (normal hemoglobin) , they are carriers of the sickle cell trait. The sickle cell trait does demonstrate incomplete dominance, which means that people with the sickle cell trait will have both normal red blood cells and sickled red blood cells. Carriers of the sickle cell trait have slightly more hemoglobin A than hemoglobin S, which keeps their red blood cells functioning as normal.

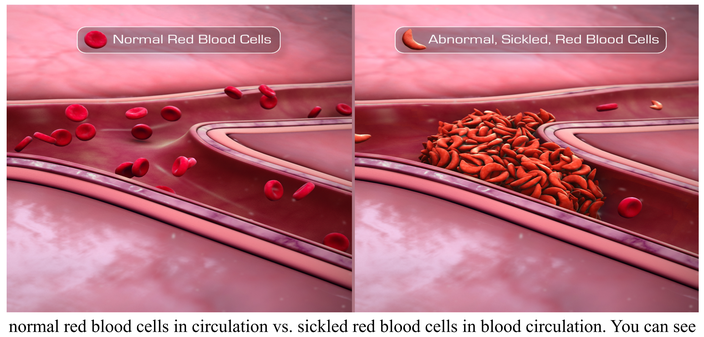
In 2010, over 305,000 babies were born with sickle cell disease, and more than 100 million people live with sickle cell trait worldwide. (hematology.org, 3/27/2021) (ncbi.nlm.nih.gov, 3/27/2021)

This shows the prescence of normal hemoglobin a inside a red blood cell. (Picture via stjude.org)

This shows the incomplete dominance of the sickle cell trait and how that results in red blood cells having both normal hemoglobin a as well as abnormal hemoglobin s in heterozygous people. (Picture via stjude.org)

How Sickle Cell Affects Malaria

By the rules of natural selection, the gene responsible for a deadly disease such as sickle cell anemia should have been removed from the population, yet we see that the gene is very prominent in certain populations. Recently, scientists found that people with the sickle cell trait, or carriers, have some protection against the fatality of malaria. People with sickle cell trait can still get infected with malaria, but after they are infected, the sickle cell mutation prevents the malaria parasite from causing damage. The sickle cell mutation also prevents the parasite from sending adhesins to the cell's surface, making the cell less sticky and therefore preventing malaria-related complications. (ncbi.nih.gov, 3/27/2021) However, people who are homozygous and have sickle cell disease do not have this protection. (malariajournal.biomedcentral.com, 3/28/2021)



normal red blood cells in circulation vs. sickled red blood cells in blood circulation. You can see the blockage that can happen with sickled cells on the right. (Picture via scientificanimations.com)

The relationship between the frequency of the sickle cell allele in the population and malaria transmission. Where there is intense malaria transmission, the sickle cell allele is in the population because of the heterozygous protection against malaria. (Picture via schoolbag.info)

Why is this important?

These observations explain why the gene still remains in the human population. Since the gene provides protection against a potentially fatal disease, individuals who have the trait tend to survive in regions where malaria is endemic. These individuals have a higher chance of passing on the gene to their offspring, leading to a higher frequency of the gene in these populations. (evolution.berkeley.edu,)

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