Sickle Cell Anemia

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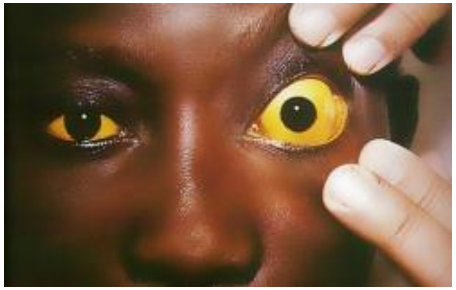
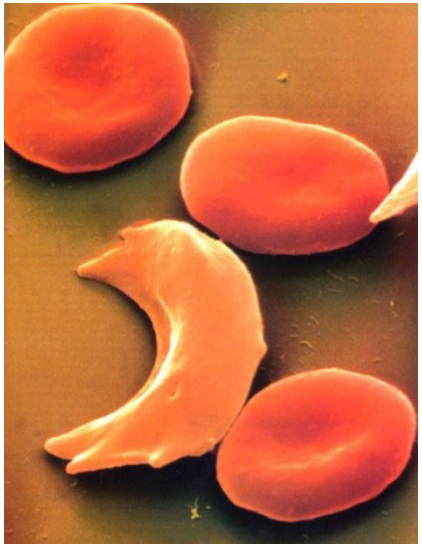
Period 6



Physiology



- 1 in every 270,000 Americans and 1 in every 400 African Americans are born with sickle cell anemia.
- Sickle cell anemia is present at birth, but cannot be determined until a child is four months of age. This is due to infants being born with fetal hemoglobin, as sickle cell anemia is a disease that targets the adult hemoglobin.
- The main symptom of sickle cell anemia is the sickled shape of the red blood cells.
- Other sickle cell symptoms include:

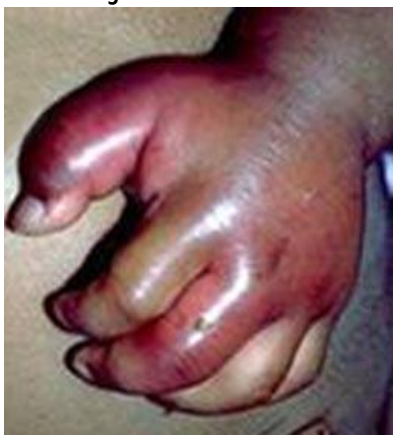
  -Anemia: Sickle cell patients have sickled shape red blood cells in place of normal red blood cells. Sickle cells are fragile, as they break apart easily and die, causing shortages of red blood cells. Red blood cells usually live for 120 days while sickle cells die after only 10-20 days.

  -Crises: Crises are periodic episodes of pain which develops when sickle shaped red blood cells block blood flow through tiny blood vessels in your chest, abdomen and joints.

  -Swollen hands and feet may appear in babies due to sickle cells blocking blood flow.

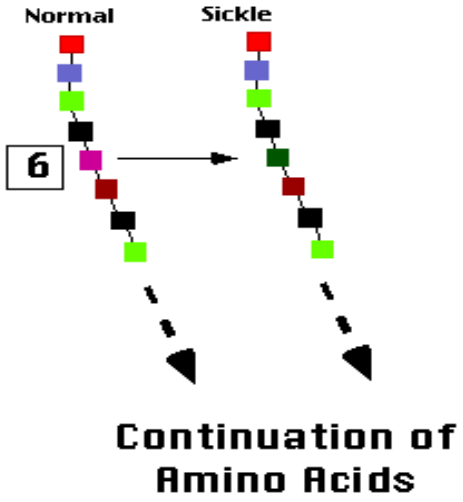
  -Sickle cell patients tend to have delayed puberty and slow growth due to shortage of healthy red blood cells providing the body with oxygen and nutrients.

  -Vision problems may also occur due to tiny blood vessels in your eye being blocked by sickle shaped red blood cells.

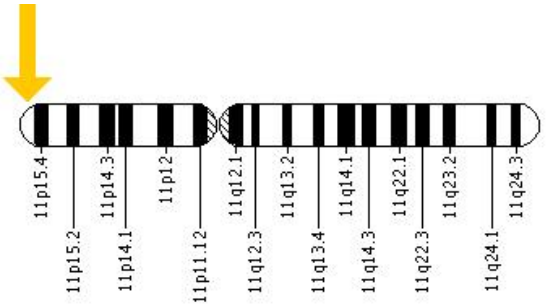


- When sickle cell anemia becomes more severe, jaundice, the yellowing of eyes and skins, and failure of the spleen may occur.

Molecular Causes



- Autosomal recessive disease.
- Beta globin (HBB) is the protein that makes up the form of hemoglobin in adult humans. The normal adult hemoglobin tetramer (protein with four subunits) consists of 2 alpha chains and 2 beta chains.
- Sickle cell anemia is caused by a point mutation of HBB in chromosome 11, 11p15.5.
- The beta subunit has the amino acid valine at position 6 instead of the glutamic acid that is normally present.



- A mutated beta globin produces HbS, or sickle cell hemoglobin, instead of HbA, adult hemoglobin. HbS, in turn, produces sickle shaped red blood cells.
- An individual can only inherit sickle cell anemia if s/he receives both alleles for sickle cell from his/her parents.
- If only one of the alleles is the sickle gene and the other is normal, the person is a carrier for sickle cell disease, called sickle cell trait. People with sickle cell trait do not have the normal symptoms of a sickle cell anemia patient. People with sickle cell trait gain resistance to malaria.

Current Treatments/Therapies

- As of today, bone marrow/stem cell transplant is the only known cure to sickle cell anemia. This process involves replacing bone marrow affected by sickle cell anemia with healthy bone marrow from a donor. However, most patients are unable to find a well-matched donor and there are risks, such as death, associated with it.
- Patients can have blood transfusions to regulate their blood level and prevent strokes as treatment for sickle cell crises (painful episodes). Patients also take Hydroxyurea, a medicine that may reduce the number of painful episodes in some people.
- Sickle cell patients also have to take antibiotics to prevent bacterial infections and receive vaccinations for infections that result from sickle cell anemia. One example is the Haemophilus influenza (does not cause influenza, mostly lifelong disabilities).
- Patients also take Decitabine, which prompts the body to make fetal hemoglobin.
- Scientists are figured out that BCL11A is a prime factor in the switching of fetal hemoglobin to adult hemoglobin and are attempting to develop a cure by silencing it.

Proposal Cure/Limits

- Fetal hemoglobin in the main oxygen transport protein in a newborn baby until it is roughly 4 months old. It is able to bind oxygen with greater affinity than adult hemoglobin.
- BCL11A is one of the primary factors involved in turning off fetal hemoglobin production. Scientists have tried silencing BCL11A in mice and have succeeded.
- My proposal will attempt to find a way to silence BCL11A in humans.
- My proposal is using siRNA (small interfering RNA or silencing RNA) to silence BCL11A. siRNA is noted to interfere with the expression of specific genes.
- Not too much is known about the BCL11A protein, so there might be side effects in humans when silencing it.
- Sickle cell anemia has an early onset, allowing only early interventions.

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