SICKLE CELL ANEMIA

INSET A CLEVER SUBTITLE HERE

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Physiology

- Prevalent amongst African populations (Around 2% of population have the disease and 30% have the trait) mainly because it conveys resistance to malaria
- Targets the circulatory system
- Early onset (from around 4 months old) with complete penetrance
- Symptoms include: anemia, periods of pains (crises), frequent infections, delayed growth, vision problems, and the hand-foot syndrome.
- Many complications arise because the body needs blood cells to supply oxygen.
  Complications include: Acute chest syndrome, Pulmonary hypertension, strokes, and anemia.

Fig. 1

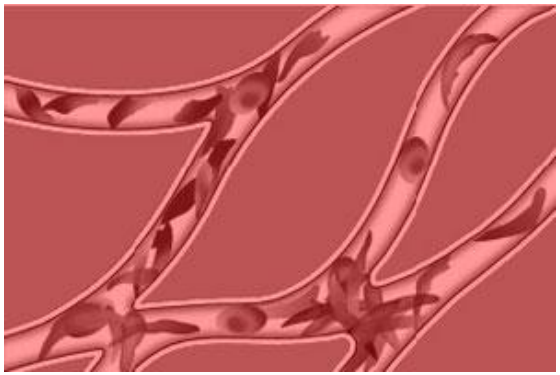
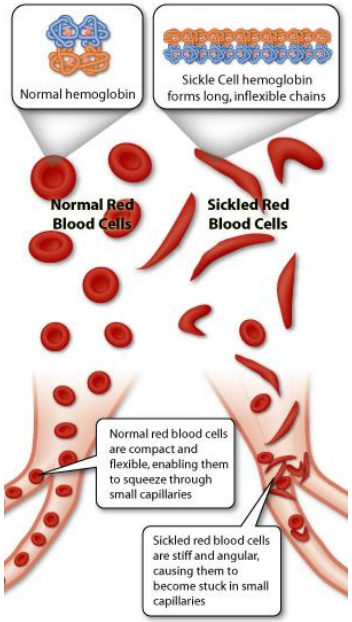
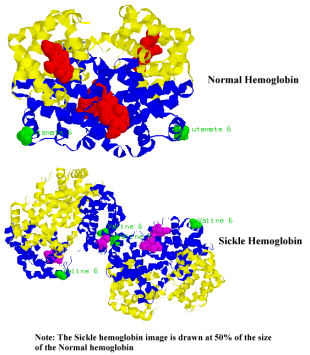


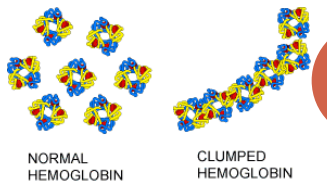
Fig. 2

Molecular Cause

- Also known as the Val6Glu mutation
- Autosomal recessive
- Mutation occurs in region 15.5 on the short (p) arm of chromosome 11
- The gene for ß globin, a subunit of hemoglobin
- The substitution of amino acid of valine for glutamic acid at amino acid 6 changes the protein structure of the ß subunit.
- This causes polymers of the deoxygenated hemoglobin to stiffen and stiffen and distort the cell, forming the “sickled” shape
- Oxygenation restores the shape of the red blood cell, repeated polymerization and depolymerization damage the hemoglobin, which irreversibly sickles the cell
- The production of blood cells in the bone marrow is unable to keep up with the destruction of sickle cells and results in a condition called anemia where the body does not have enough healthy blood cells.
- Sickle cells tend to get stuck in small blood vessels, depriving tissues and organs of oxygen and causing long term damage.







Treatments/Risks and Limits

Cure:

- Currently, bone marrow transplants is the only cure available, but is VERY risky. Only offered to the most severe of cases.

Treatments:

- Antibiotics and vaccinations to fight deadly infections at early age
- Pain-relieving medications to relieve pain from a sickle cell crisis
- **Hydroxyurea** temporarily stimulates fetal hemoglobin production and alleviates the symptoms.
- Patient can receive blood transfusions relieve anemia. Need **Deferasirox** to reduce iron levels in blood that result from transfusions.

Experimental Treatments:

- Researchers are looking for alternate sources of stem cells to make bone marrow transplants less risky.
- Also, gene therapy is currently being researched. Researchers are looking for a way to either insert a normal hemoglobin gene in, or turn off the gene responsible for the production of the ß globin.
- **Nitric Oxide** administration is currently being researched

Proposed Cure/Limits

- I propose a knockout of gene responsible for the repression of the expression of the HbF (fetal hemoglobin) gene
- Fetal hemoglobin is the main oxygen transport unit of fetuses in the last seven months of development and newborns in the first six months. After six months, the fetal hemoglobin is replaced with adult hemoglobin, the hemoglobin that we are familiar with.
- Fetal hemoglobin is composed of 2α and 2γ subunits, so any mutation in the ß subunit does not affect the fetal hemoglobin.
- Fetal hemoglobin has a better oxygen binding affinity than adult hemoglobin
- Currently, there are drugs that reactivate the production of fetal hemoglobin temporarily, but they have side effects and need to be administered daily.

Proposed Cure/Limits (Cont.)

- A transcription factor is engineered so it targets the gene responsible for the repression of the expression of HbF production gene.
- Then, the transcription factors are inserted into retroviral plasmids. Next, infectious recombinant viruses are transected with the retroviral plasmids.
- The patient is infected with the virus, preferably through the blood stream.
- Bone marrow contain numerous blood vessels and capillaries. Therefore, it should be possible for the viruses to infect the bone marrow cells, making it produce fetal hemoglobin.

Limits:

- The infectious recombinant virus can invoke an unwanted immune system reaction causing the body to attack the viruses and reject it, causing inflammation, or even organ failure.
- The infectious recombinant viruses can target the wrong cells, damaging other cells along the way causing disease or cancer.
- The virus can recover its original function once inside the body and infect the patient with another disease.
- If something went wrong with the transcription factor and if it targeted another gene, a tumor might be formed

References

Physiology

Content:

http://www.mayoclinic.com/health/sickle-cell-anemia/DS00324/DSECTION=symptoms

Images:

http://www.nwsicklecell.org/images/photos/about-trait.jpg

Molecular Cause

Images:

http://learn.genetics.utah.edu/content/disorders/whataregd/sicklecell/images/sicklecell.jpg

http://www.medindia.net/patients/patientinfo/images/sickle-cell-anemia-about.jpg

http://carnegiescience.edu/first_light_case/horn/lessons/images/hemoglobins.GIF

http://evolution.berkeley.edu/evolibrary/images/evo/hemoglobin.gif

Proposed Cure/Limits

Content:

http://www.sciencedaily.com/articles/b/bone_marrow.htm

Most of the content:

**Refer back to my works cited of my final paper