CONTENTS

AIM

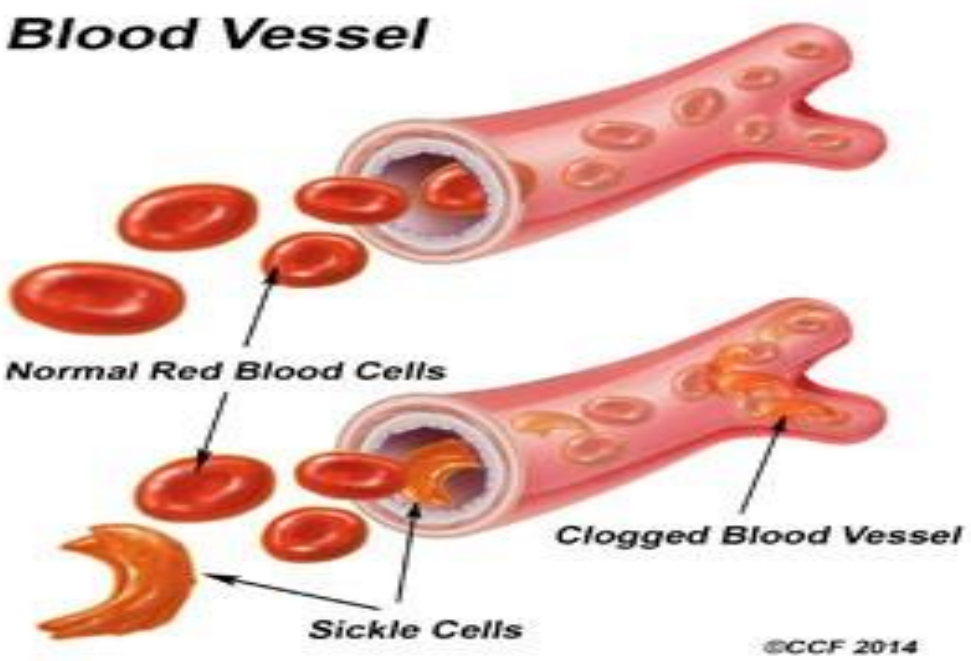
To study the signs, symptoms, genetic behavior and the evolution of the disease Sickle Cell Anaemia or SSA with special attention on bone marrow transplantation for its cure.

WHAT IS SICKLE CELL ANAEMIA? A SMALL OVERVIEW

In general, Sickle Cell Anaemia is a genetic disorder which causes the Red Blood Corpuscles in the body to lose the disc shape and break down much before than the usual life span of the RBCs that is 120 days. All these cells break quite early. In 30-40 days, is what doctors say. The sickled-cells take up the shape of a sickle(a tool used to cut small plants) and therefore called Sickle cell Anaemia.

The sickle-shaped cells stick to vessel walls , causing a blockage that slows or stops the flow of blood. As a result of this, oxygen can't reach nearby tissues. The lack of oxygen can cause attacks of sudden, very severe pain and unbearable pain, referred to as a Sickle Cell Crisis.

The abnormal hemoglobin causes distorted (sickled appearing under a microscope) red blood cells. The sickled red blood cells are fragile and prone to rupture. When the number of red blood cells decreases from rupture (hemolysis), anemia is the result. This condition is referred to as sickle cell anemia. The irregular sickled cells can also block blood vessels causing tissue and organ damage and pain.


Blood Vessel
Normal Red Blood Cells
Clogged Blood Vessel
Sickle Cells
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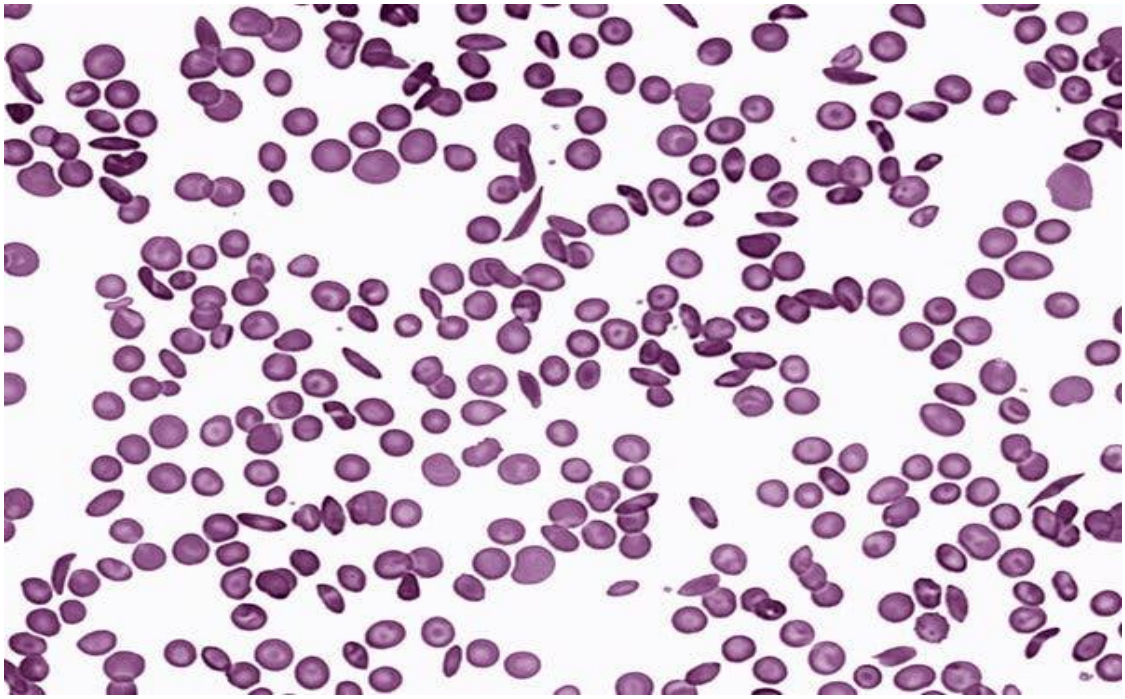


A BRIEF HISTORY OF THE DISCOVERY OF SICKLE CELL ANAEMIA

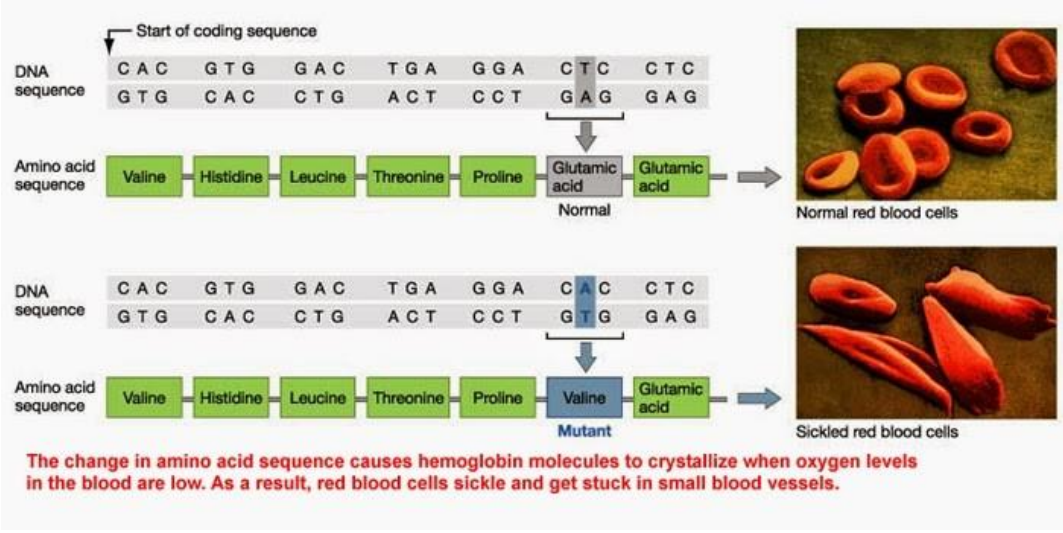
In the annals of medical history, 1910 is regarded as the date of the discovery of sickle cell disease, making 2010 the 100th anniversary of that discovery, but just what does it mean to say the disease was "discovered"? The disorder we call "Sickle Cell Disease" often abbreviated as SCD, had been present in Africa for at least five thousand years and has been known by many names in many tribal languages. What we call its "discovery" in 1910 occurred, not in Africa, but in the United States. A young man named Walter Clement Noel from the island of Grenada, a dental student studying in Chicago, went to Dr. James B. Herrick with complaints of pain episodes, and symptoms of anemia. Herrick was a cardiologist and not too interested in Noel's case so he assigned a resident, Dr. Ernest Irons to the case. Irons examined Noel's blood under the microscope and saw red blood cells he described as "having the shape of a sickle". When Herrick saw this in the chart, he became interested because he saw that this might be a new, unknown, disease. He subsequently published a paper in one of the medical journals in which he used the term "sickle shaped cells".

SICKLE CELL ANAEMIA AS A GENETIC DISORDER

This is an autosome linked recessive trait that can be transmitted from parents to the offspring when both the partners are carrier for the gene (or heterozygous).The disease is controlled by a single pair of allele, Hb(a) and Hb(s). Out of the three possible genotypes, only homozygous individuals for Hb(s){HbsHbs} show the diseased phenotype. Heterozygous [Hb(a)Hb(s)] individuals appear apparently unaffected but they are carrier of the disease as there is 50 per cent probability of transmission of the mutant gene to the progeny, thus exhibiting sickle-cell trait.

This defect is caused by the substitution of Glutamic acid(Glu) by Valine(Val) at the sixth position of the beta globin chain of the haemoglobin molecule. The substitution of amino acid in the globin protein results due to the single base substitution at the sixth codon of the beta globin gene fro m GAG to GUG. The mutant haemoglobin molecule undergoes polymerisation under low oxygen tension causing the change in the shape of the RBC from biconcave disc to elongated sickle like structure.

Courtesy- NCERT textbook



SYMPTOMS OF SSA

Signs and symptoms of sickle cell anemia, which vary from person to person and change over time, include:

•Anemia: Sickle cells break apart easily and die, leaving you without enough red blood cells. Red blood cells usually live for about 120 days before they need to be replaced. But sickle cells usually die in 10 to 20 days, leaving a shortage of red blood cells (anemia).

Without enough red blood cells, your body can't get the oxygen it needs to feel energized, causing fatigue.

•Episodes of pain: Periodic episodes of pain, called crises, are a major symptom of sickle cell anemia. Pain develops when sickle-shaped red blood cells block blood flow through tiny blood vessels to your chest, abdomen and joints. Pain can also occur in your bones.

The pain varies in intensity and can last for a few hours to a few weeks. Some people have only a few pain episodes. Others have a dozen or more crises a year. If a crisis is severe enough, you might need to be hospitalized.

Some adolescents and adults with sickle cell anemia also have chronic pain, which can result from bone and joint damage, ulcers and other causes.

•Painful swelling of hands and feet. The swelling is caused by sickle-shaped red blood cells blocking blood flow to the hands and feet.

•Frequent infections. Sickle cells can damage an organ that fights

infection (spleen), leaving you more vulnerable to infections. Doctors commonly give infants and children with sickle cell anemia vaccinations and antibiotics to prevent potentially life-threatening infections, such as pneumonia.

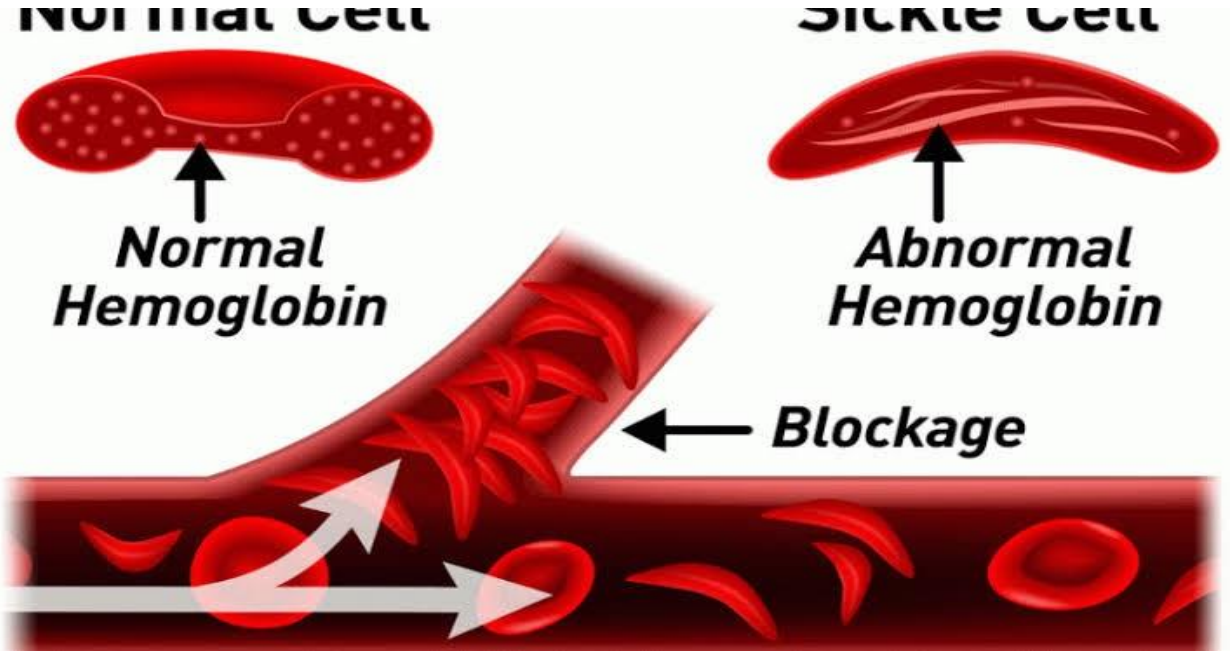
•Delayed growth: Red blood cells provide your body with the oxygen and nutrients you need for growth. A shortage of healthy red blood cells can slow growth in infants and children and delay puberty in teenagers.

•Vision problems:Tiny blood vessels that supply your eyes may become plugged with sickle cells. This can damage the retina — the portion of the eye that processes visual images, leading to vision problems.

WHAT CONDITIONS PROMOTE DISTORTION OF RED BLOOD CELLS?

Sickling of the red blood cells in patients with sickle cell anemia results in cells of abnormal shape and diminished flexibility. The sickling is promoted by conditions associated with low oxygen levels, increased acidity, or low volume (dehydration) of the blood. These conditions can occur because of injury to the body's tissues, dehydration, or anesthesia.

Certain organs are predisposed to lower oxygen levels or acidity, such as when blood moves slowly through the spleen, liver, or kidney. In addition, organs with particularly high metabolism rates (such as the brain, muscles, and the placenta in a pregnant woman with sickle cell anemia) promote sickling by extracting more oxygen from the blood. These conditions make these organs susceptible to injury from sickle cell anemia.



IS THERE A DIFFERENCE BETWEEN SICKLE CELL ANAEMIA AND SICKLE CELL TRAIT?

Yes. A person can have a mixture of normal and faulty haemoglobin in their red blood cells without having sickle cell disease. This condition is called "sickle cell trait." People with sickle cell trait have enough normal haemoglobin in their red blood cells to prevent the cells from sickling. One in 12 African-Americans in the United States has sickle cell trait.
It's important to remember that people with sickle cell trait do not have sickle cell disease. They also usually do not develop sickle cell disease, except in unusual circumstances. However, people with sickle cell trait can genetically pass the trait to their children. If two people with sickle cell trait have children together, there is a 1 in 4 chance that their children will have sickle cell anaemia.

What are the chances that your child will be born with sickle cell anaemia or sickle cell trait?

If you and your partner both have sickle cell trait, your child has a 25% chance of being born with sickle cell anaemia. If only one of you has sickle cell trait, your child cannot be born with sickle cell anaemia, but there is a 50% chance that your child will be born with sickle cell trait.
If one parent has sickle cell disease and one parent has sickle cell trait, there is a 50% chance that their children will be born with sickle cell disease.

How does a person get sickle cell anaemia?

People with sickle cell anaemia inherit the disease, which means that the disease is passed on to them by their parents as part of their genetic makeup. Parents cannot give sickle cell anaemia to

their children unless they both have the faulty haemoglobin in their red blood cells.

HOW IS SICKLE CELL CRISIS TREATED?

A sickle crises condition is a period when the sickled-cells block the flow of blood and stick to the vessel walls, hence causing unbearable pain in different intensities. A few times, the pain only lasts for a few hours and subsides on its own. But many a time, the intensity of the pain increases gradually and a medical admission is the only thing which can help. At the hospital, all they do is give enough fluids. And at a regular basis, keep injecting pain killers and antibiotics. The Hgb is also looked after because the haemoglobin percentage drops at a very high rate during a crises .So, a couple of patients require blood transfusions too. Other than these, the patient is asked to be cautious with the food and maintain a healthy diet during the stay in the hospital and later. Fatigue is a common symptom in persons with sickle cell anemia. Sickle cell anemia causes a chronic form of anemia, which can lead to fatigue. The sickled red blood cells are prone to breakage (hemolysis) which causes reduced red blood cell life span (the normal life span of a red blood cell is 120 days). These sickled red blood cells are easily detected with a microscope examination of a smear of blood on a glass slide.

Typically, the site of red blood cell production (bone marrow) works overtime to produce these cells rapidly, attempting to compensate for their destruction in the circulation. Occasionally, the bone marrow suddenly stops producing the red blood cells, which causes a very severe form of anemia (aplastic crises). Aplastic crises can be promoted by infections that otherwise would seem less significant, including viruses of the stomach and bowels and the flu (influenza).

Sickle cell anemia tends to stabilize without specific treatments. The degree of anemia is defined by measurement of the blood hemoglobin level. Hemoglobin is the protein molecule in red blood cells that carries oxygen from the lungs to the body's tissues and

returns carbon dioxide from the tissues to the lungs. Blood hemoglobin levels in persons with sickle cell anemia are generally between 6 to 8 gms/dl (normal levels are above 11 gms/dl). Occasionally, there can be a severe drop in hemoglobin requiring a blood transfusion to correct the anemia (such as in patients suffering splenic sequestration). Blood transfusion is usually reserved for those patients with other complications, including pneumonia, lung infarction, stroke, severe leg ulceration, or late pregnancy. (Among the risks of blood transfusion are hepatitis, infection, immune reaction, and injury to body tissues from iron overload.) Transfusions are also given to patients to prepare them for surgical procedures. Folic acid is given as a supplement. Sometimes a red blood cell exchange is performed. This process removes some of the sickle blood cells and replaces them with normal (non-sickle) blood cells. It is done when the sickle cell crisis is so severe that other forms of treatment are not helping.

PAIN CRISES

Pain crises in persons with sickle cell anemia are intermittent painful episodes that are the result of inadequate blood supply to body tissues. The impaired circulation is caused by the blockage of various blood vessels from the sickling of red blood cells. The sickled red blood cells slow or completely impede the normal flow of blood through the tissues. This leads to excruciating pain, often requiring hospitalization and opiate medication for relief. The pain typically is throbbing and can change its location from one body area to another. Bones are frequently affected. Pain in the abdomen with tenderness is common and can mimic appendicitis. Fever frequently is associated with the pain crises.

A pain crisis can be promoted by preceding dehydration, infection,

injury, cold exposure, emotional stress, or strenuous exercise. As a prevention measure, persons with sickle cell anemia should avoid extremes of heat and cold.

Pain crises require analgesia for pain and increased fluid intake. Dehydration must be prevented to avoid further injury to the tissues and intravenous fluids can be necessary. Other modalities, such as biofeedback, self-hypnosis, and/or electrical nerve stimulation may be helpful.

Hydroxyurea is a medication that is currently being used in adults and children with severe pain from sickle cell anemia. It is also considered for those with recurrent strokes and frequent transfusions. This drug acts by increasing the amount of fetal hemoglobin in the blood (this form of hemoglobin is resistant to sickling of the red blood cells). The response to hydroxyurea is variable and unpredictable from patient to patient. Hydroxyurea can be suppressive to the bone marrow.

WHAT IS THE OUTLOOK FOR SICKLE CELL ANAEMIA?CAN IT BE CURED?

The life expectancy of persons with sickle cell anemia is reduced. Some patients, however, can remain without symptoms for years, while others do not survive infancy or early childhood. Nevertheless, with optimal management patients can now survive beyond the fourth decade.

Most patients suffer intermittent pain crises, fatigue, bacterial infections, and progressive tissue and organ damage. Impaired growth and development is the result of the physical and emotional trauma that is endured by children with sickle cell anemia.

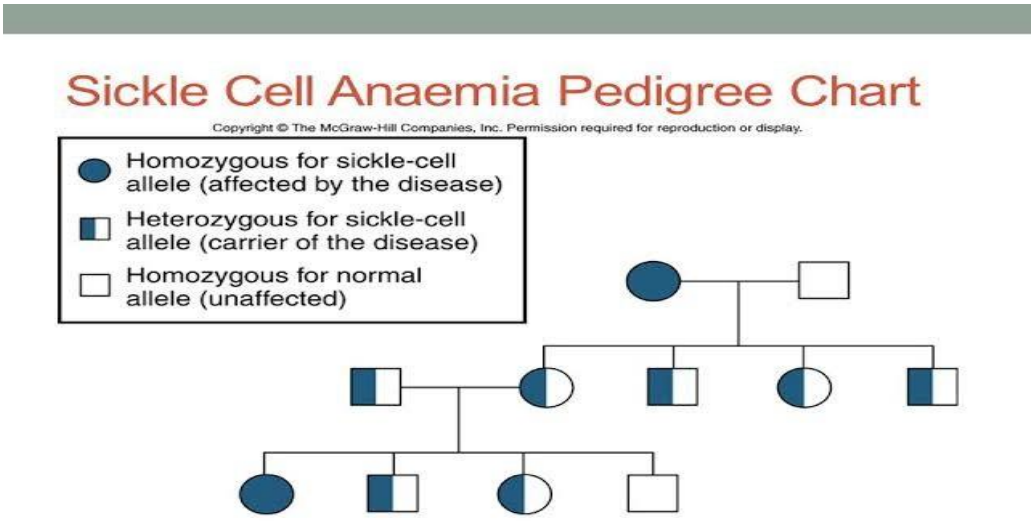
Causes of death include bacterial infection (the most common cause), stroke or bleeding into the brain, and kidney, heart, or liver failure. The risk of bacterial infections does diminish after three years of age. Nevertheless, bacterial infections are the most common cause of death at any age. Therefore, any signs of infection in a person with sickle cell anemia must be reviewed with a doctor to prevent damage and save lives.

Interestingly, the sickle cell gene somewhat protects against malaria infection. This makes those with sickle cell trait (gene carriers) at least partially resistant to malaria. Furthermore, the geographic distribution of the sickle cell gene is similar to that of malaria infection. Sickle cell anemia is a lethal condition that threatens life. However, there may be a selective advantage to being a sickle cell carrier (trait) if the person resides in an area of the world where malaria is very common. The advantage a person with sickle cell trait has over a non-carrier of the gene may explain why sickle cell anemia did not disappear from the world even though it is lethal.

The sickle cell gene is not a "black gene." It just happens to disproportionately occur in the black population. When a black person who carries a sickle cell gene has children with a non-black person, the children may inherit the sickle cell gene regardless of race. There are also people of all races who carry the sickle cell gene.

Recent research is examining further ways to promote the development of the fetal hemoglobin that delays the development of sickle cell in the newborn. Bone marrow transplantation is being used for patients with severe sickle cell anemia who have a sibling donor. Future treatments may involve genetic engineering where cures might be achieved.

Finally, genetic counseling can be helpful for parents and families to prevent sickle cell anemia. Sickle cell anemia is an inherited illness. Both parents must be carriers of the sickle cell gene for a child to be affected with sickle cell anemia. If each parent is a carrier, any child has a one chance in two (50%) of also being a carrier and a one in four (25%) chance of inheriting both genes from the parents and being affected with sickle cell anemia.



CONCLUSION

Working on this research-based-project,
we learnt about the genetic disorder Sickle cell Anaemia. We learnt how difficult life becomes for a diseased individual, and the ordeals of living with it. The signs and symptoms were studied.
Apart from all that, we also came across Bone marrow transplantation- what it is; and how it cures the disease.
We would like to conclude that by working on this project, we understood genetic diseases better and how the medicine field needs something soon to cure this and help mankind.

Bibliography

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