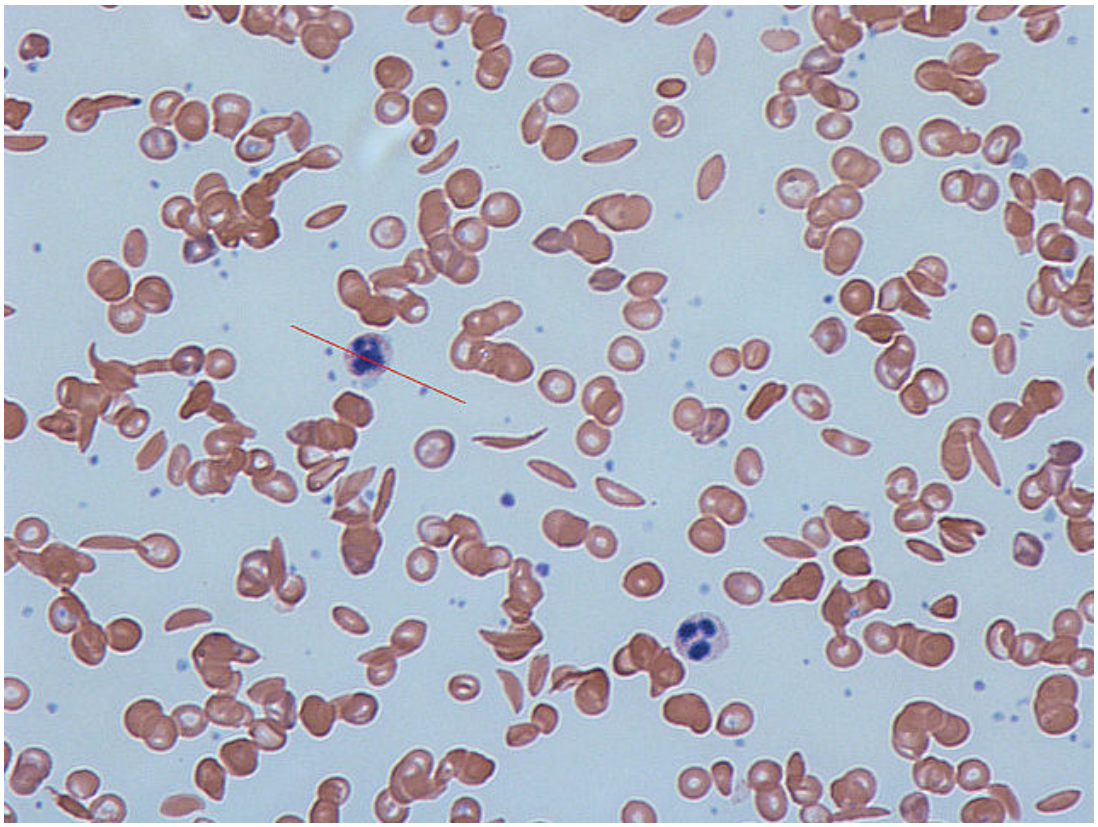
Normocytic Anemia: Sickle Cell Anemia (Sickle Cell Disease)

See online here

Sickle cell anemia leads to sickling of red cells during hypoxia. This can cause blockages in blood vessels along with a range of clinical problems. Treatment is with red cell transfusions and hydroxycarbamide.



Definition of Sickle Cell Anemia

Sickle cell anemia is a hereditary hemolytic anemia based on a point mutation. Erythrocytes contain sickle cell hemoglobin (Hb-S) instead of the normal hemoglobin.

Epidemiology of Sickle Cell Anemia

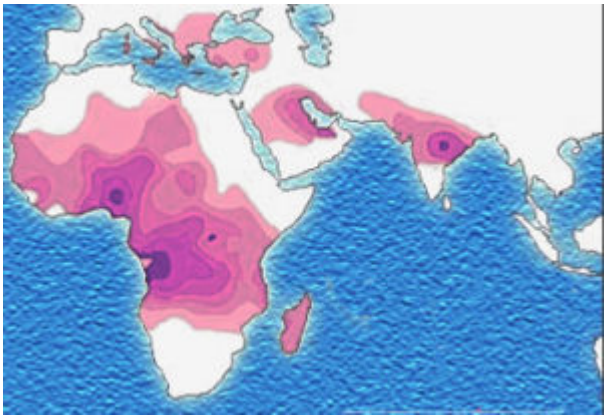


Image: “Distribution of the sickle-cell trait shown in pink and purple,” by Muntuwandi. License: CC BY-SA 3.0

Sickle cell anemia is almost exclusively present in black-skinned people.

Etiology and Pathogenesis of Sickle Cell Anemia

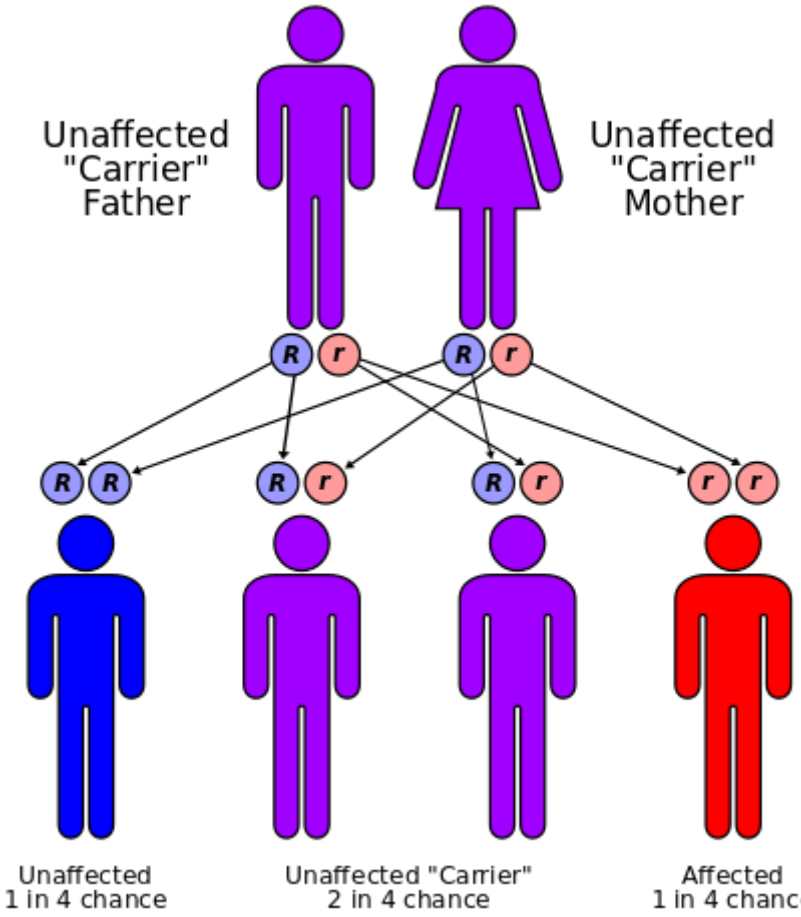


Image: “Sickle cell disease is inherited in the autosomal recessive pattern,” by Cburnett. License: CC BY-SA 3.0

As a result of a base replacement in the DNA-code (thymine instead of adenine), an exchange of an amino acid at position 6 of the ß-chain of the hemoglobin occurs. Genetically, this is a point mutation. This results in the crystallization of the altered hemoglobin in the erythrocytes. If the partial pressure of oxygen decreases, the erythrocytes assume a characteristic, sickle shaped form. This leads to micro-embolisms

and infarctions.

The severity of the disease depends on the rate of Hb-S in the erythrocytes. This rate is determined by the hereditary disposition and the inheritance mode. While heterozygosity leads to **Hb-S values** of less than 50%, homozygosity results in Hb-S values of approx. 70–99%.

Since crystallization of Hb-S depends on the partial pressure of oxygen, the symptoms mainly manifest in situations leading to hypoxia, or other similar conditions. Excessive physical exertion, as well as infections, living at higher altitudes, increased cold exposure, surgeries and the like, can lead to hemolytic crises.

- Point mutation in the b-globin gene causing glutamate-valine substitution at amino acid 6 (Hb-S).
- Autosomal recessive inheritance.

Clinic of Sickle Cell Anemia

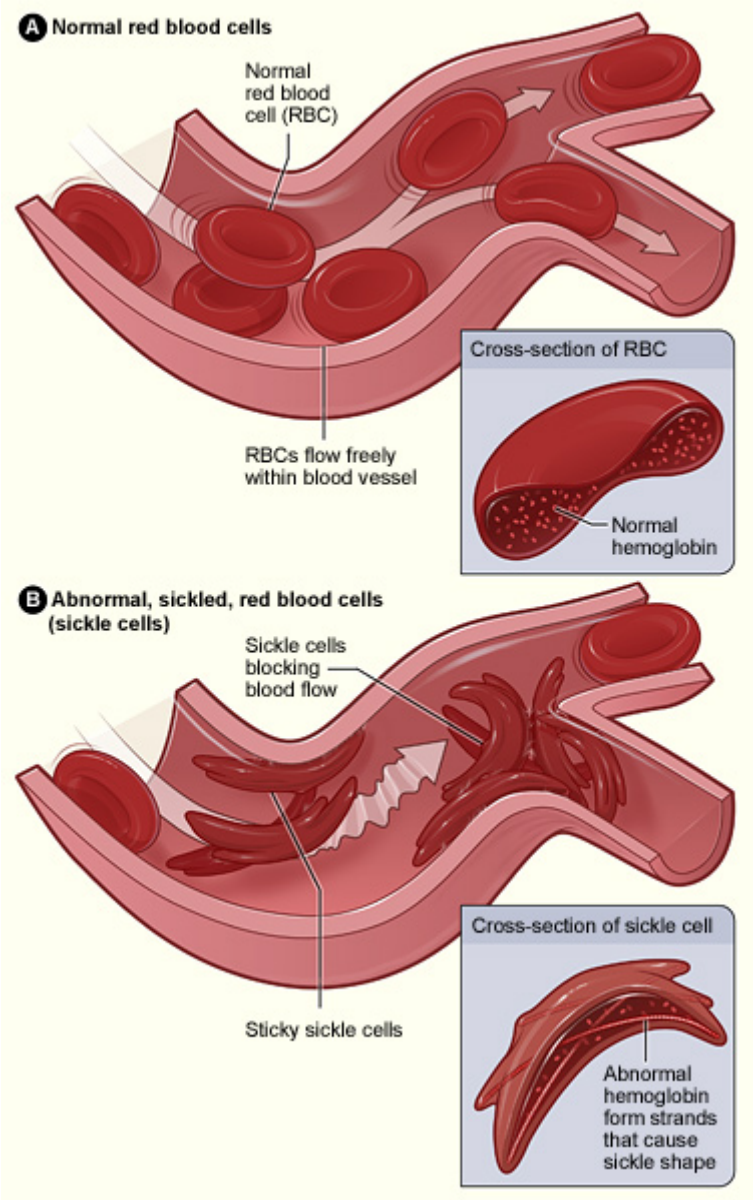


Figure A shows normal red blood cells flowing freely in a blood vessel. The inset image shows a cross-section of a normal red blood cell with normal hemoglobin. Figure B shows abnormal, sickled red blood cells blocking blood flow in a blood vessel. The inset image shows a cross-section of a sickle cell with abnormal (sickle) hemoglobin forming abnormal strands.

Patients with sickle cell anemia show the typical symptoms of chronic hemolytic anemia. Besides this, the patients suffer from abdominal, colicky complaints; bone and joint pain is also possible. Due to the pathogenesis, infarctions, especially in the kidneys and in the spleen, are frequently observed. Also, infarctions in the lung, liver and in the bone tissue are often observed. The earliest clinical hints are conspicuous shortenings of individual extremities in children (**hand-foot syndrome**).

Deoxyhemoglobin S has a tendency to polymerize. This polymerization causes sickling of red blood cells (RBCs) under conditions of low oxygen tension:

- Infection
- Dehydration
- Hypoxia

Sickled cells are cleared in the spleen, causing hemolytic anemia. They occlude the microvasculature, causing vaso-occlusive crises.

Vaso-occlusion can lead to:

- Pain crises: microvascular ischemia causing severe pain (100% of SS patients are eventually addicted to opiates).
- Acute chest syndrome: hypoxemia caused by microvascular disease of the lung.
- Stroke
- Autosplenectomy: involution of the spleen causing susceptibility to infection by encapsulated bacteria (100% of SS patients auto-splenectomized by adulthood).
- Painful priapism

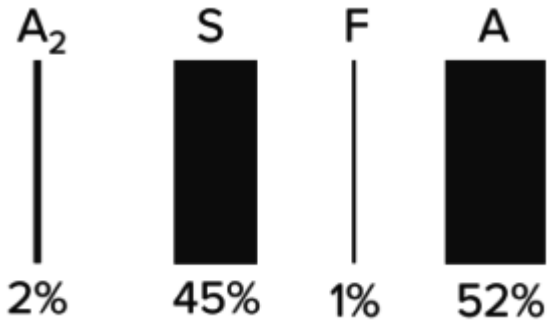
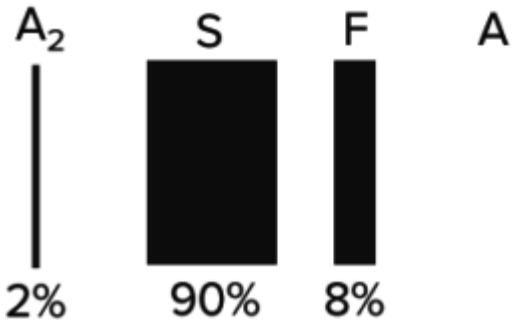
Also susceptible to:

- Aplastic crisis with parvovirus B-19 infection
- *Salmonella* osteomyelitis
- Other sequelae of chronic hemolytic anemia

Diagnosis of Sickle Cell Anemia

- Newborn screening: genetic test for *E6V* mutation
- Sickle prep: peripheral blood sickles when exposed to sodium metabisulfite (reduces oxygen tension).
- Hemoglobin electrophoresis

Hemoglobin Electrophoresis

	**No anemia**	**Sickle cell trait** Note that there is not enough HbS to cause spontaneous sickling in the peripheral blood.
	**Normocytic**	**Sickle cell disease** Note that there is no HbA. There is enough HbS to cause spontaneous sickling.

Therapy of Sickle Cell Anemia

The **minor form** usually does not need treatment. However, if not treated, the **major form** often leads to death in childhood. Thus, allogeneic **HLA-identical bone marrow**

transplantation should be attempted if there are siblings. Otherwise, therapy of the major form is symptomatic and is limited to avoiding situations of oxygen deficiency, the application of folate and the transfusion of erythrocyte concentrate.

- Hydroxyurea (increases production of fetal hemoglobin over Hb-S)
- Bone marrow transplantation
- Fluids
- Analgesics

Course and Prognosis of Sickle Cell Anemia

Due to Hb-S values between 25% and 50%, the heterozygous form barely develops symptoms and, thus, is practically not considered a disease. However, states of hypoxia, e.g., after severe exertion, or prior infectious diseases, can trigger hemolytic crises. Still, life expectancy is not decreased by the disease in any measurable way. Also, the patients exhibit a relative resistance against **malaria tropica** due to the point mutation and the resulting morphological changes of the erythrocytes.

Homozygous sickle cell anemia patients are severely ill since their Hb-S value lies between 70% and 99%. If untreated, homozygous and double heterozygous patients die in childhood.

References

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Notes