Describe the pathophysiology of the specific condition. What are the etiological factors, signs and symptoms, complications, and risk factors that contribute to the condition?

Sickle cell disease starts with a single gene mutation that changes the shape of hemoglobin, producing an abnormal version called HbS (Pecker & Lanzkron, 2021). When oxygen levels drop, HbS molecules clump together and force red blood cells into a rigid sickle shape. Once that happens, two things go wrong at the same time. The sickled cells get stuck in small blood vessels and cut off oxygen to surrounding tissue, and they break down much faster than normal red cells, which is what drives the chronic hemolytic anemia that patients live with on a daily basis (Kato et al., 2021).

The problem compounds over time. Every time a cell sickles and then returns to its normal shape, it takes damage. The membrane gets a little weaker, a little stiffer, and a little stickier than it was before. Those stickier cells are more likely to latch onto vessel walls, interact abnormally with white blood cells and platelets, and block blood flow all over again. It becomes a cycle that feeds itself, with inflammation and vascular injury building on each other with each episode (Manwani & Frenette, 2022).

Sickle cell disease is autosomal recessive, which means a person has to inherit a faulty beta-globin allele from both parents to actually have the disease. Getting only one copy from one parent results in sickle cell trait, which typically causes no symptoms but makes that person a carrier who can pass the mutation on to their children (Pecker & Lanzkron, 2021).

The reason this mutation is so concentrated in certain parts of the world comes down to survival. It shows up most often in people with ancestry from sub-Saharan Africa, the Mediterranean, the Middle East, and parts of India, and that is not a coincidence (Kato et al.,

2021). In those regions, malaria has historically been one of the most devastating diseases a person could face. Carrying one copy of the sickle cell gene turns out to offer a degree of natural protection against it. So even though inheriting two copies causes serious disease, one copy kept people alive in environments where malaria was killing others. That survival advantage is why the mutation spread and held on across generations in those populations, and it is also why sickle cell disease continues to affect people from those backgrounds at much higher rates today (Kato et al., 2021).

Signs and Symptoms (Manwani & Frenette, 2022)

• Chronic fatigue and pallor due to persistent hemolytic anemia.

• Episodic pain crises, which are the defining symptom of the disease, resulting from vascular occlusion inside bones, chest, abdomen, or joints.

• Jaundice and yellowing of the eyes from destruction of red cells.

• Hands and feet swelling, especially in infants.

• Children grow slower and enter puberty later.

• Frequent infections due to functional asplenia.

• Shortness of breath and poor exercise tolerance.

Complications.

- **Acute chest syndrome:** vaso-occlusion in the pulmonary vasculature resulting in chest pain, fever, and respiratory distress; a common cause of death.
- **Stroke:** when sickled cells build up in cerebral vessels, in particular children are susceptible.

- **Avascular necrosis:** blood supply failure to bone, most commonly the femoral head.
- **Splenic sequestration:** rapid pooling of blood in the spleen causing anemia of high risk, more common in younger children.
- **Priapism:** painful, prolonged erection from vascular obstruction.
- **Pulmonary hypertension:** develops over time as a result of chronic hemolysis and vascular damage.
- **Chronic kidney disease:** repeated sickling events can damage the renal microvasculature.
- **Leg ulcers:** especially in the legs due to poor circulation.
- **Aplastic crisis:** triggered by parvovirus B19 infection, temporarily disabling production of red cells.

Risk Factors

The most fundamental risk factor for sickle cell disease is genetic. A person has to inherit two copies of the HbS allele, one from each parent, for the disease to develop. The mutation shows up most commonly in people with ancestry from sub-Saharan Africa, the Mediterranean, the Middle East, and South Asia, largely because carrying one copy historically offered some protection against malaria in those regions (Kato et al., 2021).

For someone already living with the disease, everyday situations can become genuine triggers. Getting dehydrated, being out in the cold, traveling to high altitude, pushing too hard physically, or coming down with an illness can all set off a sickling episode. Infections are a particular concern because the spleen gradually loses its ability to filter out harmful bacteria over time. That means organisms that a healthy immune system would handle without much trouble