

Sickle Cell Crisis

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THE STORY IN ONE SENTENCE

When oxygen drops, hemoglobin S (the sickle version of the oxygen-carrying protein) turns stiff and sharp, bending red blood cells into a crescent or sickle shape.

“Sickle cell crisis happens when these bent, stiff red cells jam into tiny blood vessels like logs in a stream, blocking blood flow and starving tissue downstream—pain is just one sign of that blockage.”

Normal anatomy — the body's job

Red blood cells are soft, round, donut-shaped bags filled with hemoglobin, the protein that picks up oxygen in the lungs and carries it to every tissue in the body. Because red cells are soft and bendable, they can squeeze through capillaries (the tiniest blood vessels, narrower than a human hair) to deliver oxygen even to hard-to-reach spots. Once hemoglobin drops off its oxygen, the red cell travels back to the lungs to reload and start the trip again. A healthy red cell lives about 120 days, making thousands of round trips before it wears out and the spleen quietly pulls it out of circulation.

BODY'S JOB

Hemoglobin's job is to grab oxygen in the lungs (where oxygen is plentiful), hold it loosely during the trip through arteries, and then let it go in tissues that need it (where oxygen is lower). The red cell's job is to stay soft and flexible so it can deliver that oxygen everywhere, even through the narrowest, twistiest vessels. If you picture that—round, soft cells flowing like water through every vessel, dropping oxygen, and cycling back—you will instantly see why a stiff, sharp, crescent-shaped cell that gets stuck is such a disaster.

1. Soft, round red blood cells flow easily through capillaries, the tiniest blood vessels in the body.
2. Hemoglobin inside each cell picks up oxygen in the lungs, where oxygen levels are high.

3. Red cells carry that oxygen through arteries to tissues all over the body.
4. In the tissues, where oxygen is lower, hemoglobin gently releases the oxygen so cells can use it for energy.
5. The red cell, now carrying less oxygen, travels back through veins to the lungs to reload.
6. This cycle repeats thousands of times over the red cell's 120-day lifespan.
7. Old or damaged red cells are quietly filtered out by the spleen and broken down; the iron is recycled, and bilirubin (a yellow waste product) is sent to the liver and eventually leaves the body in stool.

What breaks

In sickle cell disease, a person inherits two copies of the hemoglobin S gene (one from each parent), so nearly all their hemoglobin is the S type instead of the normal adult type (hemoglobin A). Hemoglobin S works fine when it is holding oxygen, but the moment it releases oxygen—especially if oxygen levels drop, the blood becomes acidic, the person is dehydrated, an infection is brewing, the body is cold, or stress hormones are high—the hemoglobin S molecules stick together and form long, stiff rods inside the red cell. Those rods poke the soft, round cell into a hard, crescent or sickle shape. Sickled cells are stiff, sticky, and fragile: they pile up and block the smallest blood vessels, they break apart (hemolyze) much faster than normal (living only 10 to 20 days instead of 120), and they also switch on the lining of blood vessels (the endothelium), which calls in white blood cells and makes the vessels even stickier and more inflamed. The result is a vicious cycle: blockage cuts off oxygen, low oxygen triggers more sickling, and more sickling causes more blockage and more cell death.

CLINICAL TERM

Hemoglobin S polymerization under low-oxygen (hypoxic), acidotic, dehydrated, cold, or inflammatory conditions causes red blood cells to sickle. Sickled red blood cells (erythrocytes) are rigid, adhesive, and short-lived (10–20 day lifespan). Vaso-blockage (occlusion) results from sickled cells occluding microvascular beds, compounded by endothelial activation, white blood cell (leukocyte) recruitment, and increased expression of adhesion molecules (ICAM-1, VCAM-1, P-selectin). This triggers starved blood flow (ischemia)-reperfusion injury, local inflammation, and tissue death from blocked blood flow (infarction). Chronic intravascular and extravascular red blood cell destruction (hemolysis) releases free hemoglobin and heme, scavenging nitric oxide, impairing vasodilation, and promoting oxidative stress and endothelial dysfunction. The net effect is episodic vaso-occlusive crises and cumulative end-organ damage.

How the body compensates

The body tries to keep up by ramping up red-cell production in the bone marrow (you will see reticulocytosis, a high count of young red cells, on the blood smear), pumping the heart faster to move what red cells remain, and breathing faster to pull in more oxygen. Early in a crisis, vital signs may look okay and the person may still be talking and moving—but that does not mean things are fine. The body is working overtime to buy time, and it can only keep that up for so long. The real danger is that compensation hides how bad things are until suddenly the system crashes—acute chest syndrome with respiratory failure, stroke, or splenic sequestration with shock. By the time vital signs fall apart, the patient is already in deep trouble. The job is to recognize the crisis early (pain, fever, new cough, falling oxygen, sudden paleness or fatigue, a swollen belly in a young child) and treat aggressively before compensation fails.

1. The bone marrow cranks out new red cells as fast as it can to replace the ones breaking apart (you will see reticulocytosis and a high percentage of young, immature red cells on a blood count).
2. The heart pumps harder and faster (tachycardia) to push the remaining red cells through the body and deliver whatever oxygen is available.
3. Breathing speeds up (tachypnea) to pull more oxygen into the lungs and try to keep oxygen levels from dropping further.
4. Blood vessels in non-essential areas (like the skin) clamp down to shunt blood toward vital organs like the brain and heart.
5. These compensations can keep blood pressure and oxygen saturation looking almost normal for a while, even though tissue is being starved and damaged—this is the dangerous middle, because it hides how sick the person really is.
6. The crash point to watch for: acute chest syndrome with low oxygen (hypoxia) and respiratory failure (often triggered by infection, fat traveling clots (emboli) from bone-marrow tissue death from blocked blood flow (infarction), or in-situ pulmonary vaso-occlusion (occlusion)); stroke (from cerebral vaso-occlusion); splenic sequestration with hypovolemic shock in young children (spleen suddenly traps a huge volume of sickled cells); aplastic crisis (parvovirus B19 shuts down red-cell production and hemoglobin drops fast); or severe anemia with high-output heart failure.
7. Mortality in sickle cell crisis comes from these complications—especially acute chest syndrome, stroke, infection/sepsis, and splenic or hepatic sequestration—not from the pain itself, though pain is often the first and loudest warning sign that sickling and vaso-occlusion (occlusion) are happening.

Domino effect

1. Vaso-occlusive pain crisis (the most common type of crisis) causes severe bone and joint pain, and in babies and toddlers it causes dactylitis (painful swelling of the hands and feet). — When oxygen drops—because of dehydration, infection, cold weather, physical stress, high altitude, or even just normal sleep (when breathing slows)—hemoglobin S polymerizes and red cells sickle. Sickled cells jam into the tiny vessels that feed bones and bone marrow. Blood flow stops, and the bone tissue downstream becomes blood-starved (ischemic) (starved of oxygen). Blood-starved bone hurts terribly, and if the blockage lasts long enough, pieces of bone die (avascular tissue death (necrosis), especially in the hip and shoulder). In young children, the small bones of the hands and feet are affected first, causing dactylitis (hand-foot syndrome), often the very first sign of sickle cell disease in a baby.
2. Acute chest syndrome (ACS) causes fever, chest pain, cough, low oxygen, and a new shadow (infiltrate) on chest X-ray—it is the leading cause of death and ICU admission in sickle cell disease. — Sickling and vaso-blockage (occlusion) happen in the lungs just like anywhere else. Triggers include infection (pneumonia, often from *Streptococcus pneumoniae*, *Mycoplasma*, *Chlamydia*, or viruses), fat traveling clots (emboli) (tiny globs of fat released when bone marrow dies during a bone pain crisis), and in-situ sickling in pulmonary capillaries (especially if the person is already oxygen-starved (hypoxic) or dehydrated). Blocked vessels cause lung tissue to become blood-starved (ischemic), fill with fluid (pulmonary swelling (edema)), collapse (atelectasis), or get infected. The result is a vicious cycle: sickling lowers oxygen, low oxygen triggers more sickling, and the lungs fail. Without aggressive treatment—oxygen, incentive spirometry, hydration, antibiotics, transfusion—acute chest syndrome spirals into acute respiratory distress syndrome (ARDS) and can be fatal.
3. Stroke (cerebrovascular accident) can happen, especially in children; sickle cell disease is one of the most common causes of stroke in kids. — Sickled cells clog the large arteries at the base of the brain (especially the internal carotid and middle cerebral arteries), cutting off blood flow to brain tissue. Brain cells die within minutes without oxygen, causing sudden weakness, speech trouble, vision loss, seizures, or loss of consciousness. Chronic sickling also damages the vessel walls, causing them to narrow (stenosis) and become prone to clots. Regular transcranial Doppler (TCD) ultrasound screening in children identifies high-risk vessels, and chronic transfusion therapy (to dilute hemoglobin S and keep it below 30%) dramatically lowers stroke risk.

4. Priapism (a painful, unwanted erection lasting more than 2 to 4 hours) is a urologic emergency in males with sickle cell disease. — Sickled cells jam the tiny veins that normally drain blood out of the penis. Blood flows in but cannot flow out, so the penis fills with blood, becomes rigid and painful, and stays that way. The trapped, oxygen-poor blood triggers more sickling, making the blockage worse. If the blockage lasts more than 4 hours, the lack of oxygen kills the spongy erectile tissue (corpora cavernosa), causing permanent scarring, erectile dysfunction, and future episodes of priapism. Immediate treatment—hydration, pain control, sometimes aspiration of blood from the penis, and transfusion—is critical to save function.
5. Splenic sequestration crisis happens suddenly in infants and young children (usually under age 5), causing a swollen, tender belly, severe anemia, and shock. — In young children, the spleen is still working and full of tiny blood channels. Sickled cells get trapped in those channels and pile up, pulling a huge volume of red cells out of circulation all at once. The child's hemoglobin can drop by several grams in hours, the spleen swells (you can feel it bulging under the ribs), and blood pressure falls (hypovolemic shock). Without emergency transfusion, splenic sequestration can be fatal. After repeated episodes, or as chronic sickling damages the spleen over time, the spleen scars and shrinks (autosplenectomy), so sequestration crises stop—but the child is left without a working spleen and at high risk for life-threatening infections from encapsulated bacteria like *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis*.
6. Aplastic crisis is a sudden, severe drop in hemoglobin caused by bone-marrow shutdown, almost always triggered by parvovirus B19 infection. — Parvovirus B19 (the virus that causes fifth disease, a common childhood rash illness) infects and kills red-cell precursors in the bone marrow, stopping red-cell production for about 7 to 10 days. In a healthy person, that pause is no problem—red cells live 120 days, so there are plenty in circulation to carry you through. But in sickle cell disease, red cells only live 10 to 20 days and are breaking apart constantly, so the bone marrow is already working at full speed just to keep up. When parvovirus shuts it down, hemoglobin plummets, reticulocyte count (young red cells) drops to near zero, and the person becomes dangerously anemic. Transfusion is life-saving. Once someone recovers from parvovirus B19, they are immune for life, so aplastic crisis usually happens only once.

7. Chronic destroying red blood cells (hemolytic) anemia develops over a lifetime because sickled red cells break apart (hemolyze) much faster than normal cells. — Day after day, sickled cells are fragile and rupture as they try to squeeze through tiny vessels or get chewed up by the spleen. The bone marrow responds by running at 6 to 8 times normal speed, pouring out new red cells as fast as it can (you will see a high reticulocyte count, large numbers of young red cells, and expanded bone-marrow spaces on imaging). But even that overdrive is not enough—steady destruction outpaces production, so baseline hemoglobin in sickle cell disease is usually 6 to 9 g/dL (compared to the normal 12 to 16). The breakdown products—free hemoglobin, heme, and bilirubin—flood the bloodstream. Free hemoglobin scavenges nitric oxide, causing blood vessels to stay tight and worsening vaso-blockage (occlusion). High bilirubin causes yellowing of the skin and eyes (jaundice) (yellow skin and eyes) and over time leads to gallstones made of bilirubin (pigment stones), often requiring surgery. The heart has to pump harder to move oxygen with fewer red cells, leading to cardiomegaly (an enlarged heart) and eventually heart failure. The spleen works overtime clearing broken cells and becomes enlarged early in life, then scars and shrinks (autosplenectomy) by age 5 to 10, leaving the person without splenic immune function and at lifelong high risk for overwhelming sepsis from encapsulated bacteria.
8. Chronic organ damage accumulates silently over years, affecting nearly every system and shortening lifespan without disease-modifying therapy. — Repeated cycles of vaso-blockage (occlusion), starved blood flow (ischemia), reperfusion injury, red blood cell destruction (hemolysis), and inflammation scar and destroy organs bit by bit. The kidneys lose their ability to concentrate urine (hyposthenuria), leak protein (proteinuria), and eventually fail (sickle cell nephropathy). The lungs develop pulmonary high blood pressure (hypertension) (high pressure in lung vessels) from chronic red blood cell destruction, clots, and vessel damage. The heart enlarges and weakens. The bones develop avascular tissue death (necrosis) (dead bone, especially hip and shoulder). The retina (back of the eye) loses blood flow, causing vision loss (proliferative sickle retinopathy). The skin over the ankles breaks down into chronic leg ulcers that are slow to heal. The brain suffers silent strokes (small areas of damage that do not cause obvious symptoms but add up to cognitive problems and learning difficulties). The liver becomes enlarged and scarred. Even the penis and hearing can be affected. All of this damage is driven by the same mechanism: sickling, blockage, red blood cell destruction, and inflammation, over and over, year after year.

Symptoms · what the patient feels, and why

- Severe pain in bones, especially in the back, chest, arms, or legs: Sickled-shaped red blood cells (crescent-shaped instead of round) get stuck in tiny blood vessels and block blood flow to the bone. When the bone tissue doesn't get enough oxygen, it screams with pain — like how your muscles cramp when you hold your breath during a sprint.

- Fever (temperature above 100.4°F or 38°C): Sick cell disease damages the spleen (the body's filter that catches germs), so infections can spread fast. Fever can also signal acute chest syndrome — when sickled cells clog the lungs' blood vessels, starving lung tissue of oxygen and triggering inflammation, just like a pneumonia.
- Sudden weakness, trouble speaking, vision changes, or one-sided numbness: Sickled red blood cells can jam the arteries feeding the brain, cutting off oxygen to brain tissue — a stroke. Brain cells start dying within minutes, so every moment counts.
- Painful, unwanted erection that won't go away (priapism) in males: Sickled cells block the veins that normally drain blood out of the penis, trapping blood inside. The tissue swells and hurts intensely. If it lasts more than 4 hours, the tissue can be permanently damaged.
- Sudden shortness of breath, fast breathing, or chest pain: In acute chest syndrome, sickled cells clog lung blood vessels, fat from broken bone marrow leaks into the blood and clogs lungs, or infection inflames the lung tissue. All three cut oxygen delivery, making every breath feel like you're drowning.
- Swelling and pain in hands and feet (dactylitis), especially in babies and toddlers: Sickled cells block the small blood vessels in the bones of the fingers and toes, starving the bone and triggering swelling and throbbing pain. This is often the very first sign of sickle cell disease in young children.
- Pale skin, lips, or nail beds (worse than the person's usual color): Sickled red blood cells are fragile and break apart quickly — they only live 10 to 20 days instead of the normal 120. The body can't make new ones fast enough, so hemoglobin (the oxygen-carrying protein that gives blood its red color) drops, leaving skin and tissues looking washed out.
- Yellow tint to the whites of the eyes or skin (jaundice): When sickled red blood cells break apart, they release hemoglobin. The liver breaks hemoglobin down into bilirubin (a yellow waste product). If cells are breaking faster than the liver can clear the bilirubin, it piles up in the blood and stains the skin and eyes yellow.
- Sudden, severe belly pain (especially in the upper-right side): Sickled cells can clog blood vessels in the liver or spleen, swelling those organs fast and stretching their outer covering, which is loaded with pain nerves. The spleen can also trap huge numbers of red blood cells all at once (splenic sequestration), ballooning up and causing sharp pain and dangerous anemia.

Focused exam

- Severe bone pain in the back, chest, arms, or legs: Sickled red blood cells — shaped like hard crescents instead of soft discs — get stuck in tiny blood vessels inside bones and block oxygen from reaching bone tissue. That blockage (called vaso-blockage (occlusion)) causes severe pain and is the hallmark of a sickle cell crisis.

- Fever with cough, chest pain, or trouble breathing: This combination signals acute chest syndrome — sickled cells are blocking blood vessels in the lungs, starving lung tissue of oxygen. Acute chest syndrome is the leading cause of death in sickle cell disease and can spiral quickly, so it must be treated immediately.
- Swollen, painful hands or feet in a young child: Hand-foot syndrome (dactylitis) happens when sickled cells jam the tiny blood vessels in the small bones of the fingers and toes, blocking oxygen and causing the tissue to swell. It is often the first sign of sickle cell disease in babies and toddlers.
- Sudden weakness on one side of the body, slurred speech, or drooping face: These are stroke signs — sickled cells have blocked a blood vessel in the brain, cutting off oxygen to brain tissue. Stroke is a medical emergency in sickle cell disease just as it is in anyone else, and brain damage can happen within minutes.
- Pale or yellow skin with a hemoglobin level that has dropped sharply from the patient's usual baseline: Sickled cells are fragile and break apart easily (hemolysis), releasing their contents into the bloodstream. A fast drop in hemoglobin means red cells are dying faster than the bone marrow can make new ones, and the yellow color (jaundice) comes from bilirubin, a breakdown product of dead red cells.
- In a young child: sudden belly pain, pale skin, weak pulse, fast heart rate, and low blood pressure: Splenic sequestration crisis happens when sickled cells get trapped in the spleen, pulling a huge volume of blood out of the main circulation. The child goes into shock because there is not enough blood left in the vessels to supply the body. This is a life-threatening emergency in babies and toddlers.
- Oxygen saturation below the patient's usual baseline, even at rest: Low oxygen makes hemoglobin S (the abnormal hemoglobin in sickle cell disease) stiffen and force red cells into the sickle shape. When oxygen drops, more cells sickle, more vessels get blocked, and the crisis gets worse — creating a dangerous downward spiral.

Diagnostics · every test answers a question

- Complete blood count (CBC) with reticulocyte count → Is the patient anemic, and is the bone marrow trying to make new red blood cells to replace the ones that are breaking apart?
- Chest X-ray → Is there a new infiltrate (cloudy patch) in the lungs that could be acute chest syndrome?
- Pulse oximetry (oxygen saturation) → Is the patient getting enough oxygen into the bloodstream, or is oxygen dropping and triggering more sickling?
- Type and screen (blood type and antibody screen) → What is the patient's blood type, and do they have antibodies that will make finding safe blood for transfusion harder?

- Lactate dehydrogenase (LDH) and indirect bilirubin → How much red blood cell destruction (hemolysis) (red cell breakdown) is happening right now?
- Blood culture → Is there a bacterial infection in the bloodstream that triggered the crisis or is making it worse?
- Head CT or brain MRI (if stroke symptoms are present) → Is there a blockage or bleed in the brain causing the sudden weakness, slurred speech, or altered mental status?

Treatment logic

- Intravenous (IV) fluids at 1 to 1.5 times maintenance rate using normal saline or lactated Ringer's → Hydration dilutes the blood, making it easier for sickled cells to flow through narrow vessels without getting stuck. It also replaces fluid lost from fever, fast breathing, and poor oral intake during the crisis.
- Intravenous opioid pain medication (morphine or hydromorphone) on a scheduled basis, not just as needed, plus acetaminophen or ibuprofen if kidney function is normal → Opioids block pain signals traveling from bone tissue to the brain by attaching to opioid receptors in the spinal cord and brain. Scheduled dosing keeps pain controlled around the clock, preventing the stress and oxygen-hungry state that worsens sickling. Acetaminophen and ibuprofen reduce inflammation in the blocked tissues.
- Supplemental oxygen by nasal cannula or mask if oxygen saturation is below the patient's baseline → Raising oxygen in the bloodstream keeps hemoglobin S from stiffening and sickling. Higher oxygen levels prevent new cells from turning into crescents and joining the blockade.
- Incentive spirometry (a breathing device that encourages deep breaths) every 2 hours while awake, plus chest physiotherapy if needed → Deep breathing keeps the air sacs (alveoli) in the lungs inflated and moving, preventing collapse (atelectasis) and poor oxygen exchange. This reduces the risk of acute chest syndrome, which often starts when parts of the lung collapse and oxygen drops.
- Empiric antibiotics: ceftriaxone (a third-generation cephalosporin) plus azithromycin (a macrolide) if acute chest syndrome is suspected or fever is present → Ceftriaxone kills common bacteria (like *Streptococcus pneumoniae* and *Haemophilus influenzae*) that can trigger a crisis or cause life-threatening infection in patients with sickle cell disease, whose spleens often do not work. Azithromycin covers atypical bacteria (like *Mycoplasma*) that cause acute chest syndrome.

- Simple transfusion (adding donor red blood cells) or exchange transfusion (replacing the patient's blood with donor blood) for severe acute chest syndrome, stroke, multi-organ failure, or preparation for surgery → Transfusion replaces sickled red blood cells with normal donor cells that carry oxygen efficiently and do not stick in vessels. This restores oxygen delivery to starved tissues, stops new sickling, and gives the patient's bone marrow time to recover. Exchange transfusion also lowers the percentage of hemoglobin S in the blood (goal below 30%), reducing the chance of more blockages.
- Hydroxyurea (started or continued if already on it) as long-term disease-modifying therapy → Hydroxyurea increases fetal hemoglobin (hemoglobin F), a type of hemoglobin that does not sickle. It also reduces the stickiness of red blood cells and lowers white blood cell counts, all of which reduce vaso-blockage (occlusion) and cut the frequency of crises, acute chest syndrome, and strokes over time.

Medications

Isotonic IV fluids (normal saline or lactated Ringer's) · Crystalloid intravenous fluid

Sickle cell crisis happens when red blood cells turn stiff and pointy because they don't have enough oxygen or water. IV fluids give water directly into the blood to keep cells from drying out and clumping together. We use maintenance rate (just enough to match what the body normally uses) because too much fluid can flood the lungs and cause acute chest syndrome.

1. Fluid enters the bloodstream through an IV line in a vein
2. The extra water dilutes the blood slightly and spreads into red blood cells
3. Hydrated red blood cells stay rounder and softer, so they flow better and are less likely to get stuck
4. Better flow means more oxygen reaches tissues, which helps stop new sickling

SAFETY WATCH

Too much fluid too fast can overload the lungs and cause acute chest syndrome (fluid in the lungs) · Monitor breathing and listen to lungs for crackles (sign of fluid buildup) · Track how much urine the patient makes to be sure kidneys are working

IV opioids (morphine or hydromorphone) · Opioid analgesic (strong pain medicine)

Sickle cell crisis causes severe bone and muscle pain because sickled cells clog small blood vessels and starve tissue of oxygen. Opioids attach to pain receptors in the spinal cord and

brain and turn down the pain signal, like lowering the volume on an alarm. We give them on a schedule (every few hours) rather than waiting for pain to spike, so the level stays steady.

1. Opioid enters the bloodstream through an IV
2. Drug travels to the spinal cord and brain
3. Opioid locks onto mu receptors (special docking spots for pain control)
4. Receptors send a 'quiet down' signal that blocks pain messages from reaching the brain
5. Patient feels less pain, even though the tissue injury is still there

SAFETY WATCH

Can slow breathing (respiratory depression), especially at high doses—monitor breathing rate · Can cause severe constipation; give stool softeners and laxatives with every dose · Can cause nausea; antiemetics (anti-nausea medicine) often needed · Risk of dependence with long-term use, but undertreating pain in crisis is dangerous and unethical

NSAIDs (ketorolac or ibuprofen) · Nonsteroidal anti-inflammatory drug

Sickled cells clog vessels and cause inflammation (swelling and chemical irritation in tissues). NSAIDs block an enzyme called cyclooxygenase (COX), which the body uses to make prostaglandins (chemicals that cause pain, fever, and swelling). Blocking COX means less prostaglandin, so less pain and inflammation. NSAIDs work well with opioids because they attack pain from a different angle.

1. NSAID enters the bloodstream (by mouth or IV)
2. Drug blocks the COX enzyme in cells
3. Less prostaglandin is made
4. Pain signals weaken and swelling decreases

SAFETY WATCH

Can damage kidneys, especially if the patient is dehydrated or already has kidney disease—do NOT use if acute kidney injury is present · Can cause stomach ulcers and bleeding · Avoid in patients with low platelet count or bleeding risk

Supplemental oxygen (nasal cannula or mask) · Medical gas therapy

Sickle hemoglobin (hemoglobin S) changes shape and hardens when oxygen levels drop. Giving extra oxygen through a tube in the nose or a mask raises the oxygen level in the blood, which keeps more hemoglobin in its normal, round shape. This stops new cells from sickling. We only

give oxygen if the oxygen saturation is below 95% (hypoxia), because extra oxygen when levels are already normal does not help and wastes resources.

1. Patient breathes in oxygen-enriched air
2. Oxygen crosses from the lungs into the blood
3. Oxygen sticks to hemoglobin inside red blood cells
4. Hemoglobin S with oxygen attached stays soft and round instead of turning hard and pointy

SAFETY WATCH

Too much oxygen for too long can suppress the breathing drive in some patients (rare in sickle cell) · Check oxygen saturation with a pulse oximeter to guide dosing

Incentive spirometry (breathing exercise device) · Mechanical respiratory therapy (not a drug)

Sickle cell patients in crisis often breathe shallowly because of chest or rib pain. Shallow breathing lets parts of the lungs collapse (atelectasis), which lowers oxygen and raises the risk of acute chest syndrome (a life-threatening complication). The incentive spirometer is a plastic device that makes the patient take slow, deep breaths. Deep breaths pop open the tiny air sacs and keep lungs fully expanded.

1. Patient seals lips around the mouthpiece and breathes in slowly
2. A ball or piston rises in the device to show how deep the breath is
3. Deep breath inflates collapsed parts of the lung
4. Better lung inflation means better oxygen exchange and lower infection risk

SAFETY WATCH

Chest pain can make it hard to use—give pain medicine first · Patients need coaching and reminders every 1–2 hours while awake

Antibiotics: ceftriaxone (add azithromycin for acute chest syndrome) · Ceftriaxone is a third-generation cephalosporin; azithromycin is a macrolide

Sickle cell patients are at high risk for serious bacterial infections because the spleen (the organ that filters bacteria from blood) is often damaged by repeated sickling. Fever in a sickle cell patient is an emergency. Ceftriaxone kills common bacteria like *Streptococcus pneumoniae* and *Salmonella*. If acute chest syndrome develops (new lung infiltrate on X-ray, chest pain,

fever, cough), we add azithromycin to cover atypical bacteria like *Mycoplasma* and *Chlamydia*, which also cause pneumonia.

1. Ceftriaxone (IV): travels through blood, binds to bacterial cell walls, punches holes in the wall, bacteria burst and die
2. Azithromycin (IV or by mouth): enters bacteria, blocks the ribosome (the bacteria's protein factory), bacteria can't grow or multiply

SAFETY WATCH

Ceftriaxone: allergic reactions (rash, anaphylaxis) possible, especially if penicillin allergy; can cause diarrhea · Azithromycin: can prolong the QT interval on EKG (heart rhythm risk); check EKG if patient has heart disease

Red blood cell transfusion (simple or exchange) · Blood product therapy

In severe crises (stroke, acute chest syndrome not improving, multi-organ failure, or before major surgery), we replace the patient's sickled red cells with normal donor red cells. Simple transfusion adds new cells on top of the old ones. Exchange transfusion removes sickled cells and replaces them with normal cells, lowering the percentage of hemoglobin S in the blood. Normal red cells carry oxygen better, don't sickle, and flow smoothly, which can reverse life-threatening complications quickly.

1. Donor red cells (with normal hemoglobin A) are given through an IV
2. New cells dilute or replace the sickled hemoglobin S cells
3. Normal cells deliver oxygen better and don't clog vessels
4. Oxygen delivery improves, sickling stops, and organs begin to recover

SAFETY WATCH

Risk of iron overload with repeated transfusions (need iron chelation therapy) · Risk of alloimmunization (patient's immune system attacks donor cells in future transfusions) · Risk of transfusion reactions (fever, allergic reaction, red blood cell destruction (hemolysis)) · Risk of infections from donated blood (very rare with modern screening)

Hydroxyurea · Antimetabolite (chronic disease-modifying therapy)

Hydroxyurea is a daily pill for long-term prevention, NOT for acute crisis. It raises the level of fetal hemoglobin (hemoglobin F) in red blood cells. Fetal hemoglobin doesn't sickle. When red cells have more hemoglobin F and less hemoglobin S, they stay round and soft even when oxygen is low. Over months, this reduces the number of crises, lowers the need for transfusions, and prevents organ damage.

1. Patient takes hydroxyurea by mouth every day

2. Drug enters bone marrow and signals developing red cells to make more hemoglobin F
3. Over weeks to months, the percentage of fetal hemoglobin in blood rises
4. Red cells with more hemoglobin F are less likely to sickle, even under stress

SAFETY WATCH

Can lower white blood cells, red blood cells, and platelets (need regular blood counts) · Avoid pregnancy while taking it (can harm a developing baby) · May increase risk of skin cancer with long-term use (wear sunscreen)

L-glutamine (Endari) · Amino acid supplement (chronic disease-modifying therapy)

L-glutamine is an amino acid (building block of protein) that red blood cells use to protect themselves from oxidative damage (injury from harmful oxygen molecules). Sick cells are under constant stress and run low on glutamine. Giving extra glutamine helps cells make antioxidants (chemicals that neutralize damage), which keeps red cells healthier and reduces sickling. It is a powder taken by mouth twice a day for long-term prevention.

1. Patient mixes L-glutamine powder in water or food and swallows it
2. Glutamine is absorbed in the gut and enters the bloodstream
3. Red blood cells take up glutamine and use it to make glutathione and other antioxidants
4. Antioxidants protect the cell membrane and hemoglobin from damage, reducing sickling

SAFETY WATCH

Generally well tolerated · Can cause constipation, nausea, or stomach pain · Not safe in pregnancy or breastfeeding (limited data)

Voxelotor (Oxbryta) · Hemoglobin S polymerization inhibitor (chronic disease-modifying therapy)

Voxelotor is a daily pill that binds directly to hemoglobin S inside red blood cells and stabilizes it in the oxygenated (round, soft) form. This makes it much harder for hemoglobin S to stick together and form the long, stiff chains (polymers) that cause sickling. By preventing polymerization, red cells stay flexible, live longer, and carry oxygen better. This raises hemoglobin levels over time and reduces breakdown of red cells (hemolysis).

1. Patient takes voxelotor tablet by mouth every day
2. Drug enters bloodstream and diffuses into red blood cells
3. Voxelotor locks onto hemoglobin S and holds it in the oxygenated shape
4. Hemoglobin S cannot link together to form sickle polymers

5. Red cells stay round, flow better, and live longer in circulation

SAFETY WATCH

Can cause headache, diarrhea, stomach pain, rash · Can rarely cause allergic reactions (hives, swelling) · Monitor hemoglobin and liver tests

Crizanlizumab (Adakveo) · Monoclonal antibody against P-selectin (chronic disease-modifying therapy)

Crizanlizumab is an IV infusion given once a month to prevent crises. It blocks a sticky protein called P-selectin on the inside of blood vessel walls and on platelets. During a crisis, P-selectin acts like Velcro, grabbing onto white blood cells and sickled red cells and making clumps that clog vessels. By covering up P-selectin, crizanlizumab stops cells from sticking, so blood flows more smoothly and crises happen less often.

1. Patient receives crizanlizumab through an IV infusion over 30 minutes
2. Antibody circulates in the blood and binds to P-selectin on vessel walls and platelets
3. P-selectin is blocked and cannot grab onto passing blood cells
4. Less sticking means fewer clumps, better blood flow, and fewer vaso-occlusive crises

SAFETY WATCH

Infusion reactions (fever, chills, itching, nausea) can occur during or after infusion · May increase risk of infection (blocks part of immune signaling) · Back pain, joint pain, and diarrhea are common side effects

Red flags

- Fever above 100.4°F (38°C) — infection can turn deadly fast because the spleen is damaged
- Any sudden weakness, slurred speech, vision loss, or numbness — suspect stroke until proven otherwise
- Chest pain, trouble breathing, or coughing — may be acute chest syndrome, which can kill quickly
- Priapism (unwanted erection) lasting more than 2 hours — permanent damage starts around 4 hours
- Sudden severe belly pain or a fast-growing belly — could be splenic sequestration (spleen trapping blood) or liver crisis

Nursing priorities

1. Start IV normal saline at 1 to 1.5 times the maintenance fluid rate, watching lung sounds every 4 hours. — Hydration makes blood less thick so red cells flow better and sickle less, but giving too much fluid can cause fluid to leak into the lungs and trigger acute chest syndrome, so we give just enough to maintain good hydration without overloading.
2. Give IV opioid pain medicine on a fixed schedule every 3 to 4 hours, not waiting for the patient to ask, and add ibuprofen or ketorolac if creatinine (kidney function blood test) is normal. — Severe pain causes stress hormones that make more sickling happen and makes blood vessels tighten, so controlling pain breaks this cycle; scheduled dosing keeps pain controlled instead of letting it get bad between doses.
3. Apply oxygen by face mask or nasal cannula only if pulse oximetry (oxygen level monitor) shows oxygen saturation below 95 percent. — Low oxygen makes hemoglobin S sickle more, so we fix low oxygen right away, but giving oxygen when levels are normal can shut down the body's drive to make new red blood cells and does not help.
4. Have the patient use incentive spirometry (deep breathing device) 10 times every 2 hours while awake, and do chest physiotherapy (back patting) if ordered. — Pain makes patients take shallow breaths, which lets the bottom parts of the lungs collapse and collect mucus, creating acute chest syndrome; deep breathing keeps all lung parts open and moving.
5. Monitor temperature every 4 hours and report any fever of 100.4 degrees Fahrenheit or higher immediately to the provider. — Sick cell patients have damaged spleens (the organ that fights certain bacteria) from repeated sickling, so they cannot fight infections well and can become septic (blood infection) very quickly; fever needs blood cultures and IV antibiotics within 1 hour.
6. Check respiratory rate, oxygen saturation, and lung sounds every 4 hours, reporting any new cough, shortness of breath, or decreased air movement in lower lungs. — Acute chest syndrome often starts 24 to 72 hours after a crisis begins and shows up as new lung findings on exam before the chest X-ray looks bad; catching it early means starting antibiotics and possibly transfusion before respiratory failure happens.
7. Keep the patient warm with blankets and keep room temperature comfortable, avoiding cold drafts. — Cold temperature makes blood vessels get smaller and slows blood flow, which increases sickling and triggers more pain; warmth keeps vessels open and blood moving smoothly.
8. Assess for neurologic changes every 4 hours including speech clarity, arm and leg strength, and face symmetry, using stroke scale if any concern. — Stroke can happen suddenly when sickled cells block brain arteries, and the first few hours are critical for treatment; catching early signs like one-sided weakness or slurred speech can save brain tissue with emergency transfusion.

Sources

- American Society of Hematology (ASH) 2020 Sickle Cell Disease Guidelines
- National Heart, Lung, and Blood Institute (NHLBI) Sickle Cell Disease Evidence-Based Management
- CDC Sickle Cell Disease Resources
- UpToDate (evidence-based clinical reference)

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