SICKLE CELL DISCOVERY HANDBOOK

Crisis Prevention, Reversal and Management

Updated May 27th, 2026

For Physicians, Healthcare Workers, Patients, Caregivers and Families

RIGHT TREATMENT	RIGHT PLACE	RIGHT TIME
Inhalation oxygen	At home	Golden half hour

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Table of Contents

Foundation of Dr Sota Omoigui's Discovery (www.sicklecelldiscovery.com):

Golden Half Hour Reading Guide

Hypoxic stress Low oxygen triggers sickling	**Reversible phase** Early sickling can be restored	**Home oxygen** Start in the first 30 minutes	**Crisis stopped** Progression is prevented

Paradigm Shift

Reactive model	Proactive model
• Hospital care starts late	• Family becomes first responder
• Irreversible vaso-occlusion already occurring	• Oxygen begins at home
• Pain and organ injury already underway	• Reversible sickling is restored early

The right treatment - inhalation oxygen, in the right place - at home, at the right time - the golden half hour

Sickling

Under conditions of low oxygen - hypoxic stress (HgbS containing sickle cells) undergo shape transformation to the characteristic sickle form, progress from reversible to irreversible cells, become inflexible, obstruct the blood flow and then have to be destroyed to restore blood flow, resulting in a drop in hemoglobin.

Hgb S polymerization (sickling) under hypoxia (low oxygen) induced stress is not a single phenomenon but a two stage process, with an initial phase that is reversible by reoxygenation. See Scriver and Waugh in 1930, Franck and Chiu in 1983, Robert Hebbel in 1991, Zipursky et al in 1992, Melanie Gonick in 2015, Sota Omoigui in 2024 and 2025.

Time critical reoxygenation with home oxygen, administered in the golden half hour (30 minutes) can prevent, reverse and stop a sickle cell crisis. The consistent and rapid responses across age, geography, and severity validate the Omoigui time-sensitive model of oxygen therapy. Inhalational oxygen provided in the right place - at home, and at the right time- the golden half hour

Reactive Paradigm: By the time patients are in the hospital, they are already in an irreversible crisis and what is being implemented is the same reactive paradigm of the last 100 years after the vaso-occlusion from irreversible sickle cells had occurred and damage to all the organs was already occurring.

Pain is predictable. The greatest occurrence of a low oxygen environment occurs during sleep. Hargrove et al in 2003 concluded that low nocturnal oxygen saturation was highly significantly associated with a higher rate of painful crisis in childhood (P <.0001). In a study by Chang et al in 2024, of 21 screened participants, nine (43%) had sufficient nocturnal hypoxaemia to warrant oxygen therapy.

A Century of Failure

Lanzkron et all (2013) used the National Center for Health Statistics multiple-cause-of-death files to examine age at death and calculate mortality rates from 1979 to 2005, in patients with sickle cell disease. The median age at death in 2005 was 42 years for females and 38 years for males. The overall mortality rate increased 0.7% ($p<0.001$) each year during the time period studied. The adult (>19 years of age) mortality rate increased by 1% ($p<0.001$) each year during the time period studied. The pediatric mortality rate decreased by 3% ($p<0.001$) each year during the time period studied. Increasing hospitalizations and readmissions, are most often due to vaso-occlusive crisis, and explain the increase in mortality rates for adults observed in this study.

Vaso-occlusive crisis are the gateway to the complications of sickle cell disease, including severe pain, anemia, acute chest syndrome, avascular necrosis, kidney damage and death. Over hydration with intravenous fluids results in fluid overload with pulmonary edema, which has a mortality rate similar to that of acute chest syndrome.

Preventing, reversing and stopping a vaso-occlusive crisis is the key to reducing hospitalizations, blood transfusions and all the other complications of sickle cell disease. No medication administered orally can prevent, stop or reverse a sickle cell crisis. Not even Hydroxyurea. Only home oxygen in the golden half hour can do so.

Therefore the present reactive paradigm of the medical establishment waiting to treat an irreversible sickle cell crisis, in the hospital has failed this population.

Breaking the Cycle

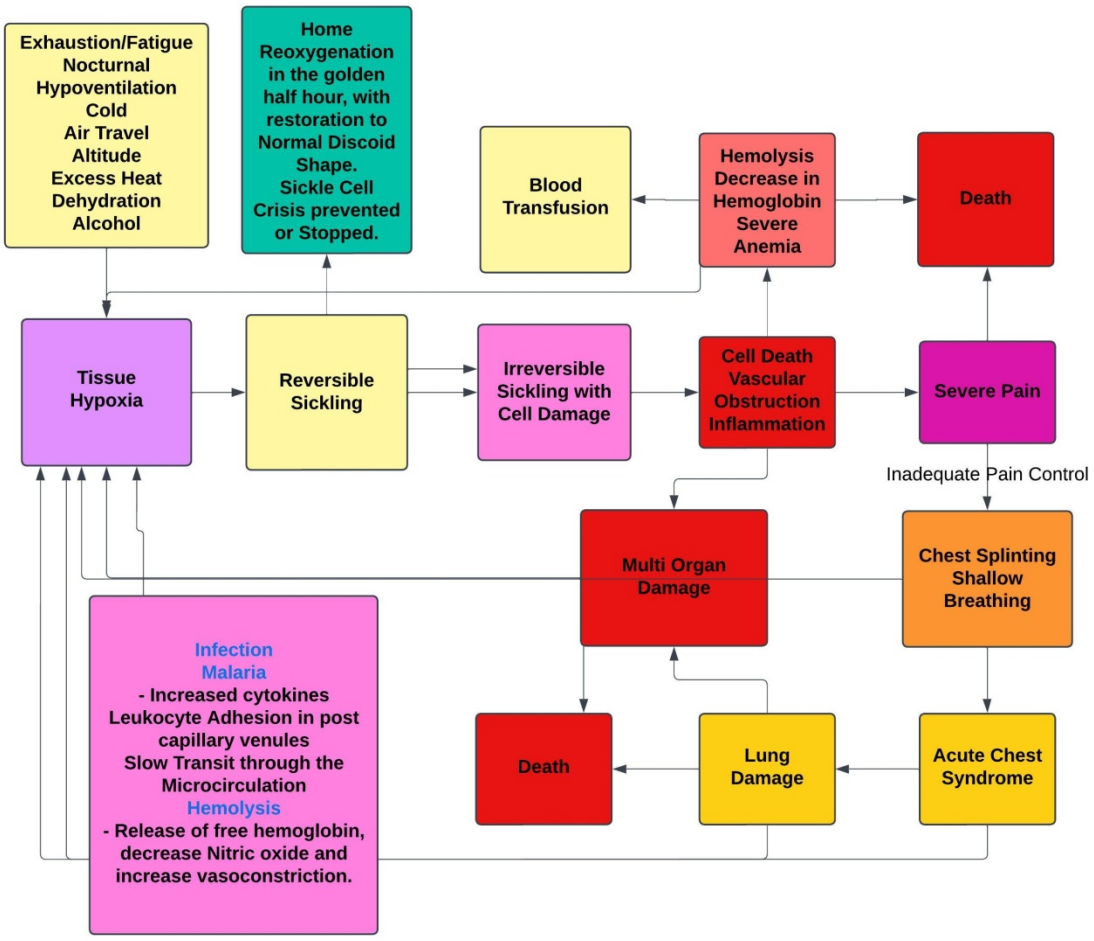

Figure 1. Breaking the Cycle diagram from the source handbook.

Inhalation Oxygen Specifications

Oxygen Equipment Summary

Cylinder	Concentrator
• Minimum size 680 liters E tank	• Continuous flow only - not pulse dose
• Preferably larger M tank	• Flow rate at least 1-2 L/min
	• Purity at least 90% +/- 3%
	• Rechargeable battery where power is erratic

Oxygen Cylinder

Minimum size 680 liters Etank, preferably bigger M tank

Oxygen Concentrator

1. Continuous flow only. Pulse dose not acceptable.

2. Flow Rate - At least 1-2 liters per min

3. At least 90% +- 3% purity across ALL flow rates. Concentrators with low quality sieve beds will have oxygen purity drop when flow rate increases.

4. Rechargeable battery - For those in Nigeria and due to erratic power supply.

Oxygen Safety

The safe use of oxygen therapy at home requires careful preparation and adherence to best practices. Below are key safety guidelines based on the provided materials:

1. Setup and Equipment

- Location: Keep oxygen equipment at least 6-10 feet away from open flames, heat sources, or electrical appliances to avoid fire hazards
- Ventilation: Place equipment in a well-ventilated area to prevent oxygen buildup, which increases fire risk
- Storage: Store oxygen cylinders upright and secure them to prevent tipping

2. Operational Safety

- Flow Rate Settings: Ensure the oxygen flow rate is set as prescribed by your healthcare provider. Improper settings can lead to insufficient oxygen or overexposure
- Monitoring Devices: Use a pulse oximeter to monitor blood oxygen levels regularly, ensuring the therapy is effective

3. Fire Safety Precautions

- No Smoking: Strictly prohibit smoking near oxygen equipment
- Fireproof Environment: Avoid using flammable products like petroleum-based ointments or alcohol near oxygen

4. Maintenance

- Regular Checks: Inspect oxygen equipment for leaks or malfunctions. Replace or repair faulty components promptly
- Battery Management: If using portable oxygen concentrators, ensure batteries are charged and maintain a backup

5. Emergency Preparedness

- Backup Plan: Have an alternative oxygen supply (e.g., cylinders) in case of equipment failure
- Contact Information: Keep emergency numbers, including oxygen suppliers and healthcare providers, readily available

6. Education and Training

- Train caregivers and family members on the proper use and handling of oxygen equipment to ensure safe and effective therapy

By following these guidelines, you can ensure the safe and effective use of home oxygen therapy for managing sickle cell disease or other conditions

Hydroxyurea

Akingbola et al found out in their 2018 study that a "fixed low-dose" regimen of 500 mg daily (10 mg/kg in children to max of 500 mg daily) of Hydroxyurea in adults to be just as effective as higher doses, with increases in hemoglobin F, reduction of pain crises, acute chest syndrome and blood transfusions, but with a lower chance of toxic side effects such as decrease in hemoglobin, decrease in white blood cells with increased risk of infection and decrease in platelets with increased risk of bleeding. (https://doi.org/10.1182/blood-2018-99-114990)

With home oxygen, the fixed low dose of 500 mg /day in adults, should work well with home oxygen and yet avoid the toxic side effects of Hydroxyurea.

Air Travel

The initial causation of hemoglobin polymerization (sickling) as due to hypoxia (low oxygen), was described by Hahn and Gillespie in 1927. Sea Level Baseline: The partial pressure of oxygen at sea level is roughly 159-160 mmHg (21% of (760 mmHg) total pressure). Aircraft cabins are pressurized to an "altitude" of 5,000-8,000 feet, which corresponds to a PO2 of approximately 118- 125 mmHg. Thus at 8,000 feet, the PO2 is about 74% of sea-level pressure. Starting after 10 mins of ascent in an aircraft, with an altitude greater than 10,000 feet, oxygen saturation in people with sickle cell disease drop from an average of 93 to 95% at sea level to 77% to 83%. Complications that have resulted in people flying without supplemental oxygen have included, pain crisis, avascular necrosis of the bones, splenic infarction and death even while still in the aircraft. The simplest solution, - Dr Sota Omoigui's discovery of providing inhalational oxygen in the right place - in the aircraft, and at the right time- the golden half hour at take-off. And for the entire duration of the flight.

> Note: Use only continuous flow oxygen concentrators or compressed medical oxygen cylinders provided by the airlines. Do NOT use pulse dose oxygen concentrators as they have to be triggered by breath and do not provide sufficient oxygenation to prevent a crisis.

InFlight Flow rate: Children 0.5-1.5 lpm Adults - 1-2 lpm

Exercise

Exercise including soccer, basketball, cricket, gym, swimming etc may be done with the following caveats:

No sauna - excess heat can precipitate a crisis

Heated pools for swimming - cold water can precipitate a crisis

After exercise, use oxygen for at least one hour before sleep - whether in the daytime or night time.

Prevention of Crisis

- A/ Vaccination against pneumococcal infection- prevena vaccine (adult and children)
- B/ Vaccination against salmonella/Typhoid infection - Typhrix vaccine (both adult and children)
- C/ vaccination against meningococcal infections (especially the warriors who live in Savannah and Sahel regions of Africa eg northern Nigeria)
- D/ Effective Antimalarial prophylaxis - (use of Paludrin) in combination with effective malaria infection control measures - regular use of insecticide treated bed nets, netting of all the doors and windows in the house, regular use of mosquito insecticides, good environmental sanitation - regular refuse disposal and prevention of water logs around the house etc in order to prevent mosquito bites which are the vectors of malaria parasites.
- D/ Hydroxyurea at low fixed dose of 500 mg daily with frequent monitoring for side effects together with the other routine medicines
- E/ Home oxygen therapy in the golden half hour at the earliest signs of crisis or after exposure to any of the triggers of the crisis.
- F/ Healthy lifestyle Behaviour -
- 1/ Avoidance of toxic substances and behaviour - Alcohol consumption, cigarette smoking, street drugs use, reckless sexual activity, coffee and caffeinated drinks
- 2/ Healthy dietary Protocol - consumption of all the vegetables and fruits in season generously without exemption. Minimise the consumption of processed and ultra processed foods etc
- 3/ Effective mental healthy management - avoiding negative emotions - anger, bitterness, anxiety, fear, depression etc and ensure positive emotions at all times - joy, peace, happiness, satisfaction, self confidence, etc

Use of Home Oxygen

When there is any stressor during the day, as listed below, the person should use oxygen as described:

Inhale oxygen for 10 minutes to 2 hours before sleep or use the oxygen for as long as needed for part or the entire duration of sleep.

Flow rate:

Children 0.5-1.5 lpm

Adults - 1-2 lpm

> Note: Sleep is the most dangerous time as the low oxygen environment will tip the person into a crisis:

Physical stress: eg from physical activity

Intellectual stress eg preparing for exams, writing papers

Environmental stress eg cold environment, high altitude, air travel

Physiological stress eg during sleep, excess heat, dehydration, pain, emotional stress, infection, malaria.

> Note: Infection and malaria, bone marrow suppression from toxic doses of Hydroxyurea or hemolytic crisis from antibodies in improperly cross matched blood transfusions, also need to be prevented and timely treated. Otherwise there will be more reversible sickle cells than oxygen can restore.

Treatment: use oxygen within the golden half hour to stop a crisis.

Mechanisms: How Malaria Triggers Sickle Cell Crisis

Malaria to Crisis Cascade

Hemolysis Hemoglobin drops	**Hypoxia** HbS polymerizes	**Inflammation** Adhesion increases	**Vaso-occlusion** Pain crisis and organ risk

A. Increased Hemolysis -> Severe Anemia

Sickle cell patients already have fragile RBCs. Malaria: Destroys infected RBCs. Also causes immune destruction of uninfected RBCs, Suppresses bone marrow temporarily

Result:

Rapid drop in hemoglobin -> tissue hypoxia -> sickling worsens.

This alone can trigger: Pain crisis, Acute splenic sequestration, Heart strain

B. Hypoxia Worsens Sickling

Malaria causes: Fever, Poor oxygen delivery, Metabolic acidosis

Low oxygen levels cause HbS to polymerize -> RBCs sickle more.

This leads to: Vaso-occlusion, Severe bone pain, Organ ischemia

> Note: Home oxygen in the golden half hour could blunt hypoxia-driven sickling.

C. Inflammation Increases Vascular Adhesion

Malaria triggers massive inflammatory cytokines: TNF-alpha, IL-1, IL-6

Inflammation causes: Endothelial activation, Increased adhesion of sickled RBCs

Microvascular blockage. This significantly increases risk of: VOC, Acute chest syndrome, Stroke

D. Splenic Stress

Malaria heavily affects the spleen. In sickle cell: the spleen may already be enlarged (children) or fibrosed (adults). Malaria can cause: Splenomegaly, Acute splenic sequestration, Splenic rupture (rare but possible)

This may explain recurrent sequestration episodes in endemic regions.

E. Increased Blood Viscosity

Malaria causes: RBC rigidity, Clumping (rosetting). Sickle cell causes:

Deformed RBCs, Sluggish blood flow.

Combined effect: Microvascular blockage risk multiplies.

Clinical Consequences in SCD Patients

Complication	Why It Happens
Severe anemia	Massive hemolysis
Pain crisis	Hypoxia + inflammation
Acute chest syndrome	Lung inflammation + sickling
Stroke	Cerebral vessel occlusion
Acute kidney injury	Hemolysis + ischemia
Death	Rapid Hb drop + organ failure

Children under 5 are especially vulnerable.

Symptoms of Sickle Cell Disease in a 6 Months-2 years old Child

Infant Recognition Guide

Common signs

- Excessive crying or irritability
- Hand-foot swelling
- Fever
- Pallor or jaundice

Emergency signs

- Enlarged spleen or abdomen
- Fast heartbeat or weakness
- Sleepy or unresponsive child
- Fast breathing or chest retractions

At this age, symptoms are often different from older children, because fetal hemoglobin (HbF) is still present but starting to decline.

1. Pain Crisis (Often the First Sign)

In infants, pain may not look obvious. Instead, you may see:

Excessive crying, Irritability, Refusal to move a limb, Fussiness when touched or carried.

Swelling of hands and feet

This is called dactylitis (hand-foot syndrome) and is often the first presentation.

2. Swelling of Hands and Feet

Usually occurs between 6 months and 2 years

Due to blockage of blood vessels in small bones

3. Fever

Fever is very dangerous in infants with sickle cell because:

They are at high risk of infection (especially pneumococcus)

The spleen may not work properly

Any fever > 38 degrees C (100.4 degrees F) should be treated as an emergency.

4. Pallor (Anemia)

You may notice:

Pale lips, Pale palms, Fatigue, Weak feeding

5. Jaundice

Yellowing of: Eyes, Skin

This happens because of rapid red blood cell breakdown.

6. Enlarged Spleen (Splenic Sequestration)

This is an emergency and requires proceeding immediately to the hospital.

Signs include:

Sudden weakness

Fast heartbeat

Enlarged abdomen

Child becoming sleepy or unresponsive

Rapid drop in hemoglobin

Parents should be trained to check spleen size daily, especially in infancy.

7. Poor Growth or Feeding

Refusal to breastfeed

Poor weight gain

Frequent illness

8. Breathing Symptoms

These may include: Fast breathing, Chest retractions, Grunting

Reduced oxygen saturation.

This can indicate:Acute chest syndrome, Severe anemia, Infection

Oxygen Flow Rate in a 6 Months-2 years old child with Sickle Cell

For infants, oxygen must be used carefully but early.

Recommended Initial Flow Rate

For home or emergency use:

0.5 to 1.5 L/min via nasal cannula

Most commonly:

Start at 0.5L/min to 1 L/min

Adjust based on symptoms

When to Use Oxygen in Infants

Use oxygen early if there is:

- Pain or irritability
- Fever
- Weakness
- Fast breathing
- Pale appearance
- Reduced feeding
- Signs of infection
- Before or during transport to hospital

Early use is especially important in resource-limited settings, such as in Nigeria

Duration

Use until symptoms improve

Continue during transport or medical evaluation

Can be used intermittently at home during early crisis

Safety Notes

Use humidified oxygen if possible

Monitor for nasal dryness

Avoid excessive high flow unless medically supervised

Priapism

Priapism Early Response Concept

Nocturnal hypoxia Occurs commonly during sleep	**Transient attack** Reversible sickling phase	**Home oxygen** Use in golden half hour	**Escalate care** Emergency care if prolonged

Priapism, a prolonged and often painful erection, is a known complication of sickle cell disease (SCD) due to sickling of the red blood cells, impaired blood flow and the occlusion of blood vessels. Up to 35% of men with sickle cell disease are affected.

Sickling in the penile circulation manifesting as priapism is no different from sickling elsewhere. Under conditions of low oxygen - hypoxic stress (HgbS containing sickle cells) undergo shape transformation to the characteristic sickle form, progress from reversible to irreversible cells, become inflexible, obstruct the blood flow and can result in fibrosis or damage to the erectile tissue. Most occurrences of priapism occur during sleep when low oxygen at bedtime increases the likelihood of nocturnal hypoxemia. Prolonged episodes of priapism that result in erectile tissue fibrosis are often preceded by periods of stuttering (recurrent) priapism or acute transient attacks which remits and relapses with or without medical intervention. These transient attacks constitute reversible sickling that can be restored to their normal discoid shape by home oxygen in the golden half hour thereby preventing progression to irreversible sickling. Home oxygen has reversed priapism in several cases sometimes as early as within 10 mins of use. Priapism can be prevented by using oxygen at bedtime for 1 hour or more including throughout sleep as needed.

When priapism becomes recurrent or prolonged, surgical treatment may be necessary to prevent tissue damage and preserve erectile function.

Home Oxygen in the golden half hour will restore reversible sickling back to normal and has reversed priapism within 10 minutes in several patients.

Home oxygen may be combined with a low daily dose of Finasteride which is an effective and safe form of treatment for recurrent priapism in SCD. Doses are 1-2 mg orally once daily in children and adolescents and 1-5 mg orally once daily in adults. Finasteride acts by inhibiting the type 2 isoform of the 5 alpha-reductase enzyme, which is responsible for the conversion of testosterone into dihydrotestosterone predominantely in hair follicles and the prostate. However, the exact mechanism through which this drug reduces the frequency of priapism attacks resulting from vaso-occlusive events is unclear. There is no significant androgenic activity in prepubertal children that would justify the use of this drug; however, it has been speculated that its effect may be mainly due to its ability to inhibit calcium efflux from smooth muscle cells . It is possible that finasteride may reduce the rate of nocturnal spontaneous erections. Finasteride has little effect on the level of serum testosterone and it has no other steroidal, androgenic, estrogenic or progestinic effects (19). Finasteride acts by inhibiting the action of 5-alpha-reductase type 2 and thus inhibiting the conversion of testosterone into DHT. This enzyme occurs most abundantly in hair follicles and prostate tissue. Therefore, the use of a low dose of finasteride might have little effect in the pubertal androgen development and epiphyseal closure. See: https://www.scielo.br/j/ibju/a/ghDqYB36cGDd69KShf4gr3S/?format=html&lang=en

Surgical Treatment Options for Priapism in Sickle Cell Disease:

Direct injection or aspiration of blood (corporal aspiration) often combined with irrigation) is a first-line, highly effective emergency treatment for ischemic priapism in sickle cell disease (SCD), particularly for episodes lasting over 4 hours. It removes viscous, deoxygenated blood from the corpora cavernosa to relieve pain and prevent permanent erectile tissue damage.

See: https://emottawablog.com/2023/07/approach-to-priapism/

https://www.medmastery.com/guides/emergency-procedures-clinical-guide/step-step-guide-two-key-procedures-treating-priapism

Your first line of treatment should involve the direct injection of phenylephrine.

Key Aspects of Injection or Aspiration in SCD Priapism:

How to perform a direct phenylephrine injection for treating priapism

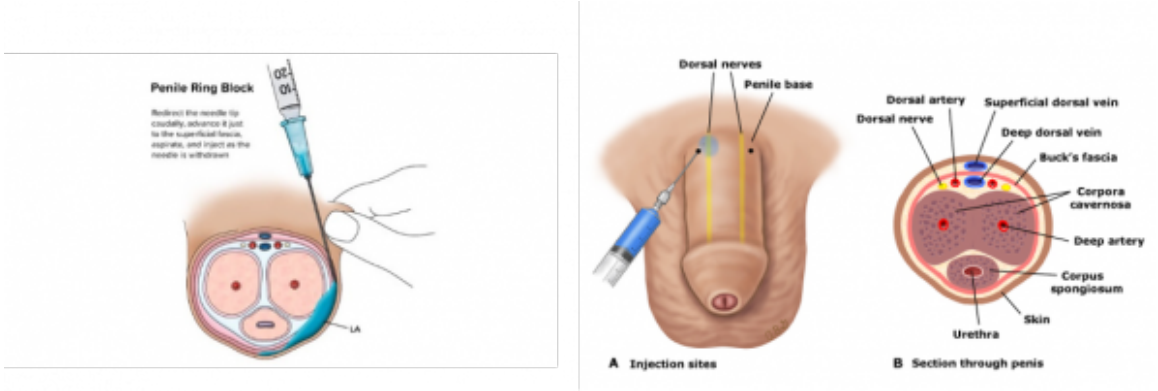

Figure 2. Priapism injection/aspiration illustration from the source handbook.

Pick a side of the penis that is most convenient for you and clean the lateral aspect with alcohol.

Draw 0.5 mg of phenylephrine into a 27 gauge (G) syringe.

Place the needle into the corpus cavernosum on the selected side, close to the base of the penis at the two or ten o'clock position.

Aspirate a little to confirm that you are in the corpus, and then inject the phenylephrine.

Remove the needle and wait to see if the priapism resolves in the next 10 minutes.

If the erection does not resolve, and the urologist is not available, it's time to perform the more invasive aspiration and irrigation procedure:

How to perform the aspiration and irrigation procedure for treating priapism

Clean the penis with a sterilizing solution and place a drape.

Perform a dorsal penile nerve block by injecting 1 cc of 1% lidocaine at the dorsal base of the penis. The nerves are shallow, so you won't need to go deep. Alternatively, you can perform a local small skin wheal at either the two or ten o'clock position where you did your phenylephrine injection.

Insert the 18 gauge (G) butterfly needle into the corpus at a 45 degrees angle toward the base of the penis (like the phenylephrine injection). Have an assistant slowly suction 20 mL of blood out. The corpus spongiosum on the ventral side of the penis is avoided as this could result in urethral injury.

If you start to get bright red arterial blood into the syringe, and the erection resolves, you can stop and remove the 18 G butterfly needle.

If the priapism persists, draw 20 mL of the prepared phenylephrine solution into a clean syringe. Keep the 18 G needle in place, attach the syringe, inject it into the corpora, then aspirate the solution out. Repeat this step twice or until the priapism resolves.

If the priapism persists (which is very unusual), you will need to have a urologist intervene surgically. More often, the erection will resolve.

Efficacy: These methods are 95% effective in producing immediate detumescence in young patients with SCD, often allowing for outpatient management.

Timing: To avoid permanent erectile dysfunction, this intervention should occur as soon as possible, ideally within 24 hours of onset.

Shunt Procedures:

Al-Ghorab Shunt: This is a surgical procedure in which a shunt is created to allow blood flow from the corpus cavernosa to the corpus spongiosum, bypassing the blocked areas. This helps relieve the pressure and prevents ischemic damage to the erectile tissue.

Winter's Shunt: This involves creating a communication between the corpus cavernosa and the glans penis. It is usually performed when priapism is refractory to conservative management or when other shunts are ineffective.

Penile Vein Shunt: This procedure is done by creating a direct connection between the venous outflow and the cavernosal system. It can help restore normal blood flow to the penis, decreasing the risk of ischemia and necrosis.

Penile Prosthesis Implantation:

In cases where priapism has caused irreversible erectile tissue damage, a penile prosthesis may be implanted to restore erectile function. This is usually considered after other management strategies fail or if priapism becomes chronic.

Other Surgical Options:

Penile Arterialization: In rare cases, surgeons may try to redirect arterial blood into the cavernous bodies to improve blood flow and prevent future episodes of priapism.

Tissue Removal: If there is extensive tissue necrosis from prolonged priapism, partial removal of affected tissue may be necessary.

Timing and Considerations:

Surgical intervention is typically considered when priapism lasts for more than 4 hours or becomes recurrent. Timely intervention is crucial to prevent erectile dysfunction and other complications.

The choice of surgery depends on the severity of the priapism, the duration of the episode, and the overall health and age of the patient.

A combination of shunt procedures and supportive care (such as home oxygen combined or medications to reduce sickling) may be used for optimal results.

Exchange blood transfusion should be avoided in these patients due to ASPEN syndrome, or Association of Sickle Cell Disease, Priapism and Exchange Transfusion and Neurologic Events. This uncommon outcome of exchange transfusion was first described in 1993 by JF Siegel described as severe headache followed by neurologic events like seizure and decreased level of consciousness requiring ventilatory support. This was conjectured to be due to cerebral ischemia from a sudden increase in percent total hemoglobin and release of vasoactive substances following penile detumescence.

Leg Ulcers

Leg Ulcer Management Framework

Prevention / physiology	Wound care
• Avoid nocturnal hypoxia	• Compression when tolerated
• Use home oxygen at bedtime as needed	• Culture-guided antibiotics if infected
• Address venostasis and edema	• Moist dressings and gentle debridement

See: https://www.woundsafrica.com/sickle-cell-leg-ulcers-1

See: https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.19584

Ulcerations in SCD are caused by local vaso-occlusive crises, resulting in cutaneous microvascular infarctions. Under conditions of low oxygen - hypoxic stress (HgbS containing sickle cells) undergo shape transformation to the characteristic sickle form, progress from reversible to irreversible cells, become inflexible, obstruct and impair the blood flow in the skin. Inadequate tissue perfusion is an important factor in the development of chronic wounds and delayed healing. Home oxygen in the golden half hour restores reversible sickle cells to their normal discoid shape thereby preventing progression to irreversible sickling. Leg ulcers can be prevented and managed by using oxygen at bedtime for 1 hour or more including throughout sleep as needed.

The majority of SCD ulcerations manifest spontaneously, without any associated trauma.5 Patients usually experience the initial symptom of spontaneous pain, followed by induration, hyperpigmentation or subcutaneous necrosis, blister formation and destruction of the epidermis.5 In some patients, leg ulcers may occur after minor trauma or scratching. Sickle cell ulcers usually show around and behind the ankle, they can also present around the base of the toes in more extreme cases. In SCD patients, microscopic examination of leg ulcer beds has revealed capillary blood stasis and venostasis. The resulting pressure from venostasis is greatest in the peri-malleolar (ankle) region, which is the primary site for SCD leg ulcers.5, 30 Stasis may also facilitate local sickling due to prolonged exposure of RBC to hypoxia and local vaso-occlusive crisis, increasing the risk of leg ulcer development.31 Venous hypertension is commonly associated with venous insufficiency, caused by poorly functioning incompetent venous valves. Venous incompetency can be diagnosed using Doppler duplex ultrasound. Venostasis around the ankle, can result in the development of leg ulcers that resemble arterial ulcers. Following the development of the ulcer, healing is hindered as a result of factors commonly observed in venous ulceration, including venous insufficiency, and tissue swelling (edema)

Venous compression stockings is essential in all SCD patients with leg ulcers, regardless of venous incompetency status. The site of the ulcer can make the standard compression therapy less effective. If the ulcer is behind the ankle, the compression bandage or sock will not generally apply the level or dosage of compression to the wound bed that it requires to heal. Consider the application of special padding to the ulcer behind the ankle or the use of compression strapping.

While sickle cell ulcers are not caused by venous hypertension, it is clear that the ankle mobility is reduced thus impacting on venous return; any wound on the leg heals faster with compression therapy.

Antibiotic Therapy

Bacterial colonization of leg ulcer area is an expected phenomenon that needs to be treated by systematic or local antibiotic therapy if signs of local infection are present. Staphylococcus Aureus has been reported to be the most common bacterium present in SCD leg ulcers.

Antibiotic therapy for sickle cell leg ulcers (SCLUs) focuses on managing bacterial colonization, treating acute secondary infections, and promoting wound healing. Because these ulcers are highly susceptible to infection, targeted antibiotic regimens are a cornerstone of treatment.

1. Topical Antibiotics

Topical preparations are used to decrease ulcer size and control superficial bacterial overgrowth (such as Staphylococcus aureus or Pseudomonas aeruginosa).

Triple Antibiotic Therapy: Clinical trials have demonstrated that topical application of a triple antibiotic (e.g., Neomycin, Bacitracin, Polymyxin B) significantly accelerates the reduction of ulcer size over 8 weeks compared to controls.

Specialized Gels: In refractory cases, specialized combinations containing agents like amikacin, levofloxacin, and vancomycin may be used.

> Note: Topical antibiotics are generally used short-term to avoid antimicrobial resistance and contact sensitization.

2. Systemic (Oral/IV) Antibiotics

Systemic antibiotics are required when there are clinical signs of deep-tissue infection, cellulitis, or systemic symptoms.

First-Line Oral Therapy: For standard infected ulcers, oral flucloxacillin is often the first-line treatment for adults, though wound cultures dictate specific therapy.

Intravenous (IV) Therapy: If the patient presents with a fever over 38■C

(100.4■F) or elevated inflammatory markers (e.g., high C-reactive protein), immediate hospitalization for IV antibiotics and close monitoring is recommended.

3. Adjunctive Wound Care

Antibiotic therapy alone is rarely sufficient to heal SCLUs. Comprehensive care must run concurrently:

Debridement: Regular surgical removal of necrotic (dead) tissue is essential to prevent bacterial harboring.

Compression & Elevation: Use of zinc oxide occlusive dressings (e.g., Unna boots) and leg elevation helps manage localized swelling and improves venous return.

> Note: Because leg ulcers are complex and bacterial colonization is inevitable, all antibiotic therapies should be guided by wound swab cultures and managed in consultation with an infectious disease specialist or a hematologist.

Pain Management

Leg ulcers are notoriously painful and frequently undertreated. Poor pain control reduces tolerance for dressing changes, compression, and debridement. Practical measures include:

procedure-related topical anesthesia where appropriate including Topical Lidocaine

systemic analgesics tailored to the patient such as nonsteroidal anti-inflammatory e.g. Diclofenac alone or in combination with opioids such as Hydrocodone or Oxycodone. Do not use Pentazocine. Effective pain management should enable a reduction in stress-induced catecholamine secretion, and can counter vasoconstriction.1

addition of neuropathic pain agents such as Pregabalin, Gabapentin or Oxcarbazepine, when the pattern suggests a neuropathic contribution

improved edema control and wound inflammation control, which often reduces pain indirectly.

Skin grafts, dermal matrices, and bioengineered skin

Advanced closure methods such as split-thickness skin grafting with healthy skin, dermal matrices, and bioengineered skin substitutes have all been used with good results for selected, well-prepared wounds after systemic and local optimization.

Hyperbaric oxygen

Hyperbaric oxygen promotes wound healing by flooding hypoxic tissues with high concentrations of oxygen, which accelerates new blood vessel growth, reduces localized inflammation, and aids in bacterial defense mechanisms.

Relieves Hypoxia: Breathing 100% oxygen under pressure increases dissolved oxygen in the blood, delivering it directly to the nutrient-deprived tissue around the ulcer.

Reduces Inflammation: Pressure and hyperoxia suppress harmful inflammation and help minimize tissue swelling.

Stimulates Angiogenesis: HBOT encourages the proliferation of fibroblasts and new blood vessels, which are essential for closing chronic, non-healing wounds

Healing protocols often pair daily hyperbaric oxygen therapy (HBOT) sessions with standard wound care and subsequent procedures like skin grafting.

Pentoxifylline

Pentoxifylline is an oral platelet aggregation inhibitor, which also enables better red-blood-cell deformation, potentially decreasing blood viscosity, platelet aggregation, thrombus formation, and plasma fibrinogen levels. This increases microcirculatory flow and tissue oxygenation, making it a good modality for treating leg ulcers in patients with sickle cell disease. One case report reported that 400 mg of oral pentoxifylline, taken three times a day, completely healed a leg ulcer in a patient with sickle cell disease within 3 months. In nine randomized clinical trials, RCTs involving 572 patients, pentoxifylline combined with compression bandages improved ulcer healing. See: https://pubmed.ncbi.nlm.nih.gov/10796661/

The 2014 clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum recommend the use of pentoxifylline for the treatment of long-standing or large venous leg ulcers. As venous insufficiency is often present in SCD patients, pentoxifylline may be a good treatment option for them.

Negative pressure wound therapy (NPWT)

NPWT can be considered in selected larger or more complex ulcers when exudate control and granulation support are needed, but pain, ischemia, and tolerance must be considered.

Surgical Treatment of Venous Insufficiency

When superficial venous insufficiency, without deep venous insufficiency, is detected by venous Doppler ultrasound, surgical treatment of the incontinent vein sections can be suggested to reduce the risk of leg ulcer recurrence, by analogy with venous leg ulcers. Endovenous ablation of superficial venous reflux may result in complete healing of small venous leg ulcers, considering that the presence of a venous incompetence worsens the healing prognosis.

Wound bed preparation

Cleansing

Use simple cleansing with normal saline or another non-cytotoxic solution. Routine harsh antiseptic scrubbing should be avoided.

Debridement

Debridement should usually be gentle and conservative. Reviews recognize that these ulcers are ischemic, painful, and prone to worsening if over-traumatized. Suitable approaches include:

Conservative sharp debridement, repeated gentle debridements at each session, is usually better than a single aggressive debridement.

autolytic debridement

enzymatic debridement, where available

Avoid aggressive repeated excision in a poorly perfused, very painful ulcer unless there is a clear surgical indication.

Dressings and moisture balance

As with other chronic wounds, use dressings based on the wound bed:

hydrogel for dry wound beds

hydrofiber/alginate for more exudative ulcers

foam as a secondary absorbent layer

Super absorbent secondary dressings for highly exudative ulcers

non-adherent silicone contact layers when the wound is painful or fragile

Antimicrobial dressings such as iodine-, PHMB-, or silver-containing products may be reasonable when bioburden is a concern. SCD-related ulcers are often colonized, and especially at the onset of the treatment, some weeks of treatment with antimicrobial dressings may be indicated.

The goal is a stable, moist environment without maceration.

Compression therapy

Compression is often underused in sickle-cell ulcers because clinicians worry about ischemia. Reviews nonetheless note that many patients also have venous stasis, edema, or mixed disease, and compression may help when used thoughtfully.

Practical approach

Ischemia is rarely an issue in younger patients with SCD, and most patients will tolerate moderate compression therapy.

begin with light to moderate compression, often around 20-30 mmHg

consider short-stretch bandaging or adjustable wraps

escalate gradually depending on pain and tolerance

Avascular Necrosis

Avascular Necrosis Pathway

Sickling Blood flow impaired	**Bone hypoxia** Perfusion decreases	**Bone injury** Necrosis/collapse risk	**Management** Oxygen, imaging, pain control, surgery if needed

Under conditions of low oxygen - hypoxic stress (HgbS containing sickle cells) undergo shape transformation to the characteristic sickle form, progress from reversible to irreversible cells, become inflexible, obstruct and impair the blood flow in the bones. The bones of the human body are made up of living cells that need an oxygenated blood supply to stay healthy. Inadequate bone perfusion is an important factor in the development of avascular necrosis. Home oxygen in the golden half hour restores reversible sickle cells to their normal discoid shape thereby preventing progression to irreversible sickling. Sickled cells can block blood flow in blood vessels that provide blood to bones in our body. When the bone does not get enough oxygen, the bone tissue can die, a complication known as avascular necrosis (AVN). When there is not enough blood reaching the bone, the joint can narrow and the bone can collapse. AVN can affect single joints or multiple joints at the same time. . AVN is a highly common and painful complication, affecting up to 50% of adults by age 35.

Avascular Necrosis can be prevented and managed by using oxygen at bedtime for 1 hour or more including throughout sleep as needed. Prolonged hypoxia as may occur in high altitude airline flights, longer than 30 minutes, without supplemental oxygen, is a risk factor for development of avascular necrosis.

Avascular Necrosis is also called:

Osteonecrosis.

Aseptic necrosis.

Ischemic necrosis of bone.

Avascular Necrosis can happen to any bone, but most often it develops in the ends of long bones, such as the:

Thigh bone (femur), especially the upper part-the ball in the hip socket. The lower end, which is part of the knee joint, is also often affected.

Upper arm bone (humerus), especially the upper part-the ball in the shoulder joint.

Less often, the bones of the elbows, knees, ankles, feet, wrists and hands are affected.

When the disease involves part of a bone in a joint, it can lead to the breakdown of the bone and arthritis.

Diagnosis

The primary symptom of Avascular Necrosis is pain, and diagnosis requires imaging methods including:

Magnetic resonance imaging (MRI) scan - The most sensitive imaging tool, often able to detect AVN before it shows up on standard X-rays.

Bone scan

Computerized tomography (CT) scan

X-rays do not always show early stages of AVN. But they do show later stages of AVN where bone collapse or joint space narrowing has occurred.

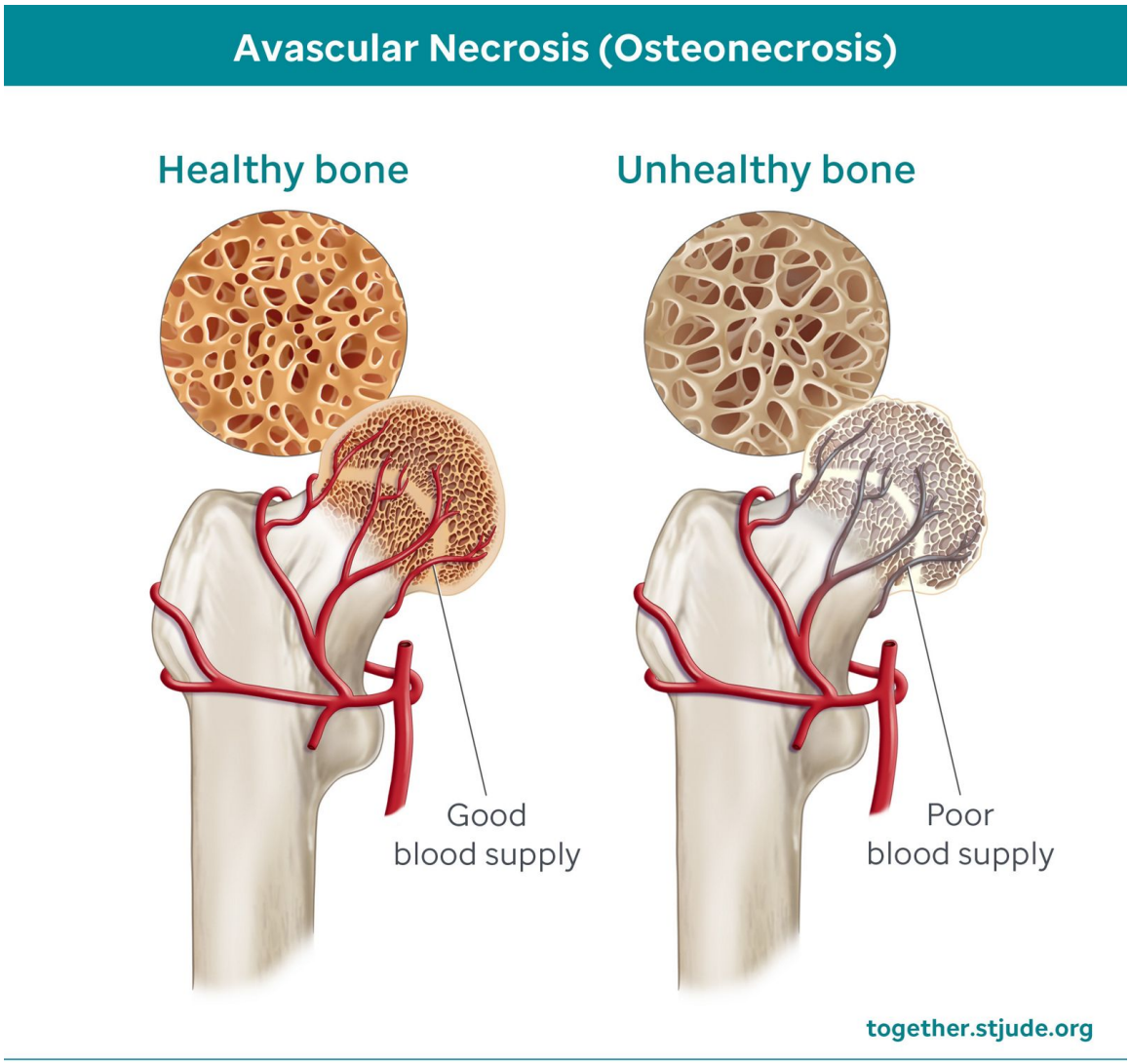

Figure 3. Avascular necrosis illustration from the source handbook.

The most common location of an AVN occurring is the hip joint, but it can also occur in other areas of the body.

Symptoms

Early stages may be asymptomatic, but as the disease progresses, it causes:

Deep, throbbing pain in the affected joint (especially the groin or thigh for hip AVN).

Pain that worsens with weight-bearing or activity.

Joint stiffness and a limited range of motion.

A noticeable limp if the femoral head begins to collapse.

What are the stages of avascular necrosis?

AVN progresses through several stages

Stage 1: mild symptoms, no visible damage on X-rays

Stage 2: bone starts to show signs of damage, but the shape remains intact

Stage 3: more significant bone damage and changes in the shape of the bone

Stage 4: bone collapse and severe joint damage, often requiring surgery

Risk factors may include:

Injury

A broken or dislocated bone or a joint injury may damage the surrounding blood vessels. This can decrease the blood supply to the bone and lead to Avascular Necrosis.

Medications

Corticosteroids. These medicines, commonly used to treat asthma, arthritis, systemic lupus erythematosus (lupus), and other conditions, act by reducing inflammation. While the reasons are unclear, they increase the risk of Avascular Necrosis when they are used for long periods at high doses. The risk of Avascular Necrosis is low when they are used on a short-term basis at lower doses.

Excessive Alcohol and Tobacco Use

Excessive use of alcohol is a risk factor for Avascular Necrosis, but why it makes people more likely to develop the disease is unclear. Overuse of alcohol can cause fatty substances to build up in the blood vessels and can increase cortisol (hormone that can cause blood vessels to narrow) levels in the blood. Together, these may decrease blood flow to the bone and lead to Avascular Necrosis. Research has also shown that excessive tobacco use is also a risk factor.

Medical Conditions

Some medical conditions may increase the risk of Avascular Necrosis, including:

Certain blood disorders, such as sickle cell disease.

Certain types of cancer, such as leukemia.

Decompression sickness, also known as divers' disease, the bends, or caisson disease.

Gaucher disease.

Gout.

HIV infection.

Pancreatitis.

Rheumatoid arthritis.

Lupus.

Medical Interventions

Some medical interventions may increase the risk of Avascular Necrosis, including:

Chemotherapy.

Kidney or other organ transplantation. The use of corticosteroids to avoid organ rejection may be a contributing factor.

Radiation treatment.

Management and Treatment

Treatment depends on the severity and stage of the bone damage:

Conservative management of AVN include:

Home Oxygen

Physical therapy to improve range of motion

Heat or cold therapy

Medication to relieve pain and inflammation

Mobility aids or assistive devices to take weight off the affected joint

Rest and avoiding activities that put extra stress on the joint

Surgery for avascular necrosis

Some patients may need surgery to improve blood flow and relieve pressure within the bone. These options can include:

Core decompression: Core decompression removes the inner layer of bone. This may reduce pressure within the bone and create an open area for new blood vessels to grow. Sometimes a piece of healthy bone with good blood vessels is put into this area to speed up the process. This procedure works best in the earliest stages of AVN.

Bone graft: Surgery to treat AVN may include a bone graft to replace and rebuild damaged bone. This involves transplanting healthy bone tissue from another part of the body or from a donor. Artificial material may also be used. If cartilage is damaged, the graft may include both bone and cartilage. In some cases, blood vessels are transplanted along with the bone tissue. In AVN, a bone graft is most often used along with core decompression.

Osteotomy: An osteotomy involves taking out a piece of bone to reposition the bone. This allows the area with blocked blood vessels to bear less weight than a healthy area next to it.

Joint replacement (arthroplasty): Joint replacement involves removing the damaged bone and replacing it with an artificial joint.

> Note: Before, during and after surgery, home oxygen needs to be continued to prevent further damage.

When Home Oxygen Does Not Work

Please go to the hospital if your pain persists. It means something else is going on and there are more reversible sickle cells than oxygen can restore and these reversible cells will progress to irreversible cells and an intractable crisis.

You need to be worked up for the following:

Blood for Full Blood Count to check for PCV, wbc, platelets, reticulocytes to evaluate anemia from destruction of irreversible sickle cells, and any toxic effects of hydroxyurea

Blood for bacteria, viral or fungal culture, and TB test

Blood smear for malaria parasites

Coombs Test - Direct and Indirect to evaluate for hemolytic crisis (red blood cell destruction) due to antibodies in improperly cross matched blood transfusions

Urine for urine analysis, culture and sensitivity

Chest X-ray - to rule out pneumonia, TB

X-rays / CT-Scans of Hips and extremities to rule out avascular necrosis

Management of Crisis in the Hospital - Physicians Take Note

Hospital Management Priorities

Pain control Treat immediately	**Continuous oxygen** 0.5-2 L/min nasal cannula	**Find triggers** Malaria, infection, anemia	**Avoid harm** Cautious fluids and selective transfusion

Quick Haematological work up - CBC, LDH, indirect bilirubin, rectic count,

Microbiology - Rapid malaria test, widal reaction , urine m/c/so etc

- A/ Control Pain, Control Pain and Control Pain immediately. Failure to control pain results in increased mortality. Implement strong analgesia with pure opioids such as Morphine, Hydromorphone or Pethidine combined with anti-inflammatory such as Diclofenac. Ketamine should be used if pure opioids are not available. Obtain from your surgical Theater or Emergency Department. If your hospital does not have pure opioids, you can request from NAFDAC. Do NOT use Pentazocine or Tramadol as these drugs are ineffective, fail to provide pain relief, and will result in chest splinting, increased hypoxia, increased sickling and acute chest syndrome. Pentazocine is banned in the United States due to its psychiatric side effects.

In adults and children with SCD and a VOC being treated with opioids, monitor for excessive sedation by measuring sedation and oxygenation levels with pulse oximetry and an objective sedation scale.

Gradually titrate down parenteral opioids as VOC resolves.

DOSES - For weight based dosing, Use Max Weight of 50kg

> Note: Patient must be on Oxygen by Nasal Cannula: Continuous Flow at 0.5 -2 liters per minute. This is to prevent further progression of reversible sickle cells to irreversible sickle cells as well as prevent hypoxia from opioid induced sedation.

Monitor patients carefully for respiratory depression and other adverse effects of opioid therapy.

Hydromorphone (Dilaudid):

Slow IV: 0.5-2.0mg (0.01-0.04mg/kg) every 30 mins as needed

IM/SC: 2-4mg (0.04-0.08mg/kg) every 4-6 hours.

Rectal: 3mg every 6-8 hours.

Morphine:

IV: 2.5-10.0-mg. every 15-30 minutes as needed (Children, 0.05-0.2-mg/kg. Maximum10 mg.)

Infusion: 0.5-10.0-mg/hr. (Children, 10- 100-mcg/kg/hr.)

IM/SC: 2.5-15 mg. (Children, 0.05- 0.2-mg/kg. Maximum15 mg.)

PO: 10-30-mg every 4 hours as needed for pain.

Rectal: 10-20-mg every 4 hours.

Pethidine (Meperidine):

PO/IM/SC: 50-150mg (1-3mg/kg) every 3-4 hours.

Slow IV: 25-100mg (0.5-2.0mg/kg) every 3-4 hours.

Ketamine:

SQ/IM/IV 5 mg to 7.5 mg (0.1-0.15 mls) (children 0.1 mg/kg) administered every 30 mins as needed and as tolerated.

> Note: Ketamine may be utilized alone or to decrease the amount of opioids required as well as decrease their side effects, while providing effective pain control. Utilize Hydralazine (IV 5-20 mg) titrated as needed for elevated blood pressure.

Combine above opioids or Ketamine with an anti-inflammatory eg Diclofenac or Ketorolac

Diclofenac:

Adult: Deep IM: 75 mg, to be repeated after 6 hours if necessary

IV infusion: 75 mg over 30 to 120 minutes, to be repeated after 4 to 6 hours if necessary. Use a solution of 5% glucose or 0.9% sodium chloride and add 0.5 ml of 8.4% sodium bicarbonate per 500 ml.

Rectal Suppositories: 12.5 - 100 mg. Do not exceed 150 mg in 24 hours.

Max Dose 150 mg in 24 hours

Children (1-14 yrs)

Rectal Suppositories 0.5 to 2 mg/kg body weight daily in 2 to 3 divided doses.

Use only 12.5 mg or 25 mg suppositories

Do not exceed 150 mg in 24 hours.

Ketorolac:

IV/IM: 30mg (0.5mg/kg) every 6 hours as needed.

PO: 10-20mg stat then 10mg every 4-6 hours.

Maximum total parenteral dose (IV/IM): 120mg daily. Maximum PO dose: 40mg daily. IV doses should be infused slowly (>15 seconds) to reduce risk of phlebitis. Combined duration of use for parenteral and oral Ketorolac in all patients should not exceed 5 days.

- B/ Home oxygen in the golden half hour and continuous oxygen therapy until patient recovers
- C/ Oral hydration. Control pain and the patient can hydrate orally. Except where there is clinically significant dehydration, IV fluids should be administered cautiously as there is risk of harm in patients with cardiopulmonary compromise. Do not over hydrate with IV fluids as it can result in fluid overload and pulmonary edema which has a mortality rate almost equivalent to acute chest syndrome. Include blood transfusions in your fluid input calculations.

D/ Acute Chest Syndrome (ACS)

Pain-associated shallow breathing and maldistribution of ventilation may contribute to the pathogenesis of acute chest syndrome, and these results support the need for adequate pain relief and monitoring of ventilatory patterns during the treatment of VOC. Hypoventilation and hypoxemia, result in increased sickling of the red blood cells. The major acute pulmonary complication of SCD is ACS, and it is a major cause of morbidity and mortality. ACS has been defined as the presence of a new pulmonary infiltrate (involving at least one complete lung segment, not atelectasis) with chest pain, a temperature of > 38.5 degrees C, tachypnea, wheezing, or cough in a patient with SCD.[3]■ Mechanisms that lead to this syndrome include lung infarction, fat emboli from infarcted bone, pulmonary infection, atelectasis from splinting due to thoracic pain during VOC, in situ thrombosis, vascular injury due to cell-cell interactions and inflammatory mediators, and thromboemboli.

Antibiotic treatment for Acute Chest Syndrome (ACS) in sickle cell disease, often triggered by community-acquired pneumonia, requires broad-spectrum coverage for both typical and atypical bacteria.

Recommended therapy typically combines a third-generation cephalosporin (e.g., ceftriaxone) with a macrolide (e.g., azithromycin) to cover S. pneumoniae, M. pneumoniae, and C. pneumoniae.

Recommended Antibiotic Regimens

Preferred Initial Coverage: Ceftriaxone (75 mg/kg IV/IM daily, max 2g) + Azithromycin (10 mg/kg on day 1, then 5 mg/kg for 4 days).

Alternative/Atypical Coverage: Respiratory fluoroquinolones (e.g., Levofloxacin) are recommended if there is a cephalosporin allergy.

Severe Cases: Consider adding vancomycin if there is severe illness or suspicion of S. aureus.

Key Considerations

Duration: Typically, a 5- to 10-day total course of antibiotics is recommended, with a shift to oral medication (e.g., amoxicillin) upon discharge.

Effectiveness: Using both a macrolide and a cephalosporin significantly reduces the risk of 30-day readmission.

Management: In addition to antibiotics, management includes oxygen supplementation, pain control, and blood transfusion if necessary.

E/ Severe Anemia

Assess patients whose hemoglobin concentration is 2 g/dL or more below their baseline (or less than 6 g/dL when the baseline is unknown) for acute splenic sequestration, anaplastic episode, a delayed hemolytic transfusion reaction, ACS, and infection.

F/ Blood Transfusions

In adults and children with SCD and a VOC, do not administer a blood transfusion unless there are other indications for transfusion, such as: simple transfusion for symptomatic ACS combined with a decreased Hb of 1g/dl below the baseline; exchange transfusion for symptomatic severe ACS (as defined by an oxygen saturation less than 90%); despite supplemental oxygen; simple transfusion for acute splenic sequestration plus severe anemia; and simple or exchange blood transfusion for stroke.

Risks of Blood Transfusion

Blood Transfusion Risk Summary

Risks	Use selectively
• Alloimmunization	• Stroke or severe ACS indications
• Delayed hemolytic transfusion reaction	• Severe anemia/sequestration indications
• Hyperhemolysis	• Phenotypically matched blood when needed
• Iron overload with chronic transfusion	

Due to the risks of alloimmunization and hemolytic transfusion reaction, the routine use of blood transfusion or chronic transfusion therapy is not recommended for prevention or treatment of VOC or recurrent SCD pain.

Red blood cell (RBC) alloimmunization occurs in approximately 30% of transfused sickle cell disease patients compared to 2% to 5% of all transfusion recipients. Among SCD patients transfused with RBCs matched only for ABO and D antigens, the rate of alloimmunization to non-ABO RBC antigens is much higher than for other transfused patient populations, ranging from 18% to 37%. This is due to the differences in RBC antigen expression frequencies between the mostly Caucasian donor base and the mostly African-American SCD patients.

In SCD patients, many partial D, C, and e antigens are described, and importantly, the resulting antibodies are associated with delayed hemolytic transfusion reaction (DHTR) cases. Such allo-immunized patients should be transfused with antigen-negative units (D-negative RBCs for a partial D patient). One of the common alloantibodies made by SCD patients is against the Rh antigen E. In recent years, phenotypic matching protocols are now the standard of care for SCD patients in

order to prevent RBC alloimmunization. Such protocols include matching for C, E, and K1 even for non-allo-immunized patients, to extended antigen matching for Fy, Jk, and Ss blood groups in patients who have made one or more alloantibodies.

DHTR, as a result of allo-immunization against transfused blood cells, is a dreaded complication of transfusion. In the severest cases, hyperhemolysis, defined by the destruction of both transfused and autologous RBCs, occurs and may be life-threatening.

Blood transfusion may be indicated where all other measures have failed and for reasons other than pain (eg, stroke, silent stroke, abnormal transcranial Doppler ultrasound, or pregnancy).

Where indicated, blood transfusion aims to increase the oxygen-carrying capacity of blood and to decrease the proportion of sickle hemoglobin (HbS) relative to hemoglobin A (HbA). In the acute situation, simple transfusion will increase oxygen-carrying capacity but with a risk of hyperviscosity if the Hb is increased to significantly over the patient's baseline. Therefore, the target Hb should be 10 g/dL in patients with homozygous HbS (HbSS).■■ Exchange transfusion has the advantage of both increasing oxygen-carrying capacity and reducing HbS percentage

Chronic Transfusion Therapy

Chronic transfusion therapy is used primarily to reduce the risk of stroke in high-risk individuals with SCD 31, 32. However, it can also be used to reduce the levels of circulating sickled RBCs, and thereby decrease the number of vaso-occlusive crisis (VOCs) when used as prophylactic therapy 33. Complications of chronic transfusion therapy include the risk of allo-immunization, iron overload, and its related complications. The utility of chronic transfusion therapy in SCD is limited by the availability of a compatible blood donor population. Individuals undergoing transfusion for SCD may also generate antibodies against the transfused RBCs, resulting in unpredictable, delayed hemolytic transfusion reactions and thus require phenotypically matched blood.34

Despite improved implementation of Hydroxyurea (HU) and chronic transfusion therapy for disease management in SCD, recurrent VOCs continue to be associated with disease severity and mortality. Of greater concern is the increased risk of early mortality in individuals with more frequent VOCs. In a study of 264 subjects with SCD, there was a significantly younger age of death (55.8 years versus 66.2 years; p = 0.04) and a higher risk ratio (RR) of death (RR = 2.68; p = 0.03) among individuals with high rates of VOCs (defined as ■1 ED/hospitalization for pain in the prior 12 months) compared with those with low rates of VOCs (defined as 0 ED visits/hospitalizations in the prior 12 months).35 In this study, 41% of participants reported HU use, and 39% reported >10 RBC transfusions during their lifetime. Major trials investigating transfusion therapy, including SIT, SWITCH, and TWITCH, showed a lower incidence of VOCs with transfusion therapy, although VOCs continued to occur despite chronic transfusion therapy.36,37.

Conclusion - Preventing, reversing and stopping crisis is the key to stopping pain, suffering, reducing hospitalizations and blood transfusions as well as preventing premature death in sickle cell disease. Nothing in the past 100 years is as effective as Dr Sota Omoigui's discovery of home oxygen in the right place - at home and at the right time - the golden half hour.

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G/ Fever:

Treatment in patients with fever should include potent antimalarial as indicated (to achieve early total parasitaemia clearance), intravenous antibiotics that provide coverage against community-acquired pneumonia and gram-negative enteric organisms, as well as simple or exchange blood transfusion where indicated.

H/ Aplastic Crisis

Manage aplastic events with immediate red blood cell transfusion aimed at restoring the hemoglobin to a safe (not necessarily baseline) value. Isolation of hospitalized patients (droplet precautions) is required to prevent the spread of the parvovirus B19 to pregnant women and others with SCD or compromised immunity. In people with hypovolemia due to severe acute splenic sequestration, immediately provide IV fluid resuscitation.

Strict compliance of this management protocol will ensure a good response to the home oxygen therapy, prevent hospitalization or reduce significantly long hospitalization. While on hospital admission, the attending physician must maintain continuous oxygen administration. This will prevent further sickling of the red blood cells while the body tries to mop up the already irreversibly sickled red blood cells (by phagocytosis and sequestration etc) which are responsible for the ongoing crisis. Also note that as long as malaria and infections are not successfully treated and anaemia is not corrected, the vaso occlusive crisis will persist even with the continuous oxygen therapy. Please note, all the patients must endeavour to own a home oxygen therapy appliance - either an oxygen concentrator or an oxygen cylinder.

Pulse Oximetry and Oxygen Saturation

In sickle cell disease, there is a poor correlation between oxygen saturation measured by pulse oximetry (which primarily reflects arterial oxygen saturation) and venous oximetry, meaning that a seemingly normal pulse oximetry reading may not accurately represent the actual oxygen saturation in the venous system due to the abnormal blood flow dynamics caused by sickling red blood cells; therefore, careful interpretation is crucial when monitoring oxygenation in sickle cell patients, often requiring further evaluation with blood gas analysis. [1, 2, 3]

> DISCOVERY NOTE: A normal oxygen saturation > 90% can occur in the presence of sickling and provides no reassurance or guarantee against a crisis. What is more significant is a sudden change in the baseline oxygen saturation.

A low oxygen saturation < 90% however and especially if lower than the baseline and at bedtime increases the likelihood of nocturnal hypoxemia and sickling during sleep. This can be prevented by using oxygen at bedtime for 1 hour or more including throughout sleep as needed.

Key points about this correlation: [3, 4, 5]

Sickle cell pathology: Sickle hemoglobin (HbS) polymerizes under low oxygen conditions, causing red blood cells to become rigid and sickle-shaped, which can obstruct blood flow in small vessels, leading to tissue hypoxia even with seemingly normal arterial oxygen saturation. [3, 4, 5]

Venous oxygen extraction: Due to impaired blood flow in sickle cell patients, tissues may extract a higher percentage of oxygen from the blood, resulting in a lower venous oxygen saturation even if the arterial oxygen saturation is normal. [3, 4, 6]

Pulse oximetry limitations: Pulse oximetry can underestimate oxygen saturation in sickle cell patients because it relies on the difference in light absorption between oxygenated and deoxygenated hemoglobin, which can be affected by the altered blood flow dynamics and the presence of abnormal hemoglobin variants like HbS. [1, 7, 8]

Clinical implications: [1, 3, 6]

Monitoring oxygenation: When managing sickle cell patients, relying solely on pulse oximetry may not be sufficient, and more invasive monitoring like central venous oxygen saturation (ScvO2) may be necessary to assess tissue oxygenation. [1, 3, 6]

Treatment decisions: Low venous oxygen saturation, even with seemingly normal pulse oximetry readings, could indicate the need for interventions to improve blood flow and oxygen delivery. [1, 4, 6]

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Oxygen Toxicity or Side Effects

Oxygen toxicity from low flow oxygen in a hypoxia induced crisis is a non possibility. In sickle cell disease, the problem is a low oxygen environment that induces a crisis. Supplemental oxygen normalizes the low oxygen environment. There are no side effects. As you are reading this, you are inhaling air which is 21 % oxygen, several times a minute. Oxygen 2 liters per minute by nasal cannula is 28% oxygen. Liguoro I, et al. in 2021, concluded that long-term oxygen therapy (LTOT) administered from 2014 to 2019, was a safe and feasible treatment option for children (age range 6-15) with SCD and chronic hypoxaemia. No child discontinued LTOT because of intolerance or poor adherence. No major adverse events were reported. Laboratory data did not show significant changes in haemoglobin and reticulocyte count after 1 year of follow-up. Furthermore, it is the same oxygen that is administered in the hospital, and for a much longer duration of time, when the person is in an irreversible crisis, and when the oxygen cannot restore irreversible cells but only prevent more reversible cells from progressing to irreversible cells.

Workup of Shortness of Breath

Shortness of Breath Workup

Assess	Rule out	Treat	Escalate
CBC and chest imaging	ACS, PE, fluid overload, anemia	Oxygen and targeted therapy	Antibiotics, anticoagulation, transfusion when indicated

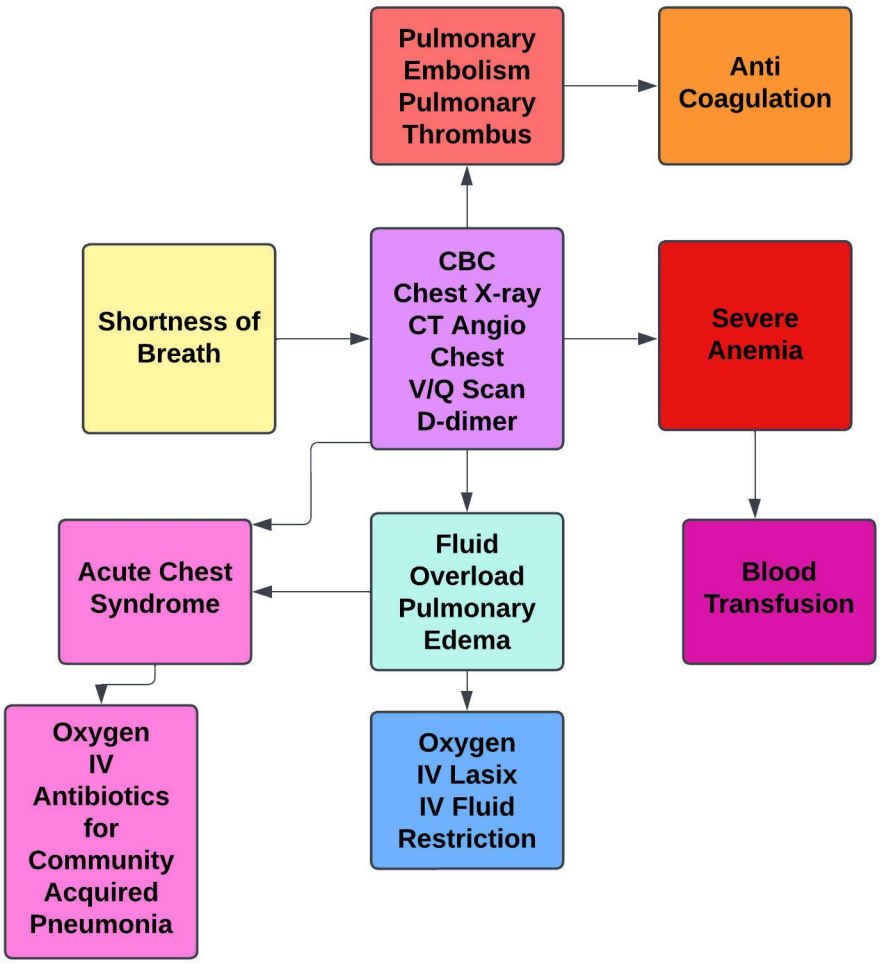

Figure 4. Workup of shortness of breath diagram from the source handbook.

Case Series - 2025

Home Oxygen Therapy in the Golden Half Hour for Sickle Cell Disease: A Prospective Real-World Cohort Demonstrating Reduced Pain, Hospitalizations, and Transfusions in Nigeria - 2025

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Abstract

Background: Hospital-based oxygen is standard to treat irreversible sickle cell crisis, but there has been no previous use of home oxygen to restore reversible sickle cells back to their normal discoid shape in the golden half hour, thereby prevent, reverse and stop a sickle cell crisis. Methods: We conducted a prospective observational cohort (N = 98) of sickle cell patients in Nigeria using a structured digital questionnaire and daily symptom logs. Patients with home oxygen served as their own controls, comparing 6-month pre-oxygen and post-oxygen periods. Patients without oxygen served as a natural comparison group. Results: Pain crisis were prevented or aborted in 80-90% of early oxygen users with a drop from 7-10 -> 0-2 within 20-60 minutes. Home oxygen reduced hospitalizations by 79% with most users going months without needing emergency care. Blood transfusions drop 80%. Quality-of-life (qoL) items revealed substantial baseline functional impairment, with patient reports of improved sleep, emotional outlook, and social participation and reduced fear of hospitalization, after obtaining home oxygen. Non-oxygen patients continue to suffer high crisis burden reporting persistently high crisis frequencies (most with >=3 crises/year). This confirms the treatment effect is real, not due to regression or bias. Conclusions: Home oxygen therapy dramatically reduces pain, transfusions, and hospitalizations and improves the qoL for sickle cell patients. This the first use of a medical gas in the history of medicine to reverse the pathologic basis of a disease by restoring reversible sickle cells back to their normal discoid shape - instead of just treating the symptom of a disease such as using oxygen for an asthmatic attack.

About the Discoverer - Sota Omoigui MD

"I tackle problems that have not been solved for thousands of years - not because they are difficult but because they are impossible"

Sota Omoigui MD - July 4th, 2024

Sota Omoigui M.D. is CEO of State-of-the-Art Technologies Inc and Medical Director of the L.A. Pain Clinic in Hawthorne, California. He is board certified in Anesthesia with subspecialty certification in Pain Medicine. He has served as an adviser to the United States, FDA Advisory Committee on Anesthetics and Life Support Devices. He is author of several drug handbooks published in six languages.

He has 1050 plus Google Scholar citations for his scientific research work.

He is a Recipient of the US FDA Advisory Committee Service Award, in recognition of his distinguished service to the people of the United States of America.

Since the dawn of time, 300,000 years ago, Mankind has tried to understand the origins of pain. From Athenian philosopher Plato (c. 428 to 347 B.C.) to the 1644 pain theory, by the French philosopher Renee Descartes to the 1965 gate control theory by Melzack and Wall. None of these theories have withstood the test of time.

In his seminal book titled: The Biochemical Origin of Pain and published in 2002, Dr Sota Omoigui proposed his theoretical law that the origin of pain is due to inflammation and the inflammatory response. His subsequent publication of his theory as a journal article in 2007 has been cited as of this date by 504 medical publications. In his 2002 theory, he demonstrated a clear association between migraine and the release of inflammatory mediator calcitonin gene-related peptide (CGRP) and substance P (SP). In 2019, seventeen years later, the US FDA approved members of a new class of drugs specifically designed to treat migraine by targeting calcitonin gene-related peptide (CGRP). Those drugs have been the greatest advance in the treatment of migraine.

Finally

He is also a co-author of the All Nigerian 1978 national anthem - Arise O'Compatriots

On July 4th, 2024, he described the

The First Solution in 7300 years to prevent, reverse and stop a sickle cell crisis in the golden half hour

Let Oxygen be your medicine

Dr Sota Omoigui's discovery heralds the beginning of a new century of transformation for patients, their families, their communities and the world.

He is an independent translational researcher, analyzing and applying patterns in basic science research to discover novel clinical applications. Dr Sota Omoigui's discovery has come to offer a solution to a problem 7300 years old. It is bringing a Paradigm Shift

From

A reactive treatment approach of the last 100 years of modern medicine, wherein patients are treated in a hospital after going into an irreversible sickle cell crisis, experiencing severe pain, suffering and multi organ damage and death

To

A preventive proactive symptomatic approach where patients and family, empowered by knowledge, are transformed from hopeless and helpless bystanders, to first responders utilizing home oxygen therapy in the golden half hour, to restore reversible sickle cells to their normal discoid shape, prevent, reverse and stop a crisis making hospitalizations, and blood transfusions few and far between, saving and changing lives all over the world.

More than 200 patients in different continents, in collaboration with their physicians, are currently implementing his discovery using inhalational oxygen in the right place - at home and at the right time- the golden half hour, and experiencing a dramatic change in their lives and a significant reduction in hospitalizations, blood transfusions and all the complications of a sickle cell crisis. Testimonies and the scientific foundation of his discovery may be seen on his website at sicklecelldiscovery.com

About the Discovery

Dr Sota Omoigui's Discovery - Announced on July 4th, 2024.

1. The first solution in 7300 years to prevent, reverse and stop a sickle cell crisis in the golden half hour

2. A solution that has confounded the biggest and most resourced pharmaceutical companies and researchers that have spent billions of dollars looking for a solution to stop a vaso-occlusive sickle cell crisis but that has eluded them
3. A discovery that has changed the entire paradigm of treatment for a chronic disease since Banting and Best isolated insulin in 1921 and changed the entire paradigm for treatment of diabetes that had hitherto been a uniformly fatal disease killing diabetics in their 20's and 30's.
4. The first use of a medical gas in the history of medicine to reverse the pathologic basis of a disease by restoring reversible sickle cells back to their normal discoid shape - instead of just treating the symptom of a disease such as using oxygen for an asthmatic attack.
5. A discovery now preventing hundreds of hospitalizations, hundreds of blood transfusions, hundreds of organ damage and death in Nigeria, the United States and all over the world.