Sickle Cell Disease

Acute crises · Analgesia fast, watch the chest, and know what still works

ANALGESIA < 60 MIN
a quality standard

VASO-OCCLUSIVE CRISIS *the commonest presentation, and the most poorly managed*

1. **Give analgesia within 30–60 minutes of arrival** and reassess every 30 minutes. **Believe the reported pain** — there is no objective marker, and these patients are systematically under-treated and mislabelled as drug-seeking.
2. **Use the patient's individualized plan** if one exists. Strong opioids by the fastest reliable route, titrated, then **patient-controlled analgesia** for ongoing pain. **Avoid meperidine (meperidine)** — normeperidine accumulates and causes seizures.
3. **Add adjuncts:** acetaminophen and an NSAID if renal function allows, plus warmth and reassurance. Prescribe **laxatives and antiemetics routinely** alongside opioids.
4. **Hydrate to euvolemia, not beyond.** Over-hydration precipitates acute chest syndrome and pulmonary edema. Oral where possible; maintenance IV if not.
5. **Incentive spirometry every 2 hours while awake**, plus oxygen only if hypoxic. This is a genuinely evidence-based intervention that **prevents acute chest syndrome**, and it is the step most often omitted.
6. **Watch the sedation score, not just the pain score.** Opioid-induced hypoventilation with atelectasis is a direct route into acute chest syndrome.

ACUTE CHEST SYNDROME *a leading cause of death — treat on suspicion*

DEFINITION

A **new pulmonary infiltrate** plus fever and/or respiratory symptoms — chest pain, cough, tachypnea, hypoxia. Often develops **2–3 days into an admission for a painful crisis**, so the deterioration is on your watch.

TREAT ALL OF IT AT ONCE

Antibiotics covering typical and atypical organisms (a cephalosporin plus a macrolide) · **oxygen** · **incentive spirometry** · bronchodilators if wheezy · careful fluid balance · adequate analgesia so they can breathe deeply · **transfusion**: simple for moderate disease, **exchange transfusion for severe or deteriorating** disease, targeting HbS below about 30%. **Escalate early** — deterioration is rapid.

THE OTHER ACUTE EMERGENCIES *each has a distinct trigger and treatment*

Emergency	Recognition and action
Stroke	Any focal deficit. **Urgent imaging and urgent exchange transfusion.** Children are screened with **transcranial Doppler**, and abnormal velocities are an indication for a chronic transfusion program.
Splenic sequestration	**Rapidly falling hemoglobin with an enlarging, tender spleen** and hypovolemia, mainly in children. **Transfuse and resuscitate urgently**; it can exsanguinate into the spleen within hours.
Aplastic crisis	**Parvovirus B19** shuts down erythropoiesis. Profound anemia with a **low reticulocyte count** — the reticulocyte count is the discriminator from sequestration or hemolysis. Transfuse and isolate.
Priapism	**More than 4 hours is an emergency.** Hydration, analgesia, and **urgent urology** for aspiration and irrigation. Untreated episodes cause permanent impotence.
Fever	**Functional asplenia** means encapsulated organism sepsis. **Cultures and empirical antibiotics immediately** — treat fever in sickle cell disease as a medical emergency, not a routine review.

DISEASE-MODIFYING THERAPY *the landscape changed recently — two agents are no longer what they were*

Agent	Status
Hydroxyurea	**The mainstay.** Raises fetal hemoglobin, reduces crises, acute chest syndrome, transfusion need and mortality. **Under-prescribed** — offer it to anyone with recurrent crises. Monitor the blood count; it is teratogenic.
Voxelotor	**Withdrawn from worldwide markets in September 2024.** Pfizer withdrew all lots after data suggested an **imbalance in vaso-occlusive crises and fatal events**, such that benefit no longer outweighed risk. **Should not be prescribed.**
Crizanlizumab	The phase 3 **STAND** trial found **no significant reduction in vaso-occlusive crises versus placebo** at either dose, though no new safety concerns emerged. Its role is now substantially in question.
L-glutamine	Approved for reducing acute complications; modest effect, and tolerability limits use for some patients.
Gene therapy	**Exagamglogene autotemcel (Casgevy)** and **lovotibeglogene autotemcel (Lyfgenia)**, both approved in 2023, produce very high rates of freedom from vaso-occlusive crises in trials. Access, cost, and conditioning toxicity are the limiting factors.
Transplant	**Allogeneic hematopoietic stem cell transplantation remains the established curative option**, with success depending on donor match, age, and disease severity.

CHRONIC CARE *the preventive work that keeps them out of hospital*

ROUTINE HEALTH MAINTENANCE

Penicillin prophylaxis in young children and **full encapsulated-organism vaccination** (pneumococcal, meningococcal, Haemophilus) for life · **folic acid** · annual **retinal screening** for proliferative retinopathy · blood pressure, urine protein and creatinine for sickle nephropathy · screening for **pulmonary hypertension** and iron overload in transfused patients.

PLAN AHEAD

Give every patient an **individualized analgesia plan** they can bring to the emergency department. Discuss **hydroxyurea** at every opportunity in anyone with recurrent crises. Pre-operative assessment matters — **transfusion before surgery** reduces perioperative complications. Address **contraception, pregnancy planning and transition** from pediatric to adult services deliberately.

PEARLS & PITFALLS

- **Under-treated pain is the defining failure in sickle cell care.** Delayed analgesia and stigma are documented and measurable harms.
- **Over-hydration and over-sedation both cause acute chest syndrome.** Aim for euvolemia and watch the respiratory rate.
- **Incentive spirometry prevents acute chest syndrome.** Prescribe it on admission, every time.
- **Do not prescribe voxelotor** — it was withdrawn worldwide in 2024 over an excess of crises and deaths.
- **Fever with functional asplenia is sepsis until proven otherwise.** Antibiotics go in immediately.
- **A low reticulocyte count** in a profoundly anemic patient points to parvovirus aplastic crisis, not hemolysis.

References: FDA safety statement and Pfizer withdrawal of voxelotor (Oxbryta), 2024 · STAND trial of crizanlizumab (Lancet Haematology, 2024) · ASH guidelines on sickle cell disease · NHLBI evidence-based management of sickle cell disease.

Educational aid; verify against local hematology protocol and patient-specific plans.