Sickle Cell Disease in the 21st century

Rob Cronin, MD, MS
Associate Professor of Internal Medicine
Department of Internal Medicine
Division of General Internal Medicine and Geriatrics
The Ohio State University Wexner Medical Center

MedNet21
Center for Continuing Medical Education

The Ohio State University
Wexner Medical Center

Objectives

- Describe barriers for individuals with sickle cell disease (SCD) to obtain primary care providers (PCPs)
- Describe preventive care for people with SCD, including nuances for this population
- Describe some common acute and chronic issues in SCD that intersect with primary care and how to manage them

Individuals with SCD face many barriers when seeing a PCP

- Barriers to access – insurance, location, cost, time
- Barriers to providers
  - Lack of provider knowledge about SCD
  - Negative attitudes towards adults with SCD
  - Concerns about opioid management for pain
  - Concerns about hematology support
- Expectations of the PCP may not be clear
  - Patient perceptions that PCPs have nothing to offer
  - What hematologist expects of the PCP

Transition from pediatric to adult models of care

- High rates of mortality, comorbid conditions (cardiac, renal, lung complications), hospitalizations/re-admissions
  - Some have cognitive dysfunction
- Quality of care decreases from pediatric to adult care
  - Challenges with access to specialists (including hematologists)
    - About 66% of adults with SCD on Medicaid
  - Patients report dissatisfaction with quality of care they receive
  - Healthcare providers report dissatisfaction with quality of care they can provide
- Emerging adults become disengaged from healthcare system
  - Decrease in routine preventative and screening visits
  - More likely to seek care for acute medical evens in emergency room

Preventive care

- Vaccines
- Screening
- Vitamin D and bone health
- Women's health

Vaccines

- The typical vaccines in childhood and adult and yearly influenza
- SCD-specific vaccines
  - Pneumococcal
  - Meningitis (ACWY and B)
  - Hib
  - Hepatitis B (for chronic transfusions)
- CDC immunization schedule:
  - https://www.cdc.gov/vaccines/schedules/index.html
  - https://www.cdc.gov/vaccines/schedules/hcp/imz/child-indications.html#table-indications
- Mobile app
  - https://www.cdc.gov/vaccines/schedules/hcp/schedule-app.html

Screening – SCD-related

- Eye screening – every 1-2 years
- Kidney screening – yearly microalbumin
- Brain – transcranial dopplers in children and an MRI before transition to adult model of care
- Heart screening – with symptoms – echocardiogram
- Lung screening – with symptoms – pulmonary function test

Other screening – particularly important for SCD

- Pediatric anticipatory care - development
- BMI – high and low
- Blood pressure (≤130/80)
- Smoking status
- Depression/anxiety
- Typical cancer screening, but increased cancer risk
  - Colon, hematologic, thyroid, kidney, non-melanoma skin cancer

Vitamin D and bone health

- Low vitamin D levels highly prevalent among individuals with SCD
- Low vitamin D may lead to pain episodes
- No clear guidance on how often to monitor vitamin D levels
- Supplement low levels
- Bisphosphanates have been used in osteoporosis and early avascular necrosis

Women's Health

- Menstrual cycles
  - Over 1/3 of females report having sickle cell related pain during menstrual cycles
- Sickle cell pain while menstruating treatments:
  - Heating pad
  - Ibuprofen around the clock, starting a few days before period starts
  - Methods to attenuate menstrual cycles (contraceptives without estrogen)
- Contraception
  - Important on ACEi/ARBs or SCD modifying therapies like Hydroxyurea
  - Estrogen increases risk of blood clots in SCD – an inherited thrombophilia
    - IUD's that don't contain estrogen
    - Progesterone only -- Depo is popular
- Menopause
  - The changing hormone levels may trigger sickle cell pain or joint pain
  - Women with SCD may have premature menopause due to disease specific factors

Chronic conditions that intersect with primary care

- Depression
- Hypertension/albuminurea
- Diabetes
- Sleep

Depression

- Compared to the general population, the rate of depression among patients with SCD is 5 times higher
  - 20-47% in SCD
- Associated with worse clinical outcomes and mortality
- Diagnosis
  - PHQ-9, BDI – screening tool
  - DSM-5 – diagnosis

Depression - management

- Initial treatment pharmacotherapy and psychotherapy recommended
  - Pharmacotherapy – typically start with SSRI, but SNRIs can help with pain (e.g., Cymbalta)
  - Psychotherapy – primarily CBT
- Follow up
  - Depressed outpatients started on antidepressants should be seen one to two weeks after starting an antidepressant
  - Subsequently monitored (by phone or visit) at least every two to four weeks for six to eight weeks

Hypertension/Albuminuria

- American Society of Hematology (ASH) guidelines (2019): A blood pressure goal ≤130/80 mm Hg in adults with SCD
  - Extrapolating to children (≤ 90%)
- Interventions - diet and exercise, no clear guideline on what medication to start
- Albuminuria - ASH guidelines suggest ACEis or ARBs to slow progression of kidney disease

Pulmonary hypertension

- Pulmonary hypertension present in ~6 to 10% of SCD population
- Guidelines differ on screening with echocardiogram
  - Get echo if symptoms concerning for pulmonary hypertension, such as shortness of breath, swelling, or decreased exercise tolerance
  - Tricuspid jet velocity > 2.5m/s is associated with early mortality
- A right heart catheterization is needed for diagnosis
- Treatment varies, depending on the type of pulmonary hypertension
- A pulmonary hypertension specialist involved in the care is critical

Diabetes

- Likely underreported
- Diagnosis is different than typical patient
  - A1C is **not** a good test
  - Consider other criteria – fasting glucose, glucose tolerance test
- Fructosamine good to monitor treatment but not for diagnosis
- Treatment is similar, watch for medication side effects

Sleep

- Issues with sleep is a pervasive problem in SCD
- Not a lot of data about best treatments
- Personalize to patient
  - Sleep hygiene
  - Consider hypoxia at night and overnight pulse oximetry test
  - Ask about priapism and **pain** at night
  - Referral to sleep doctor for evaluation of sleep apnea
    - Even if normal BMI – tonsillar enlargement can cause sleep apnea
    - Consider central sleep apnea with opiate use
  - Consider underlying conditions like depression or anxiety
  - Cautious about pharmacotherapy

Acute issues

- GERD
  - Typical management
- Headaches
  - Ensure no neurological deficits
  - Avoid triptans (newer agents are beneficial, e.g., Rimegepant)
- Musculoskeletal injuries and pain
  - Can have infarcts of bones or avascular necrosis: check imaging Xray vs MRI
  - Avoid steroids (can precipitate vaso-occlusive pain episodes)
- Rheumatologic diseases
  - Psoriasis, SLE, etc.
- Upper respiratory infections (URIs)
  - Can be masking acute chest syndrome so be sure to evaluate patient in office

Fevers

- Fevers (>= 38.5°C (101.5°F)) can be deadly
- Should have immediate evaluation (within 4 hours) including
  - Vitals including O2 saturation
  - Physical including spleen and neurologic evaluation
  - Labs including blood cultures, CBC and retic count
  - Other labs and imaging depending on symptoms, physical, and other evaluation
- Give antibiotics – EARLY - within an hour of patient presentation
  - SCD is considered immunosuppressed due to asplenia
  - Ceftriaxone or Clindamycin
- Inpatient vs outpatient management
  - Keep in clinic until evaluation of CBC returns (as may need to go to the ER)
  - If clinically stable could have next day follow up
  - The patient/family must be able to recognize worsening of the patient's condition and have a reliable means of transportation

51 y/o with Sickle Cell Disease (SCD) referred to you for primary care

- Recently discharged following admission for “pain episode”
  - Received 2 units of PRBCs due to Hgb of 6 gm/dl
  - Chronically transfused
- Hx of pulmonary HTN, cerebral infarcts, avascular necrosis, and chronic kidney disease (CKD)
  - BP 160/98
  - Creatinine 2.5 and urine microalbumin > 30
  - On 2L nasal cannula O2 chronically
  - Chronically in pain
- Native of Congo
  - Unemployed and on Medicaid
- What would you do for him?

51 y/o with Sickle Cell Disease (SCD) referred to you for primary care

- How is his access to specialists?
  - Hematology, pulmonary hypertension specialist, orthopedic, nephrology
  - Communication with these providers is key
- What are his primary care needs?
  - Preventative screening
  - Vaccines
  - Hypertension management
  - Mental health
- Are his social needs being addressed?

25 y/o female with SCD calling for a cough

- Calls into the office this morning
- Started 4 days ago with rhinorrhea and cough
- No shortness of breath
- One episode of chest pain when coughing yesterday, not like her typical sickle cell pain which is usually in her legs
- States she checked her temperature once and it was 100.2
- Should she monitor at home with supportive care, come into the office, or go to the ER
- If you bring her in, what would you do for her, how would you plan to manage her depending on the results

25 y/o female with SCD calling for a cough

- She should be seen by a healthcare provider
- Will get vitals including O2 saturation, physical exam, CBC with reticulocytes, chest X-ray, and may need additional tests
- If the chest X-ray shows a new opacity, should consider acute chest syndrome which requires hospitalization

25 y/o female with SCD calling for a cough

- Everything was normal, but two days later she calls back with a fever of 102.0
- She needs to come back in for vitals including O2 saturation, physical exam, CBC with reticulocytes, chest X-ray, and blood cultures.
- She should get antibiotics (ceftriaxone, or clindamycin if allergic) and plan to see her back the next day if everything comes back normal.

Resources

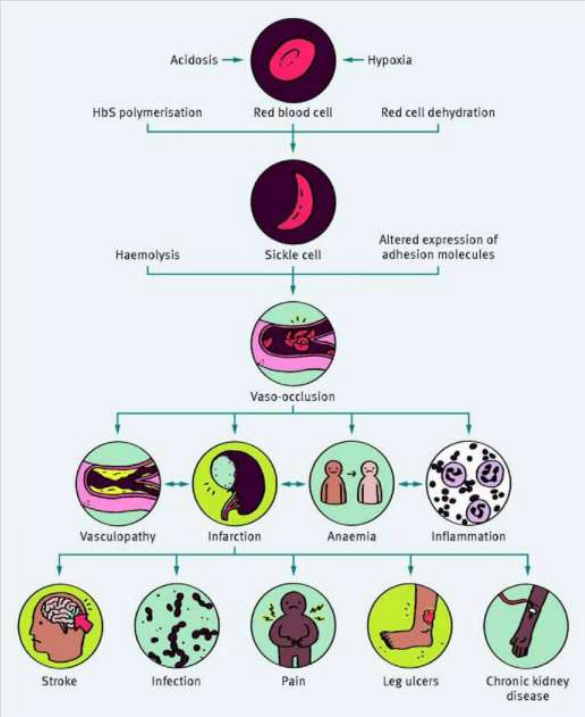
- 2014 NHLBI guidelines
  - https://www.nhlbi.nih.gov/health-topics/evidence-based-management-sickle-cell-disease
- 2019 ASH guidelines
  - https://www.hematology.org/education/clinicians/guidelines-and-quality-care/clinical-practice-guidelines/sickle-cell-disease-guidelines
  - https://apps.apple.com/us/app/ash-practice-guidelines/id1444327980?platform=iphone
- CDC vaccination schedule
  - https://www.cdc.gov/vaccines/schedules/hcp/imz/child-indications.html#table-indications
  - https://www.cdc.gov/vaccines/schedules/hcp/schedule-app.html
- Patient resources
  - SC101: https://www.sc101.org/
  - SCDAA: https://www.sicklecelldisease.org/

Sickle Cell Disease: Pathophysiology and Pain Management

Andrew Schamess, MD
Associate Professor
General Internal Medicine
The Ohio State University Wexner Medical Center

MedNet21
Center for Continuing Medical Education

The Ohio State University
Wexner Medical Center



Brousse V, Makani J, Rees DC. Management of sickle cell disease in the community. BMJ. 2014;348:g1765. Open access.

Effects of RBC contents on endothelium after hemolysis

- Liberated hemoglobin and arginase reduce bioavailability of nitrous oxide, leading to vasospasm
- Liberated hemoglobin generates free radicals that activate the innate immune system, leading to and inflammatory and pro-adhesive state
- ATP/ADP activate P2Y12 receptors on platelets, causing release of platelet contents and increasing the risk of thrombosis

Xue J, Li XA. Therapeutics for sickle cell disease intravascular hemolysis. Front Physiol. 2024;15:1474569.

Treatments for sickle cell disease that attenuate hemolysis and its effects

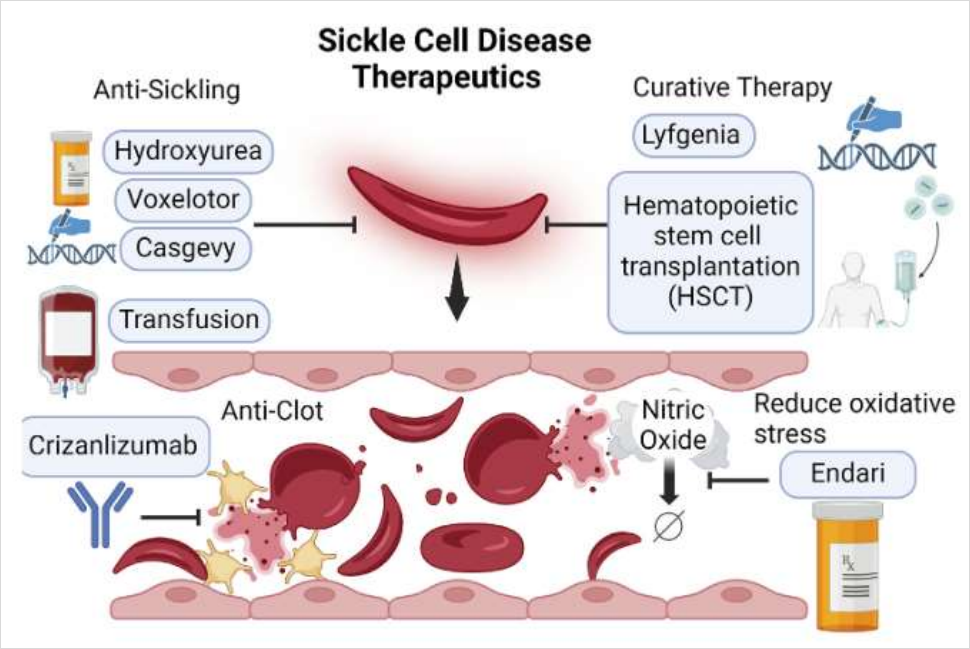
- **Hydroxyurea** – induces fetal hemoglobin, which slows the polymerization of mutated adult hemoglobin that would otherwise cause red cell sickling.
- **Crisper-cas9 gene editing** ("Casgevy") re-activates genetically suppressed production of fetal hemoglobin.
- **L-glutamine** reduces oxidative stress in endothelium.
- **Crizanlizumab** is a monoclonal antibody that inhibits p-selectin, blocking platelet-endothelium interaction and reducing intravascular clotting.
- **Transfusion** improves oxygen delivery and dilutes sickle cells

Xue J, Li XA. Therapeutics for sickle cell disease intravascular hemolysis. Front Physiol. 2024;15:1474569.

Curative treatments for sickle cell disease

- Hematopoietic stem cell transplantation - requires a matched related donor - only available to 15% of patients.
- Gene therapy - "Lyfgenia" - uses a viral vector to add a working copy of the beta hemoglobin gene to patient's stem cells ex-vivo and then re-infuses the cells. Cost: $3.1 million.
- Both are arduous, involving months in the hospital, painful complications of chemotherapy such as mucositis, and a risk of organ damage and death.
- “Even though I say ‘this is a dangerous therapy, high risk, you could die,’ no one hears that. All they hear is ‘I could be cured.’” - Dr. Akshay Sharma, NYT 10/21/2024

Xue J, Li XA. Therapeutics for sickle cell disease intravascular hemolysis. Front Physiol. 2024;15:1474569.



Xue J, Li XA. Therapeutics for sickle cell disease intravascular hemolysis. Front Physiol. 2024;15:1474569. Open access.

American Society of Hematology 2020 guidelines for management of pain in sickle cell disease

Acute pain

- Use a standard protocol to treat pain in the acute care setting.
- Tailored opioid dosing based on consideration of baseline opioid therapy and prior effective therapy
- Consider subanesthetic (analgesic) ketamine infusion as adjunctive treatment of pain that is refractory or not effectively treated with opioids alone

Brandow AM, Carroll CP, Creary S, et al.. Blood Adv. 2020;4(12):2656-2701.

Vasoocclusive crisis versus chronic pain

- The clinical hallmark of Sickle Cell Disease (SCD) is the painful crisis, sometimes called a vasoocclusive crisis (VOC).
- The medical literature for some time used acute care visits for VOC as a proxy measure for the pain burden of SCD. However, many adults with SCD have a high burden of chronic pain as well.
- Clinicians attempting to alleviate chronic pain in patients with SCD have limited evidence to guide management.
- Chronic opioid therapy is often used, although its long-term efficacy is not established in SCD.

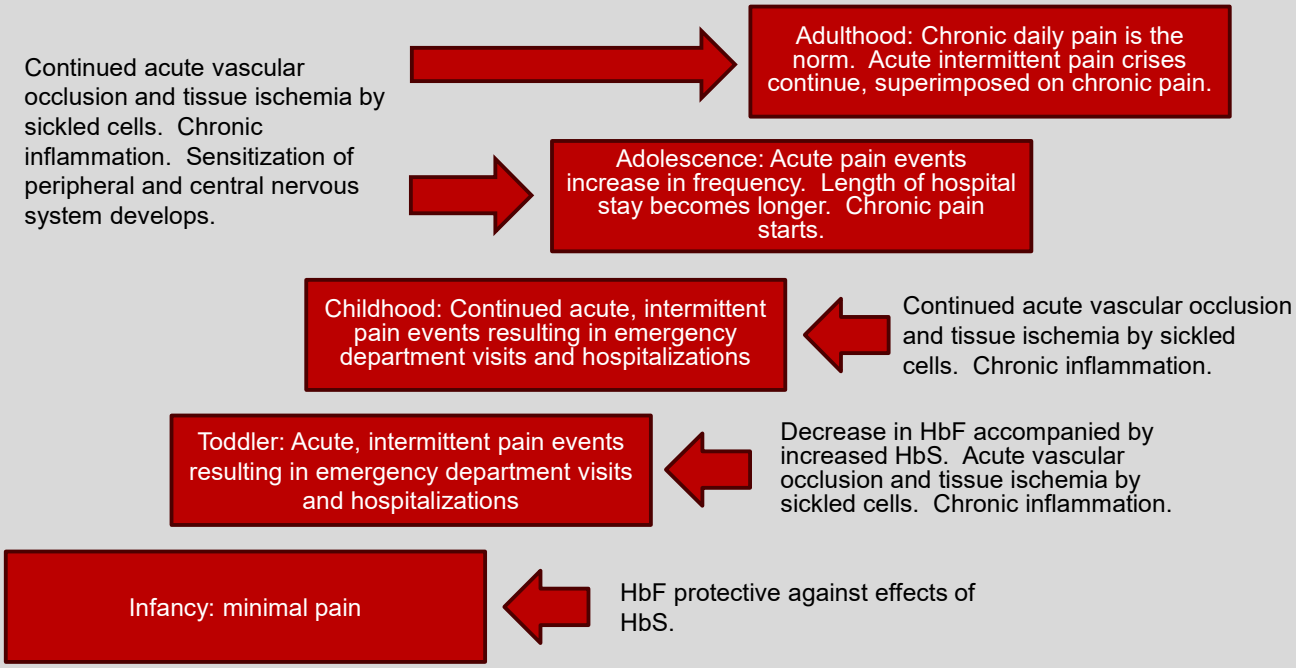
Patrick Carroll, et al

Carroll CP, Lanzkron S, Haywood C Jr, et al. Chronic Opioid Therapy and Central Sensitization in Sickle Cell Disease. Am J Prev Med. 2016;51

Prevalence of chronic pain in sickle cell disease

- Prospective cohort of 232 persons aged 16 and over with sickle cell disease completed daily pain diary for 6 months.
- 29% had pain on > 95% of days
- 14% had pain on < 5% of days
- Pain was reported on 54.5% of total diary days.
- Acute care services were utilized on only 3.5% of days.
- Chronic pain is the most prevalent complication of sickle cell disease in adults.
- Persons with more chronic pain used more opioids.

Smith WR, Penberthy LT, Bovbjerg VE, et al. Daily assessment of pain in adults with sickle cell disease. Ann Intern Med. 2008;148(2):94-101.



Brandow AM, Zappia KJ, Stucky CL. Sickle cell disease: a natural model of acute and chronic pain. Pain. 2017;158 Suppl 1:S79-S84. Graphic my own.

Current model of chronic pain

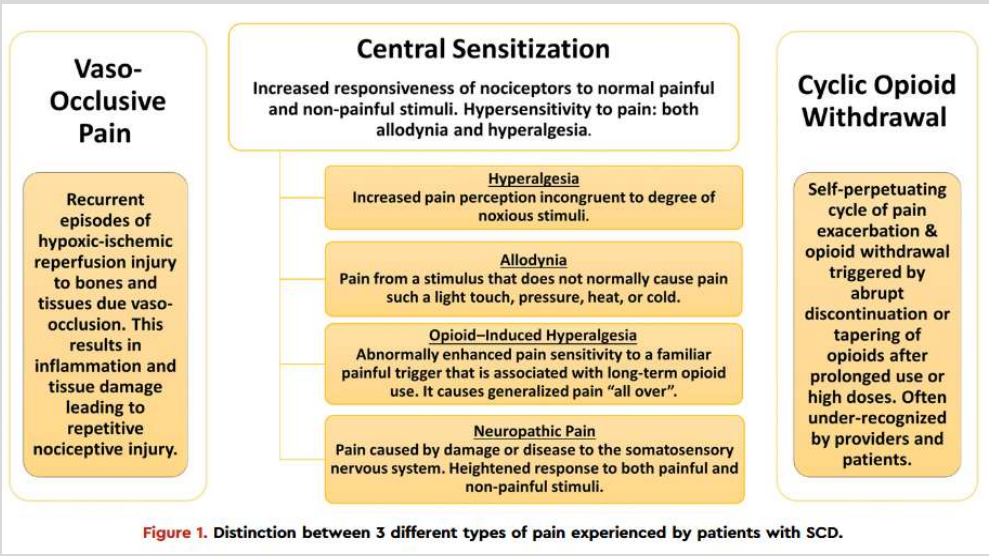
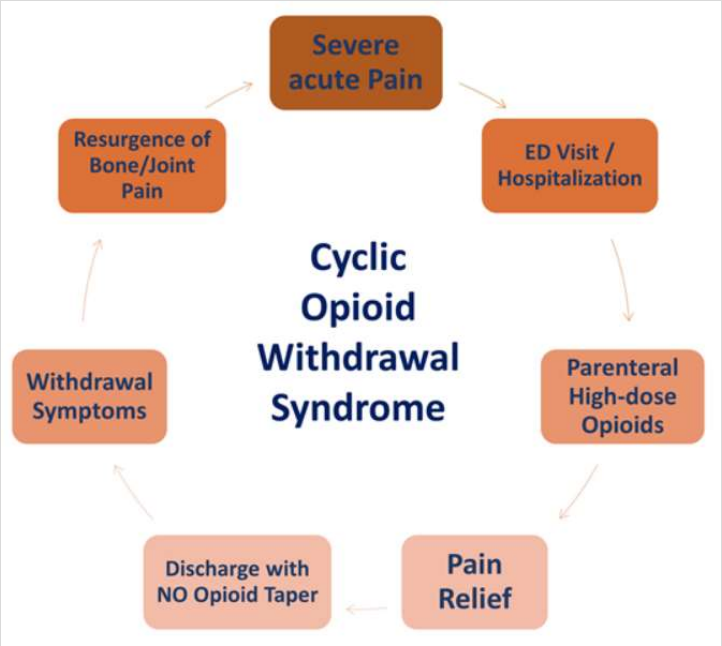


Figure 1. Distinction between 3 different types of pain experienced by patients with SCD.

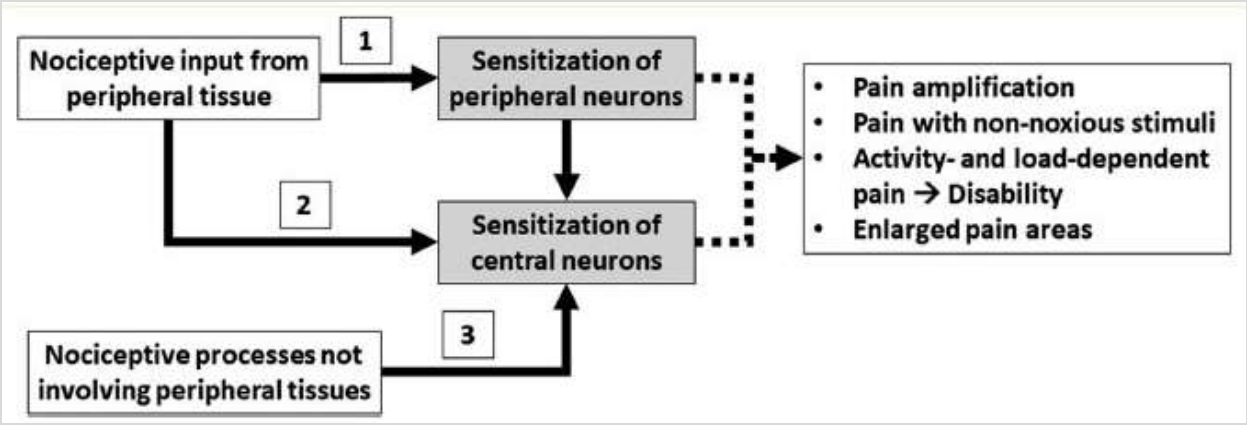
Osunkwo I, O'Connor HF, Saah E. Optimizing the management of chronic pain in sickle cell disease. Hematology Am Soc Hematol Educ Program. 2020;2020(1):562-569. Open access.



Osunkwo I, O'Connor HF, Saah E. Optimizing the management of chronic pain in sickle cell disease. Hematology Am Soc Hematol Educ Program. 2020;2020(1):562-569. Open access.

Central Sensitization to Pain – Basic Model

Curatolo M. Central sensitization and pain: Pathophysiologic and clinical insights. Curr Neuropharmacol. 2024;22(1):15-22. Open access.

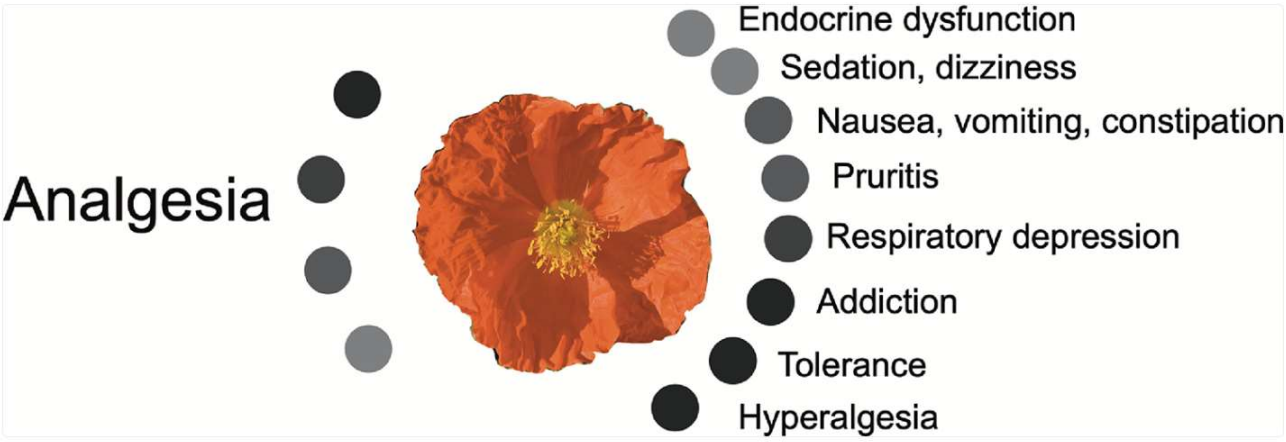


Psychosocial factors that enhance pain sensitivity and intensity in persons with sickle cell disease

- Repeated social defeat (such as attempting and failing to obtain treatment for acute pain) [1]
- Discrimination in health care settings [2]
- Stress-related depression and insomnia [3]
- Catastrophizing (exaggerating the potential negative consequences of an event such as going to the ED to seek treatment) [4]

1. Biltz RG, Sawicki CM, Sheridan JF, Godbout JP. The neuroimmunology of social-stress-induced sensitization. Nat Immunol. 2022;23(11):1527-1535.
2. Mathur VA, Kiley KB, Haywood C Jr, et al. Multiple levels of suffering: Discrimination in health-care settings is associated with enhanced laboratory pain sensitivity in sickle cell disease. Clin J Pain. 2016;32(12):1076-1085.
3. McGill LS, Hamilton KR, Letzen JE, et al. Depressive and insomnia symptoms sequentially mediate the association between racism-based discrimination in healthcare settings and clinical pain among adults with sickle cell disease. *J Pain*. 2023;24(4):643-654.
4. Mathur VA, Kiley KB, Carroll CP, et al. Disease-related, nondisease-related, and situational catastrophizing in sickle cell disease and its relationship with pain. J Pain. 2016;17(11):1227-1236.

Figure 1: Ying and Yang of Opioid use.

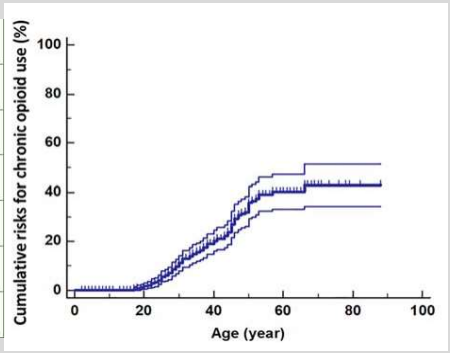


Sagi V, Mittal A, Tran H, Gupta K. Pain in sickle cell disease: current and potential translational therapies. Transl Res. 2021;234:141-158. Open access.

Opioid use increases steadily with age

Age (years)	N	Median (mg)	IQR (mg)	Mean (mg)	SD (mg)
0–9	86	0.54	0.32–1.07	3.10	9.73
10–19	449	1.07	0.49–2.52	6.85	23.77
20–29	237	3.70	0.83–19.59	38.20	123.01
30–39	253	3.70	0.82–22.53	42.36	175.12
40–49	210	3.37	0.82–36.37	52.69	123.72
50+	162	6.03	1.23–36.99	63.49	167.34

Han J, Zhou J, Saraf SL, Gordeuk VR, Calip GS. Characterization of opioid use in sickle cell disease. Pharmacoepidemiol Drug Saf. 2018;27(5):479-486. Open access.



Mo G, Jang T, Stewart C, et al. Chronic opioid use in patients with sickle cell disease. Hematology. 2021;26(1):415-416. Open access.

Prevalence of Substance Use Disorders in Sickle Cell Disease Compared to Other Chronic Conditions

Data from a population-representative sample of Black Americans with SCD, other chronic conditions, and no chronic conditions were obtained from the National Survey of American Life database

Sample consisted of 4,238 African-American and Black Caribbean participants 18 years of age or older.

Controlling for age, sex, and socioeconomic status, there were no differences in odds of a drug use disorder when comparing individuals with SCD to Black adults with other chronic conditions (OR = 1.12; p = 0.804) or no chronic condition (OR = 2.09; p = 0.102).

Jonassaint CR, O'Brien J, Nardo E, et al. J Gen Intern Med. 2023;38(5):1214-1223

CDC 2016 Prescribing Guidelines for Opioids for Chronic Pain

Determining When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.

Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain - United States, 2016. MMWR Recomm Rep. 2016;65(1):1-49.

Opioid Prescribing and Outcomes in Patients With Sickle Cell Disease Post-2016 CDC Guideline

This retrospective cohort study analyzed claims data from the Merative MarketScan Commercial Database from 2011 through 2019.

The cohort included 14,979 patients with SCD (mean age, 25.9).

Compared with the pre-guideline trends, the study found:

- Decrease in opioid dispensing rate ($p < .001$)
- Increase in VOC-related hospitalizations ($p = .001$)

Kang HA, Wang B, Barner JC, et al. JAMA Intern Med. 2024;184(5):510-518.

Desire to alleviate pain

Concern about long-term harm

Opioid deprescribing mandates

Implicit bias

Institutionalized racism

Trust / mistrust

Original graphic and photo (no copyright)

"I can't cry on cue": Exploring distress experiences of persons with sickle cell

Theme 1: Pain has performative features

- I feel like I have to perform or show that I'm in pain. Which is really just to make them feel comfortable about treating me, even though they are supposed to, no matter what. [Participant 3]
- Doctors do an exam, and they assume because we're not balled up, freaking crying and screaming our hearts out, they don't think that we're in pain. [Participant 5]
- Sometimes they ask me, "Well, how does the pain feel? You don't look like you have sickle cell." Well, how am I supposed to look? [Participant 4]

Childerhose JE, Emerson B, Schamess A, Caputo J, Williams M, Klatt MD. SSM - Qualitative Research in Health. 2024;5:100426.

"I can't cry on cue": Exploring distress experiences of persons with sickle cell

Theme 2: Stigma and racism surround care

- I need more pain medication then what I've been given. But I can't ask for it. Because I'm black, I'll be seen as drug-seeking. I've had several comments made to me before that suggest that a doctor or a nurse thought that I was drug-seeking because of my race and strictly because I had sickle cell. I feel like my nurses and doctors don't trust me. [Participant 3]
- Don't judge me based off of my skin color. I want to have the same, equal care that a person from a different ethnicity would have. The same exact care that you would give to your loved one is the same exact care that I should be able to have. [Participant 13]

Childerhose JE, Emerson B, Schamess A, Caputo J, Williams M, Klatt MD. SSM - Qualitative Research in Health. 2024;5:100426.

"I can't cry on cue": Exploring distress experiences of persons with sickle cell

Theme 3: Sickle cell is a neglected disease

- It's because it's a black disease that people just don't know about it, and it's not talked about. [Participant 12]
- They mention their cancer patients a lot. It's annoying because I have to go to a hospital that's mainly dedicated to cancer. I'm always in spaces that say cancer on the door. [Participant 3]
- They were going to stop providing monthly prescriptions of pain medications for pretty much everyone unless you are a cancer patient. If you are not a cancer patient, then you are limited to getting a week's worth of pain medication. [Participant 7]

Childerhose JE, Emerson B, Schamess A, Caputo J, Williams M, Klatt MD. SSM - Qualitative Research in Health. 2024;5:100426.

"I can't cry on cue": Exploring distress experiences of persons with sickle cell

Theme 4: Participants lack control over their pain management plan

- When we're in the hospital, many times I tried to tell doctors like this will work, this is what I need, let's get this going so I can get out of here. I know my body. If I'm there, I'm there for a reason. I hate the hospital. I feel like it's jail. [Participant 12]
- Listen to us when we say, because we know our bodies, if we don' t have ports, we know the best thing to do is to start an IV. Just listen to us. That's all we want: for you to listen to us and fully understand us because we're coming to you for help. [Participant 5]

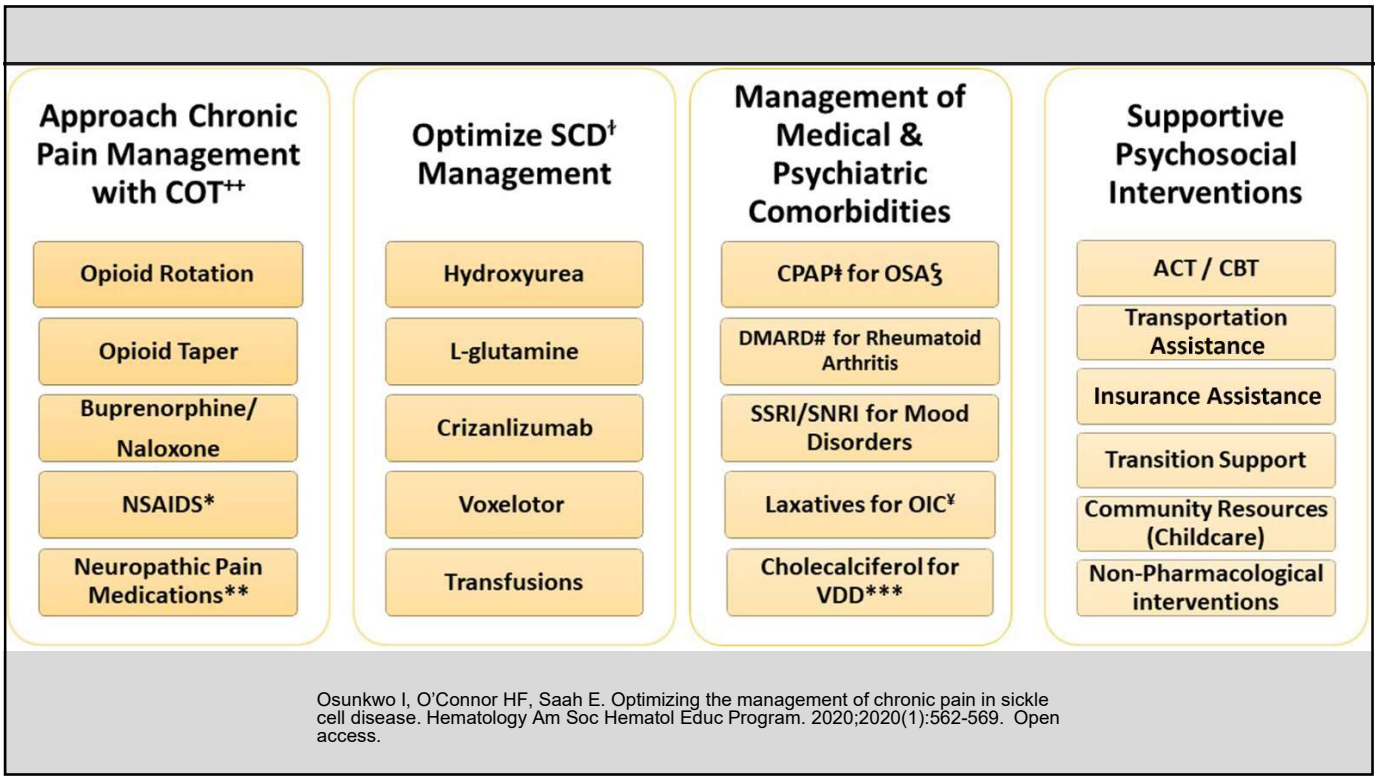
Childerhose JE, Emerson B, Schamess A, Caputo J, Williams M, Klatt MD. SSM - Qualitative Research in Health. 2024;5:100426.

American Society of Hematology 2020 guidelines for management of acute and chronic pain in sickle cell disease

Chronic pain

- Cognitive and behavioral pain management strategies in the context of a comprehensive disease and pain management plan
- Integrative approaches (eg, massage therapy, acupuncture) conditional upon individual patient preference and response.
- Panel suggests against the initiation of chronic opioid therapy unless pain is refractory to multiple other treatment modalities.
- Optimization of SCD management is a priority.

Brandow AM, Carroll CP, Creary S, et al.. Blood Adv. 2020;4(12):2656-2701.



Osunkwo I, O'Connor HF, Saah E. Optimizing the management of chronic pain in sickle cell disease. Hematology Am Soc Hematol Educ Program. 2020;2020(1):562-569. Open access.

Suggestions for pain management

- Form therapeutic alliance with patient.
- Implement early disease modifying treatment to prevent or delay the development of chronic pain.
- Offer non-opioid therapies including integrative and behavioral approaches.
- Take measures to minimize traumatic healthcare experiences.
- Validate and respond to patient-reported experience of pain.
- Chronic opioids may be necessary and dose requirement may increase over time.
- Opioid failure is a potential complication.