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CENLA POTPOURRI
ALEXANDRIA LOUISIANA

Sickle Cell Care for the General Pediatrician

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I have no relevant financial relationships with manufacturers of any commercial products and/or providers of commercial services discussed in this CME activity.

I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

I have not used artificial intelligence in the development of this presentation.

Objectives

- At the conclusion of this activity, learners will be able to:
  - Describe ways to care for children living with sickle cell disease.
  - Apply evidence-based sickle cell preventive care strategies.
  - Recommend specific disease modifying treatments for children with sickle cell disease.
  - Connect the patients with sickle cell resources in Louisiana.

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Sickle Cell Disease Epidemiology

- 100,000 people living with SCD in the US
- 1/365 African-American; 1/16,300 Hispanic American live births
- Sickle cell trait in 9% of AA population
- Average life expectancy 52.6 years
- Louisiana
  - ~80 infants born each year
  - 3,000 individuals living with disease (~0.05% of population)
  - Pediatric patients (<18 years) ~ 1,400
  - ***One of the highest SCD populations per capita in the US***

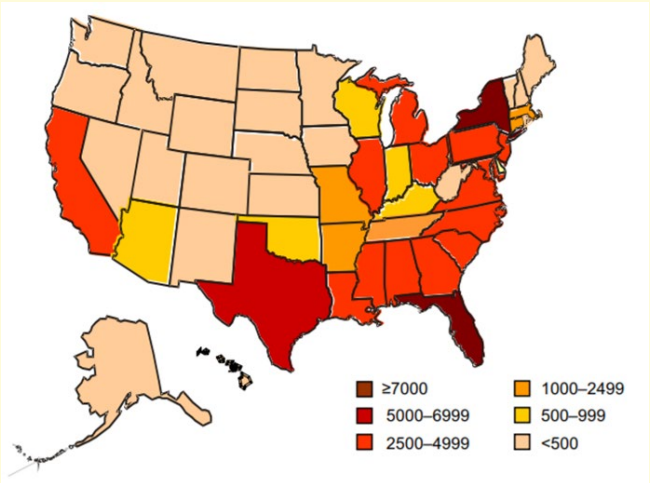

Figure 3. Estimated number of individuals with SCD, based on state-specific African-American and Hispanic birth-cohort disease prevalence and 2008 U.S. Census population, corrected for early mortality
SCD, sickle cell disease

Hassell / Am J Prev Med 2010;38(4S):S512–S521

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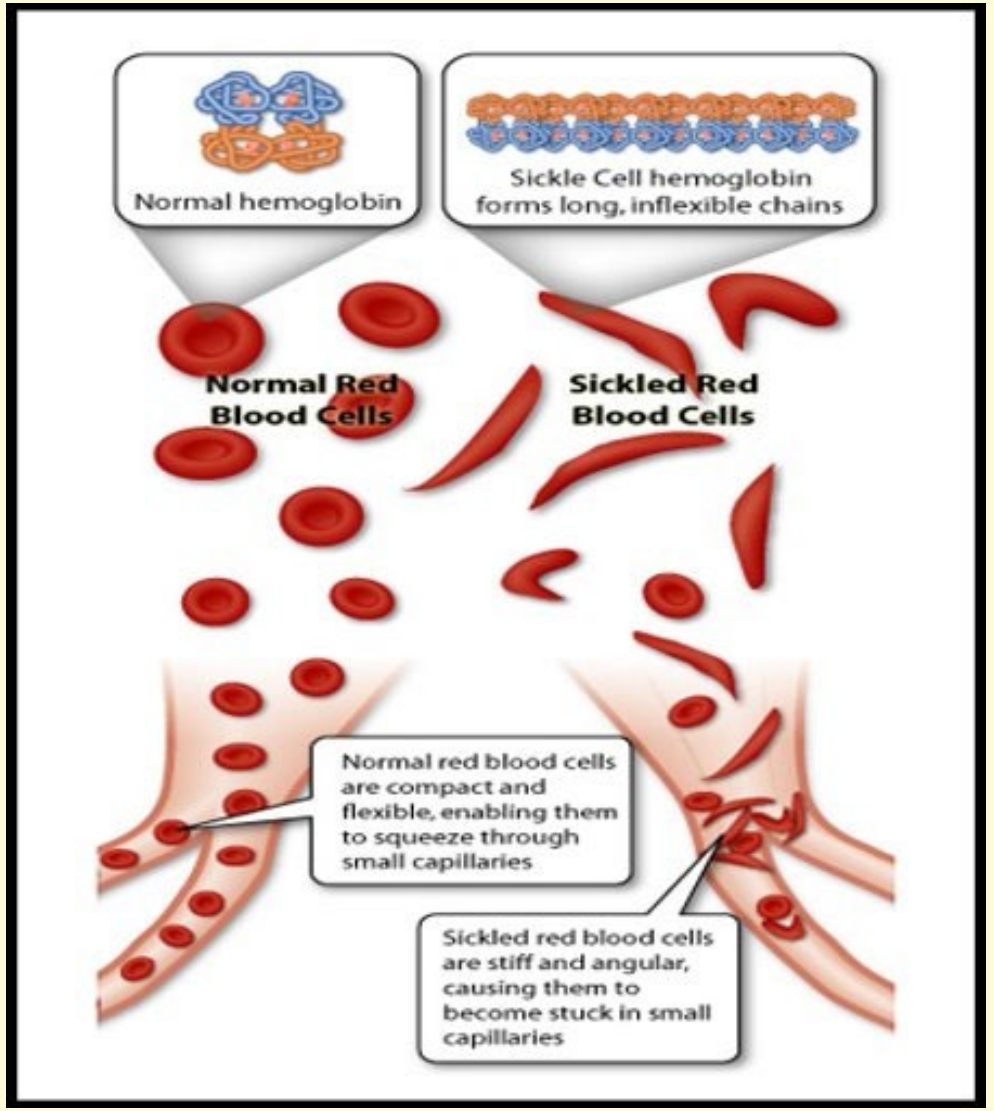
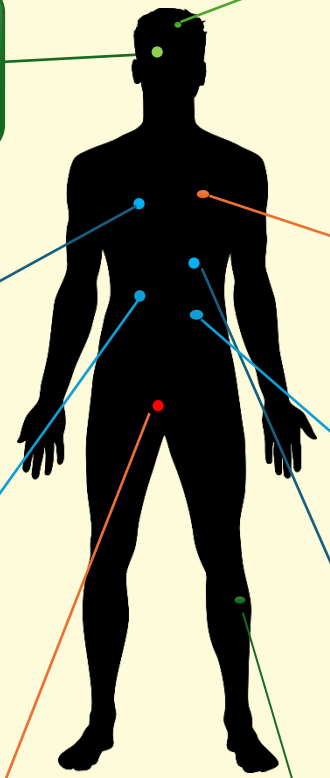
Pathophysiology Review

- Hemoglobin Polymerization
- Hemolysis
- Vaso-occlusion
- Endothelial dysfunction
- Inflammation



Complications



- Ophthalmic
- Respiratory
- Hepatobiliary
- Reproductive
- Neurologic/ Psychiatric
- Circulatory System
- Spleen
- Kidney
- Bone and Soft tissue

Vaso-occlusive Crisis

Chronic Pain

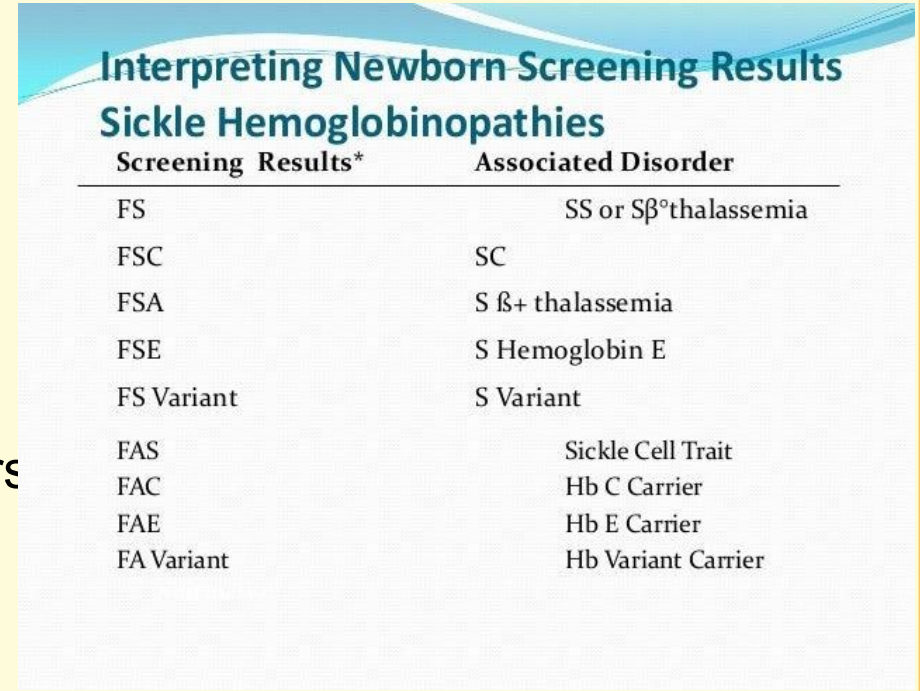
Sickle Cell Genotypes and Severity

Type	Hemoglobin (g/dL)	Clinical Features
Sickle Cell Trait (SCT)	13-18	Asymptomatic, extreme exercise in high heat may provoke hematuria
Sickle Cell β^{+}-thalassemia	10-14	Rare crises HgA production – milder severity
Sickle Cell Hemoglobin C (HbSC)	10-12	Mild anemia; hematuria; vaso-occlusive crises are less common; complications more frequent in older patients
Sickle Cell β^{0}-thalassemia	7-10	Severity similar to HbSS No HgA production
Sickle Cell Anemia (HbSS)	7-10	↑ incidence of vaso-occlusive crises; chronic anemia; microvascular organ injury common

Case #1

- Term newborn first well-child check.
- Birth was uncomplicated and mother reports he is doing well, breast and bottle fed, gaining weight.
- **Upon reviewing the newborn screen, you notice his hemoglobinopathy screen shows FS**
- Your clinic is in Southwest Louisiana, at least 3 hours away from a comprehensive sickle cell center.

What should you do next?



Interpreting Newborn Screening Results
Sickle Hemoglobinopathies

Screening Results*	Associated Disorder
FS	SS or Sβ°thalassemia
FSC	SC
FSA	S ß+ thalassemia
FSE	S Hemoglobin E
FS Variant	S Variant
FAS	Sickle Cell Trait
FAC	Hb C Carrier
FAE	Hb E Carrier
FA Variant	Hb Variant Carrier

www.sicklecellspeaks.com

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Education/Counseling

- Refer to Comprehensive Sickle Cell Center
- Counseling on pathophysiology and inheritance
- Fever precautions:
  - Temp > 101.3F or 38.5C in children >2 months of age.
  - Temp >100. 4 in chidlren <2 months of age
- Pain symptoms, dactylitis, splenomegaly
- Penicillin, Vaccinations
- Connect with local sickle cell support resources

Prevention of Invasive Pneumococcal Infection

- Functional asplenia develops as early as 4 months
- Penicillin prophylaxis reduced incidence by 84% (Gaston, 1986)
- Start by 2 months of age in ALL patients
- Dosing: **<3 yo 125mg and ≥3 yo 250mg twice daily**
- Continue until 5 years old, completed necessary vaccines.
  - Indefinitely if splenectomy or history of bacteremia
- Only 18% of children received ≥300 days of antibiotics (Reeves, 2018)

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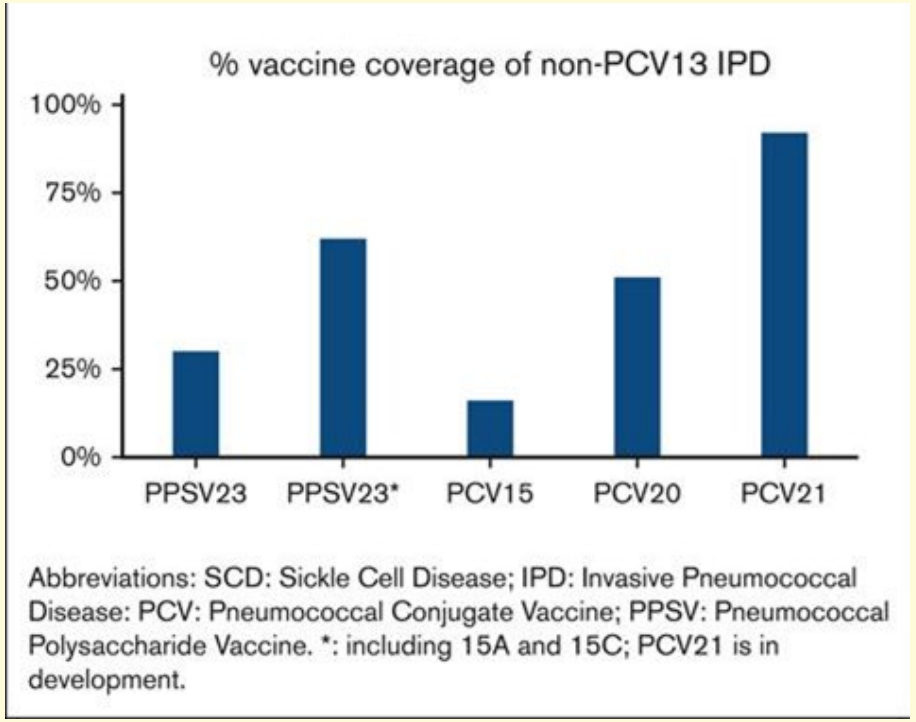
Immunizations: Pneumococcal

- Pneumococcal Conjugate Vaccine (PCV, Prevnar)
  - IPD incidence after intro of PCV13 decreased by 86%
- PPSV23 boosts response to PCV serotypes
  - Give >2yo; then boost after 3-5 years
- PCV20 may provide better coverage
  - 4 dose primary series
  - Single dose at least 8 weeks after last PCV
  - OR 5 years after last PPSV23



Abbreviations: SCD: Sickle Cell Disease; IPD: Invasive Pneumococcal Disease: PCV: Pneumococcal Conjugate Vaccine; PPSV: Pneumococcal Polysaccharide Vaccine. *: including 15A and 15C; PCV21 is in development.

Adamkiewicz et al, 2023

Immunizations: Meningococcal

- Quadrivalent Meningococcal (ACYW)vaccines:
  - Menactra or Menveo (not MenQuadfi)
  - 2 doses 8 weeks apart starting 24 months
  - Boosters given:
    - <7 yo for first dose: 3 yrs after primary series, then q5 years
    - >7 yo for first dose: 5 yrs after primary series, then q5 years
- Monovalent Meningococcal (B) Vaccines: starting age 10
  - Trumenba 3 dose series: 0, 2, 6 months
  - Bexsero 2 dose series 1 month apart
    - Boost 1 year after and then q2-3 years

Case#2

- 9mo F with HbSS presents to the ED with fever of 101.4°F at home, increased fussiness, decreased PO intake, and cough.
- Exam reveals baby in distress, tachycardic and tachypneic, retracting with with SpO2 93%, belly is distended but difficult to palpate spleen.
- Labs: WBC 15k, Hb of 5, retic 4%, Plts 100k

What actions should be taken?

Fever and Splenic Sequestration

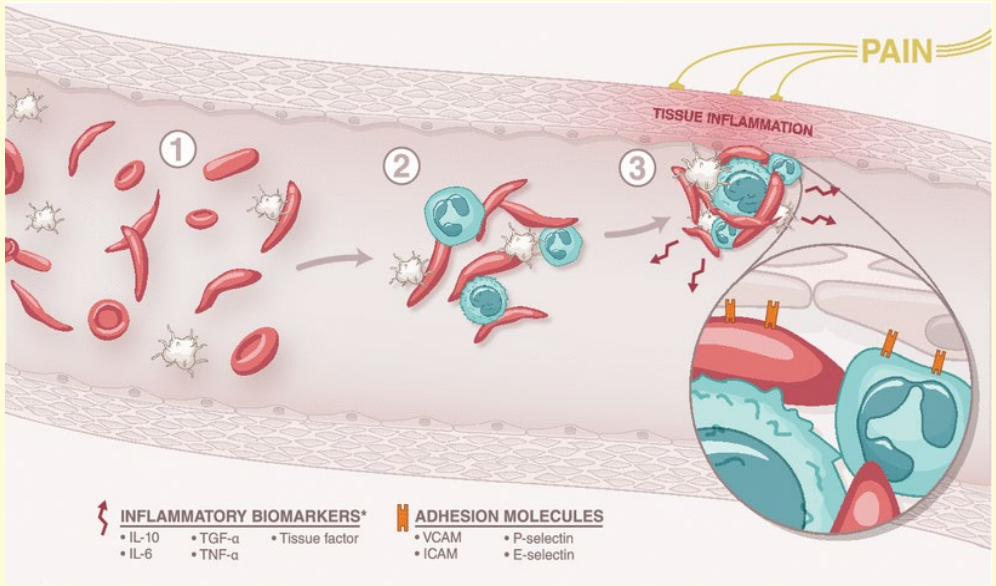
- All patients with fever > 38.5 °C need a sepsis workup
  - **Blood Culture and give Ceftriaxone ASAP**
  - Urine culture, Chest Xray, Abdominal Ultrasound, viral studies SHOULD NOT DELAY ANTIBIOTICS
- Admit children <2 yo or other high-risk factors
- **Splenic sequestration is an emergency**
  - Drop in Hb ≥2 g/dL, splenomegaly, hemodynamic instability
  - Transfuse pRBCs in small aliquots (5-10mL/kg) to avoid hyperviscosity
  - >2 episodes of splenic sequestration requiring transfusion, consider splenectomy

Case#3

- 9yo F with HbSβ^0 disease presents with pain in her abdomen and legs refractory to motrin and tylenol
- Typical VOC pain is in her legs
- No fever, mild tachycardia, no other VS abnormalities
- Appears only mildly uncomfortable, but having difficulty walking at home

Vaso-occlusive Crisis/Event (VOC/VOE)

- Mostly occurs in the extremities, chest, and back
- Risk Factors:↑ HgS ↓HbF
- Triggers: Infection, Dehydration, Extreme Temperatures, Hypoxia, Stress
- There are no tests to rule in/out a VOC
- **Provider bias can interfere with care**



N Engl J Med 2008;359:2254-65.

Approach to Pain Management

- Acute Pain
  - **Scheduled** NSAIDs +opioids (oral or IV)
  - Conservative fluid administration
  - Heat, lidocaine patches, topical NSAIDs, distraction, early ambulation
- Chronic Pain
  - Pharmacological, psychosocial support, pain specialists, physical therapy
- Prevention of Pain:
  - Minimize triggers, increase fluid intake, disease modifying agents

Management of pain MUST be guided by patient reports of pain severity

Acute Chest Syndrome

- **Leading cause of death in SCD**
- Etiology multifactorial
  - Infection (29%), pulmonary infarction (16%), fat embolism (9%)
- Diagnosis: New infiltrate on chest X-ray + 1 or more:
  - Fever >38.5°C, Hypoxia, Respiratory changes, Chest pain, abnormal lung sounds
- Mild pneumonia to acute respiratory failure
- ↑ risk during acute illness, severe VOC, after general anesthesia

Vichinsky et al. *N Eng J Med.* 2000

Acute Chest Syndrome Management

- Antibiotics: Cephalosporin + macrolide
- Maintain oxygen saturation >92%
- Incentive spirometry
- Cautious hydration
- Transfusion if > 1g/dl below baseline
- Consider bronchodilators, AVOID steroids

Case #4

- 12yo F with HbSβ^0 comes to your clinic for evaluation.
- Mother describes a history of weakness on one side that she was hospitalized for at age of 5, received blood transfusions, but then lost to follow up
- Sickle cell center is more than 3 hours away
- What type of screening and interventions do you recommend for this patient?

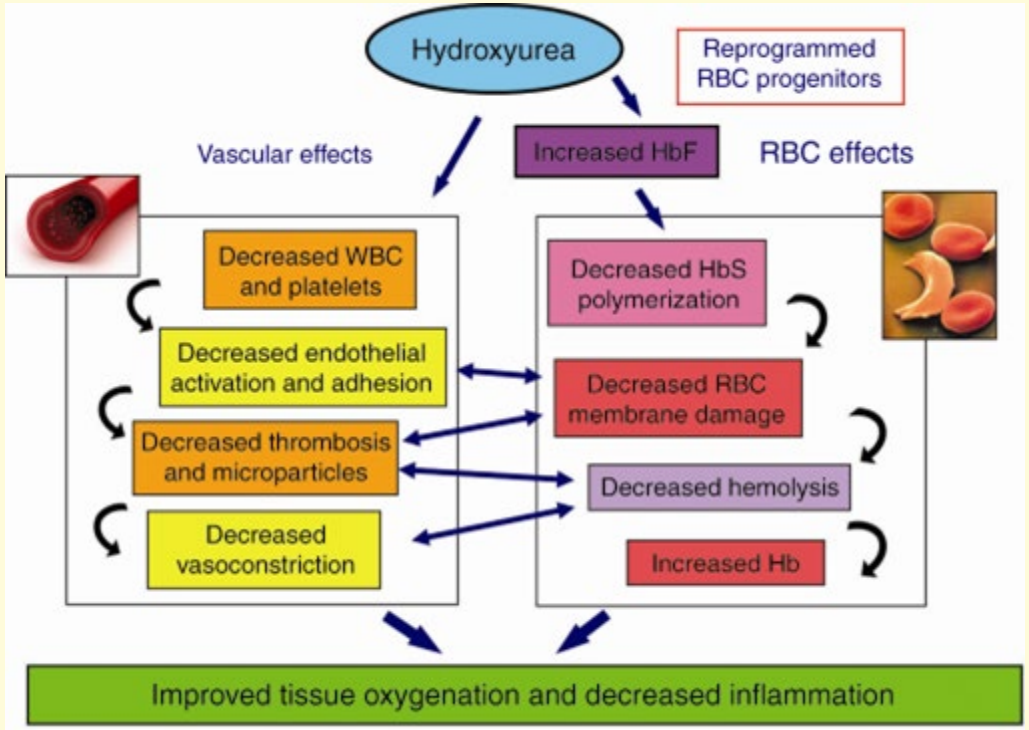
Stroke

- Cerebrovascular occlusion of internal carotid or middle cerebral artery
- Headaches, hemiparesis, parasthesia, aphasia, visual disturbance
- 10% of children will have stroke by age 20
- Primary Prevention
  - Transcranial Doppler yearly age 2-16 with HbSS or Sβ°
  - Elevated (>200 cm/sec) TCD results, refer to a specialist for chronic transfusion therapy
  - TWiTCh trial: HU non-inferior to chronic transfusions
- Secondary Prevention
  - Chronic transfusion therapy every 3-4 weeks
  - Maintain the HbS concentration below 30%

Other Screening Recommendations

- Retinopathy:
  - Ophthalmology screening yearly starting age 8
- Nephropathy:
  - Blood pressure checks at all visits
  - Random Urine microalbumin/creatinine ratio yearly from age 10
  - Referral to renal if abnormal on more than one occasion
- Cardiovascular
  - Regular monitoring BP, O2 Saturations – ECG and Echo if needed
- Cholelithiasis
  - Abdominal US if needed

Disease Modifying Agents: Hydroxyurea

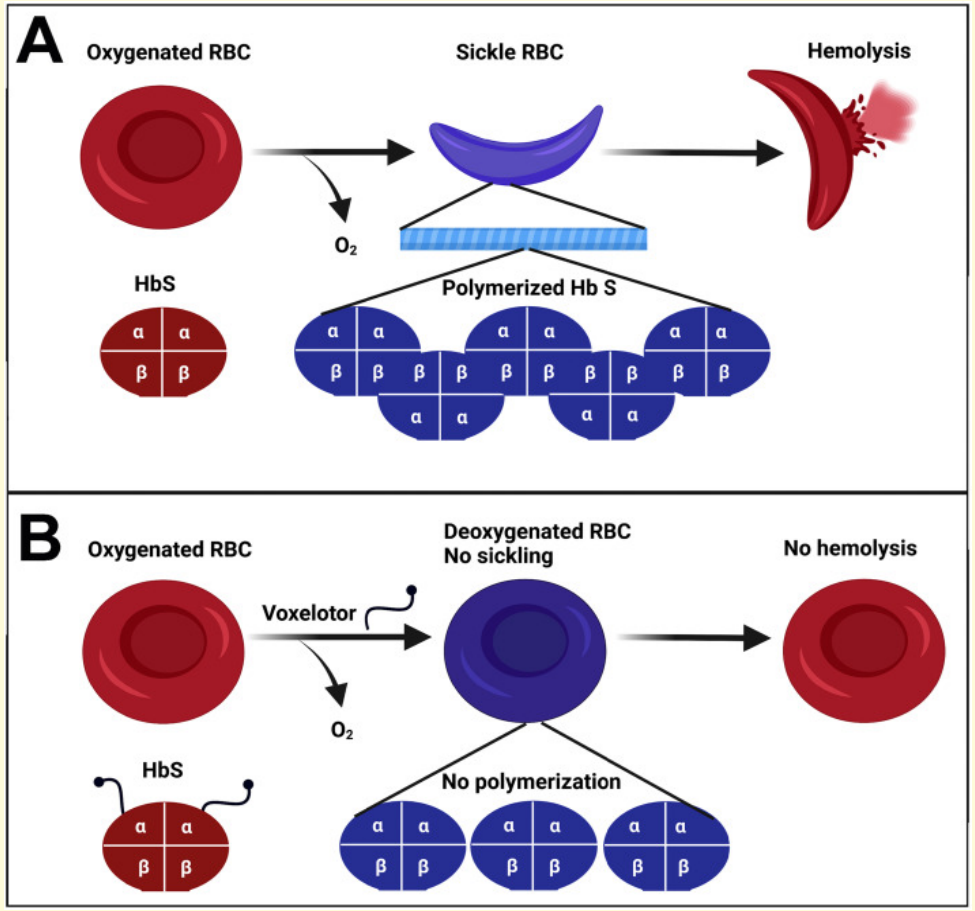


Green and Barral. 2014

- Decreased pain crises, ACS, blood transfusions, mortality
- HgSS and Sβ° infants starting 9 mo (BABY HUG 2012)
- **Once daily starting at 20mg/kg/day**
- Increased HbF, MCV, and Hb, decreased WBC, ANC, and reticulocyte
- Toxicity that is dose dependent and reversible

Disease Modifying Agents

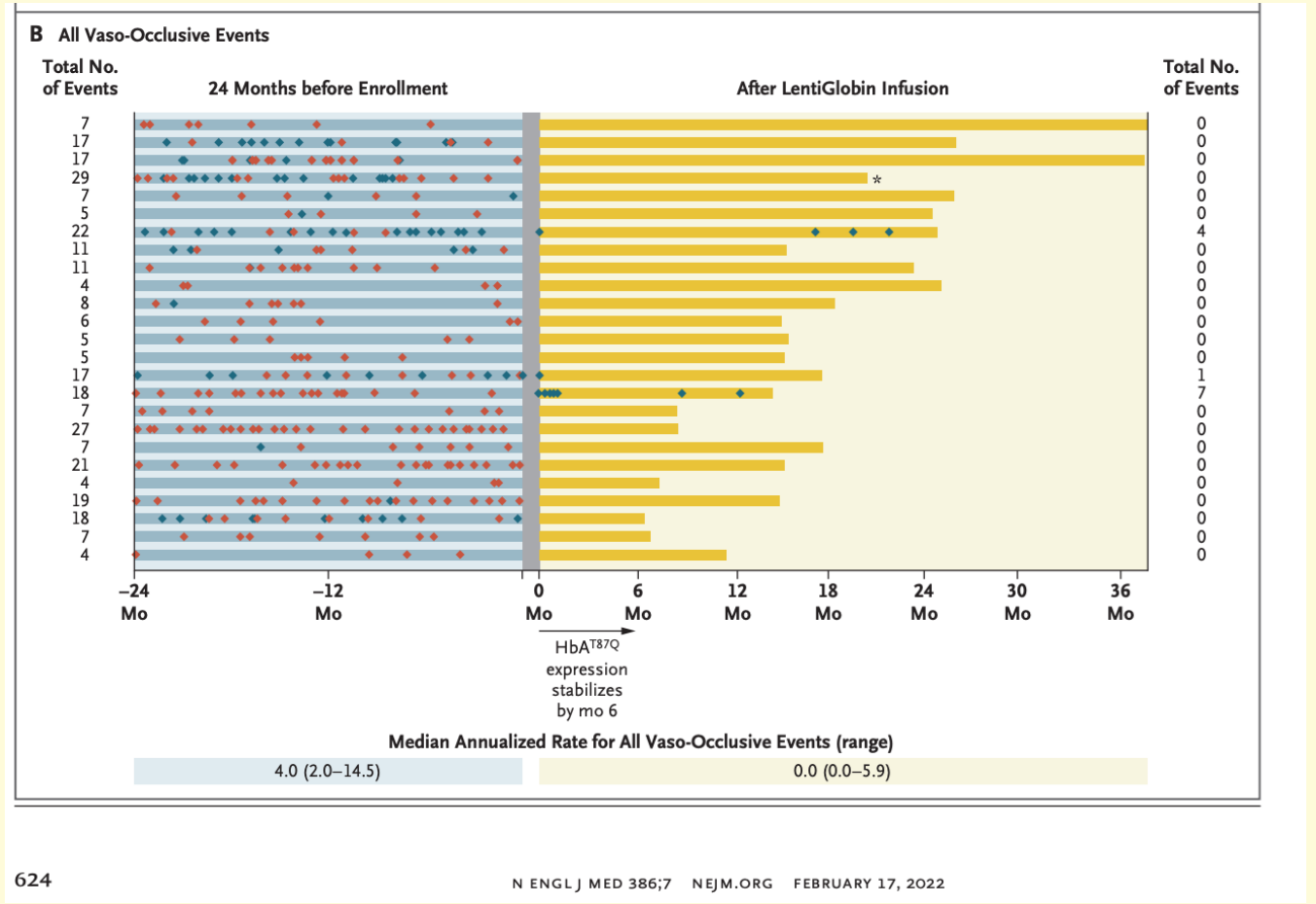
- Oxbryta (Voxeletor) - ages 4+
- Adakveo (Crizanlizumab) - ages 16+
- Endari (L-glutamine) – ages 5+
- Folic Acid – no longer recommended



Leibovitch et al. 2022

Curative Therapies - Update

- Stem Cell Transplant
- LentiGlobin – lentivral gene therapy
- Exa-Cel - CRISPR gene therapy
- Who is the right patient?



Sickle Cell Trait

- Carried in about 3 million people in USA
- Risk of compound heterozygosity
- Mostly asymptomatic
- Extreme conditions --> pain, splenic infarct, rhabdomyolysis
- Risk of glaucoma, kidney disease
- Sudden death in SCT is very rare and should not exclude anyone from sports!
- Counseling for family planning

Athletes: Don't Get Sidelined by Sickle Cell Trait! Play it Safe with These Helpful Tips!

Participating in regular physical activity is one of the most important things you can do for your health. This is true for everyone, including those with Sickle Cell Trait (SCT). You just have to be aware of the warning signs and complications of exercise-related illness, listen to your body, and take steps to protect yourself. Below are answers to some commonly asked questions about SCT, participation in sports, exercise related illness, and what to do to stay safe and healthy while engaging in physical activity.

Should people with SCT be allowed to play sports?

Absolutely! People with SCT can safely participate in all sports provided they take a few general precautions, such as

- Drinking enough water;
- Taking breaks when needed; and
- Not overdoing it, especially when starting a new exercise program.

CDC, ASH, Sickle Cell Association of America

Sickle CellClinics Louisiana

CLINIC	LOCATION
LSU & Tulane/Children's Hospital Comprehensive Clinic	**New Orleans**
Sickle Cell Center of Southern LA (Adult/Transition) - Tulane	**New Orleans**
Ochsner Foundation Hospital	New Orleans
Moss Memorial Health Clinic*	Lake Charles
St. Jude Children's Research Hospital Affiliate Clinic	Baton Rouge
Our Lady of the Lake Adult Sickle Cell Clinic	Baton Rouge
Children's Hospital Specialty Clinic	Lafayette
Ochsner Health Center for Children	Lafayette
Women's and Children's Rapides Specialty Clinic	Alexandria
Willis-Knighton Health Specialists	Shreveport
Ochsner LSU Health -Feist-Weiller Cancer Center	Shreveport
Monroe Sickle Cell Center	Monroe

Sickle Cell Resources

- Louisiana Department of Health:
  - State Newborn Screening
  - Toolkits for Schools and Emergency Departments

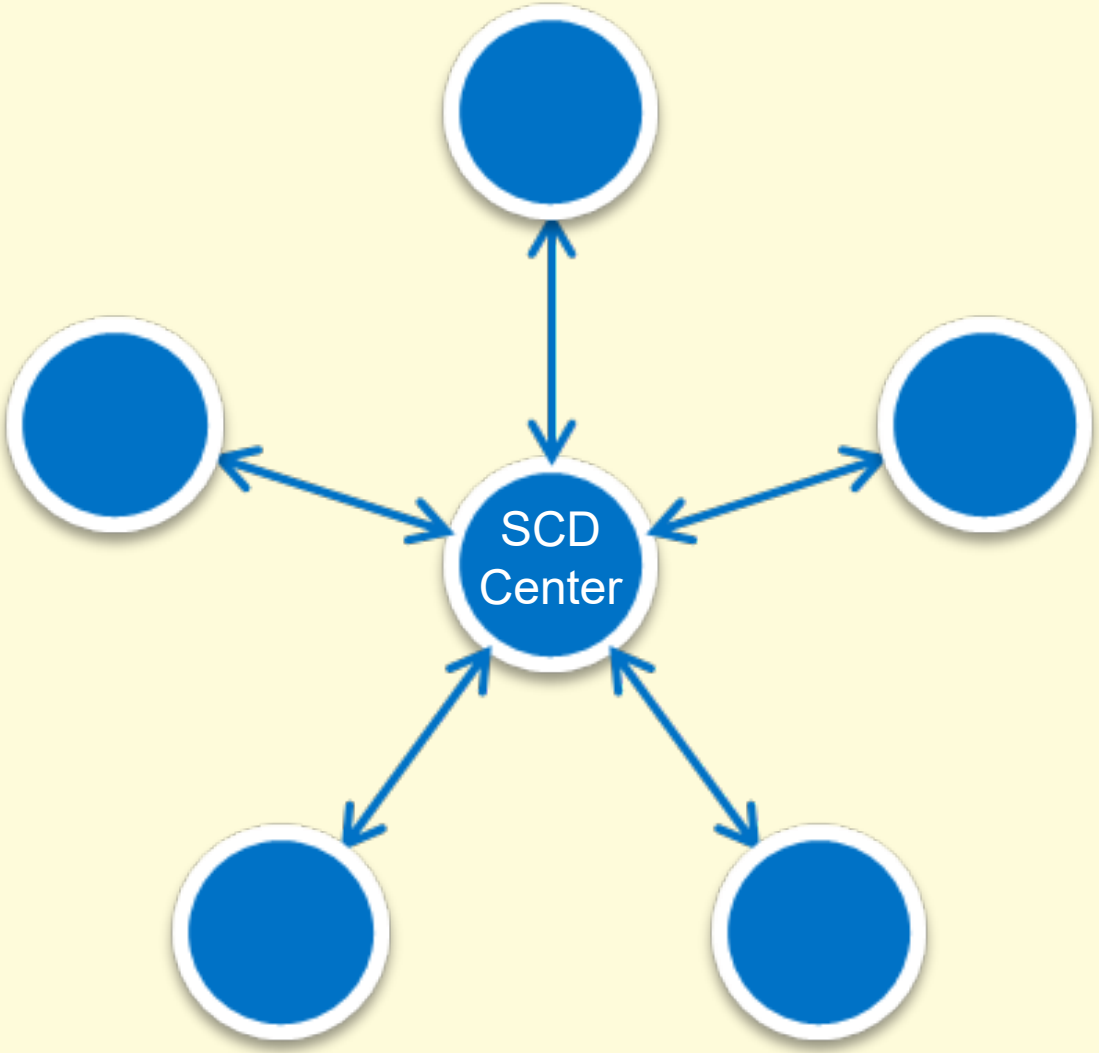
- Louisiana Sickle Cell Commission:
  - ***"to ensure adequate services to all persons living with SCD and formulate new actions to reduce the burden of SCD in Louisiana."***
  - Patient navigation, State advocacy, SCD registry

Regional Sickle Cell Foundations

Region	Foundation Address	Foundation Staff
Region 2 Ascension, E. Baton Rouge, E. Feliciana, Iberville, Pointe Coupee, W. Baton Rouge, W. Feliciana	**Baton Rouge Sickle Cell Association of South Louisiana** 2301 North Boulevard Baton Rouge, LA 70806 (225) 346-8434	Erin Fulbright, Executive Director
Region 5 Allen, Beauregard, Calcasieu, Cameron, Jefferson Davis	**Etta Pete Sickle Cell Anemia Foundation, LLC** 1901 Harless Street Lake Charles, LA 70601 (337) 302-3929	Leticia Pete, Executive Director
Region 6 Avoyelles, Catahoula, Concordia, Grant, LaSalle, Rapides, Vernon, Winn	**Sickle Cell Anemia Research Foundation, Inc.** 2625 Third Street Alexandria, LA 71302 (318) 625-7266	Shay Hardison, Executive Director
Region 7 Bienville, Bossier, Caddo, Claiborne, DeSoto, Natchitoches, Red River, Sabine, Webster	**Sickle Cell Disease Association of America Northwest Louisiana Chapter** 3658 Judson Street Shreveport, LA 71109 (318) 636-5300	Rosalind Spain, Executive Director
Region 8 Caldwell, E. Carroll, Franklin, Jackson, Lincoln, Madison, Morehouse, Ouachita, Richland, Tensas, Union, W. Carroll	**Northeast Sickle Cell Anemia Foundation** 1604 Winnsboro Road Monroe, LA 71202 (318) 322-0896	Donna Thaxton, Executive Director

Sickle Cell Centers as a Hub

CALL US!
504-896-9740



MOC Questions in Slido

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Review of Content

- With prevention strategies, once a fatal pediatric illness now a chronic disease
- Penicillin ppx should be start by 2 months of age in all patients
- Additional pneumococcal and meningococcal vaccinations
- TCDs starting age 2 for primary stroke prevention
- Rapid antibiotics for fevers
- Multimodal pain management and recognizing Acute Chest
- Hydroxyurea starting at 9 months
- There is a cure...but it's complicated

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Action Items

- Ensure all patients with sickle cell disease are on penicillin prophylaxis until at least age 5 up to date on all recommended vaccines
- Refer patients for TCDs starting at age 2-16 if not following at sickle cell center
- Consider starting Hydroxyurea and know how to monitor if unable to see hematologist regularly

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