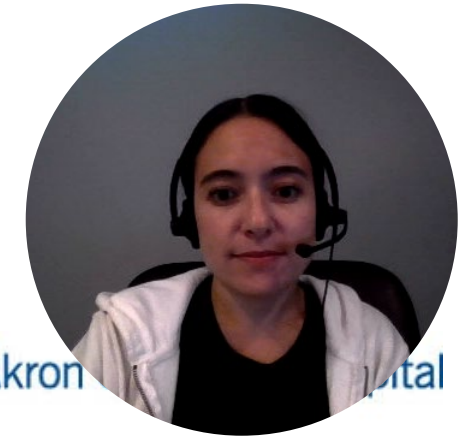
Pharmacologic Management of Sickle Cell Disease

Lauren Beck, APRN-CNP

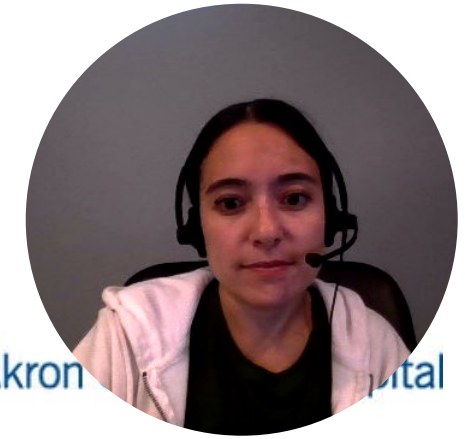
Disclosures

- I have no relevant financial relationships to disclose.



Objectives

- Describe sickle cell treatment in the outpatient setting.
- Discuss maintenance medications and newer therapies for patients with sickle cell disease.
- Review pharmacologic management of common acute issues related to sickle cell disease.



Review of Sickle Cell Disease

- **Most common inherited blood disorder**
- Point mutation in 6th position of HBB gene replaces glutamate with valine → creates Hemoglobin S
- Deoxygenated HgbS molecules polymerize and change the shape of the red blood cell
- Altered RBC shape impairs blood flow

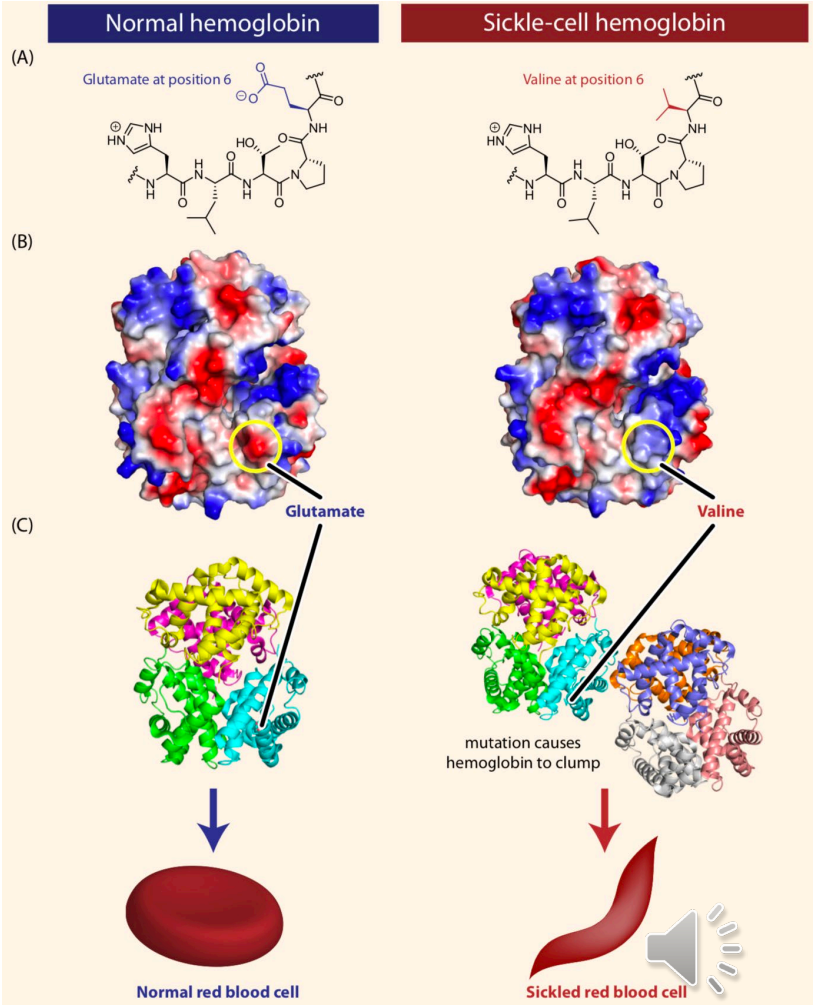


Image: LabXchange

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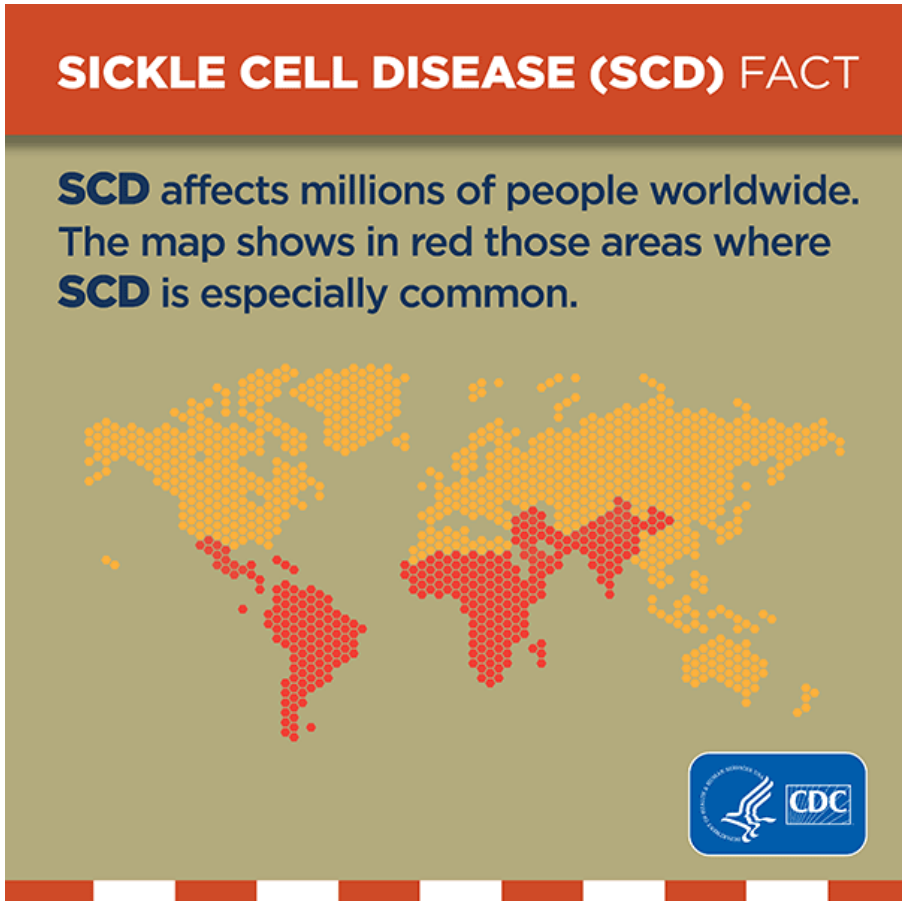
Prevalence of Sickle Cell Disease



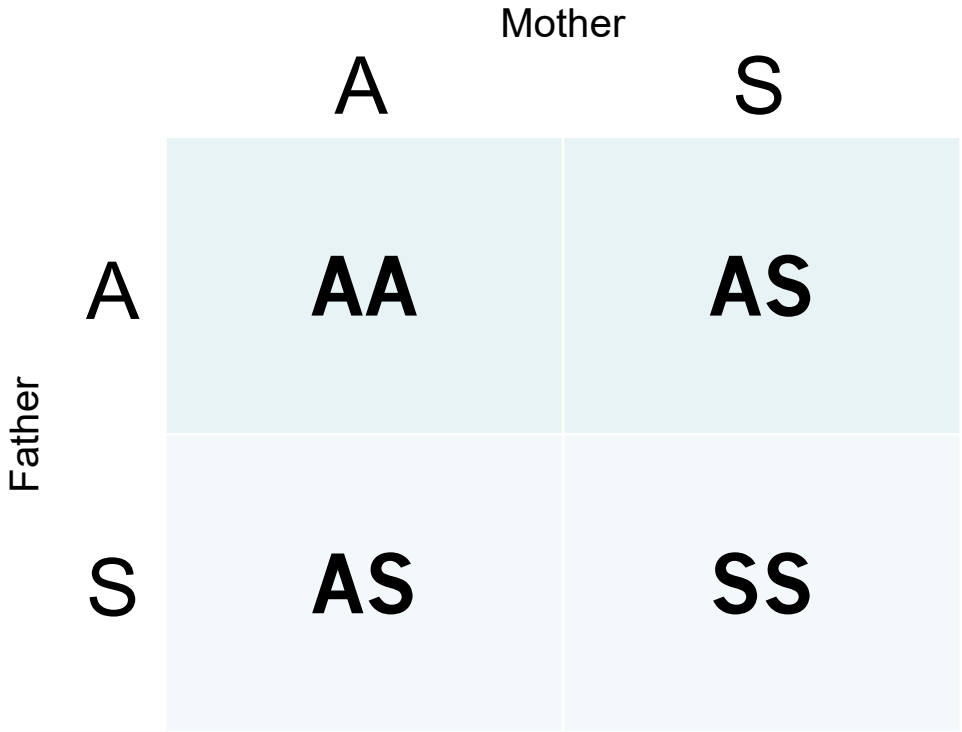
- ~100,000 people in the US have SCD
  - 1 in 365 Black American births
  - 1 in 16,300 Hispanic American births
- ~90% of people with SCD in the US are Black or African American
- 3–9% are Hispanic or Latino

- Affects ~8 million people globally
- The highest concentrations of people with SCD live in Africa, Central & South America, India, Saudi Arabia, and the Mediterranean

- 1 in 13 Black American babies are born with sickle cell trait

Image: CDC

Inheritance Pattern for HgbSS



AA = Normal adult hemoglobin

AS = Sickle cell trait

SS = Hemoglobin SS disease

Different Types of Sickle Cell Disease

- Hemoglobin SS — Sickle cell anemia
- Hemoglobin SC
- Hemoglobin S/beta-0 thalassemia — Sickle cell anemia
- Hemoglobin S/beta+ thalassemia
- Hemoglobin SD
- Hemoglobin SE
- Hemoglobin S/Variant

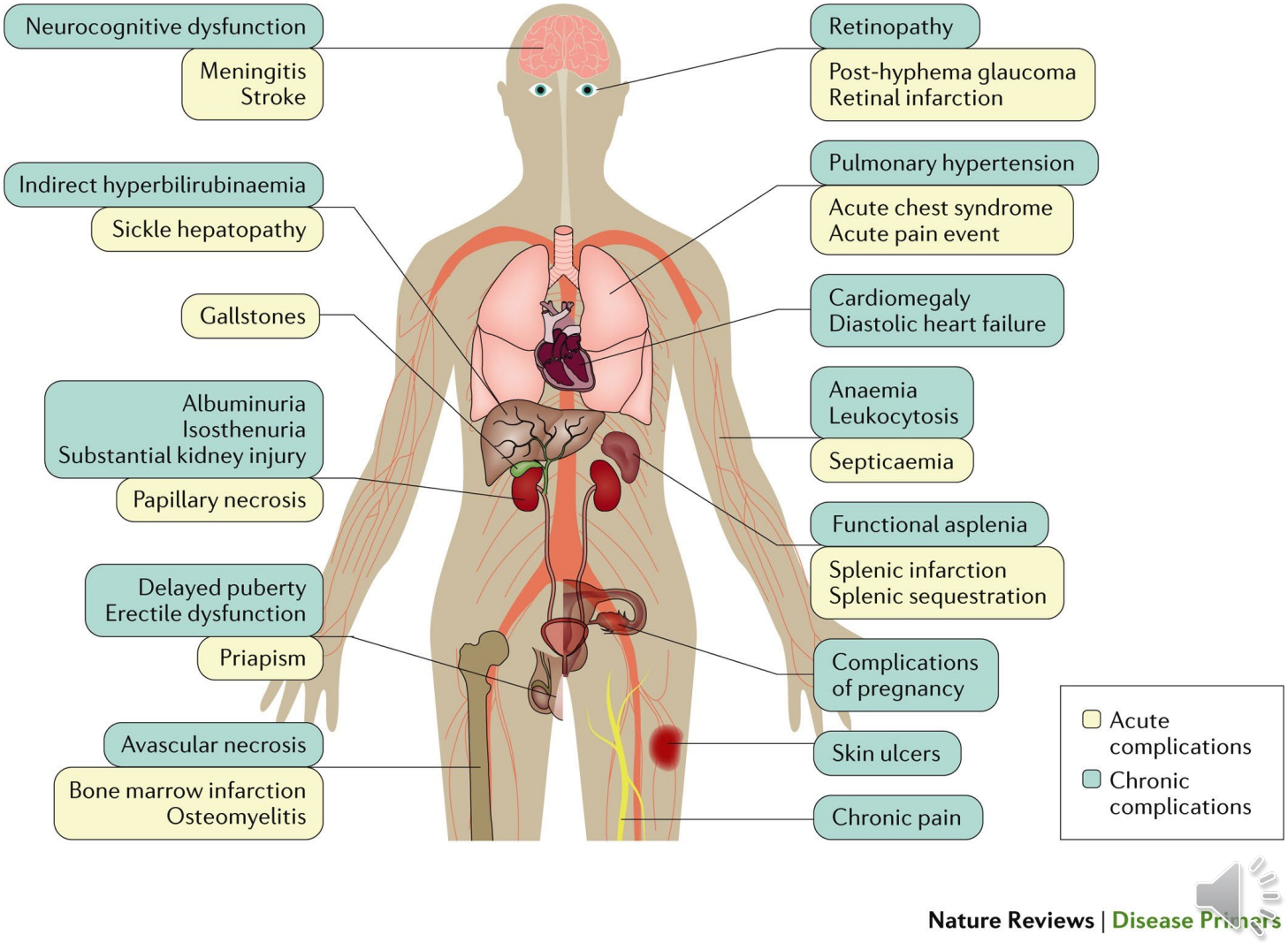


Image: Nature Reviews

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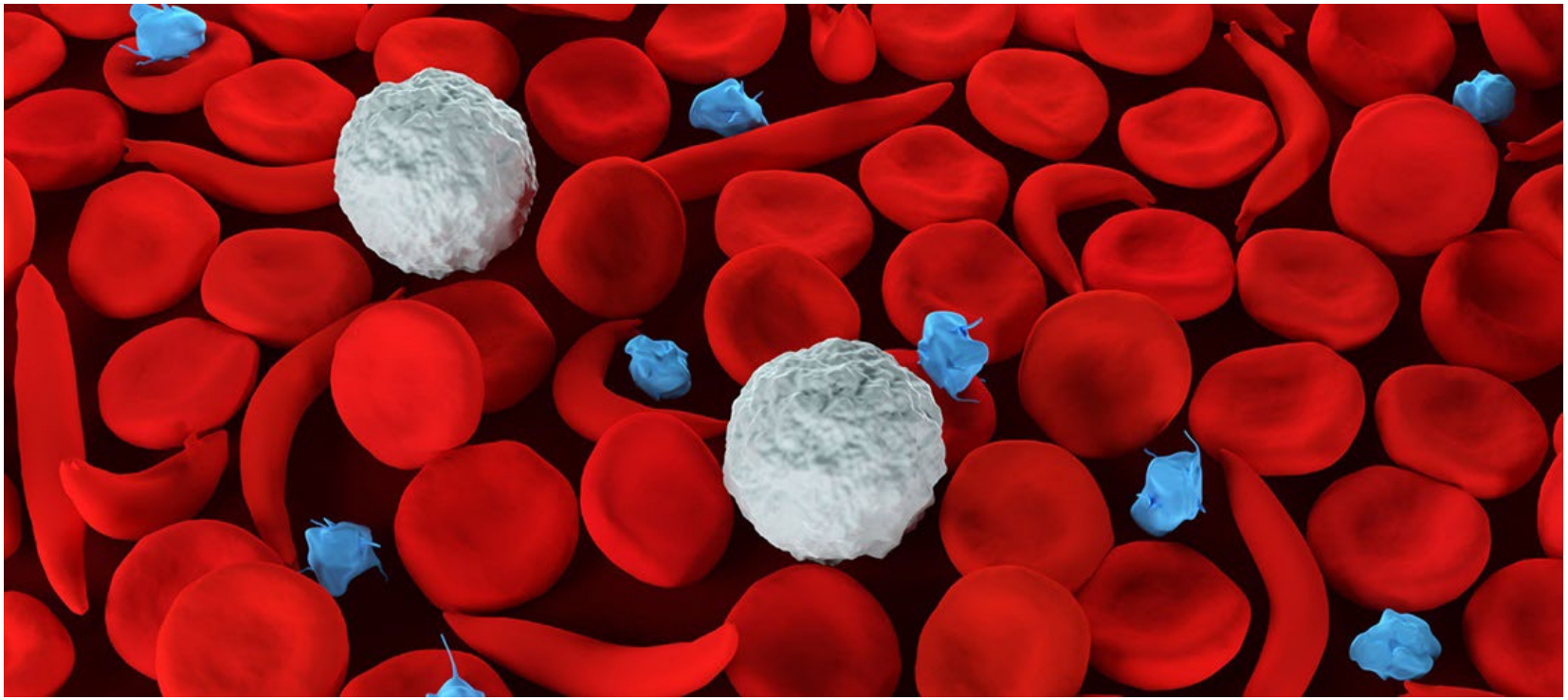

Medications Commonly Used in the Care of Patients with Sickle Cell Disease

Image: Johns Hopkins Medicine

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Pfizer Press release | Research and Pipeline | Diseases & Conditions

Pfizer Voluntarily Withdraws All Lots of Sickle Cell Disease Treatment OXBRYTA® (voxelotor) From Worldwide Markets

Wednesday, September 25, 2024 - 05:00pm

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) announced today that it is voluntarily withdrawing all lots of OXBRYTA ® (voxelotor) for the treatment of sickle cell disease (SCD) at this time, in all markets where it is approved. Pfizer is also discontinuing all active voxelotor clinical trials and expanded access programs worldwide.

Medication Reconciliation Example 1

Home Medications

	Taking?	Last Dose	Start Date	End Date	Provider
acetaminophen (TYLENOL) 160 MG/5ML suspension Take 6 mL (192 mg) by mouth every 6 hours as needed for Pain		--	08/23/24	--	Inpatoutpat, Md, MD
Cholecalciferol 25 MCG (1000 UT) CHEW Take 1 Tablet by mouth daily		--	08/23/24	--	Inpatoutpat, Md, MD
hydroxyurea (HYDREA) 100 mg/mL oral suspension Take 4.6 mL (460 mg) by mouth daily		--	08/23/24	--	Inpatoutpat, Md, MD
ibuprofen (ADVIL; MOTRIN) 100 MG/5ML suspension Take 8 mL (160 mg) by mouth 3 times daily as needed for Pain		--	08/23/24	--	Inpatoutpat, Md, MD
penicillin V potassium (VEETID) 250 MG/5ML solution Take 2.5 mL (125 mg) by mouth 2 times daily		--	08/23/24	--	Inpatoutpat, Md, MD

Mark as Reviewed Last Reviewed by Inpatoutpat, Md, MD on 8/23/2024 at 11:28 AM History

Medication Reconciliation Example 2

acetaminophen (TYLENOL) 325 MG tablet Take 2 Tablets (650 mg) by mouth every 6 hours as needed for Pain	--	08/23/24	--	Inpatoutpat, Md, MD
albuterol 108 (90 Base) MCG/ACT inhaler Inhale 2 Puffs into the lungs every 4-6 hours as needed for Wheezing or Shortness of Breath Notes: 1 Each = One 200 dose inhaler; Pharmacy may dispense any albuterol 90 mcg HFA, brand or generic, including Ventolin HFA, ProAir HFA, or Proventil HFA.	--	08/23/24	--	Inpatoutpat, Md, MD
cholecalciferol (VITAMIN D3) 25 mcg (1000 units) tablet Take 1 Tablet (1,000 Units) by mouth daily	--	08/23/24	--	Inpatoutpat, Md, MD
famotidine (PEPCID) 20 MG tablet Take 1 Tablet (20 mg) by mouth 2 times daily	--	08/23/24	--	Inpatoutpat, Md, MD
fluticasone HFA 110 mcg inhaler Inhale 1 Puff into the lungs 2 times daily Notes: 1 Each = 1 Inhaler	--	08/23/24	--	Inpatoutpat, Md, MD
hydroxyurea (HYDREA) 500 MG capsule Take 3 Capsules (1,500 mg) by mouth daily	--	08/23/24	--	Inpatoutpat, Md, MD
ibuprofen (MOTRIN) 200 MG tablet Take 2 Tablets (400 mg) by mouth 3 times daily as needed for Pain Take with meals.	--	08/23/24	--	Inpatoutpat, Md, MD
lidocaine (LIDODERM) 5 % PTCH patch Place 1 Patch over 12 hours onto the skin daily as needed for Pain	--	08/23/24	--	Inpatoutpat, Md, MD
loperamide (IMODIUM) 2 MG capsule Take 1 Capsule (2 mg) by mouth 3 times daily as needed for Diarrhea	--	08/23/24	--	Inpatoutpat, Md, MD
ondansetron (ZOFRAN-ODT) 8 MG disintegrating tablet Take 1 Tablet (8 mg) by mouth every 8 hours as needed for Nausea	--	08/23/24	--	Inpatoutpat, Md, MD
penicillin V potassium (VEETID) 250 MG tablet Take 1 Tablet (250 mg) by mouth 2 times daily	--	08/23/24	--	Inpatoutpat, Md, MD
pseudoephedrine (SUDAFED) 60 MG tablet Take 1 Tablet (60 mg) by mouth every 12 hours as needed (priapism)	--	08/23/24	--	Inpatoutpat, Md, MD
sildenafil (VIAGRA) 50 MG tablet Take 1 Tablet (50 mg) by mouth daily	--	08/23/24	--	Inpatoutpat, Md, MD
Spacer/Aero-Holding Chambers DEVI 1 Device by Does not apply route as needed (Use with inhaler.)	--	08/23/24	--	Inpatoutpat, Md, MD
Voxelotor 500 MG TABS Take 3 Tablets (1,500 mg) by mouth daily	--	08/23/24	--	Inpatoutpat, Md, MD

Penicillin V Potassium

Rationale	Children with SCD are functionally asplenic and therefore susceptible to infections with Strep pneumoniae
Mechanism of Action	Inhibits cell wall biosynthesis of pneumococcal bacteria, causing lysis
Age Group	Newborn & up (can discontinue at age 5)
Dose	125mg PO twice a day for ages 0-2 250mg PO twice a day for ages 3+
Available Forms	**250mg/5ml** & 125mg/5ml solution, 250mg tablets
Monitoring	None
Common Side Effects	• GI upset (nausea/vomiting/diarrhea) • Rash
Special Considerations	• Take with food • For PCN allergy, may take amoxicillin or erythromycin instead (dose is the same)

The New England
Journal of Medicine

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PROPHYLAXIS WITH ORAL PENICILLIN IN CHILDREN WITH SICKLE CELL ANEMIA

A Randomized Trial

MARILYN H. GASTON, M.D., JOEL I. VERTER, PH.D., GERALD WOODS, M.D., CHARLES PEGELOW, M.D., JOHN KELLEHER, M.D., GERALD PRESBURY, M.D., HAROLD ZARKOWSKY, M.D., ELLIOTT VICHINSKY, M.D., RATHI IYER, M.D., JEFFREY S. LOBEL, M.D., STEVEN DIAMOND, M.D., C. TATE HOLBROOK, M.D., FRANCES M. GILL, M.D., KIM RITCHEY, M.D., AND JOHN M. FALLETTA, M.D., FOR THE PROPHYLACTIC PENICILLIN STUDY GROUP

Abstract Children with sickle cell anemia have an increased susceptibility to bacterial infections, especially to those caused by *Streptococcus pneumoniae*. We therefore conducted a multicenter, randomized, double-blind, placebo-controlled clinical trial to test whether the regular, daily administration of oral penicillin would reduce the incidence of documented septicemia due to *S. pneumoniae* in children with sickle cell anemia who were under the age of three years at the time of entry. The children were randomly assigned to receive either 125 mg of penicillin V potassium (105 children) or placebo (110 children) twice daily. The trial was terminated 8 months early, after an average of 15 months of follow-up, when an 84 percent reduction in the incidence of infection was observed in the group treated with penicillin, as compared with the group given placebo (13 of 110 patients vs. 2 of 105; P = 0.0025), with no deaths from pneumococcal septicemia occurring in the penicillin group but three deaths from the infection occurring in the placebo group. On the basis of these results, we conclude that children should be screened in the neonatal period for sickle cell hemoglobinopathy and that those with sickle cell anemia should receive prophylactic therapy with oral penicillin by four months of age to decrease the morbidity and mortality associated with pneumococcal septicemia. (N Engl J Med 1986; 314:1593-9.)

FOR 20 years, children with sickle cell anemia have been known to have an increased susceptibility to severe bacterial infections, particularly those due to *Streptococcus pneumoniae*. Meningitis, pneumonia, and septicemia caused by this organism have been recognized as the major causes of death among children with the disorder, with those under three years of age at highest risk.[1-5] The incidence of pneumococcal septicemia among children with sickle cell anemia under the age of five years appears to have remained remarkably constant, at 7 to 8 per 100 person-years of observation.[6-8] This illness is often fulminant, progressing from the onset of fever to death in less than 12 hours; the case fatality rate may be as high as 35 percent.[7,9,10]

The recent widespread availability of pneumococcal vaccines and improved programs of care for chil-

Address reprint requests to Dr. Gaston at the Sickle Cell Disease Branch, Federal Bldg., Rm. 504, 7550 Wisconsin Ave., Bethesda, MD 20892.

Sponsored by the Sickle Cell Disease Branch, Division of Blood Diseases and Resources, National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), Bethesda.

The clinical centers in the Prophylactic Penicillin Study (PROPS) group and their principal investigators and project coordinators were Interfaith Medical Center, Brooklyn — Steven Diamond, M.D., and Margaret Allen, R.N.; Boston City Hospital — Lillian McMahon, M.D., and Jane Luff, R.N.; Yale University, New Haven, Conn. — Kim Ritchey, M.D., and Yolanda Rooks, P.N.P.; Children's Hospital, Philadelphia — Frances Gill, M.D., and Cynthia Allen, R.N.; Children's Hospital, Washington, D.C. — John Kelleher, M.D., and Iola Williams, P.N.P.; Duke University, Durham, N.C. — John Falletta, M.D., and Marilyn Hockenberry, R.N.; University of Miami — Charles Pegelow, M.D., and Mavis Eaton, P.N.P.; Michael Reese Hospital, Chicago — Nasrin Talishy, M.D., and Joyce Meyers, R.N.; Washington University, St. Louis — Harold Zarkowsky, M.D., and William Bishop, P.N.P.; University of Tennessee — St. Jude Children's Research Hospital, Memphis — Gerald Presbury, M.D., and Julie Dahl, R.N.; Children's Hospital, Oakland, Calif. — Elliott Vichinsky, M.D., and Ann Earles, P.N.P.; San Francisco General Hospital — William Lande, M.D., and Patricia Gibbons, P.N.P.; Children's Hospital, Cincinnati — Jeffrey Lobel, M.D., and Eula Hawkins, R.N.; University of South Alabama, Mobile — Vipul Mankad, M.D., and Patricia Davis, R.N.; University of Illinois, Chicago — Sudha Rao, M.D., and Sandra Gooden, R.N.; Children's Mercy Hospital, Kansas City, Mo. — Gerald Woods, M.D., and Wanda Boyd, R.N.; East Carolina University, Greenville, N.C. — C. Tate Holbrook, M.D., and Cindy Gaskins; University of Mississippi, Jackson — Rathi Iyer, M.D., and Jennie Nugent; Arkansas Children's Hospital, Little Rock — Dasilee H. Berry, M.D., and Kathryn Bailey, R.N.; University of Alabama, Birmingham — Robert Castleberry, M.D., and Nancy Brown, R.N.; Grady Memorial Hospital, Atlanta — Iris Buchanan, M.D., and JoAnn Harris, R.N.; Children's Memorial Hospital, Chicago — Helen Maurer, M.D., and Carol Ingrisano, R.N.; and the Sickle Cell Comprehensive Center, Milwaukee — Betty Malone, M.D., and Denise Lockhart, R.N. The chairman of the PROPS group was John Falletta, M.D., Duke University, the staff at the project office (NHLBI) were Marilyn H. Gaston, M.D., and Sharon Brown, B.S., and the staff at the Data Coordinating Center (NHLBI) were Joel Verter, Ph.D., and Pat Strobell. The Policy Advisory Board consisted of Harold Ballard, M.D. (chairman), Darleen Powars, M.D., Marcus Kjelsberg, Ph.D., George Honig, M.D., Helen Ranney, M.D., Andrew Keller, M.D., Wendell Rosse, M.D., Paul Levy, Ph.D., and Clarice Reid, M.D. Participants at the National Hemoglobinopathy Laboratory (Centers for Disease Control) were Rosalie Baine, Ph.D., and Solomon Holland, M.T. (A.S.C.P.); at the National Institute of Allergy and Infectious Diseases (NIH), Michael Frank, M.D., and Stephanie Simmons, M.T.; and at the Drug Dispensing Center (Duke University), Donald Holloway, Pharm.D.

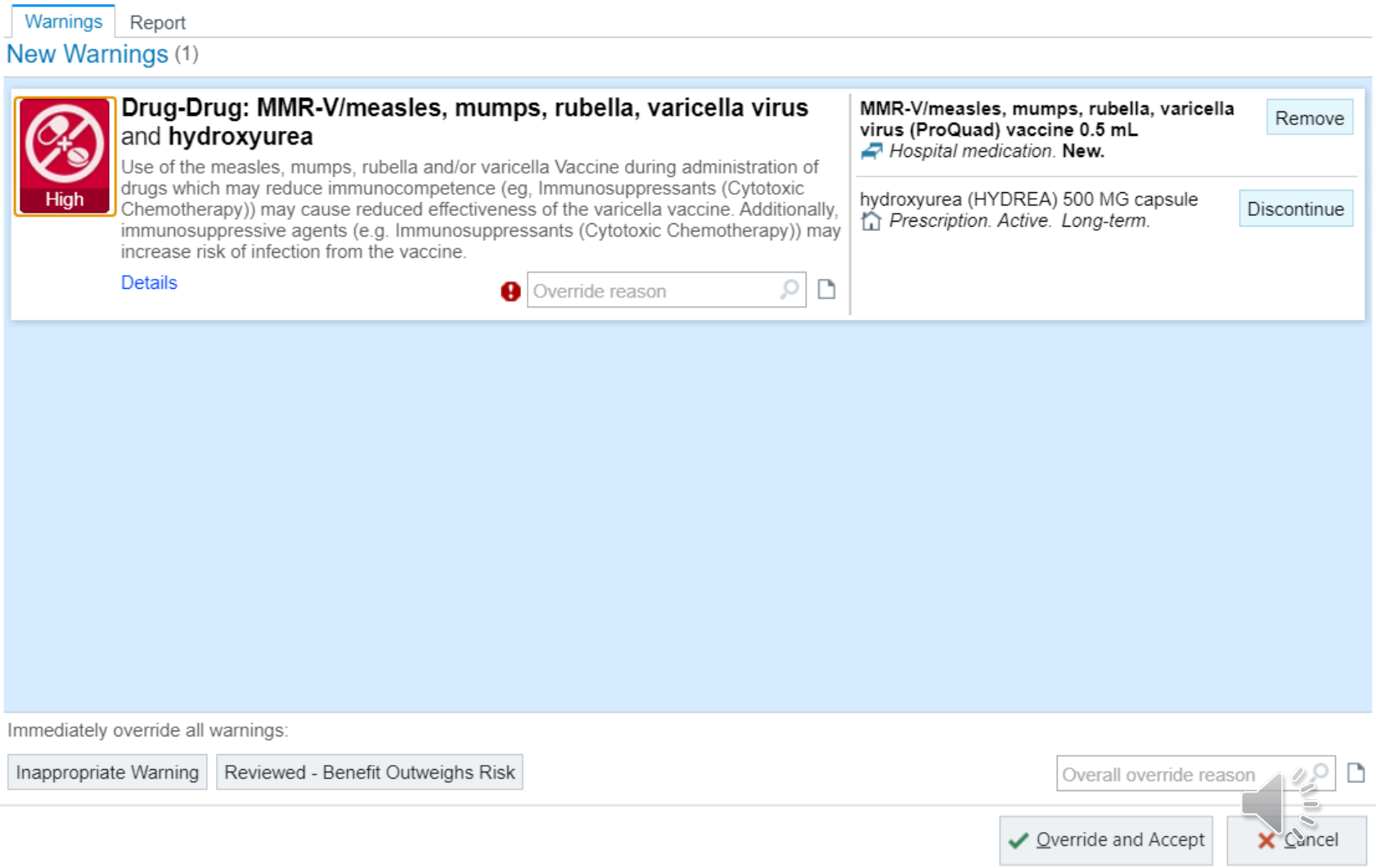
Vaccines

Vaccine	2mo	4mo	6mo	12-15mo	2y	3y	4y	5y	6y	7y	8y	9y
Hib	X	X	X	X								
PCV	X	X	X	X	X*							
MenACWY	X	X	X	X			X					X
MenB												

*PCV20 if not given previously.

Vaccine	10y	11y	12y	13y	14y	15y	16y	17y	18y	19y	20y	21y
Hib												
PCV												
MenACWY					X					X		
MenB	X x2											

Hydroxyurea and Live Vaccines



Vitamin D Supplementation

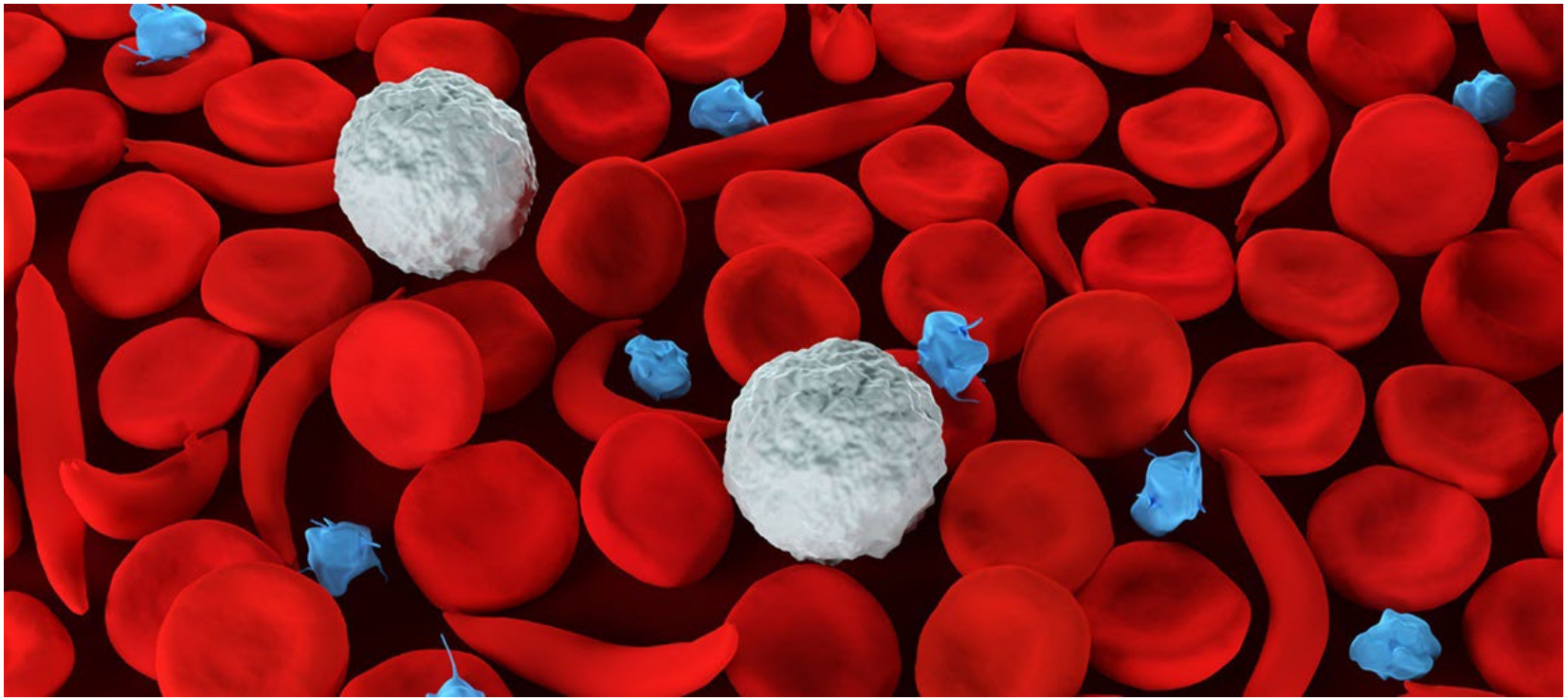
Cholecalciferol (D3), Ergocalciferol (D2)

Rationale	• **Vitamin D deficiency is prevalent among patients with sickle cell disease.** • **Vitamin D is essential for bone growth.**
Mechanism of Action	Stimulates calcium and phosphate absorption from the small intestine to enable normal bone mineralization
Age Group	Newborn & up
Dose	Treatment: 2,000 IU PO daily or 50,000 IU PO weekly x6 wks Maintenance: 600-1,000 IU PO daily
Available Forms	Numerous liquid, tablets, chewables
Monitoring	• Vitamin D 25 hydroxy levels every 3-6 months starting around age 1 • Normal level is 30-100 ng/ml
Common Side Effects	Lexicomp says none!
Special Considerations	For patients with SCD, vitamin D deficiency can contribute to chronic pain, osteoporosis, muscle weakness, poor bone growth, bone fractures, shorter height than expected

Vitamin D Stoss Dosing

Vitamin D 25-hydroxy Level (ng/mL)	Cholecalciferol Dose (IU/kg) *Max dose 600,000 units
< 10	14,000
10-29	12,000
30-50	7,000

- **STOSS DOSING**
  - Dose able to be administered over 4 hours PO or NG
  - Provides a 2-3 month store of vitamin D
- **Goal level:** 30-100 ng/mL
- **Products available for Vitamin D3:**
  - Capsules: 5,000 units; 50,000 units
  - Tablets: 1,000 units
  - Liquid preparations: 400 IU/ml; *1000 IU/0.028mLs (DDrops) preferred due to volume*



Medications for Prevention of Sickle Cell Complications

Image: Johns Hopkins Medicine

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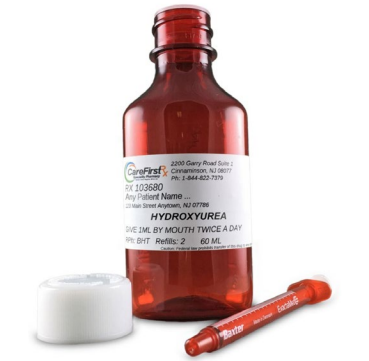

FOR ILLUSTRATION PURPOSE ONLY. ACTUAL PRODUCT MAY VARY.

Hydroxyurea (Droxia, Hydrea, Siklos, XROMI)

FDA approved 1998

Hydroxyurea (Droxia, Hydrea, Siklos, XROMI)

Mechanism of Action	• Antimetabolite chemotherapeutic agent • Increases RBC water content → less likely to become deformed & rigid • Alters RBC adhesion to endothelium (makes environment "less sticky") • Increases fetal hemoglobin levels (goal >20%)
Age Group	6-9 months & up
Dose	Start at 20mg/kg/day PO daily, advance as tolerated to optimal dosing of 30-31mg/kg/day, maximum dosing is 35mg/kg/day
Available Forms	Liquid 100mg/ml, 200/300/400mg capsules (Droxia), 500mg capsules (Hydrea), 100/1000mg dissolving tablets (Siklos)
Monitoring	Labs every 4 weeks until optimal dosing reached, then every 3-4 months Hemoglobin HPLC at least yearly Urine hcG Qvisit for menstruating females
Common Side Effects	• Bone marrow suppression, increased infection risk due to mild neutropenia (HU takes ANC out of inflammatory range) • GI upset • Headache • Rash
Special Considerations	• Wear gloves when handling liquid or pills, wash hands before & after • Clean up spills with a damp paper towel, dispose in a plastic bag • Protect your skin from the sun • Discontinue if pregnant (unknown if it causes fetal harm)

Hydroxyurea Benefits

- Safe and effective
- Prevents sickling through multiple mechanisms of action
- Well studied in children and adults
- Inexpensive
- Low side effect profile
- Can be stored at room temperature
- Widely available

L-glutamine (Endari)

Mechanism of Action	• Reduces oxidative stress on the RBC, prevents sickle cell pain • Glutamine is considered a "conditionally essential" amino acid during metabolic stress and injury. It regulates cell growth & regeneration.
Age Group	5 years & up
Dose	<30kg → 5g PO BID 30-65kg → 10g PO BID >65kg → 15g PO BID
Available Forms	5g packets
Monitoring	None
Common Side Effects	• Headache • GI upset • Pain • Cough
Special Considerations	• Mix with 8oz of a cold/room temperature beverage or a soft food • Must obtain from specialty pharmacy

Crizanlizumab (Adakveo)

Mechanism of Action	• Humanized monoclonal antibody which binds to P-selectin and blocks interaction with other ligands. This prevents adhesion of sickle cells to vessels and the development of vascular occlusion. Goal is to maintain blood flow and minimize sickle cell pain crises.
Age Group	16 years & up
Dose	5mg/kg/dose IV every 2 weeks x2, then every 4 weeks indefinitely. Infuse over 30 minutes (no need to ramp up or ramp down), flush with D5W or NS.
Available Forms	100mg/10ml vial
Monitoring	Vital signs at beginning and end of infusion, monitor patient in clinic for 30 minutes following completion
Common Side Effects	• Nausea • Arthralgias • Back pain • Fever
Special Considerations	• May falsely decrease automated platelet counts • Infusion reactions may occur, have anaphylaxis medications ready

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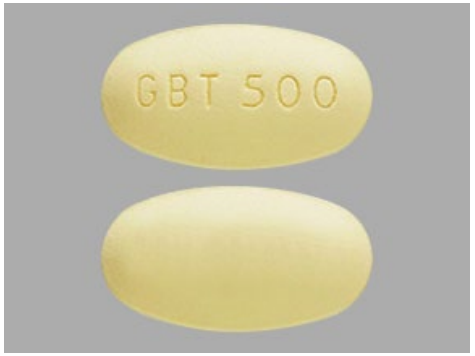
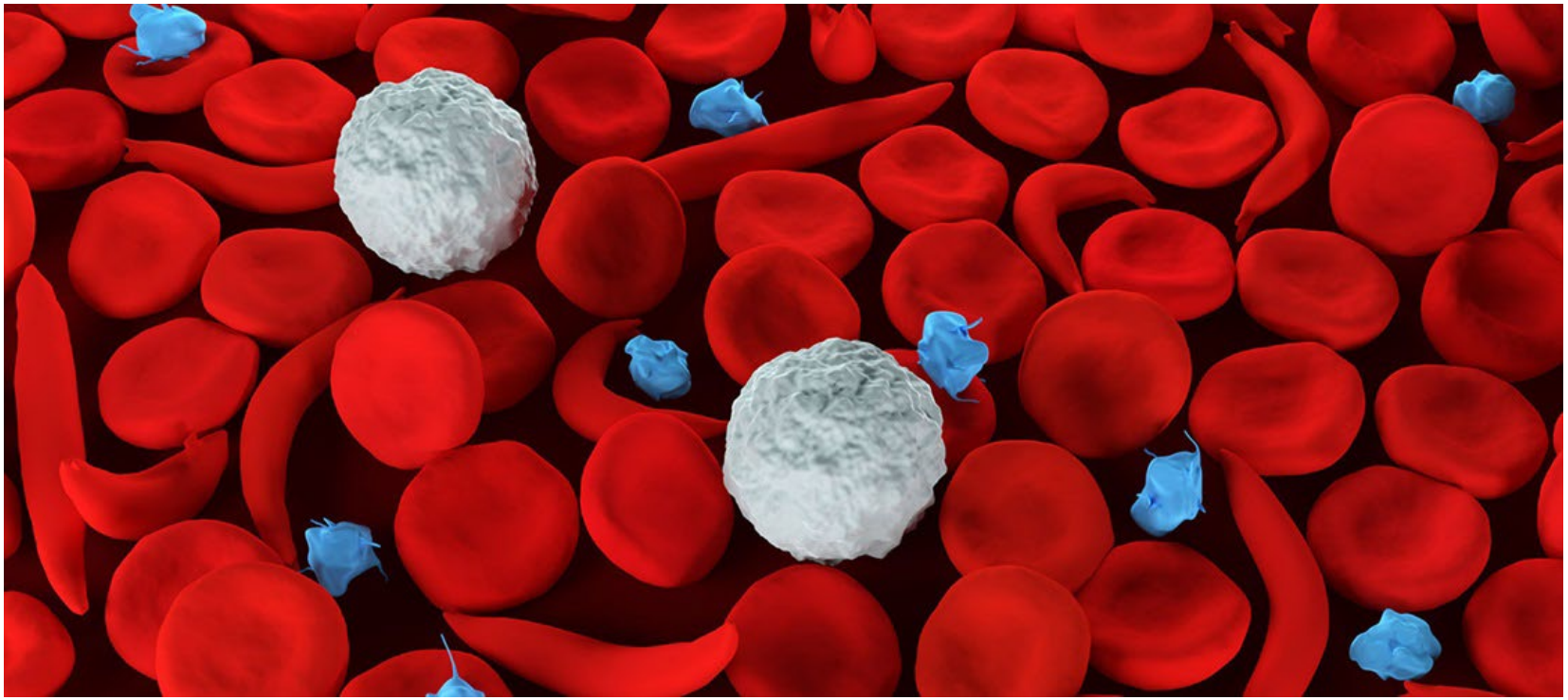
Voxelotor (Oxbryta)



Mechanism of Action	• Binds to Hgb and stabilizes the oxygenated Hgb state, which inhibits HgbS polymerization. This will then inhibit RBC sickling, improve RBC deformability, reduce whole blood viscosity, extend RBC half-life, and reduce anemia and hemolysis. • Increases Hgb by an average of ~1g/dl.
Age Group	4 years & up
Dose	10 to <20kg: 600mg PO daily 20 to <40kg: 900mg PO daily ≥40kg: 1,500mg PO daily (dose for age 12+ no matter what weight) *May reduce dose for side effects
Available Forms	500mg & 300mg tablets, 300mg soluble tablets
Monitoring	Routine lab work
Common Side Effects	• GI upset • Headache • Fatigue • Rash • Fever
Special Considerations	• Cannot crush tablets, must be swallowed whole • Mix soluble tablets with a clear drink (at least 5ml per tablet) • Drug interactions with fluconazole, erythromycin, & other CYP3A4 inhibitors (may need to decrease Oxbryta dose) • May interfere with HPLC lab results

Barriers to Medication Adherence

- Lack of Access to Healthcare
- Cost/Insurance Denial
- Pharmacy Issues
- Transportation Issues
- Language Barrier
- Forgetfulness/Time Management
- Toleration Issues (Side Effects/ Tastes Bad)
- Decreased Health Literacy
- Inadequate Provider Knowledge
- Mental Health Issues
- Missed Appointments



Curative Treatment Options:
Bone Marrow Transplant

Image: Johns Hopkins Medicine

Akron Children's Hospital

BMT: History

- The first HSCT in a patient with HgbSS was conducted in 1983:
  - Patient was an 8yo female with AML
  - Preparative regimen included cyclophosphamide & fractionated total body irradiation, followed by stem cells from a matched sibling donor
  - Prevention of GVHD included a short course of methotrexate & 28 days of methylprednisolone
  - Patient is still alive and doing well!

BMT: Indications

- Frequent vaso-occlusive pain events
- Multiple episodes of acute chest syndrome
- Stroke
- Frequent hospitalizations
- Poor quality of life

BMT: Donation

- Types: HLA-matched sibling or unrelated donor, haploidentical, or cord blood
- Donor receives a stem cell mobilizing medication in advance, like filgrastim
- Stem cells can be collected peripherally, via bone marrow aspiration from the pelvis, or via the umbilical cord in newborn babies

BMT: Conditioning Regimen

- Myeloablative Conditioning **Most Common**
  - Busulfan ± Cyclophosphamide ± Fludarabine
  - Melphalan + Fludarabine
  - Thiotepa
- Reduced Intensity Conditioning & Nonmyeloablative Conditioning
  - TBI
  - Cyclophosphamide ± ATG ± Fludarabine
  - Busulfan
  - Melphalan
  - Thiotepa

BMT: Risks

Infection

Bleeding

Graft vs. host disease

- ACUTE: 13% risk in <16 yo, 16% risk in 16+ yo
- CHRONIC: 15% risk in <16yo, 23% risk in 16+

Transplant rejection

Seizures

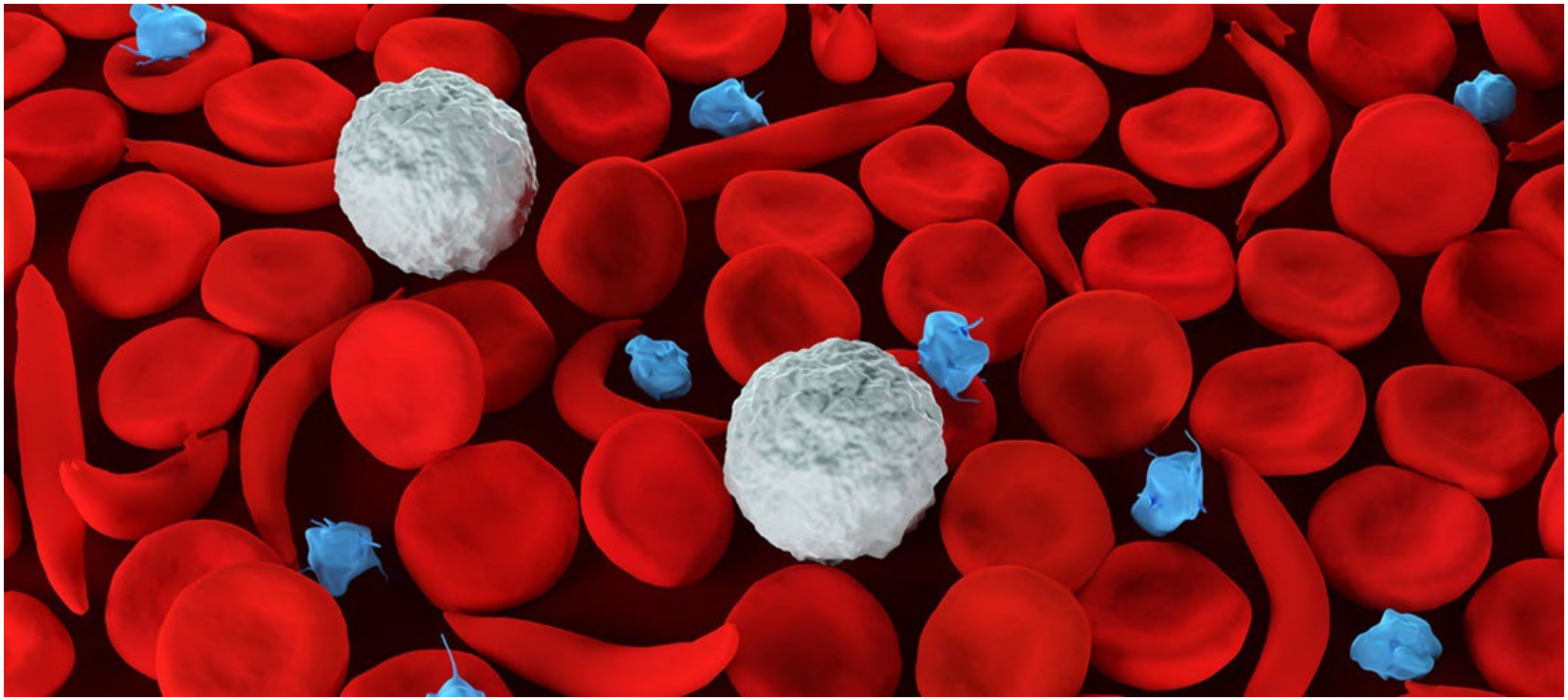
Infertility

- Offer fertility preservation in advance

Secondary malignancy

Death

- 5% risk in patients <16 years old
- 9-18% risk in patients ≥16 years old

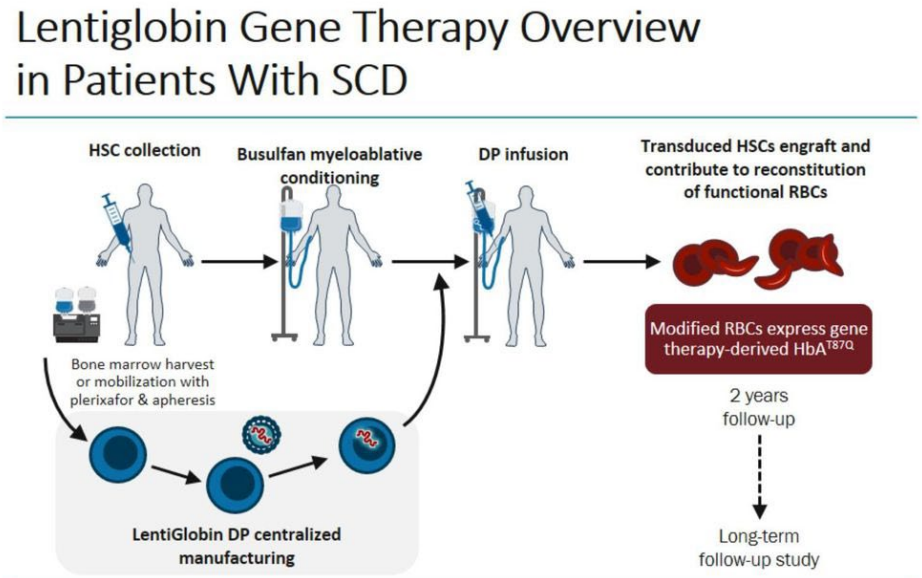


Curative Treatment Options:
Gene Therapy

Image: Johns Hopkins Medicine

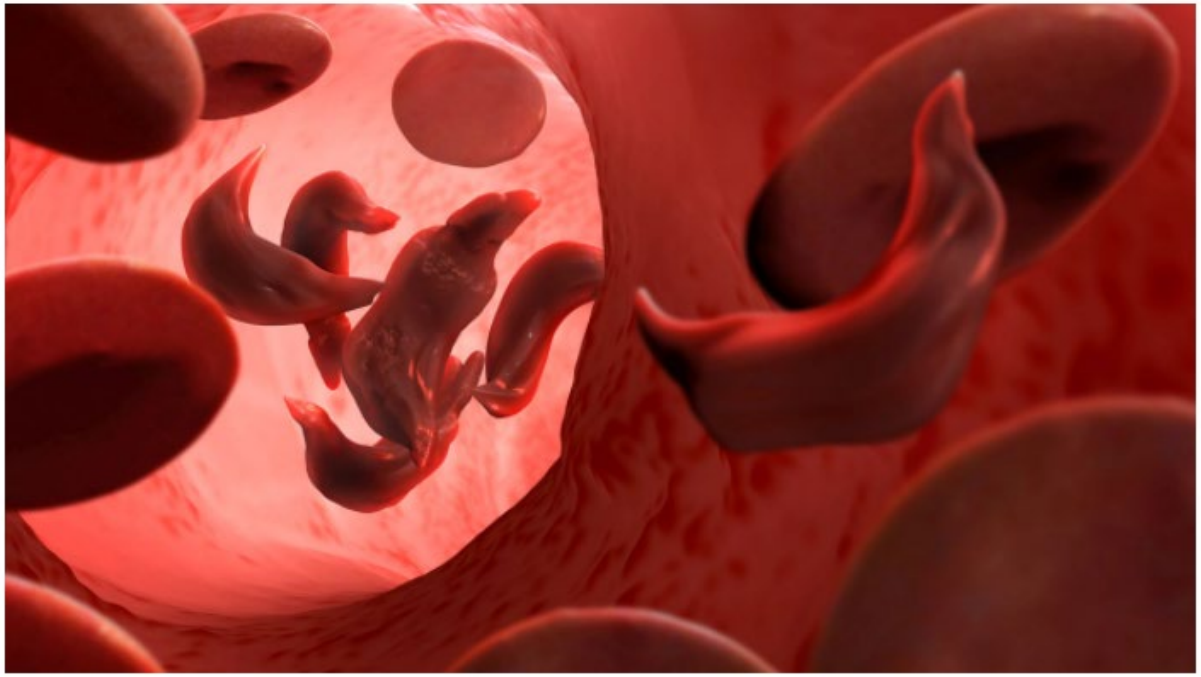
Akron Children's Hospital

Gene Therapy: Lentiviral Vector



- **Lovotibeglogene autotemcel (Lyfgenia)**
- Patient's CD34+ hematopoietic stem cells are removed via apheresis following stem cell mobilization
- The mutated HBB gene in these stem cells is replaced with a healthy, functioning copy of the gene in a lab
  - Delivered via lentiviral vector (modified virus r/t HIV)
- Genetically modified cells are transplanted back to patient
  - New cells will repopulate the bone marrow and produce healthy red blood cells with Hgb A^{T87Q} instead of Hgb S

Image: Medscape



There are new cancer concerns swirling around a gene therapy approach designed to prevent the sickling of blood cells (above). TIM VERNON/SCIENCE SOURCE

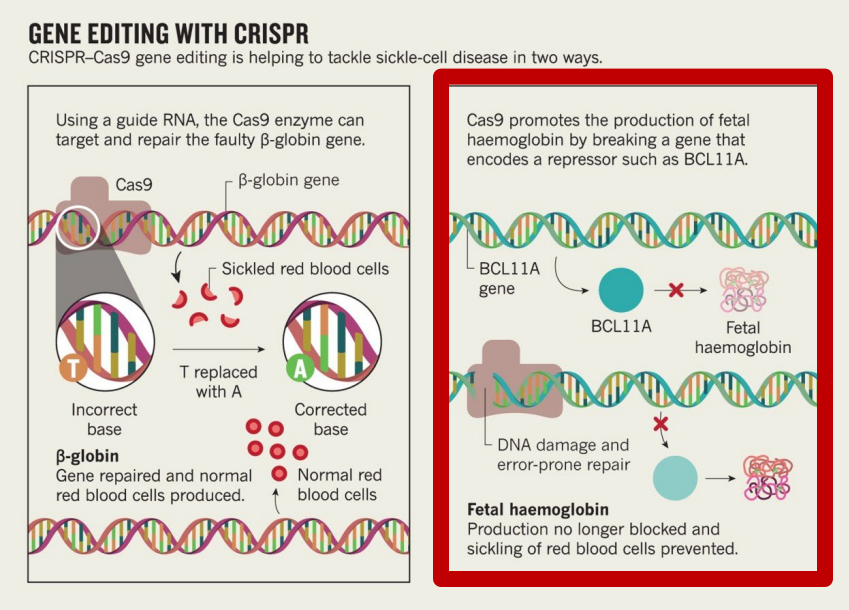
Gene therapy trials for sickle cell disease halted after two patients develop cancer

By Jocelyn Kaiser | Feb. 16, 2021 , 6:15 PM

Image: Science Magazine

Akron Children's Hospital

Gene Therapy: CRISPR/Cas9



- **Exagamglogene autotemcel (Casgevy)**
- Patient's CD34+ hematopoietic stem cells are removed via apheresis following stem cell mobilization
- CRISPR is a gene-editing technique that utilizes a highly specific enzyme (Cas9) to:
  - Target a gene that suppresses Hgb F production (i.e., a gene containing BCL11A) and cut the stem cell's DNA → cell repairs its own DNA, which disrupts expression of BCL11A → increased production of Hgb F
- Genetically modified cells are transplanted back to patient
  - New cells will repopulate the bone marrow and produce healthy red blood cells with Hgb F instead of Hgb S

Image: Blood Journal

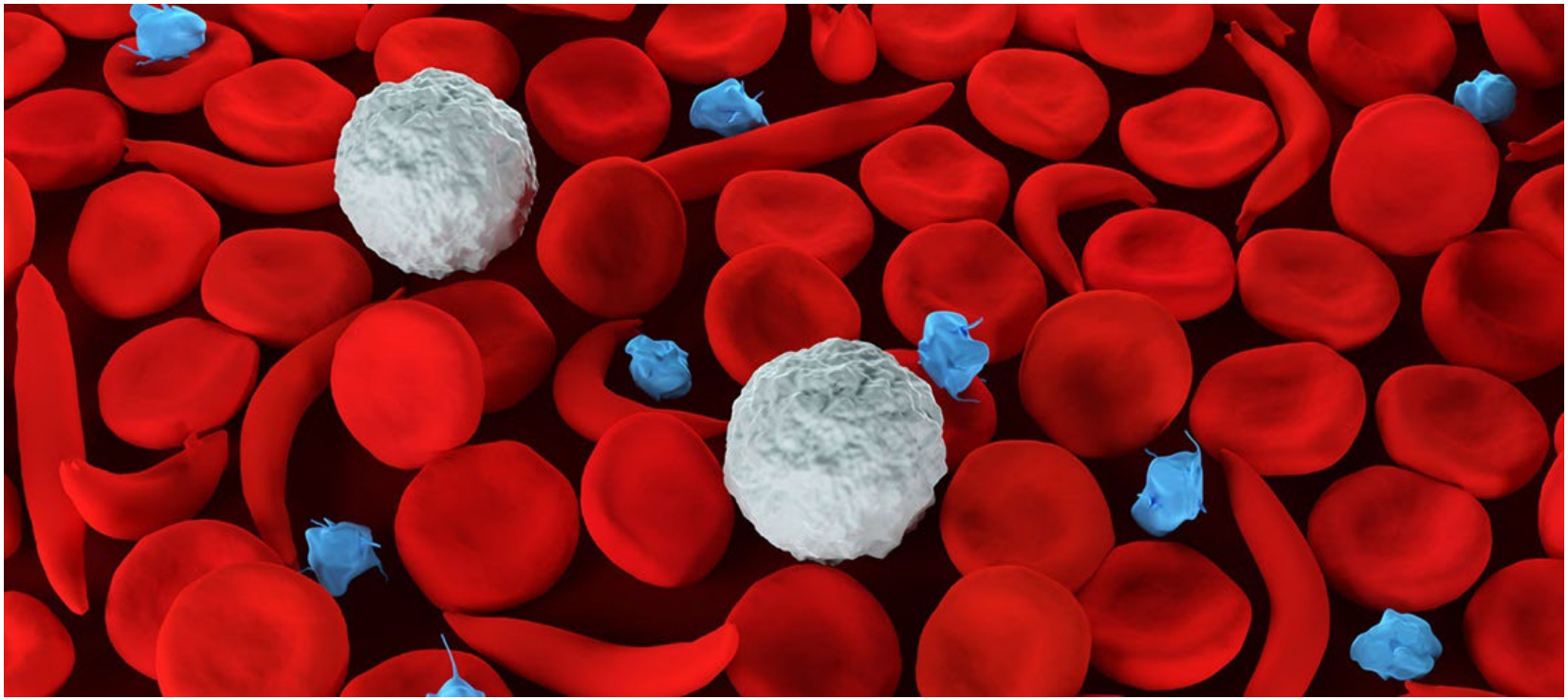
Gene Therapy cont.

Benefits

- Don't need to find matched donor
- Autologous = fewer immune-mediated adverse effects (GVH)
- Could be a permanent cure

Risks

- Need more data on long-term effects
- Adverse Effects of Preparative Regimen:
  - Short-Term Risks: infection, bleeding, mucositis
  - Long-Term Risks: infertility, secondary malignancy
- Cost



Management of Common Sickle Cell Complications:

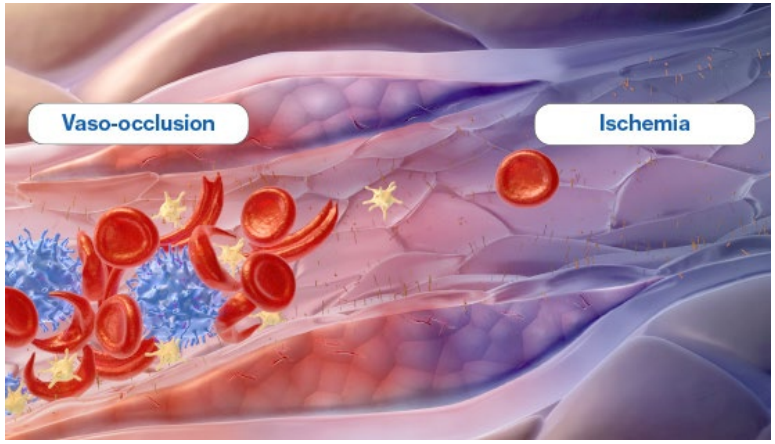
Pain Crisis

Image: Johns Hopkins Medicine

Akron Children's Hospital

Pain Crisis

Acute Vaso-occlusive Crisis



- Pain is the #1 reason patients with SCD present to the hospital
- Diagnosis of exclusion
- Requires rapid assessment & administration of analgesia, *ideally within 1 hour*
- More frequent VOCs associated with higher morbidity & mortality
- Treatment is multimodal

Image: Rethink Sickle Cell Disease

Pain Crisis: Treatment Modalities

Pharmacologic	Non-Pharmacologic

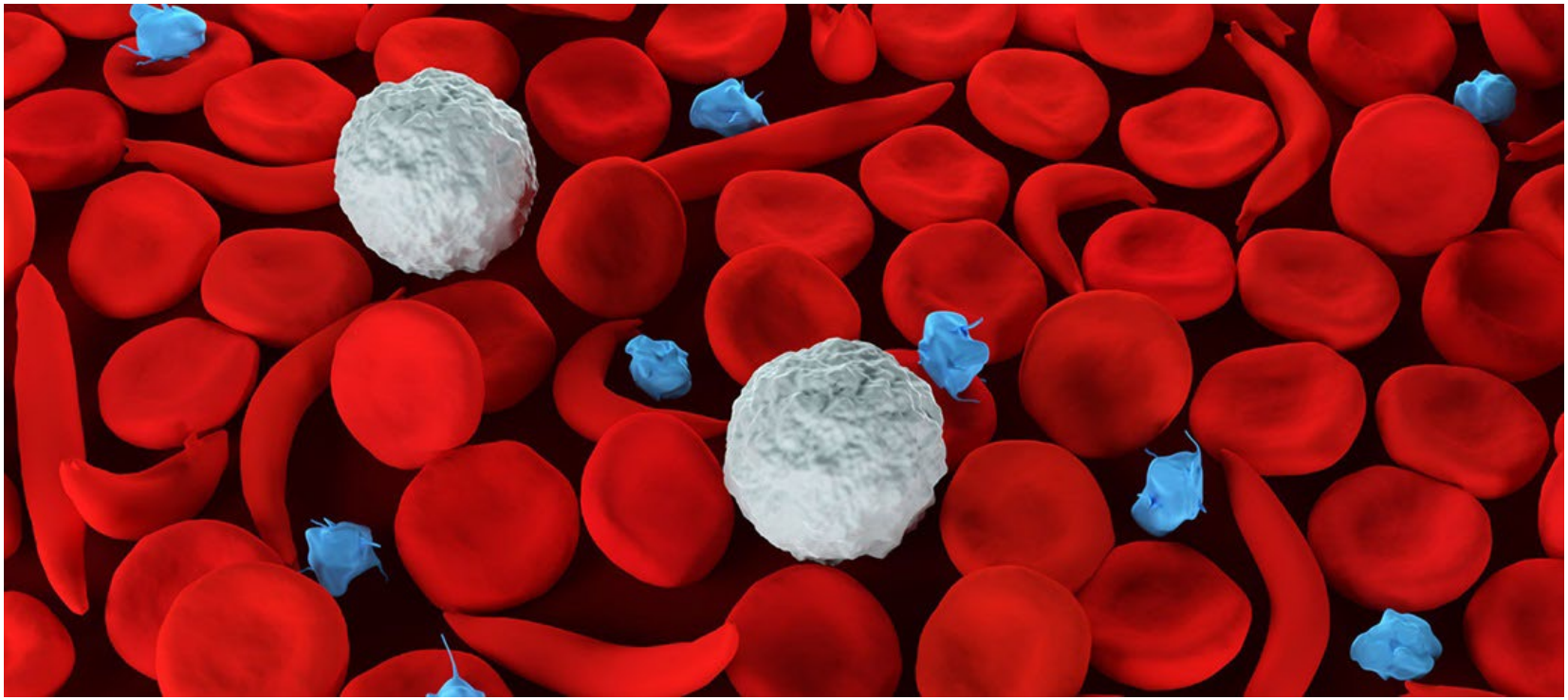
• Opioids
  • IV Morphine vs. Dilaudid vs. Fentanyl
  • Intranasal Fentanyl
  • PO Oxycodone
• Ketamine infusions
• Inhaled nitric oxide
• NSAIDs
• Tylenol
• Topical lidocaine patches
• Topical pain cream
• Regional nerve blocks
• Lyrica/Neurontin
• Muscle relaxers
• Antacids
• Vitamin D supplementation
• Bowel regimen
• Antidepressants
• ¾ maintenance IV fluids
	• Heat (heating pad, warm bath/shower) – *NO ICE*
	• Hydration
	• Incentive spirometry
	• Physical therapy
	• Occupational therapy
	• Manual therapy
	  • Massage
	  • Reiki
	  • Acupuncture
	• Gentle exercise
	  • Walking, yoga
	• TENS unit
	• Distraction techniques
	  • Virtual reality
	  • Hypnosis
	  • Guided meditation/relaxation
	• Mental health support
	  • Cognitive behavioral therapy

Table 1 Comparing number of deaths due to opioid pain relievers of non–sickle cell disease patients with the number of deaths due to opioid pain relievers of sickle cell disease patients from 1999 to 2013 in the United States

Year	Non-SCD Patients Who Died Due to OPR	SCD Patients Who Died Due to OPR
1999	4,022	8
2000	4,393	7
2001	5,521	7
2002	7,450	6
2003	8,513	4
2004	9,856	1
2005	10,922	6
2006	13,717	6
2007	14,401	7
2008	14,795	5
2009	15,594	3
2010	16,641	10
2011	16,907	10
2012	16,002	5
2013	16,225	10
Totals	**174,959**	**95**

OPR = Opioid Pain Reliever; SCD = Sickle Cell Disease.

Reference: Multiple Cause of Death Data, 1999-2013. CDC WONDER Online Database. 2015. Available at http://wonder.cdc.gov/mcd.html .



Management of Common Sickle Cell Complications:

Fever/Infection

Image: Johns Hopkins Medicine

Akron Children's Hospital

Fever/Infection

Table 1

Summary of immune system dysfunction and mechanisms leading to increased susceptibility to infections in patients with sickle cell disease.

System	Mechanism
INNATE IMMUNE DYSFUNCTION	
Neutrophil dysfunction (20)	Impaired neutrophil chemotaxis, migration, and killing ability
Splenic dysfunction (21, 22)	Repeated sickling within the spleen leads to compromised splenic filtration of microorganisms
Reduced opsonization (23, 24)	Reduced opsonin production, leading to decreased ability to destroy encapsulated organisms
ADAPTIVE IMMUNE DYSFUNCTION	
Decreased humoral immunity (25)	Loss of splenic marginal zone leads to reduced number of Memory B cells and reduced antigen-specific immunoglobulin M secretion
Impaired virus-directed immunity (26)	Decreased Th1 response with reduced CD4+:CD8 suppressor T Cells
MECHANICAL FACTORS	
Increased susceptibility to osteomyelitis (27)	Bony infarction secondary to sluggish circulation leading to infarcts, which then act a nidus for bacterial proliferation
NUTRITIONAL	
Impaired virus-directed immunity (28, 29)	Zinc deficiency leads to lymphopenia and decreased Th1 response

Image: National Library of Medicine

Fever

- Labs: blood culture, CBC, retic, CMP
  - Consider: respiratory panel film array, rapid strep & strep culture, urinalysis, urine culture, wound culture
- Cefepime IV
  - <13kg → 50mg/kg
  - 13-19kg → 1000mg
  - 20-30kg → 1500mg
  - >30kg → 2000mg
  - Subsequent doses 50mg/kg
- For cefepime allergy: Meropenem 20mg/kg IV
- NS bolus 10ml/kg
- Anti-pyretic

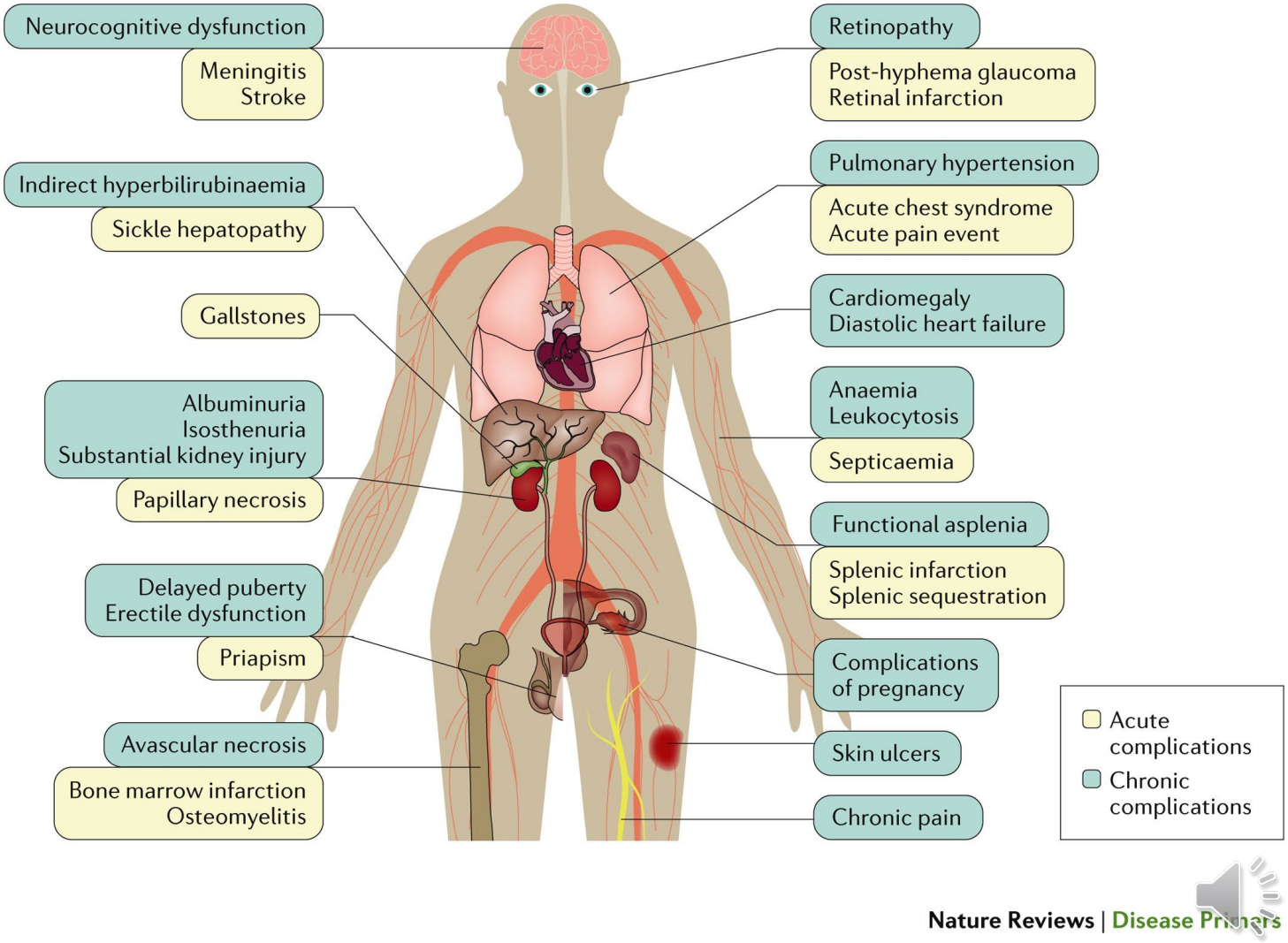


Image: Nature Reviews

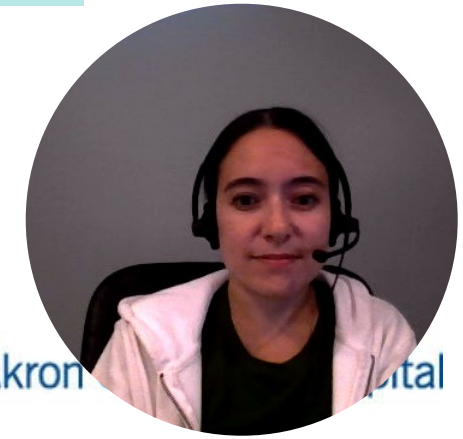
Akron Children's Hospital

Our Sickle Cell Team

- **Dr. Prasad Bodas**, Sickle Cell Director
- **Lauren Beck**, Sickle Cell Nurse Practitioner
- **Bobbi Moser**, Sickle Cell Nurse
- **LaTonya Johnson**, Program Director, Newborn Screen Counselor, & Outreach Education Coordinator
- **Psychologists**
  - **Dr. Jordan Weith**
  - **Dr. Jessica Feinstein**
  - **Dr. Mallory Zehe**
- **Social Worker Team**
  - **Maria Hartland**
  - **Leah Mallinos**
  - **Doug Palmer**
  - **Sam Dunn**
- **Renee Redenshek**, Child Life
- **Dr. Brittney Williams**, Neuropsychologist
- **JoEllen Weilnau**, Pharmacist
- **Comprehensive Clinic Team**
  - **Melinda Aylward & Jodi Leiter**, School Teachers
  - **Vicki Vitale**, Dietician
  - **Madeline Frederick**, Genetics Counselor
  - **Katherine Pritchard**, Physical Therapist
  - Echo Services
- **Apheresis Team**
  - **Tori Thompson**, Apheresis Nurse
  - **Kayla Davis**, Apheresis Nurse
- **Mahoning Valley Team**
  - **Alyssa Pidgeon**, Sickle Cell RN & Clinical Coordinator
  - **Nancy Fingerhood**, Social Worker
  - **Meghan Ball**, Physical Therapist

Questions?

lbeck2@akronchildrens.org



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