Sickle Cell Disease Lifespan:

CASE MANAGEMENT CONSIDERATIONS

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Learning Objectives

1. Review history of sickle cell disease (SCD) from molecular discovery
2. Describe SCD pathophysiology and its medical complications.
3. Discuss the transition of care from Pediatric to Adult care with SCD
4. Understanding of the multi-disciplinary team approach to the care of individuals living with SCD and the importance of case management. Also, how improving social factors can enhance healthcare outcomes.
5. Provide practitioner and patient perspectives on sickle cell, race, and advocacy.

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History of Sickle Cell Disease

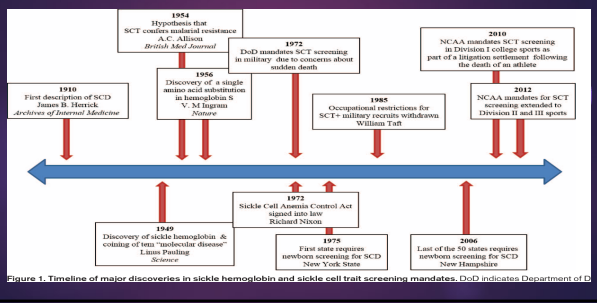

Figure 1. Timeline of major discoveries in sickle hemoglobin and sickle cell trait screening mandates. DoD indicates Department of D

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Polling question #1

- How many people have Sickle Cell Disease in the United States?
  - 10,000
  - 30,000
  - 100,000
  - 300,000

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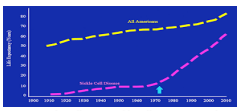
Sickle Cell Disease

- SCD affects approximately 100,000 Americans. SCD occurs among about 1 out of every 365 Black or African-American births. SCD occurs among about 1 out of every 16,300 Hispanic-American births. About 1 in 13 Black or African-American babies is born with sickle cell trait (SCT).
- 4 major types of SCD: SS, SC, $S\beta^0$thalassemia, $S\beta^+$thalassemia
- Compared to the general population decreases life expectancy by 25-30 years.



A Legacy of Excellence in Sickle Cell Disease Research: Extending Life Expectation

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Sickle Cell Disease

- Red blood cells play a very important role as the agents responsible for delivering oxygen to every part of the body.
- Normal red blood cells are flexible and rounded, which is crucial to their ability both to carry oxygen and to pass through small blood vessels
- Sickle cell disease (SCD) is a group of inherited (autosomal-recessive) red blood cell disorders.
- In sickle cell disease, a very small mutation in the structure of hemoglobin makes the red blood cell much more prone to becoming deformed and assuming the shape of a sickle.

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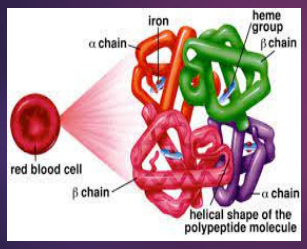
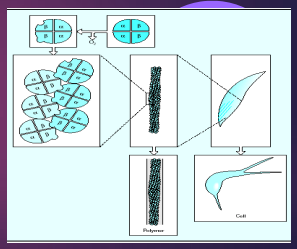
SCD – Hemoglobin S polymer





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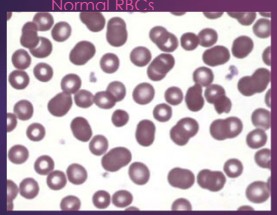
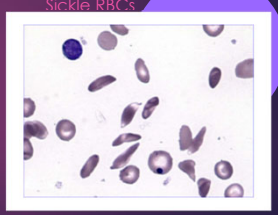
SCD – Microscopic comparison

Normal RBCs



Sickle RBCs



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SCD – Complications (every organ)

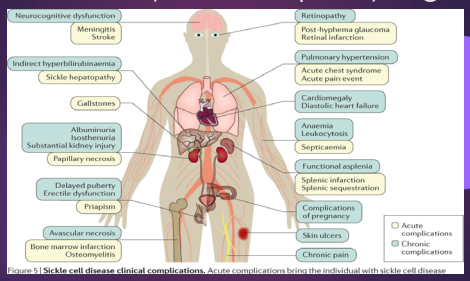

Figure 5 | **Sickle cell disease clinical complications.** Acute complications bring the individual with sickle cell disease

Hallmark symptom – Vaso-occlusive crisis/pain (acute/chronic)

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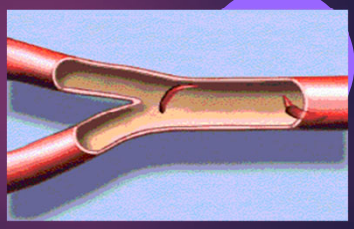
Vaso-occlusive Crisis

- Rigid RBC obstruct blood flow
- Decreased blood flow leads to tissue hypoxia
- Severe tissue hypoxia leads to tissue damage manifested by localized pain swelling.
- Repeated low grade obstruction leads to organ damage



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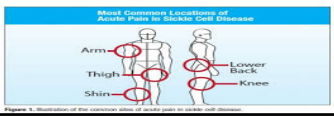
SCD – Pain Management

- Pharmacological
  - Acetaminophen
  - NSAIDs
  - Opioids
  - Topical lidocaine
  - "Adjunctive" meds
    - Antidepressants
    - anticonvulsants
  - Medical marijuana (?)
- Non-Pharmacologic
  - Local heat/cold
  - Distraction
  - Massage
  - Guided Imagery
  - Meditation



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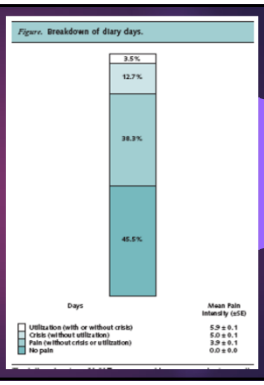
SCD – Pain & stigma

- 232 patients age 16 years or older with sickle cell disease
- Daily diary for up to 6 months
- Pain reported on 54.5% of 31,017 analyzed patient-days

Ann Intern Med. 2008;148:94-101.



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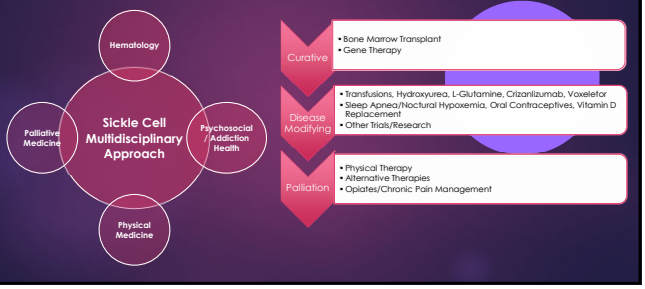
SCD – Management



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SCD – Disease Modifying Therapy

Simple Transfusions

- Symptomatic anemia
- Acute neurologic event
- Acute chest syndrome
- Acute multiorgan failure
- Preparation for major surgery
- Acute splenic or hepatic sequestration
- Sepsis and meningitis

Exchange Transfusions

- Acute neurologic event
- Severe acute chest syndrome
- Acute multiorgan failure
- Preparation for major surgery
- Chronic use, as for simple transfusion, to avoid/reduce iron loading

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Polling Question #2

- How long did it take for the FDA to approve a new medication for the treatment of Sickle Cell Disease?
  - 5 years
  - 12 years
  - 20 years
  - 36 years

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SCD – Disease Modifying Therapy

Drug	Year FDA Approval
Hydroxyurea	1998
L-Glutamine	2017
Crizanlizumab	2019
Voxeletor	2019

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Disease Modifying Therapy - Hydroxyurea

What is it?

- Hydroxyurea first line therapy for those with SCA (frequent crises & symptomatic anemia)
- Oral capsule prescribed/titrated by Hematology
- The cost for hydroxyurea oral capsule 500 mg is around $78 for a supply of 100 capsules (out of pocket)

How does it work?

- Increases HbF (fetal Hgb), improves RBC morphology and deformability, reduces hemolysis, releases of nitric oxide

Results?

- Decrease in number of crises/yr, decrease in ACS, decrease in patients undergoing transfusion

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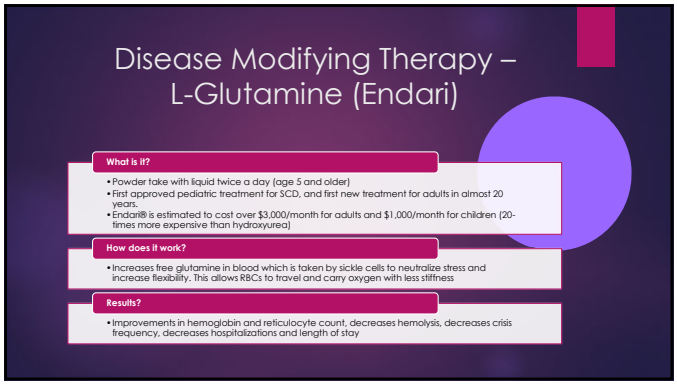
Disease Modifying Therapy – L-Glutamine (Endari)
What is it?
• Powder take with liquid twice a day (age 5 and older)
• First approved pediatric treatment for SCD, and first new treatment for adults in almost 20 years.
• Endari® is estimated to cost over $3,000/month for adults and $1,000/month for children (20-times more expensive than hydroxyurea)
How does it work?
• Increases free glutamine in blood which is taken by sickle cells to neutralize stress and increase flexibility. This allows RBCs to travel and carry oxygen with less stiffness
Results?
• Improvements in hemoglobin and reticulocyte count, decreases hemolysis, decreases crisis frequency, decreases hospitalizations and length of stay

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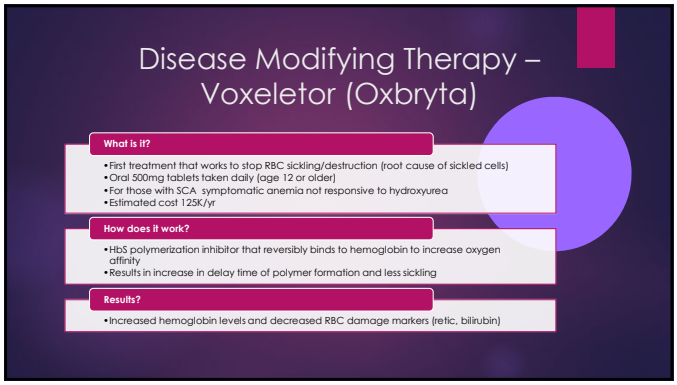
Disease Modifying Therapy – Voxeletor (Oxbryta)
What is it?
• First treatment that works to stop RBC sickling/destruction (root cause of sickled cells)
• Oral 500mg tablets taken daily (age 12 or older)
• For those with SCA symptomatic anemia not responsive to hydroxyurea
• Estimated cost 125K/yr
How does it work?
• HbS polymerization inhibitor that reversibly binds to hemoglobin to increase oxygen affinity
• Results in increase in delay time of polymer formation and less sickling
Results?
• Increased hemoglobin levels and decreased RBC damage markers (retic, bilirubin)

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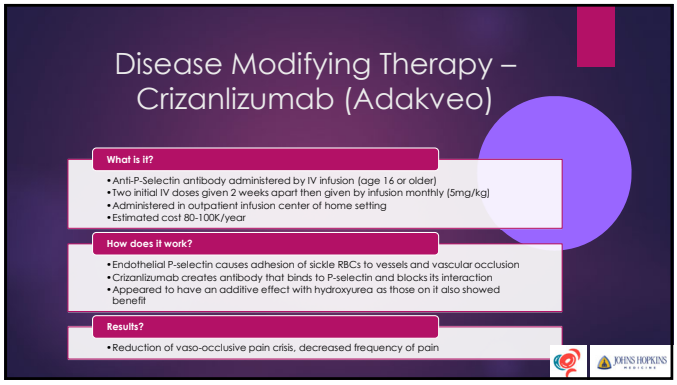
Disease Modifying Therapy – Crizanlizumab (Adakveo)
What is it?
• Anti-P-Selectin antibody administered by IV infusion (age 16 or older)
• Two initial IV doses given 2 weeks apart then given by infusion monthly (5mg/kg)
• Administered in outpatient infusion center of home setting
• Estimated cost 80-100K/year
How does it work?
• Endothelial P-selectin causes adhesion of sickle RBCs to vessels and vascular occlusion
• Crizanlizumab creates antibody that binds to P-selectin and blocks its interaction
• Appeared to have an additive effect with hydroxyurea as those on it also showed benefit
Results?
• Reduction of vaso-occlusive pain crisis, decreased frequency of pain
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Sickle cell patients fight uphill battle for research, treatment — and compassion

By Jenny Gold — Kaiser Health News Dec. 26, 2017

- Sickle cell funding pales in comparison to other diseases. *Cystic fibrosis, which affects 30,000 people in the U.S., for example, gets seven to 11 times more funding per patient than sickle cell disease*, according to a 2013 study in the journal Blood. The ALS challenge in 2014 raised $115 million for approximately 20,000 patients in the U.S.
- With *annual costs to treat the disease soaring past $1 billion*, new efforts are afoot to improve the lot of patients. But each of these developments faces limitations and obstacles
- Physician associations are working to disseminate guidelines to *improve care and reduce discrimination against sickle cell patients, who often are assumed to be drug addicts when they come to emergency rooms in severe pain*. Still, there has been so little research on sickle cell that it is difficult even to write evidence-based protocols.
- *Legislation in Congress to fund research and treatment, stalled since 2009*, is finally moving out of committee. But the bill would provide *only $4 million — less than half its original funding level*.

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Case Management Considerations: Lifespan of an Individual

- Pediatric population

- Adult population

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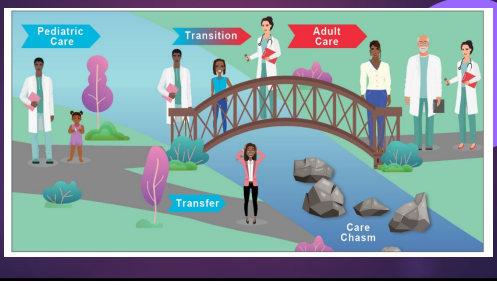
Case Management Considerations: Transition of Care



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Comprehensive Needs Assessment

- A Comprehensive Assessment describes in detail the client's medical, physical and psychosocial condition and needs. It identifies service needs being addressed and by whom; services that have not been provided; barriers to service access; and services not adequately coordinated.
  - Elements to a complete CNA:
    - Demographics
    - History
    - Functionality
    - Nutrition
    - Developmental Concerns
    - Support/Community resources
    - Psychosocial History

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Polling Question #3

- Social Determinates of Health (SDoH) make up what percentage of health outcomes?
  - 20%
  - 30%
  - 50%
  - 60%

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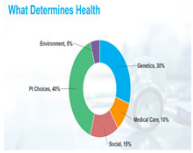
Social Determinants of Health (SDoH)



- Health care spending per person has risen in the United States for as long as expenditures have been tracked, yet population health appears to be deteriorating.
- In 2016 health care spending increased 4.3 percent in the United States, reaching $3.3 trillion, but life expectancy declined for the second consecutive year, which has not happened since 1963.

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Social Determinants of Health (SDoH)

- Social determinants of health (SDoH) are the conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks
- According to the World Health Organization, over 60% of health outcomes are the result of social determinants of health. These social risk factors in people's lives create significant impacts in their health outcomes, utilization patterns, and costs.

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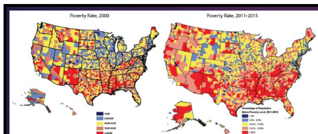


Percentage of Population Below the Federal Poverty Level, United States, 2000 and 2011-2015 (3,143 Counties)
Source: Data derived from the 2000 Census and 2011-2015 American Community Survey.

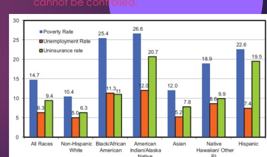
Currently black infants have 2.3 times higher mortality than white infants (11.4 vs. 4.9 per 1,000 live births). Black infants and children in poor, rural communities have nearly three times higher mortality rate compared to those in affluent, rural areas.

Chronic disease prevalence continues to grow, and 60 percent of the population is now reported to have one or more chronic conditions.

Unlike the other social determinants that address an individual's surroundings, one's race and their socioeconomic status (SES) at birth are factors that cannot be controlled.

Recent estimates attribute 10 to 20 percent of health outcomes to medical care, 30 percent to genetics, 40 to 50 percent to behavior, and 20 percent to the social and physical environment.

Individuals with an annual family income <$35,000 were 10.6 times more likely to forgo needed medical care due to cost than those with annual family incomes of $100,000 or more. Individuals without a job were 1.7 to 1.8 times more likely to forgo or delay needed medical care due to cost than those with a full-time job.



Poverty, Unemployment, and Health uninsurance Rates (%) by Race/Ethnicity, United States 2015
Source: US Census Bureau. 2015 American Community Survey.

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SDoH and Sickle Cell Disease

Universal screening for social determinants of health in pediatric sickle cell disease: A quality-improvement initiative

Alexandra Power-Hays Stephanie Li Akosua Mensah Amy Sobota

First published: 01 October 2019 https://doi.org/10.1002/pbc.28006

- Through prospective, quality-improvement methods, we introduced universal screening for SDoH into our pediatric hematology clinic. The intervention was a paper screener followed by a referral to local community organizations for the specific needs endorsed.
- Between August 2017 and November 2018, 156 screens were completed. 60% percent were positive for at least one unmet social need for which 80% were referred to a relevant community organization. Forty-five percent of patients available via follow-up phone call reached out to the community organization.
  - Food was the most frequently unmet social determinant of health (25.6% of screens),
  - Utilities and education (24.3% each),
  - Employment (19.2%),
  - Transportation to the hospital (14.1%),
  - Adequate housing (10.9%),
  - Available childcare (7.7%),
  - Ability to pay for medication (2.6%).

  Note: 45% of families with whom a social worker followed up reported they had reached out to a community organization.
- Patients with SCD have a chronic illness and are typically minorities, both of which can increase susceptibility to a high burden of social determinants of health. Clinically implemented, guideline-recommended universal screening and resource referral programs could improve social determinants of health for these vulnerable pediatric patients and their caregivers.

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SDoH Questions to Consider

Housing

- Home/apartment/shelter/ Structural housing needs
- Can individual independently navigate into and throughout home
- DME needs (personal cane/walker/wheelchair)
- Is housing safe/adequate?
- Risk for becoming homeless
- Concerns with electric or heating?

Transportation

- Mode of transportation
- Can patient get to and from all appointments and high-priority errands independently? Is current transportation reliable?
- How far/distance from medical appointments?
- Current transportation needs/concerns?

Food Access

- Height/weight/BMI
- How many meals on average are eaten in a day?
- What diet does individual maintain? Snacking?
- Distance to nearest grocery store from home.
- Are there current concerns with obtaining and preparing food?

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SDoH Questions to Consider

Social Support

- Patient's family/social support
- Social support concerns/ability to comply to treatment plan
- Psychiatry/therapy history for individual. PHQ2 completed
- Are social support members complying to Covid-19 precautions?
- Does individual have trouble taking care of a child, family member, or friend?

Financial Considerations

- Patient employed or unemployed? Are they receiving benefits?
- Is workplace supportive and knowledgeable of sickle cell disease/complications?
- Are bills routinely paid? Delay in paying?
- Is individual able to pay for prescription medications
- How adequate is current insurance coverage? Copays paid?

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SCD – Empathy & Rapport

- People with sickle cell disease have been told since childhood they will not live long, they shouldn't have babies, and they cannot work.
- Sickle cell patients are hospitalized for 1-2 weeks away from their families, most are on disability, those who work often lose their job due to hospitalization, resulting in low self esteem.
- Their disease often forces individuals to rely on opioid pain management.
- Our job is to not only treat their pain but teach them coping skills to find other ways to deal with their pain.

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SCD – Race & Advocacy

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Thank you!

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