The Overlap Between Sickle Cell and Effective Chronic Disease Treatment and Management

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Objectives

1. Understand how to identify and treat SCD ‘emergencies’
2. Review strategies to help patients grow up, transition, and successfully manage SCD
3. Recognize the resources available to help treat patients with SCD
70,000 to 100,000 People in the United States Have SCD¹

- SCD includes all conditions with clinical manifestations of sickle Hb (HbS)²
  - Approximately 70% of SCD patients have homozygous SCD (HbSS), which is often referred to as sickle cell anemia (SCA)²
  - Many other patients have heterozygous hemoglobin SC disease (HbSC)²

Hb, hemoglobin.

Brief Pathophysiology

- Mutation at sixth position of beta globin chain changes glu → val
- With deoxygenation, the HbS molecule polymerizes within the RBC leading to characteristic shape changes
- Sickled erythrocytes are rigid and obstruct small blood vessels leading to tissue ischemia
- Deformed sickle cells adhere to endothelium & macrophages
  - induces hemolytic process
- Inflammation and ongoing adhesion
Sickle Cell Disease – ‘light’

- An inherited disease of red blood cells
- Affects hemoglobin
- Polymerization of hemoglobin leads to a cascade of effects decreasing blood flow
- Tissue hypoxia causes acute and chronic damage
Key Trials and Developments Correlate With Greatly Improved Patient Survival

- 1910 – Discovery of SCD
- 1949 – Identification of HbS
- 1976 – RBC transfusion for treatment of secondary stroke
- 1986 – Antibiotic prophylaxis in infants
- 1987 – NIH recommends newborn screening
- 1995 – MSH trial
- 1998 – STOP trial
- 2011 – BABY HUG trial
- 2012 – SWiTCH trial
- 2016 – TWiTCH trial

Life expectancy for patients with SCA (years)

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Adult Emergencies

- Acute chest syndrome
- Severe pain
- Fever/infection
- Stroke
Acute Chest Syndrome
A leading cause of death in sickle cell disease

- **Diagnosis:**
  - New infiltrate on chest x-ray + additional symptom/sign
    - Acute onset of fever
    - Respiratory symptoms
    - Hypoxia
    - Lower lobes most commonly; 1/3 bilateral
  - Infection, sickling, fat embolism, atelectasis

Since you cannot distinguish between acute chest syndrome and pneumonia clinically there is no change in treatment.
Management of ACS

- Antibiotic therapy for encapsulated bacteria and *Mycoplasma pneumoniae*
  - IV Cefuroxime
  - Azithromycin (even in young children)
- Cautious IV hydration (max of 3/4X maintenance)
- Analgesia for chest pain
- Incentive spirometry
- Oxygen for $O_2$ sats < 92%
Acute Chest Syndrome

- Consider:
  - Simple transfusion
  - Exchange transfusion
Management of VOE

Acute pain

• Hand-foot syndrome (dactylitis)
• Painful episodes: vaso-occlusion
• Splenic sequestration
• Acute chest syndrome
• Priapism
• Cholelithiasis
• Avascular necrosis
Management of VOE

Pain is an emergency

- Hydration but not over hydration
  - Need maintenance intake IV+PO

- Assess pain level and treat
  - Do not withhold opioids
  - Frequently reassess pain control
Management ofVOE

Mild-moderate pain

• Acetaminophen
  • Hepatotoxic

• Non-steroidal anti-inflammatory agents (NSAIDs)
  - Contraindicated in patients with gastritis/ulcers and renal failure
  - Monitor renal function if used chronically
Pain Management

• Moderate or less severe pain
  • NSAID's in combination with opioids

• Moderate-severe pain
  • Opioids are first-line treatment
  • Morphine sulfate or hydromorphone
  • Meperidine NOT recommended
    • (Metabolite causes seizures & renal toxicity)
Management of VOE

• Adequate pain control
  • Narcotic - BASAL + demand
    • Basal: IV >> po (oxycontin)
    • Demand: IV > po (oxycodone)
  • Continual assessment of narcotic requirements

• Incentive spirometry
• Bowel regimen
• Discharge on appropriate home regimen
Fever and Infection

- Fever > 38.5°C (101°F) is an EMERGENCY
- IV/IM Ceftriaxone
  - Vancomycin if ill-appearing
- Basic laboratory evaluation:
  - CBC/diff and reticulocyte count, and blood culture
- Consider:
  - urine, and throat cultures, urinalysis, chest x-ray

Indications for hospitalization & IV antibiotics:
- Age <1 year
- Surgically splenectomized or history of pneumococcal sepsis
- Unsure f/u
- Ill appearing
- Infiltrate on CXR
- ANC <2000 or >30k
Stroke

Any acute neurologic symptom other than mild headache, even if transient, requires urgent evaluation.

- Historically 8 to 10% of children with SS
- “Silent Stroke” in 22% of children with hemoglobin SS
Stroke

- Thrombotic or infarctive event involving large intracranial arteries
- Present with weakness, aphasia, seizures, LOC
- Often results in permanent neurological damage and long-term disability
Treatment of Stroke

- IV Fluids at 1X maintenance
- Transfer to Sickle Cell Center and notify Blood Bank ASAP
- PRBC exchange transfusion to goal of Hgb 9.0 gm/dL and < 30% HbS
- MRI/MRA of brain not immediately necessary
- Chronic monthly transfusions to prevent secondary stroke

No evidence for antiplatelets or anticoagulation
Remember

• **Acute Emergency** Treatment with e-pheresis:
  • Stroke (Strongest Evidence based support)
  • ‘Significant’ ACS
  • Refractory priapism

• Consider transfusion for:
  • ACS
  • History of stroke or elevated TCDs
  • Significant anemia (as compared to baseline)
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A Definition of Transition

- “Transition is a multifaceted, active process that attends to the medical, psychosocial, and educational/vocational needs of adolescents as they move from the child-focused to the adult-focused health care system. Health transition facilitates transition in other areas as well (eg, work, community, and the school)”

- “Transition proceeds at different rates for different individuals and families (and programs)”
Transitioning Poses Many Challenges for Patients

Challenges for Any Patient With a Chronic Condition

- Inability to effectively manage their disease
- Need for effective coping strategies
- Concerns about cost of care and insurance coverage
- Uncertainty about future as an independent adult

Challenges of Particular Concern for SCD Patients

- Increased socioeconomic challenges
- Large number of older SCD patients, placing strain on the system
- Adult "transition patients" ending up in the pediatric emergency room
- Lack of a medical home with an adult hematologist
  - Result: suboptimal care with poor tracking of medication and transfusion histories

References:
**Key Quality Indicators for Transition to Adult Care***

<table>
<thead>
<tr>
<th>Process</th>
<th>Patient Factors</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Transition counseling prior to transfer</td>
<td>• Patient keeps clinic appointments</td>
<td>• Overall quality of life</td>
</tr>
<tr>
<td>• Written transfer summary sent to adult provider</td>
<td>• Patient remains adherent to treatment and medications</td>
<td>• Trust in adult provider</td>
</tr>
<tr>
<td>• Direct communication between pediatric and adult providers</td>
<td>• Patient self-efficacy: ability to manage their illness day-to-day</td>
<td></td>
</tr>
<tr>
<td>• First visit to adult provider within appropriate interval</td>
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</tbody>
</table>

*Based on a modified Delphi survey to reach a consensus on the quality indicators of a successful transition. The survey was carried out by an expert panel consisting of members of the Sickle Cell Adult Provider Network.

A Transition Plan Helps Patients Navigate into Adulthood

Planning for transition with SCD is a process\(^1,^2\)

<table>
<thead>
<tr>
<th>12-13 years of age</th>
<th>14-15 years of age</th>
<th>16-17 years of age</th>
<th>≥18 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients and caregivers discuss transition planning with their doctor</td>
<td>Patients and caregivers develop transition plan with their doctor</td>
<td>Review and update transition plan</td>
<td>Implement transition plan as patients enter adult care</td>
</tr>
</tbody>
</table>

Planning for transition is critical to help patients work with their doctors and other health care providers to stay on top of their treatment\(^3\)

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A WHO/WHAT/WHERE Framework to Guide Patient Understanding Of Transition

Level I (WHO)
Know who they are

“我是_____，我有_____型的镰状细胞病。”

Level II (WHAT)
Know what to do in different situations

“I am _____, and I have sickle cell type ___. Sickle cell is when your blood looks like a banana and can cause blood to have problems going places. Stress to the body can cause issues.

I know what I need to do when _____ happens with sickle cell.”

Level III (WHERE)
Know where they are going

“I am _____, and I have sickle cell type ___. Sickle cell is when your blood looks like a banana and can cause blood to have problems going places. Stress to the body causes issues.

I know what I need to do when _____ happens with sickle cell.

I am going to ____ college/university and/or I am going to work at ____. I know about what is bad for me and who/what are bad influences.”

Know WHO They Are

Level I
(WHO)
Know who they are

“l am _____, and I have sickle cell type ____.”

Basic points to understand¹,²

- Shape of a sickle cell
- Genetics
- Types of sickle cell
- How sickle cell causes complications
- ‘Stressors’ that cause sickling

Know WHAT to do in Different Situations

**Level II**
**WHAT**

Know what to do in different situations

**Basic points to understand**

- Types of blood cells
  - Hb
  - MCV
  - Reticulocyte count
  - WBCs
  - Platelets
  - Transfusions, serum ferritin

- Management of pain

- Medications taken daily

- Warning signs for complications
  - Fever, shortness of breath, neurologic symptoms

- Complications
  - Acute chest syndrome, stroke, infection, priapism

- Sports and hydration

- Implications of laboratory results

“**I am _____, and I have sickle cell type _____. Sickle cell is when your blood looks like a banana and can cause blood to have problems going places. Stress to the body can cause issues.**

I know what I need to do when _____ happens with sickle cell.”

Patients Should Understand the Implications of Their Lab Results

<table>
<thead>
<tr>
<th>Hb(^1)</th>
<th>MCV(^1,2)</th>
<th>Reticulocyte count(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carries oxygen</td>
<td>How big</td>
<td>How much blood is made</td>
</tr>
<tr>
<td></td>
<td>How much</td>
<td>Reflects HbF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hydroxyurea effect</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>WBCs(^1)</th>
<th>Platelets(^1)</th>
<th>Transfusions, serum ferritin(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fight infection</td>
<td>Stop bleeding</td>
<td>May reflect risk of chronic iron overload</td>
</tr>
</tbody>
</table>

MCV, mean corpuscular volume.

# What Patients Need to Know

## Pain management\(^1,^2\)
- Know their medications
  - Have a pain action plan
- Take main pain medication with anti-inflammatory
- Drink fluids, rest, reduce ‘stress’ to body
- Interplay between stress, swelling, and pain

## Shortness of breath\(^2\)
- Can be an emergency
- Risk for acute chest syndrome
- Asthma increases their chances of having issues
- May need immediate transfusion or exchange transfusion

## Neurologic complications\(^1,^3\)
- Emergency
- Weakness, slurred speech, visual changes
- Need immediate transfusion or exchange transfusion

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Know WHERE They Are Going

Level III (WHERE)
Know where they are going

Basic points to understand

• Health maintenance
• School and/or work (limits and resources)
• Insurance
• Adult provider
  • Coordination of transfer
  • Inpatient management differences
  • Transfusions/exchange transfusion

“I am _____, and I have sickle cell type ___. Sickle cell is when your blood looks like a banana and can cause blood to have problems going places. Stress to the body causes issues.

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Toolkits Have Been Developed to Facilitate Transition Planning

• Disease-specific tools to help young adults transition successfully to self-care
• Components include
  • Transition readiness and self-care assessments
  • Medical summary/transfer record
• The American Society for Hematology (ASH) participated in the initiative and developed a SCD-specific toolkit

Evidence-Based Management of Sickle Cell Disease

Expert Panel Report, 2014

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute

http://www.nhlbi.nih.gov/guidelines
Recommendations and Tools

• Health Maintenance
  • Pediatric and Adult

• Problem-focused—Acute and Chronic
  • Fever
  • Respiratory Symptoms/Hypoxia
  • Anemia
  • Neurological
  • Pain

• Tip Sheet - New Recommendations and Clinical Pearls
Emergency Department
Vaso-occlusive Crisis Management

Developed by the CCNC Sickle Cell Task Force with representation from
the NC College of Emergency Physicians and NC Emergency Nurse’s Association

Patient presents with vaso-occlusive crisis

Are there signs of other complications (e.g., aplastic crisis, neurologic event, pulmonary, sepsis, abdominal or orthopedic complication)?

Yes

Triage as high priority ESI Level 2, higher than VOC alone
Facilitate placement
Notify EM physician

No

Triage as high priority ESI Level 2
Facilitate placement

Provide pain management according to protocol (see next page)

After administration of 3 doses of opioids, reassess pain for improvement

Discharge home according to discharge protocol (see next page)

Yes

Pain resolved and patient states they can manage pain at home?

No

Pain Improving?

Yes

Continue analgesic management either in ED or consider transfer to observation status and/or unit (Goal: avoid hospital admission)

No

Admit to Hospital if minimal or no progress on pain score
鼓励PCP或SCD提供者在几天内进行随访。

[tps://nccsrph.hidinc.com](tps://nccsrph.hidinc.com)
NHLBI guidelines
Available to download in the Apple App Store for free.

Use password 1234 for general use or email Dr. Nirmish Shah at Nirmish.shah@duke.edu for specialty access
Thank you!

Questions?