Older Adults Living with Sickle Cell Disease

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Goals and Objectives

*The participant will:*

- Understand the demographics of sickle cell disease are changing.
- Learn some of the problems that occur in adults with sickle cell disease.
- Understand the hydroxyurea may improve quality and quantity of life in sickle cell disease.
- Understand that we lack data and understanding of the real face of sickle cell disease in older patients.
Dr. James Eckman,

Personal/Professional Financial Financial Relationships with

<table>
<thead>
<tr>
<th>External Industry Relationships *</th>
<th>Company Name(s)</th>
<th>Role</th>
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<tbody>
<tr>
<td>Equity, stock, or options in biomedical industry companies or publishers**</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Board of Directors or officer</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Royalties from Emory or from external entity</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Industry funds to Emory for my research</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>None</td>
<td></td>
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</tbody>
</table>

No off label use of drugs
Sickle Survival
Quinn et al Blood 2010;103:4023
Age Specific Sickle Cell Death Rate: California and Georgia RuSH Data

Improved Survival in Hb SS


- 102 older than 60 from 1943 to 2003
- 40 alive ages 60 to 87
- Increased fetal hemoglobin associated with survival
- Fewer pain crisis as they age
- Progressive anemia
- Progressive increase in creatinine
Objectives of our Sickle Cell Center

- Provide a medical home from birth to death
- 24 Hour Urgent Care
- Comprehensive Primary Care
- Tertiary Care
- Model of Cost Effective Disease Management
- Education
- Research
24 Hour Urgent Care

All patients over 18, except during pregnancy or for acute trauma.

Treated by MD-PA, RN, Clinic Assistant using problem specific clinical guidelines developed over 25 years.

Aggressive pain and fluid management is used.

Admitted if not improved by 8 Hours of treatment

- 80% of patients go home

Instant Medical Records

- Shadow chart and online database
Age of Active Patients

Number of Patients

Ages

2001 vs. 2016
Pain is a/the Major Adult Issue
Sickle Cell Disease: 60 Years of Study: Diggs LW & Bell A
PAIN RATES BY PHENOTYPE


Percent of Phenotype

Hb SS  Hb SC  SB⁺ Thal  SB⁻ Thal

Legend:
- $r = 0$
- $0 < r < 1$
- $1 < r < 3$
- $3 < r < 6$
- $> 6$
Georgia RuSH Experience

Average Number of Hospital Encounters from 2004 through 2008 per Individual with SCD, by Age Group in Georgia

 Average number of in-patient stays per person in 5 years
Average number of ER visits per person in 5 years

Patient Age in Years as of 2008
ER Visits in Sickle Cell
Health care utilization does not adequately characterize the sickle cell pain experience!

Pain Frequency

Breakdown of Diary Days


- Crisis & U 3.5%
- Pain C no U 12.7%
- Pain No C or U 38.3%
- No Pain 45.5%
Sickle Pain In The Adult Is Unique
Severe Acute and Chronic Pain

Barnhart, MI et al. Sickle Cell Upjohn1976. p51
Sickle Pain is Complex

- Initially acute, self limited - nociceptive
- Chronic pain from tissue and organ damage
- Chronic pain syndrome – neuropathic or mixed
- Good prognosis for survival
Neuroanatomy of Pain


Apkianarian AV et al. PAIN 2011;152:S 49–S64
Sickle Pain Is Unique

A Life-long Pain Experience

- Repeated and/or constant exposure to opioids
  - Tolerance
  - Physical dependence
  - Opiate induced hyperalgesia
  - Addiction

www.deamuseum.org/
Sickle Pain Is Unique
A Life-long Pain Experience

• Many interactions with health professionals.

• For the Patient:
  – Often positive and rewarding
  – May be negative

• For the health professional.
  – Interactions with patient and family may be positive and rewarding
  – May be negative

• Carryover to next encounter

Sickle Pain Dimensions

Emotions & Motivation
Depression, Fear, Anger, Arousal, & Behavioral Adaptations

Tissue Damage

Cognitive & Conceptual
Past Experiences, Current Expectations, Secondary Gain & Loss, Threat Perception

Social & Cultural Experiences
Familial Expectations, Age, Sex & Race, Social Identity, Peer Support / Pressure
Impact of Frequent Visitors

Number of Visits - 1988

- No Visits: 271
- 1 to 6 Visits: 535
- 6 to 12 Visits: 433
- 12 to 52 Visits: 1016
- > 52 Visits: 2767

Visits per Year

- Patients: Green
- Visits: Red
Protocol For Patients With Frequent Pain Episodes

Complete evaluation and detailed care plan:

- **Health Problems**
  - Medical Problems
  - Psychological Functioning
  - Psychiatric Evaluation

- **Social Functioning**
  - Education
  - Support Systems
  - Vocational Evaluation
MULTIDISCIPLINARY PAIN TEAM

- Medical Care
- Psychological Support
- Social Services
- Physical and Vocational Rehabilitation
- Clinical Pharmacology
Model of Cost Effective Disease Management

CENTER EMERGENCY VISITS
166 Active Patients 1985-1992
Bone Density and Vitamin D in Male Adults with Sickle Cell Disease

- Vitamin D deficiency in 142 adults with SCD
  - 139 of 142 (98%) had suboptimal levels (<30 ng/mL)
  - 85/142 (60%) were severely deficient (<10 ng/mL).
  - Vitamin D level was not related to age, sex, hydroxyurea use, sickle cell type, or date of lab draw.

Renal Disease

Figure 2. Age and the prevalence of albuminuria in adults with sickle cell hemoglobinopathies. □, normoalbuminuria; ■, microalbuminuria; ▪, macroalbuminuria.

Renal Failure in Sickle Cell Disease

- A prospective, 25-year clinical cohort study of 725 patients with Hb SS and 209 with Hb SC disease.
- Renal failure in 36 patients: 4.2% of patients with Hb SS and 2.4% of patients HB SC.
- Median age of onset was 23.1 and 49.9 years, respectively.
- Survival time after onset was 4 years despite dialysis. The median age at death was 27.
- Relative risk for mortality was 1.42 (95% CI, 1.12 to 1.81; P= 0.02) compared with patients who did not develop renal insufficiency.

Cardio-Pulmonary Disease

- Boston Pulmonary function tests normal in 10%: Decreased total lung capacity (70% of predicted) and decreased DL$_{CO}$ (65% of predicted). Restrictively physiology in 74% and isolated decreased DL$_{CO}$ in 13%.


- Duke Medical Center 43 Deaths in a 5 year period with a median age of death of 39 years for and 40 years for males. Cardiac causes 11 (25.6%); pulmonary, 6 (14.0%); other SCD related 14 (32.6%); unknown, 6 (14.0%); and others, 6 (14.0%).

- Pulseless electrical activity arrest, pulmonary emboli, acute multi-organ failure, and stroke were the most frequent causes of death.

- Most common premorbid conditions were cardiopulmonary: acute chest syndrome/pneumonia (58.1%), pulmonary hypertension (pHTN; 41.9%), systemic HTN (25.6%), congestive heart failure (25.6%), myocardial infarction (20.9%), and arrhythmias (14.0%).

Pulmonary Thromboembolism

- History of non-catheter associated PE in 100 of 404 adults, median age 29.9
- More common in Hb SC and Hb Sβ+ Thal; RR 1.77
- Associated with increased TRV
- Independently associated with death; RR 3.63

Naik et al Amer J Med. 213;126.
<table>
<thead>
<tr>
<th>Genital-Urinary</th>
</tr>
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<tbody>
<tr>
<td><strong>• Females</strong></td>
</tr>
<tr>
<td>- Delayed puberty</td>
</tr>
<tr>
<td>- Menstruation associated pain crisis</td>
</tr>
<tr>
<td>- Pregnancy</td>
</tr>
<tr>
<td>- Menopause</td>
</tr>
<tr>
<td><strong>• Males</strong></td>
</tr>
<tr>
<td>- Delayed Puberty</td>
</tr>
<tr>
<td>- Priapism</td>
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<tr>
<td>- Erectile dysfunction</td>
</tr>
</tbody>
</table>
Neurocognitive

- Subarachnoid hemorrhage and stroke
- Neuropsychological deficits
  - WAIS-III Performance IQ 86.69 for patients vs 95.19 for controls, $P = .008$
  - Correlated with age and hemoglobin level
    Vichinsky et al. JAMA. 2010;303(18):1823-1831

- Role of transfusion or hydroxyurea in prevention?
Hydroxyurea

NIH Consensus Development Conference

HYDROXYUREA

Treatment for Sickle Cell Disease

February 25-27, 2008
Natcher Conference Center
National Institutes of Health
Bethesda, Maryland

Information/Registration
Online: consensus.nih.gov
E-mail: consensus@mail.nih.gov
Telephone: 1-888-644-2667
### MULTICENTER HYDROXYUREA TRIAL

<table>
<thead>
<tr>
<th>Group</th>
<th>Hydroxyurea</th>
<th>Placebo</th>
<th>p value*</th>
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<tbody>
<tr>
<td>Pain Episodes</td>
<td>2.5 / year</td>
<td>4.5 / year</td>
<td>p &lt; 0.001</td>
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<tr>
<td>Pain Admits</td>
<td>1.0 / year</td>
<td>2.4 / year</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Acute Chest</td>
<td>25 episodes</td>
<td>51 episodes</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Transfused</td>
<td>48</td>
<td>73</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Total Units</td>
<td>336</td>
<td>586</td>
<td>p = 0.004</td>
</tr>
</tbody>
</table>

*Van der Waerden’s test.

Hydroxyurea Improves Survival

Adults: 131 treated with Hydroxyurea and 199 usual care for up to 17 years (median 8 versus 5 years)

10 Year Predicted Survival

<table>
<thead>
<tr>
<th>Group</th>
<th>Hydroxyurea</th>
<th>No Hydroxyurea</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>86 %</td>
<td>65 %</td>
<td></td>
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<tr>
<td>Hb SS</td>
<td>100 %</td>
<td>10 %</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hb S β⁰</td>
<td>87 %</td>
<td>54 %</td>
<td>&lt;0.001</td>
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<tr>
<td>Hb S β⁺</td>
<td>82 %</td>
<td>66 %</td>
<td>0.369</td>
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</table>

Voskaridou E et al.  Blood 2010; 115: 2354-2363
Usual Adult Onset Diseases

• Patients are now living long enough to deal with many of the diseases common in the general population
  – Hypertension
  – Diabetes
  – Heart disease
  – Cancer
  – Rheumatoid arthritis
  – Many others
My Conclusions:

- Individuals with sickle cell disease are living longer. Sickle geriatrics is real.
- Most patients live full and productive lives despite considerable challenges from their disease.
- Many have long, almost normal, and very productive lives.
- We have almost no population based data to support this conclusion or understand the challenges they may face.
  - There is a desperate need for ongoing surveillance and a registry to collect prospective data.
  - Need to define the disease and document impact of treatment in adults.

Thank You!