Lessons in Management of Sickle Cell Disease

CME Conference, Lloyd Erskine Sandiford Centre, November 15, 2015
Age at Death in African SS Disease

The greatest chance of death is in the first 5 years.

Analysis of this period shows that the greatest deaths occur in the first year. Considering that little pathology occurs in the first 6 months, the 2nd 6 months are a very high risk period.
The Spleen

Central to much of the early pathology of sickle cell disease

1. Loss of splenic function renders patients prone to overwhelming blood infections especially with Streptococcus pneumonia.

2. Acute enlargement may trap the blood causing serious morbidity and death – acute splenic sequestration.

3. Chronic enlargement causes sustained anaemia and the metabolic demands limit growth – chronic hypersplenism.
Pneumococcal Septicaemia

Early loss of splenic function; posterior scans.

Normal function showing liver (right) and spleen (left)

Loss of splenic function occurs in most children with African disease during the 1st year rendering them prone to overwhelming septicaemia.
Pneumococcal Septicaemia

*mostly under 2 years*

*incidence falls sharply after 5 years*
Pneumococcal septicaemia
**Lessons learnt**

Prophylactic penicillin works but pneumococcal vaccine does not work well when it is most needed.

Penicillin is given as monthly IM injections to avoid compliance problems.

Given 4 months to 4 years when last injection is given with 23V vaccine.

Protocol will need modifying with rapid emergence of penicillin resistance and conjugate vaccine.

Nurse Jackson giving penicillin in home visiting programme
Acute Splenic Sequestration

- sudden increase in spleen size, fall in Hb, and increase in retics.
- after attack, spleen decreases in size.
- accounted for 24% deaths in first 10 years of study.

Cohort 6 - age 3 m, Hb ↓ 2g, retics ↑, spleen 4 cms – resolved spontaneously.
Acute Splenic Sequestration

Cohort 12 - 4.5 years old, died in 3rd attack of ASS, Hb 1.9 g, retics 38%, spleen 8 cms below costal margin.
Acute Splenic Sequestration

Teaching splenic palpation – does it work?

Education programme

<table>
<thead>
<tr>
<th>Before ‘74-’78</th>
<th>After ‘79-’83</th>
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<tbody>
<tr>
<td>ASS per 100 pt/yr</td>
<td>4.6</td>
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<tr>
<td>Death rate</td>
<td>10/36 (28%)</td>
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### Chronic Hypersplenism

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before</th>
<th>After</th>
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<tbody>
<tr>
<td>Hb (g/dl)</td>
<td>4.5</td>
<td>9.2</td>
</tr>
<tr>
<td>Retics (%)</td>
<td>27</td>
<td>12</td>
</tr>
<tr>
<td>Platelets (x10⁹/l)</td>
<td>112</td>
<td>588</td>
</tr>
<tr>
<td>Red cell mass (ml/kg)</td>
<td>12</td>
<td>30</td>
</tr>
<tr>
<td>Plasma volume (ml/kg)</td>
<td>75</td>
<td>60</td>
</tr>
<tr>
<td>Blood volume (ml/kg)</td>
<td>87</td>
<td>90</td>
</tr>
<tr>
<td>Mean cell life (days)</td>
<td>3.0</td>
<td>9.0</td>
</tr>
<tr>
<td>Height velocity (cm/yr)</td>
<td>7.0</td>
<td>13.4</td>
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**Cohort 290. 3.5 year-old SS with chronic hypersplenism**
Aisha T, born 8/8/98. By age 3.9 years, 32 admissions, 29 transfusions underwent splenectomy July 2002

Left: At home in Katosi on shores of Lake Victoria Jan 2003, right August 2004
Chronic Hypersplenism in India

December 2011
69 transfusions

Splenectomy Feb 4, 2012
April 2012 - no transfusions

Divyash MP aged 12 years, Gujarat, India
September 2013 1½ y post-op
No transfusions, growing rapidly

November 2015
3½ years post-op, no transfusions.
Gallstones
Gallstones

Complications

- Acute cholecystitis
- Chronic cholecystitis
- Obstruction of common bile duct
- Empyema
The Bones

Bones are affected because of the increased bone marrow expansion and its metabolic demands

1. To compensate for the rapid red cell destruction, bone marrow expands and turns over more rapidly.

2. If the increased metabolic demands are not met, bone marrow may undergo avascular necrosis causing pain – the painful crisis.

3. Dead bone marrow is prone to infection especially by the Salmonella organisms - osteomyelitis.
Dactylitis
Dactylitis

Haemophilus influenzae osteomyelitis complicating dactylitis
Age 2.8 years

Permanent shortening of affected small bones
Age 10.5 years
Painful crisis

Precipitating factors

- Skin cooling: 90%
  - Seasonal: 74%
  - Rain: 50%
  - Swimming: 40%
- Exercise: 66%
- Infection: 24%
- Psychological stress: 22%

Avascular necrosis of lumbar vertebrae

Photos courtesy of the late Prof. Lemuel Diggs
Risk factors

Pregnancy: especially the last trimester and immediate post partum period.

Haematology:

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<tr>
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<th>Regression coefficient</th>
<th>t</th>
<th>p</th>
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<tbody>
<tr>
<td>Hb</td>
<td>0.357</td>
<td>4.51</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Reticulocytes</td>
<td>0.554</td>
<td>2.18</td>
<td>0.032</td>
</tr>
<tr>
<td>MCV females</td>
<td>-0.041</td>
<td>2.25</td>
<td>0.026</td>
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Painful crisis
Most patients with bone pain of severity to require narcotic analgesia are treated in a day care facility and 92% elect to return home.

Cohort 14 most frequent painful crises in the cohort. Note 4 year pain free window from 14-18 yrs.
Painful Crisis

Treatment

Prevention
- Identify and avoid precipitating factors.

Treatment of established pains
- Rest
- Reassurance, education: many patients do not understand the cause of the severe pain, they think that it is serious and that they are going to die.
Treatment

Treatment of established pains (contd.)

- **Warmth**: many patients find local warmth helpful.

- **Fluids**: sick patients rapidly become dehydrated because they do not drink, have high obligatory insensible losses with fever, and cannot concentrate urine normally; give fluids orally or if necessary intravenously.
Painful Crisis

Treatment

Pain relief: WHO Analgesic ladder

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<tr>
<th>Level</th>
<th>Agent</th>
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<tr>
<td>1</td>
<td>Paracetamol or paracetamol/codeine.</td>
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<tr>
<td>2</td>
<td>Codeine, +/- anti-inflammatory agents.</td>
</tr>
<tr>
<td>3</td>
<td>Narcotic analgesia: pethidine, pentazocine, morphia.</td>
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Pain relief:

**Level 1**

Paracetamol: weak analgesic but can be effective with other supportive measures.

Paracetamol/codeine tablets (500mg paracetamol: 8mg codeine): much more effective, Jamaican patients keep at home where many manage pains.
Pain relief:

Level 2

Codeine tablets (30mg): stronger analgesic but can cause constipation.

Non-steroidal anti-inflammatory (NSAID’s): effective, but major problems with gastric symptoms; beware of impaired renal function.
Pain relief:

**Level 3**

Pethidine, demerol (75mg ampoules): strong analgesic given i/m, preferred by patients because of rapid pain relief. Disadvantages include muscle fibrosis at injection sites.

Pentazocine, sosegon, talwin: effective, but about 10% patients get vestibular symptoms.
Pain relief:

**Level 3 (contd.)**

Morphia: strong analgesic given i/v or by PCA pump, preferred by physicians because they feel they get more even pain control at lower total doses; often disliked by patients because of side effects of constipation, pruritus.
Avascular Necrosis of the Femoral Head

Damage to the immature femoral head results in flattening with ‘mushroom’ deformity, good joint space and often good function.

Damage to the mature femoral head is usually segmental and continued weight bearing results in progressive damage and a painful limitation of movement.
Acute chest syndrome

Rib infarction is risk factor for acute chest because breathing hurts and is shallow.

with rib infarction, incentive spirometry may prevent acute chest syndrome.
Acute chest syndrome

- complex pathology resulting from infection, infarction, fat embolism, acute pulmonary sequestration.
- major cause of death at all ages after 2 years
- monitor closely with pulse oximetry
- exchange transfusion may be life-saving
Proliferative Retinopathy

Visual impairment in sickle cell disease is usually secondary to proliferative retinopathy (PSR).

PSR is more common in sickle cell-haemoglobin C (SC) disease than SS disease. Despite high frequencies of PSR, serious visual loss is unusual.

The role of laser treatment is undefined.
From 1981, Professor Alan Bird of Moorfields Eye Hospital in London and a team has conducted annual eye exams on Cohort children from age 5 years and fluorescein angiography from age 6 years.
Proliferative Retinopathy

Cohort 158 VB
SC disease

13 May 1985 age 8y 6m

21 May 1985 age 8y 6m

28 Jan 1987 age 10.2yr

13 Jan 1986 age 9y 2m
Gallbladder age 13 years

Patient minus gallbladder age 29 years
Dactylitis

Permanent shortening of small bones - age 10.5 years

Birthday party age 30 years
Age 3 months

Cohort 6

Age 33 years
Age 24 years perfect health

Age 3.5 years with chronic hypersplenism

Cohort 290
Jamaica is an island laboratory which has allowed many of these observations. And so is Barbados; we both have unique opportunities for disease follow-up and research.