Sickle Cell Trait and the Athlete

Kimberly G. Harmon, MD
Professor, Department of Family Medicine and Orthopaedics and Sports Medicine

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Disclosures

- Grant from Sonosite

Hemoglobin S

- Hemoglobin composed of 2 α-chains and 2 β-chains
- Hemoglobin S results from the substitution of a valine for glutamic acid at the sixth amino acid of the beta globin chain
Hemoglobin S

- Produces a hemoglobin tetramer that is poorly soluble when deoxygenated

Sickle Cell Disease

- Occurs when an individual is homozygous for Hgb S
- Vaso occlusion and hemolysis are hallmarks
- Incompatible with strenuous exercise

Sickle cell trait

- Heterozygous for Hgb S
- 1 in 12 African Americans have sickle cell trait
- 1 in 625 – 10,000 Caucasians
- 3,000,000 Americans have sickle cell trait
Challenges

- Exercise
- Altitude
- Heat

- Elevated temperature
- Hypoxia
- Acidosis
- Dehydration

Associations

- Splenic infarct
- Gross hematuria
- Hyposthenuria
- Exertional rhabdomyolysis
- Sudden death

Splenic Infarct

- Occurs with unacclimated athletes at altitude
- Can occur as low as 5,550 ft.
- Presents with:
  - LUQ pain
  - Nausea
  - Vomiting
Treatment

• Stop exertion
• O₂
• Descend
• Rarely require splenectomy if diagnosed and treated quickly

Ryan Clark

• Denver 2005 – diagnosed with splenic contusion
• Denver – 2007 – splenic infarct led to splenectomy and missed the rest of the season
• Held out in 2009
• Sat out of play off game 2012

Gross Hematuria

• Results from sickling in the renal medulla
• Papillary necrosis will sometimes be present
Treatment

• Rest
• Hydration
• Iron if needed

Hyposthenuria

• Inability to concentrate urine
• Cumulative effects of renal papillary necrosis
• May contribute to dehydration when exercising

Sudden Death and SCT

• First reported in 1970
• Reviewed one year of Army basic training
• 4,000 recruits total
• 4 recruits died, 3 had SCT
• Training was at Ft. Bliss, TX — elevation 4,050 ft.

Sudden Death and SCT

• Retrospective review of all deaths during basic training among active-duty military 1977 – 1981.
• 2 million military recruits
• All deaths are reported and autopsy confirmed.
• Risk of sudden unexplained death (SUD) in African American recruits with SCT was 28X that of those without SCT.
• Absolute risk of death with SCT was 1 in 3200.

Kark, JAMA 1987

Sudden Death SCT

• Non-traumatic deaths in basic training from 1977 – 2001 (25 years).
• 139 exercise related non-traumatic deaths.
• 26 recruits who died had SCT (18%)
• Death rate of those with SCT was 1 in 37,000 recruit-years.


Proposed mechanism

Combination of high intensity exercise, dehydration, thermal strain

Causes hyperthermia, hyperosmolality, acidosis, and red cell dehydration

Erythrocyte sickling, inflammation, microvascular occlusion
Proposed mechanism

- Ischemic pain
- Muscle weakness
- Massive release of potassium
- Arrhythmia
- Death

Unproven . . . and Implausible?

- Proposed pathology does not exist in those with SCD
- Sickling does not occur in the muscle in those with SCD
- Infarcts occur most commonly in bone, spleen, lung

“Exertional Sickling has become the leading killer in NCAA Div-I football”

“SCT is the leading killer in NCAA football/conditioning”
Screening - NCAA

- Dale Lloyd of Rice University collapsed and died after an intense football practice in 2006.
- Family filed suit
- NCAA now recommends screening as required by settlement

NCAA Legislation

- Proposal 2009-75-B-1
- 17.1.5 Mandatory Medical Examination.
- “The examination or evaluation shall include a sickle cell solubility test (SST), unless documented results of a prior test are provided to the institution or the student-athlete or student declines the test and signs a written release.”
Screening

- Began August 2010 in Division I
- Division II began screening August 2012
- Division III passes screening at Jan 2014 conference and began screening in August 2014

American Society of Hematology: ASH

- Policy Opposes Mandatory SCT Screening for Athletic Participation
  - Recommends universal training interventions and additional research
- Believes NCAA Division I policy, as currently written and implemented, has potential to harm student athletes and larger community of individuals with SCT.

Others agree...

Universal Precautions

- Mandatory hydration
- Limiting physical activity in all
- Limiting practice/play in certain environmental conditions
- Letting any athlete who was struggling recover

Control contributing factors

- Dehydration
  - Sickling eliminated when fluid losses replaced
  - More difficult b/c of impaired renal concentrating ability
- High temperature
- Asthma
- Illness
- Altitude

Intervention

- 1982 U.S. Army implemented strict hydration policies
  - Direct observation of recruit drinking
  - Measurement of wet bulb globe temperature (WBGT) with modification of training if a certain threshold was reached.
Intervention

- From 1982-1991
  - No deaths in SCT recruits in the intervention group and all exertional deaths decreased (2.3 million recruits)
  - Unchanged rate of deaths in non-participating centers (1.2 million recruits).
- Study was never published in peer-reviewed journal
- Revisiting policy now

Screening in the Military

- Screen
  - Navy
  - Marine Corps
  - Air Force
- Does not screen
  - Army

ACSM DoD Consensus Conference on SCT – Sept 2011

- Dr. John Kark
- Dr. Randy Eichner
- Dr. Kwaku Ohene-Frempong
- Dr. Alexis Thompson
Exercise Collapse Associated with SCT – ECAST
Further research needs to occur regarding etiology of increased death rate
Possibility exists that SCT is surrogate for another contributing factor

1. Team physicians/ATCs should familiarize themselves with literature
2. Unwarranted restrictions should not be placed on individuals with SCT
3. SCT testing should be voluntary and accompanied by genetic counseling if positive

4. All exercising individuals including those with SCT should:
   – Avoid dehydration
   – Acclimatize gradually to heat and humidity
   – Condition carefully before exhaustive exercise
   – Acclimatize to altitude
   – Refrain from extreme exercise during illness
Questions

• What is the magnitude of the problem in NCAA athletes?
• Is screening effective in preventing death?
• Is screening cost effective?
• Is it harmful?

NCAA Deaths 2004 - 2008

Harmon, Circulation, 2011

All-Cause Football Deaths 2004 – 2008

Harmon, BJSM 2012
“Exertional sickling has become the leading killer in NCAA Div-I football”


“SCT is the leading killer in NCAA football/conditioning”

What is the magnitude of the problem in the NCAA?

- 5 deaths in the 5 years (2004-2008)
- 9 deaths from 2000 – 2010
- All in African American football players
- All in football conditioning

<table>
<thead>
<tr>
<th></th>
<th>Number of Athletes 2004-2008</th>
<th># of athletes (all ethnicities) with SCT</th>
<th>Risk of exertional deaths in athletes with SCT</th>
<th># of athletes (all ethnicities) without SCT</th>
<th>Risk of exertional deaths in athletes without SCT</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All divisions, all sports</td>
<td>1,909,663</td>
<td>23,529</td>
<td>1,4,706</td>
<td>1,960,134</td>
<td>28</td>
<td>1:69,505</td>
</tr>
<tr>
<td>Div I athletes, all sports</td>
<td>798,033</td>
<td>12,512</td>
<td>1,2,302</td>
<td>775,521</td>
<td>16</td>
<td>1:48,470</td>
</tr>
<tr>
<td>All divisions, football athletes</td>
<td>308,042</td>
<td>7,432</td>
<td>1,1,486</td>
<td>300,610</td>
<td>7</td>
<td>1:42,944</td>
</tr>
<tr>
<td>Div I football athletes</td>
<td>126,447</td>
<td>4,134</td>
<td>1,027</td>
<td>122,313</td>
<td>4</td>
<td>1:30,578</td>
</tr>
</tbody>
</table>

Annual risk of death

- Lightening strike – 1:7,000,000
- Airplane crash – 1:400,000
- In a fire – 1:88,000
- NCAA with SCD – 1:43,000
- Motor vehicle accident – 1:6,500
- Athlete with SCT – 1:4,170
- Motorcycle – 1:1,200
- Member of sky diving club – 1:1,000

- 101,450 African American football athletes
- 7,102 presumed with SCT
- 5 deaths
- Risk of death associated with SCT 1:805

Is screening effective in preventing deaths?

- Division I began screening all athletes in 2010
- Prior to 2010 there was an average of 1 death per year associated with SCT
- No deaths associated with SCT from 2010 – 2013
- Recent death in a known SCT + football athlete in conditioning (Feb. 2014)

Athletes with death related to SCT in the last decade

<table>
<thead>
<tr>
<th>Student-Athlete</th>
<th>Institution</th>
<th>Date of Activity</th>
<th>Status Known?</th>
<th>Lawsuit?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preston Birdsong</td>
<td>Tennessee Technological University</td>
<td>8/13/2000</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>DeAngelo Darby</td>
<td>Florida State University</td>
<td>2/26/2001</td>
<td>Known</td>
<td>Awarded</td>
</tr>
<tr>
<td>Aaron Richardson</td>
<td>Bowling Green State University</td>
<td>9/15/2004</td>
<td>Unknown</td>
<td>Filed</td>
</tr>
<tr>
<td>Aaron O’Neal</td>
<td>University of Wisconsin</td>
<td>7/12/2005</td>
<td>Unknown</td>
<td>Awarded</td>
</tr>
<tr>
<td>Dale Pinkston</td>
<td>Rice University</td>
<td>9/24/2006</td>
<td>Unknown</td>
<td>Awarded</td>
</tr>
<tr>
<td>Ereck Plancher</td>
<td>University of Central Florida</td>
<td>3/18/2008</td>
<td>Status known</td>
<td>Awarded</td>
</tr>
<tr>
<td>Erek Wiley</td>
<td>North Carolina A&amp;T</td>
<td>7/30/2008</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Bennie &quot;Frank&quot; Abrams</td>
<td>Western Carolina</td>
<td>7/8/2009</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Ja’Quayvin Smalls</td>
<td>Minnesota University</td>
<td>11/4/2013</td>
<td>Status known</td>
<td></td>
</tr>
</tbody>
</table>
Screening

- Allows education and counseling of individual
- Allows education of training and coaching staff
- Extra attention to hydration
- Extra attention to difficulty with conditioning
- If someone is in crisis it narrows (or reorders) the differential

Assuming all deaths in SCT athletes could be prevented if their status was known . . .

Cost Effectiveness Analysis Sickle Cell Screening 2004 - 2008 (no start up costs)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>African American Football</th>
<th>All Football Athletes</th>
<th>African American All Athletes</th>
<th>All Athletes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per Year Life Saved</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;Simple SS Test&quot;</td>
<td>$307</td>
<td>$1,610</td>
<td>$1,410</td>
<td>$9,982</td>
</tr>
<tr>
<td>Sickle Dex/isolectric focusing</td>
<td>$6,361</td>
<td>$12,938</td>
<td>$12,512</td>
<td>$83,678</td>
</tr>
<tr>
<td>Hemoglobin Electrophoresis</td>
<td>$15,218</td>
<td>$46,206</td>
<td>$44,607</td>
<td>$298,850</td>
</tr>
</tbody>
</table>
Screening sub-populations

• Football players?
• African Americans?
• Males?
• Discriminatory?

NCAA policy ... “has potential to harm student athletes and larger community of individuals with SCT”

• Concern about recreational athletes being discouraged from exercise because of fear
• Concern that athletes who are known to be SCT+ will be discriminated against
  — “Coaches have no right to know athletes’ private health care information”
• Concern about a lack of appropriate genetic counseling when positives are found

Harm?

• Recommendations of “universal precautions” for football is profoundly reasonable but ultimately not practical
  — Workouts should be conducted by a certified strength and conditioning coach
  — Conditioning should not be used as punishment
  — Medical personnel should have “unchallengeable authority”
Prevention of Sudden Death

- Primary Prevention
  - Universal Precautions vs. Targeted Interventions
- Secondary Prevention
  - Recognition and Treatment

Treatment of SCT crisis

- Rapid recognition
- Early treatment
- Transport if needed
- Communication with ER

Chain of Survival

- Early Access
- Early CPR
- Early Defibrillation
- Early Advanced Care
- Rapid Recognition
- Early Treatment
- Transport if needed
- Communicate with ER
Emergency Action Plan

- Practice annually
- Practice with ATCs, strength and conditioning coaches
- Practice with local EMS
- Review with facilities
- Coordinate with local ER

Rapid Recognition

Struggling Athlete

- Heat illness
- SCT crisis
- Cramps

Rapid Recognition
Unconscious Athlete

- Sudden cardiac arrest
- Fulminant rhabdomyolysis
- Heat stroke

Rapid Recognition

Recognition of SCT crisis

- Muscle pain is ischemic
  - Sometimes described as cramping
  - Often weak
  - Muscle are usually not tense or hard
- Athlete may collapse but will be conscious

Sodium depletion cramps

- Electrolyte drinks
- Stretch
- Ice massage
- IV Fluids

Struggling Athlete

Sick Cell Crisis

- Oxygen
- Apply AED
- Establish IV access
- Transport failing immediate improvement
Sudden Cardiac Arrest

- CPR
- AED
- Transport

Exertional Rhabdomyolysis

- AED
- Cool
- IV access
- Transport
- Communicate with ER

Heat Stroke

- Pulse
- Rectal temp > 104°F

No pulse

Pulse

SCT?

Conclusions

- SCT is a preventable cause of death in NCAA athletes with some populations at significantly higher risk
- Screening appears to have decreased the rate of death
- The cost effectiveness of screening largely depends on the cost of the test and the population screened
- There is no proof screening is harmful
- Early recognition, treatment and a coordinated response are critical to prevent death