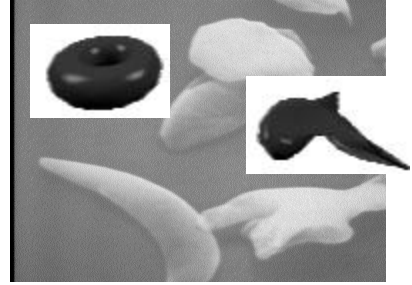


The Student Athlete with Sickle Cell Disease / Trait

Cynthia Gauger, MD
Nemours Children's Clinic

What is Sickle Cell Disease?



The Student Athlete with Sickle Cell Disease/Trait

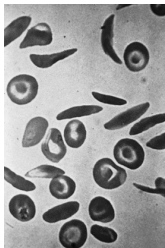
Objectives

- Differentiate Sickle cell Trait (AS) from Sickle Cell Disease (SS)
- Define the Population at Risk
- Discuss the Clinical Complications of Sickle Cell Disease vs Trait, with regard to the Student Athlete
- Recognize *Sickling Collapse* of the Athlete
- Discuss the benefits of Screening for Sickle Cell Trait in the Preparticipation Physical

The Sickle Mutation

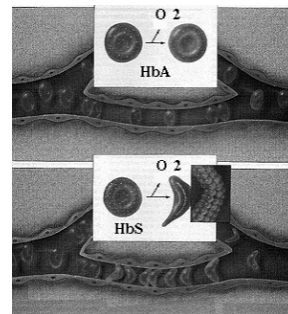
- Most common genetic disorder in No Am - Hb S
 - single amino acid substitution
 - alters the structure of oxygen carrying hgb
 - deoxygenated sickle hgb polymerizes
 - red blood cells become distorted into the sickle shape
- Sickle-shaped red cells interrupt blood flow by blocking small blood vessels
- The result is a chronic hemolytic anemia and painful vaso-occlusive crises
- May lead to ischemic tissue injury and significant end-organ damage

Morphology of the Sickled Cell



- Western observers named SSA for its microscopic morphologic features
- African cultures named it for its painful episodes '*chwechwechwe*' relentless repetitive chewing

Blood flow of normal and sickle red blood cells



Normal vs. Sickle Hemoglobin

Normal

- disc-Shaped
- soft(like a bag of jelly)
- easily flow through

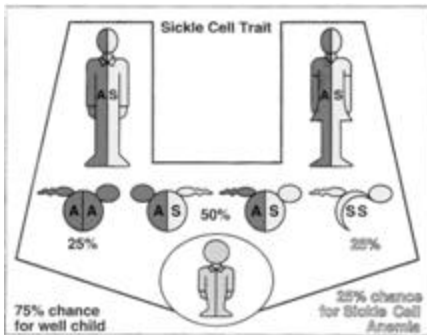
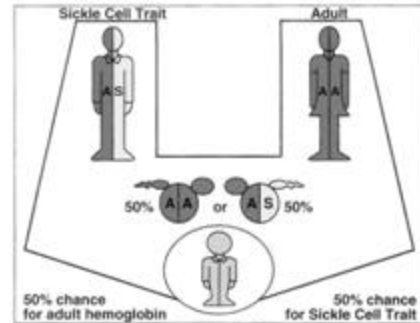


Sickle

- sickle-Shaped
- hard (like a piece of wood)
- often get stuck in small blood vessels
- lives for 20 days or less



Inheritance Pattern of Sickle cell Disease



How Common is SS Trait vs Disease

- SSD affects millions of people throughout the world.
- In this country about 100,000 people are affected by sickle cell disease
- The disease affects 1 in 500 AA births with an estimated 1,000 babies born each year with SS
- Approx 2.5 million Americans will have sickle trait
- An estimated 1 in 10- 12 AA have inherited the trait ~ 8%; 1 in 2,000 - 10,000 white Americans

Florida Newborn Screening

- Jacksonville began newborn screening for hemoglobinopathies in 1984
- Entire state of FL began universal screening in 1988
- Population of Greater Jacksonville: 1,344,504
 - 21.6% AA = 290,412 people
 - 9% AA have sickle cell trait
 - 26,137 AA with sickle cell trait
 - 588 AA with sickle cell disease

Diagnosis

The most widely used blood test for sickle cell disease and trait is the hemoglobin electrophoresis. A blood sample is placed in an electric field on filter paper and the different hemoglobins travel at different speeds to the negative pole.



Complications From Sickle Cell Disease

- Varying degrees of anemia
- Yellowing of the eyes/skin
- Predisposition to Vaso-occlusive pain crisis
- Damage to major organs (spleen, liver, kidney, lung)
- Increase vulnerability to severe infection
- Stroke
- Delayed growth and sexual maturation
- Aseptic necrosis of the hip/shoulder
- Sickle retinopathies

Hand Foot Syndrome - Dactylitis

Sickle dactylitis is one of the first complications in sickle cell syndromes with the highest incidence between ages six months and two years.

The sickle red cells cause painful swelling of the hands and feet.

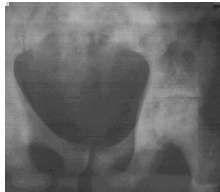


Bone Pain

More prolonged and constant pain can be seen with bone infarction, sickle arthritis, and aseptic necrosis of the femur or humerus.



Most common complication and the most common reason for hospitalization.



Common triggers: dehydration, low oxygen, exhaustion, temp extremes, acidosis, infection

"Ten Revisited"



Splenic Sequestration

- Sudden trapping of blood within the spleen
- Usually occurs in infants under 2 years of age
- May be associated with fever, pain, and respiratory symptoms.
- Circulatory collapse and death can occur in less than thirty minutes.



Acute Chest Syndrome

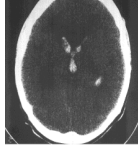
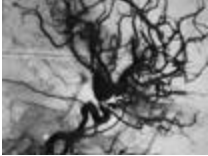
Pneumonias or infections in the lung, and acute chest syndrome, caused by sickling red cells blocking blood vessels in the lung, are the most common complications.



Strokes

Strokes are a blockage of blood flow to a part of the brain caused by the sickle cells. The symptoms include one sided weakness, numb feelings, seizures, slurred speech or facial weakness.

More common in children than adults



Eye Problems

Sickle cells can cause damage to the blood vessels in the eye, especially in SC disease. New weaker blood vessels may form and break open and bleed. Early treatment with laser therapy can prevent such bleeds.



Kidney

Kidney damage starts very early and progresses throughout life causing complications in many individuals with sickle syndromes. The kidneys may not filter normally, passing protein and/or excessive amounts of water.



Leg Ulcers

Leg ulcers are seen in 10 to 15% of older children and adults with sickle cell anemia. They may start as a simple insect bite or cut that will not heal. They are likely caused by poor circulation to the skin.



Sports Participation in Adolescents with SS Disease

- Adolescents should be encouraged to participate in exercise
- Exercise tolerance greatly depends on the severity of the anemia
- Individuals with SS will transition to anaerobic metabolism more quickly → results in lactic acidosis and muscle cramping, → heat exhaustion or heat stroke
- High risk of VOC pain crisis
- Exercising too hard on the hips - AVN
- If the patient has a large spleen - contact sports would carry a risk of splenic rupture

Sports Participation in Adolescents with SS Disease

- Individuals with SSD should avoid extreme endurance sports such as long distance competitive racing, football, etc which push the body to exhaustion/dehydration
- Avoid sports that involve cold temp or low oxygen concentration that will trigger VOC pain
- Avoid repetitive jumping

Sickle cell Trait (AS)

- Inheritance of one gene for normal hgb A and one gene for sickle hemoglobin
- Trait will not turn into disease, nor will it go away
- AS is not associated with anemia
- Red blood cells have normal morphology under light microscopy
- No difference in the height and weight of children with AS
- No data to suggest that AS is associated with painful events or crises

Sickle cell Trait

- People with AS are normal with few exceptions
- AS is no barrier to outstanding athletic performance
- About 40% of the hemoglobin is sickle hemoglobin, but the red cells can sickle under severe conditions of low oxygen
- So,
What are the possible clinical consequences of sickle cell trait?

Concerns for the Athlete with sickle cell trait

- Gross Hematuria and renal Issues
- Splenic Infarction
- Exertional Rhabdomyolysis
can be life threatening

Renal Issues

- Gross hematuria
 - massive often recurrent bleeding
 - 3 - 4:1 ratio from left kidney
 - thought to be secondary to renal papillary necrosis
 - Treatment: hydration, alkalinization, observation
- Hyposthenuria - impaired concentrating ability
- Cause? Relative hypertonia, acidosis, hypoxia of renal medulla predisposing to "sickling"

Splenic Infarction

- Can occur in AS, typically at altitude
- Typically causes LUQ pain, often with N/V and splenomegaly
- The risk may begin at 5,000 feet and increases with increasing altitude
- The lower oxygen environment predisposes to intravascular polymerization of sickle hgb
- Vigorous exercise may increase the risk
- Racial predisposition: higher average percentage of Hgb S in caucasians vs AA

Exertional Rhabdomyolysis

Makaryus, et al, Hematology 2007;12: 349

- In AS, strenuous exercise may contribute to sickling:
 - severe hypoxia
 - metabolic acidosis
 - hyperthermia in muscles
 - red cell dehydration
- Skeletal muscle injury resulting in release of myoglobin and creatine kinase into circulation
- Hyponatremia, hyperkalemia, hyperphosphatemia, hypocalcemia, lactic acidosis, and hyperuricemia

Exertional Rhabdomyolysis

Makaryus, et al, Hematology 2007;12: 349

- Severe cases result in renal failure and death
- Risk factors: high temperatures and humidity, poor physical conditioning and inadequate fluid intake, underlying/recent viral illness

Military Training

- US Armed Forces linked AS to sudden unexplained death during basic training
- N Engl J Med:
 - 1970 – 4 deaths among 4000 AA at 4,000 feet altitude
 - 1987 – 42 sudden deaths in 37,300 blacks with AS in a total of 2,087,600 recruits
 - Relative risk of sudden unexplained death was 27.6 in AS compared to AA recruits without AS and 39.8 compared to all recruits
 - Main cause of death – rhabdomyolysis
 - Risk of death increased with age

College athletes with AS

- 15 athletes, most college football players, have died in the past decade associated with AS
- 1974: First documented NCAA case of death resulting from AS: Polie Poitier
- 2001 Devaughn Darling; FSU
- 2006: Dale Loyd; Rice University
- 2008: two players collapsed at UCF; Ereck Plancher

Sickle Cell Trait and the Athlete



NCAA CONSIDERS AS
The Student-Athlete
with Sickle Cell Trait



Consensus Statement: Sickle Cell Trait and the Athlete

Sickling Collapse

- The setting and syndrome in most cases have been similar
- ? Sickling players may be on the field only briefly, sprinting only 800 – 1,600 meters, often early in season
- ? Can occur during repetitive running of hills or stadium steps, during intense sustained strength training, if the tempo increases late in intense one-hour drills, or at the end of practice when players run “gassers”
- ? Sickling can even occur rarely in the game, as when a running back is in constant action during a long, frantic drive downfield
- Not limited to football

Recognizing Sickling Collapse

- A sickling collapse is a medical emergency
- Often confused with heat cramping
- Athletes described as having ischemic pain and muscle weakness (not cramping)
- Physical findings are different:
 - Cramping: writhe in pain, muscles visibly contracted and rock-hard
 - Sicklers: lie fairly still, not yelling in pain, muscles look and feel normal
- The athlete is typically experiencing major lactic acidosis, impending shock, and imminent hyperkalemia from sudden rhabdomyolysis

Sickling Collapse – Medical Emergency !!

- Check vital signs
- Administer high-flow oxygen, 15 lpm with a non-rebreather face mask
- Cool the athlete if necessary
- If the athlete is obtunded or as vital signs decline, call 911, attach an AED, start an IV, and get the athlete to the hospital
- Tell the doctors to expect explosive rhabdomyolysis and the metabolic complications

Screening for Sickle cell Trait

- Nearly all 50 states screen for hemoglobinopathies at birth
- Trait notification is inconsistent
- Education programs are limited
- Consensus of the Task Force of the National Athletic Trainer's Association:
 - Efforts should be made to document newborn screening results during the PPE
 - In the absence of NB screening, institutions should carefully weigh the decision to screen
 - Irrespective of screening, institutions should educate staff, coaches, and athletes

NCAA – screening for Sickle Trait



- 2008 NCAA formally recommended sickle testing as a result of the legal settlement
- April 2010: NCAA's Division I Legislative Council approved a measure that requires all athletes to be screened for sickle trait unless they can show results of a previous test or they sign a release to decline testing
- Must still be reviewed by the Division I board of Directors – would go into effect August 2010

Sickle Trait

Education and precautions

- Set their own pace
- Slow and gradual preseason conditioning regimen
- Adequate rest and recovery between repetitions
- Do not urge all out exertion beyond 2 to 3 minutes without a breather
- Stop activity immediately if struggling
- Exclude performance tests such as mile runs, serial sprints
- Stay well hydrated at all times
- Maintain proper asthma management
- Refrain from extreme exercise during acute illness, if febrile
- Access supplemental O₂ at altitude as needed
- Seek prompt medical care if experiencing unusual distress

Sickle Trait

Education and precautions

- Ambient heat stress, dehydration, asthma, and altitude predispose the athlete with sickle cell trait to an onset of crisis in physical exertion

? Adjust work/rest cycles for environmental heat stress

? Emphasize hydration

? Control asthma

? No workout if an athlete with sickle cell trait is ill

? Watch closely the athlete with sickle cell trait who is new to altitude. Modify training and have supplemental oxygen available for competitions

Sickle cell Trait: Conclusions

- Sickle cell trait is common
- AS is usually a benign condition but... may be associated with renal, splenic, ocular problems and a risk of vascular collapse with extreme exercise particularly in association with heat, altitude, hypoxia, and dehydration.
- Under these extreme conditions sickle cell trait cells may "sickle" transforming silent sickle cell trait into a syndrome with risk of organ damage from vaso-occlusion
- None of the clinical consequences of AS are frequent or predictable

Sickle cell Trait: Conclusions

- Real risk of sickle cell trait remains genetic
 - Persons with AS must know their trait status and their risk of having a child with disease
- All positive testing MUST be followed with counseling / education
- www.NCAA.org/health-safety
 - The Student Athlete with Sickle Cell Trait
 - Educational Materials
 - Fact Sheet for the Student Athlete
 - Fact Sheet for Coaches
 - The Student Athlete with Sickle cell Trait - Video