Searching for Conditions Associated with Sudden Cardiac Death in the Young: Can We Prevent a Rare Event?

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Disclosures:
Medical Advisory
• August Heart

Ignorance and Fate…

"Must helpless man, in ignorance sedate,
Roll darkling down the torrent of his fate?"

Samuel Johnson (1709-1784)

Extinguishing a Rising Star…

The date is 4 March 1990, a sunny Saturday afternoon in southern California…

"I’m honest about it. I’m in college to play basketball. The degree is important to me, but not that important."

Hank Gathers (1967-1990)

Extinguishing a Rising Star…

Outstanding Issues:
• Doctor Shopping
• Medication Titration and Compliance
• Medical Care in Sports
• Role of BLS/AEDs in Sports

Helplessly… Torrent of Our Fate

• Spring Valley Hall High School Varsity Football
• Collapsed during First Day of Fall Conditioning Drills
• Trainer “tended to teen” until EMS arrived
• “Heat exhaustion” speculated…
• …Hypertrophic cardiomyopathy confirmed at autopsy
• History of antecedent chest pain later reported by friends

Hank Gathers (1967-1990)

Daniel Lule (1995-2012)

http://ksi.uconn.edu/research/real-time-registry-of-sudden-death-in-sport/
Where We’re Going…

- Defining the Scope of the Problem
- Understanding the Causes
- Challenges of Screening
- What is Happening Now in San Antonio
- Future Directions

Defining the Problem…

Sudden death in the young is a rare event

<table>
<thead>
<tr>
<th>Population Group</th>
<th>Age Distribution</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organized HS/College Athletes¹</td>
<td>14-21 years</td>
<td>1:135,000 (male)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1:750,000 (female)</td>
</tr>
<tr>
<td>USAF Recruits²</td>
<td>17-28 years</td>
<td>1:735,000</td>
</tr>
<tr>
<td>Rhode Island joggers³</td>
<td>&lt;30 years</td>
<td>1:280,000</td>
</tr>
<tr>
<td>Overall⁴</td>
<td>14-21 years</td>
<td>1:200,000</td>
</tr>
</tbody>
</table>


Defining the Problem…

Defining the Problem…

Cardiac causes of sudden death usually predominate

<table>
<thead>
<tr>
<th>Region / Era</th>
<th>Age</th>
<th>N</th>
<th>Top Diagnoses</th>
<th>C/V Causes</th>
<th>Exertion-related?</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV Registry¹</td>
<td>7-35 yrs</td>
<td>50</td>
<td>1. C/V</td>
<td>1. MVP</td>
<td>16%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. Pulmonary</td>
<td>2. Myocarditis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3. HCM</td>
<td>3. ACAD</td>
<td></td>
</tr>
<tr>
<td>Israeli Defense Forces²</td>
<td>17-30 yrs</td>
<td>44</td>
<td>1. C/V</td>
<td>1. Myocarditis</td>
<td>86%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. Unexplained</td>
<td>2. HCM</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3. Heat Stroke</td>
<td>3. MVP</td>
<td></td>
</tr>
<tr>
<td>Osaka Prefecture³</td>
<td>5-19 yrs</td>
<td>64</td>
<td>1. C/V</td>
<td>4. ACAD</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. Pulmonary</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3. Neurologic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allegany Co, PA⁴</td>
<td>1-21 yrs</td>
<td>207</td>
<td>1. Infectious</td>
<td>1. Myocarditis</td>
<td>8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. CV</td>
<td>2. Cardiomegaly</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3. Epilepsy</td>
<td>3. Arrhythmia Hx</td>
<td></td>
</tr>
</tbody>
</table>

¹Topaz and Edwards, 1985; ²Kramer, 1988; ³Kitada, 1990; ⁴Neuspiel and Kuller, 1985

Defining the Problem…

Summarizing statistics begins to tell the story...

Death rates are highest in...

- Males
- African descent
- College Athletes (versus High School)
- Older Individuals
- Football/Basketball/Soccer participation

Non-cardiac causes account for ~ 1/3rd of deaths.

Disease epidemiology changes in the third decade of life: from predominantly congenital to ‘acquired’.

* Compared with athletes in "other sports"
Primary cardiac causes of sudden death (SCD) are roughly divided into several categories:

- **Abnormal Muscle**
  - HCM, ARVD, Myocarditis
- **Abnormal Coronaries**
  - Congenital Anomalies, Accelerated CAD
- **Abnormal Valves/Vessels**
  - Marfan Syndrome, MVP, Aortic Stenosis
- **Abnormal Electricity**
  - WPW, Ion Channelopathies
- **Bad Timing**
- **Environment**

Hypertrophic cardiomyopathy is usually considered number 1 in the list of causes in the US. Causes of death may include arrhythmia, obstruction or primary coronary ischemia. Hypertrophic cardiomyopathy is usually considered number 1 in the list of causes in the US. Myocarditis is usually an infrequent cause of SCD among young athletes, but the most common cause after congenital heart disease in pediatrics. Myocyte Necrosis and Inflammatory Response.

Congenital coronary anomalies (CCA) are the second most common (after HCM) cause of SCD in the US. Left main coronary artery from right aortic sinus most common. "Myocardial bridging" also important. Coronary-Cameral & AV Fistula may also be at risk.
Understanding the Causes...
Accelerated coronary artery disease typically occurs in the third decade.
- Family history is often positive for multiple affected family members
- A history of prior Kawasaki's Disease may also play a future role
- Signs/Symptoms mimic those in adults

Index of Suspicion must be high!

Understanding the Causes...
Marfan Syndrome is often suspected before sports participation.
- Not all patients have classic stigmata
- Dissection and rupture of aorta key concern
- MVP may also contribute

Understanding the Causes...
Other valvular abnormalities such as mitral valve prolapse or aortic stenosis/insufficiency are usually recognized, when severe, before sports participation.

Mitral Valve Prolapse
Aortic Valve Disease

Understanding the Causes...
One common pathway for SCD in valve disease may be the inciting of malignant ventricular arrhythmias.

SCD in 13 year old with aortic valve disease wearing a Holter monitor. Patient was at rest at time of event.

Understanding the Causes...
The role of arrhythmias in SCD is believed to be underestimated in most series because of the difficulty with making a post-mortem diagnosis.

- Wolf-Parkinson-White Syndrome
  - Presumed antegrade rapid conduction of atrial fibrillation to ventricles
  - Some evidence for "atrial myocarditis"

Understanding the Causes...
Congenital long QT syndrome is the most common (and best understood) of the family of disorders known as "ion channelopathies."

Ion Channelopathies:
- Long QTc
- Short QTc
- Brugada Syndrome
- Catecholaminergic Polymorphic VT
- ? Idiopathic VT

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SCD has also been reported in the previously normal heart under "extreme conditions."

Commotio cordis
$\text{K}^+_{\text{ATP}}$ channel opens when blunt trauma to heart applied during precise timing of ventricular repolarization


Cardiac stimulants, factors predisposing to coronary thrombosis and environmental extremes (or the interplay of all of them) should always be considered.

Len Bias (1964-1986)
Sickled Red Blood Cells

The challenge is identifying "the really bad players" and minimizing them.

Dihydrogen Monoxide

Dihydrogen monoxide is colorless, odorless, tasteless, and kills uncounted thousands of people every year. Most of these deaths are caused by accidental inhalation of DHMO, but the dangers of dihydrogen monoxide do not end there. Prolonged exposure to its solid form causes severe tissue damage. Symptoms of DHMO ingestion can include excessive sweating and urination, and possibly a bloated feeling, nausea, vomiting and body electrolyte imbalance. For those who have become dependent, DHMO withdrawal means death.

The challenge is identifying "the really bad players" and minimizing them.

Rules for an Effective Screening Program

- Conditions to be screened should be:
  - Sufficiently important
  - Have a modifiable natural history
- Any screening test (and confirmatory testing) should be:
  - Inexpensive
  - Readily available
  - Acceptable to those being screened and the screeners
  - Highly sensitive and specific

Example of an Effective Screening Program

Newborn screening for Congenital Hypothyroidism

Incidence ~ 1/3,500
Sensitivity ~ 97.5%
Specificity ~ 100%
Cost per Screen ~ $1

Fisher DA, et al. J Peds 1979:94(5); 700-705

Challenges of Cardiovascular Screening

The Epidemiologic Argument

--- Assume a disease prevalence of 1 in 200,000 sudden deaths
--- Assume the existence of a screening test with 99% sensitivity and specificity

...then for every patient correctly diagnosed with a condition predisposing to sudden death, ...

1,999 will be "incorrectly diagnosed" with the same condition
Challenges of Cardiovascular Screening

The “Barriers”:

- Are we trying to prevent sudden death or identify/treat disease(s)?
- Can the tenets of an effective screening program be fulfilled for any of them?
- Who will bear the costs of screening?
- Are philanthropic efforts sufficient? Should screening be mandated?
- Do families understand what we are doing and why?
- Will they follow through with recommended additional testing?
- Texas data would suggest only 25% of the time1

Challenges of Screening…

- Abnormal Muscle
  - HCM, ARVD, Myocarditis
- Abnormal Coronaries
  - Congenital Anomalies, Accelerated CAD
- Abnormal Valves/Vessels
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- Abnormal Electricity
  - WPW, Ion Channelopathies
- Bad Timing
- Environment

Heterogeneity can exist within families on the basis of age at time of screening and gene expression.

- 2 year old boy with harsh murmur
  - Septal thickness 20mm (normal < 6mm)

Heterogeneity can exist within families on the basis of age at time of screening and gene expression.

- 12 year old asymptomatic brother
  - Septal thickness 18mm (normal < 10mm)

Have any other programs enjoyed success?

"Voluntary" Cardiovascular Screening Programs…

Physician Initiatives
- Performed by physicians (typically) for schools that their children (or close friends) attend
- Volunteer staff & facilities
- Screening Questionnaire/ECG/ECHO-based
- Positive referrals advised of options for care
- Assistance with follow-up evaluations

Community Initiatives
- Directed by an independent non-profit group
- Volunteer physicians & facilities
- Screening Questionnaire/ECG/ECHO-based
- Positive referrals sent back to their practice

What’s Happening Now…


What’s Happening Now…

Results (up to 30 June 2013):

<table>
<thead>
<tr>
<th>TOTAL SCREENINGS</th>
<th>TOTAL REFERRALS</th>
</tr>
</thead>
<tbody>
<tr>
<td>3713</td>
<td>160</td>
</tr>
</tbody>
</table>

Overall Referral Rate: 4.3%

Identified Abnormalities:
- Wolff-Parkinson-White syndrome
- Dilated Cardiomyopathy
- Suspected Long QT Syndrome
- Cardiac Hypertrophy

Latest Initiatives…

Targeted Screening of Selected Conditions…

Conditions to Be Detected:
- Hypertrophic Cardiomyopathy
- Dilated Cardiomyopathy
- Aortic Root Dilation
- Long QT Syndrome
- Wolff-Parkinson-White Syndrome

Reduces Screen Positive Rate to < 1%

Method of Screening:
- 12-Lead ECG
- Limited Echocardiogram

Future Directions…

Advocacy for Secondary Prevention…

Project ADAM®

My wish is that all schools have the opportunity to participate in Project ADAM, a Wisconsin-based program that Children’s Hospital of Wisconsin began in 1988. The program is designed to help every school place defibrillators in their buildings and have staff and students certified in CPR.

- 17 children successfully resuscitated since implementation
- 14 children left the hospital with little to no neurologic sequelae
- Chapters now exist in 30 states and more than 11 countries

Where We’ve Been…

- Defining the Scope of the Problem
- Understanding the Causes
- Challenges of Screening
- What is Happening Now in San Antonio
- Future Directions

What We’ve Learned…

- Sudden cardiac death among previously healthy adolescents is a rare event
- If a sudden cardiac event happens to someone in your community, the rarity of the event is somewhat more subjective
- We can improve our ability to identify cardio disorders, but preventing sudden cardiac death is less certain.
- Screening & advocacy are not panaceas
- Screening & advocacy are OUR JOBS as Health Professionals!

Perseverance

“Perseverance is more prevailing than violence; and many things which cannot be overcome when they are together, yield themselves up when taken little by little.”

Lives, Sertorius, sec. 16

Plutarch  AD 46-123