SYNCOPE: A Guide For the Beginner

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SYNCOPE

• The transient loss of consciousness and postural tone with spontaneous recovery

• Derived from the Greek word ΣΥΝΧΩΠΑ, meaning “to cut short”

Frequency of Syncope

In a community based study of American adults 45 years and older, 19 % admitted to at least one episode of syncope

Impact of Syncope

Cost

• 40% will experience syncope at least once in a lifetime
• 1-4% of hospital admissions
• 3% of ER visits per year
• 10% of falls by elderly are due to syncope
• Syncope evaluation and treatment exceeds $750 million per year in the U.S.
• Estimated U.S. hospital costs are in excess of $10 billion

Quality of Life Impact

Anxiety/Depression 73% 71%
Daily Activities 71%
Restricted Driving 60%
Change Employment 37%

References:

Comparison of annual health care costs for syncope vs. other chronic diseases 2010

<table>
<thead>
<tr>
<th>Disease</th>
<th>Annual Dollars in Billions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syncope</td>
<td>2.4</td>
</tr>
<tr>
<td>HIV</td>
<td>2.0</td>
</tr>
<tr>
<td>COPD</td>
<td>2.2</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.9</td>
</tr>
</tbody>
</table>

US Congressional Budget Office Analysis 2011

Indirect Economic Effects-USA Quality of Life Impact

Percent of Patients

- Anxiety/Depression 73%
- Daily Activities 71%
- Restricted Driving 60%
- Change Employment 37%

References:
Indirect Adverse Economic Effects
Disabilities: - UK Norms vs. Syncope Patients

![Graph showing % Prevalence of disabilities between Normal Controls and Syncope Patients]

37% 36%
49% 43%
19% 19%

Normal Controls
Syncope Patients

“Those who suffer from frequent and severe fainting without obvious cause often die suddenly.”

Hippocrates
Aphorisms 2.41

Syncope and Sudden Death are the same thing, except in one you wake up…
Each year in the U.S. alone there are 400,000 sudden deaths, in 45% the only warning was syncope.
UT athlete dies during workout at campus track

School tries to cope with loss of British basketball player

Oct. 10, 2006
Potentially lethal conditions that may present with syncope:

1. VT/VF post MI
2. Heart block
3. Hypertrophic cardiomyopathy
4. Dilated cardiomyopathy
5. Long QT syndrome
6. RV dysplasia
7. Anomalous coronary arteries

Coronary Artery Anomalies: Congenital or Acquired
Congenital Coronary Artery Anomalies
Left From The Right

Coronary anomalies: magnetic resonance imaging (MRI) versus computed tomography (CT).


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A 66 yr old man seen in an ER for syncope, sent home, syncope again, suffered a hip fracture, is brought to your ER. Diagnosis?
16 yo Female with Syncope

Table 1. Summary of LQTS Genotypes Identified.3

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Genes</th>
</tr>
</thead>
<tbody>
<tr>
<td>LQT1</td>
<td>KCNQ1/4/5/QT1</td>
</tr>
<tr>
<td>LQT2</td>
<td>LQT2/HERC</td>
</tr>
<tr>
<td>LQT3</td>
<td>SCN5A (sodium channel)</td>
</tr>
<tr>
<td>LQT4</td>
<td>HERG (potassium G)</td>
</tr>
<tr>
<td>LQT5</td>
<td>KCNE1/MIR6h</td>
</tr>
<tr>
<td>LQT6</td>
<td>KCNE2/PM5h</td>
</tr>
<tr>
<td>LQT7</td>
<td>KCNE2 (Anderson-Famili syndrome)</td>
</tr>
<tr>
<td>LQT8</td>
<td>CACNAAC</td>
</tr>
<tr>
<td>LQT9</td>
<td>GYF2/SCHIT</td>
</tr>
<tr>
<td>LQT10</td>
<td>SCHIB</td>
</tr>
</tbody>
</table>

*Please note that other genes have been identified in addition to this list.
Polymorphic VT in a patient with suspected Long QT Syndrome

The Long QT Syndrome
Syncope in this case would be most likely:
- With emotional stress
- With exercise
- At rest

Moss AJ. Long QT Syndrome. JAMA. 2003;289:2041-4

Syncope and Drowning

HEART RHYTHM AND THE QT INTERVAL

- Prolonged or abnormal QT interval
- Heart rhythm when the QT interval is long

Moss AJ. Long QT Syndrome. JAMA. 2003;289:2041-4
Potassium Voltage gated channel
Subfamily H: hERG (human ether related gene)

Incidence: 1 in 2534 People !!!

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Case: LQTS (near sudden infant death syndrome)

9 year old referred for evaluation of recurrent syncope and “seizures”. Echo WNL. EKG reported to be “normal”. Tilt negative. Several family members died unexpectedly (father, uncle, 2 cousins) autopsy negative in each.
9 yr old with recurrent syncope, father died suddenly

Recording made during a episode of syncope with convulsions after ILR insertion

**Short QT Syndrome**

<table>
<thead>
<tr>
<th>SQT Type</th>
<th>Subject Code</th>
<th>Reported Mutation(s)</th>
<th>Number of Cases (Gene(s))</th>
</tr>
</thead>
<tbody>
<tr>
<td>NQTL</td>
<td>RCSM</td>
<td>MSSH</td>
<td>10 (2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R151X</td>
<td>3 (1)</td>
</tr>
<tr>
<td>NQTC</td>
<td>RCSM</td>
<td>F204L</td>
<td>1 (1)</td>
</tr>
<tr>
<td>SQTS</td>
<td>LCSM</td>
<td>V277L</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Genotype unknown</td>
<td>—</td>
<td>—</td>
<td>44 (20)</td>
</tr>
</tbody>
</table>

*ILR was implanted in a case of reported short QT syndrome (SQT2), identified in cases in association with complete heart block, this patient was not included in our cohort due to the additional presence of complete heart block (25).
Short QT syndrome
Brugada Syndrome - Survival

Priori S. Circulation 2002;105:1342-1347
Brugada Syndrome
Before Procainamide

Brugada Syndrome
After Procainamide

Types of Brugada Syndrome
Catheter Ablation of Brugada Syndrome

Soccer Star with syncope x 2 dies during game
Right Ventricular Cardiomyopathy

ARVD

Epsilon Wave in ARVD
Arrhythmogenic right ventricular cardiomyopathy (ARVC).

What is the diagnosis?

22 yr old woman has syncopal episode one week after removal of a subclavian line used for chemotherapy.
Non-Compaction Syndrome

LV Noncompaction: Diagnosis by Echo

1. Noncompacted portion of the myocardium is at least 2 times thicker than the normal compacted myocardium.
2. There are prominent and discrete trabeculations—most often localized to the apex, the midventricular septal wall, or the midventricular inferior wall—less commonly along the midventricular septal or inferior wall.
3. There are deep recesses that are filled with flow from the LV cavity that can be identified by Color Doppler or Stedial.
4. Differentiation from hypertrophic hearts or normal hearts—Prominent LV trabeculations can be found in up to 60% of healthy hearts, and in hypertrophic hearts, where trabeculation predominates on anterior base wall or IVS.
Dilated cardiomyopathy/non-compaction cardiomyopathy.

Even if the cause is benign, recurrent syncope places a huge psychologic burden on both patients and their families.

16 yr old with recurrent NCS had syncope at school and fell down 2 flights of concrete stairs.
Any phenomena which can cause an 8-10 second interruption in cerebral blood flow or a reduction in mean arterial BP below 40 mmHg can cause syncope.
Somatic Nerve

A linear System

Autonomic Nerve

A non-linear system
The autonomic centers control most of the functions considered essential to life itself:

1. Heart Rate
2. Blood Pressure Control
3. Body Temperature
4. Bowel Motility
5. Sweating
6. Breathing
7. Genital-urinary function

The Structures of the Central Autonomic Network

1. Insular Cortex
2. Central nucleus of the Amygdala
3. Several Nuclei of the hypothalamus
4. Periaqueductal gray of the midbrain
5. Parabrachial nucleus in the dorsolateral pons
6. Several medullary regions:
   a. the nucleus of the solitary tract
   b. ventrolateral reticular formation of the medulla
   c. medullary raphe
Figure 2.1 Components of the central autonomic network. (From Berne J. Basic Neuroscience with Clinical Application. Philadelphia: Lippincott; 2006. By permission of Mosby Foundation for Medical Education and Research. All rights reserved.)

Figure 2.2 Main hypothalamic output to autonomic nuclei of the brain stem and to sympathetic preganglionic neurons of the intermediolateral cell column. Other outputs originate from the arcuate (inframammillary) nucleus and the dorsomodal nucleus (not shown).

Figure 3.1 Main connections of the reticular nuclei of the medulla.
Periods of autonomic decompensation resulting in hypotension (with or without Bradycardia) may have a wide variety of clinical manifestations, such as:

- Vertigo/dizziness
- Lightheadedness
- Convulsive Activity
- TIAS
- Syncope/near syncope
- Fatigue
- Cognitive Impairment
Normal and Abnormal Tilt Response Patterns
### Venous Pooling in POTS

<table>
<thead>
<tr>
<th></th>
<th>Supine</th>
<th>Upright</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td><img src="image1" alt="Normal Image" /></td>
<td><img src="image2" alt="Pooling Image" /></td>
</tr>
</tbody>
</table>

### Symptoms in POTS Pts. (%)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lightheadedness</td>
<td>85-95</td>
</tr>
<tr>
<td>Dizziness</td>
<td>60-80</td>
</tr>
<tr>
<td>Palpitations</td>
<td>40-55</td>
</tr>
<tr>
<td>Exercise Intolerance</td>
<td>50-85</td>
</tr>
<tr>
<td>Blurred Vision</td>
<td>70</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>60</td>
</tr>
<tr>
<td>Clamminess</td>
<td>60</td>
</tr>
<tr>
<td>Near Syncope</td>
<td>50</td>
</tr>
<tr>
<td>Anxiety</td>
<td>50</td>
</tr>
<tr>
<td>Flushing</td>
<td>50</td>
</tr>
<tr>
<td>Syncope</td>
<td>40-45</td>
</tr>
<tr>
<td>Fatigue</td>
<td>45-75</td>
</tr>
<tr>
<td>Headache</td>
<td>50</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>40</td>
</tr>
</tbody>
</table>
Chronic Secondary Acute Autonomic Neuropathy

Primary Secondary

NCS: Neurocardiogenic Syncope
CSH: Carotid Sinus Hypersensitivity
POTS: Postural Orthostatic Tachycardia Syndrome
JHS: Joint Hypermobility Syndrome

Disorders of the Autonomic Nervous System Associated with Orthostatic Intolerance

Figure 1: Subtypes of POTS

POTS

Primary

Hypothyroidism

Diabetes

Addiction

JHS

POTS = Postural Tachycardia Syndrome
JHS = Joint Hypermobility Syndrome
Evaluation of Syncope in the ED

Causes of Syncope
Framingham Study (n=692)

- Medication: 0.1%
- Inner: 7.5%
- Common: 9.7%
- Vasovagal: 21.2%
- Syncope or transient ischemic attack: 4.1%
- Labyrinth: 56.0%

Fig. 12: An algorithm for management of syncope. This may confuse more than help.
Evaluation

1. Careful History
2. Complete Physical (including neurologic exam)
3. ECG
4. Echocardiogram

<table>
<thead>
<tr>
<th>Table 1.7 History: important data to obtain.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Witnesses</strong></td>
</tr>
<tr>
<td><strong>Situation</strong></td>
</tr>
<tr>
<td><strong>Age elderly (&gt;65 years)</strong></td>
</tr>
<tr>
<td><strong>Age young (&lt;40 years)</strong></td>
</tr>
<tr>
<td><strong>Heart disease</strong></td>
</tr>
<tr>
<td><strong>Family history of sudden death</strong></td>
</tr>
<tr>
<td><strong>Number of episodes</strong></td>
</tr>
<tr>
<td><strong>Previous evaluation</strong></td>
</tr>
<tr>
<td><strong>Medications</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 1.8 Early symptoms related to syncope spell.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptom</strong></td>
</tr>
<tr>
<td>Nose, rhinorrhea, fever</td>
</tr>
<tr>
<td>Anxiety</td>
</tr>
<tr>
<td>Ocular complaints</td>
</tr>
<tr>
<td>Palpitations, diaphoresis</td>
</tr>
<tr>
<td>Vestibular complaints</td>
</tr>
<tr>
<td>Breathless, dizziness</td>
</tr>
<tr>
<td>Migraines</td>
</tr>
<tr>
<td>Visual change, neurologic abnormalities</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Chest pain</td>
</tr>
<tr>
<td>Syncope</td>
</tr>
<tr>
<td>Additional pain</td>
</tr>
<tr>
<td>Early loss</td>
</tr>
<tr>
<td>Flushing</td>
</tr>
<tr>
<td>Hypoglycemic (hyperglycemic)</td>
</tr>
<tr>
<td>Syncope</td>
</tr>
</tbody>
</table>
Usual Workup

Holter monitor
CT scan
EEG
MRI scan
Glucose tolerance test
ETT
Echocardiogram
Treatment

- Identify the Problem!
- Education
- Avoid predisposing factors
- Support hose

Agents that may cause or exacerbate orthostatic hypotension

- Tricyclic Antidepressants
- Ethanol
- Angiotensin Converting Enzyme Inhibitors
- Alpha Blockers
- Calcium Channel Blockers
- Phenothiazines
- Opiates
- Bromocriptine
- Beta-Blockers
- Sildenafil citrate

Table 1.1: The electrocardiogram to evaluate syncope

<table>
<thead>
<tr>
<th>Sign</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal or non-specific</td>
<td>Common, does not rule out serious cause</td>
</tr>
<tr>
<td>Complete heart block</td>
<td>Possible indication</td>
</tr>
<tr>
<td>Second-degree heart block</td>
<td>Complete with symptoms, pacemaker may be indicated</td>
</tr>
<tr>
<td>First-degree heart block</td>
<td>No obvious significance in most cases</td>
</tr>
<tr>
<td>Delta waves</td>
<td>Wolff-Parkinson-White pattern, possible supraventricular tachycardia</td>
</tr>
<tr>
<td>T wave abnormality</td>
<td>Non-specific, may indicate sick sinus syndrome</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Acute myopathy, hemodynamic problem</td>
</tr>
<tr>
<td>QRS</td>
<td>QRS &lt; 0.10 second, atrial or ventricular</td>
</tr>
<tr>
<td>Epsilon waves</td>
<td>Right ventricular tachycardia</td>
</tr>
<tr>
<td>Bundle branch block</td>
<td>Possible bundle branch block</td>
</tr>
<tr>
<td>QP &gt; 300 (p 8-300)</td>
<td>Possible bundle branch block</td>
</tr>
<tr>
<td>ECG traces</td>
<td>No known significance</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>May indicate underlying structural heart disease, arrhythmic cause</td>
</tr>
<tr>
<td>Supraventricular tachycardia</td>
<td>RR: Likely cause of syncope</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>RR: Likely cause of syncope</td>
</tr>
<tr>
<td>Paced rhythm</td>
<td>Paced heart malfunction</td>
</tr>
</tbody>
</table>
Is the heart normal?
Is there any history of sudden death in the family?

A 16 year old woman with recurrent syncope and a family history of sudden death in a cousin and aunt.

Male 39 years

A 17 year old man with a family history of sudden death (father age 21 and uncle age 32) who had 2 episodes of syncope while playing baseball, preceded by severe palpitations.
Physical exam WNL
ECG - WNL echo - normal. Now what?
12 Lead ECG of induced VT

12 lead ECG after VT termination
MRI of Heart demonstrates thinning of the RV, consistent with Right Ventricular Dysplasia.
48 yr old woman with a 9 yr history of recurrent syncope and seizures. Episodes are intermittent, no prodrome, associated with convulsive activity. LOC of 5 - 10 min. Mild post-ictal state, some episodes accompanied by urinary incontinence. Has suffered multiple traumas to face and arms. Extensive cardiac and neurologic workups negative. Episodes labeled “psychogenic”. After seen in clinic had ILR implant. One day later she had a typical episode…
16 yr old girl with recurrent syncope, complete evaluation WNL. Diagnosed with a conversion disorder "Psychogenic asystole"
CLS Measures Impedance as an Ohm-meter

\[ Z_{\text{total}} = Z_1 + Z_2 + Z_3 \]
\[ Z_1 + Z_2 \gg Z_3 \]
\[ Z_{\text{total}} = Z_1 + Z_2 \]

During systole, Z1 (lead) is constant,
\[ \Delta Z_{\text{total}} = \Delta Z_2 \]

![Diagram of heart and impedances](image)

Figure 1 Kaplan-Meier estimates of probability of remaining free of surgical reoperations in 25 patients in clipless atrioventricular stimulation group (blue line) and 16 patients in control group (red line).

Table 1.11 Criteria for hospitalization.

- Malignant arrhythmia or cardiovascular cause suspected
- New neurologic abnormality present
- Severe injury present
- Multiple frequent episodes
- Severe orthostatic hypotension
- Uncontrolled "malignant" vasovagal syncope
- Elderly patient
- Treatment plans not possible as an outpatient
“Doctors pour drugs of which they know “little” into patients about whom they know “less” with diseases of which they know nothing.”

-Voltaire

Pharmacotherapy
1. Fludrocortisone / DDAVP
2. Methylphenidate
3. Midodrine
4. Beta blockers
5. SSRIs
6. Clonidine
7. Erythropoietin
8. Yohimbine
9. Pyridostigmine
10. Norepinephrine reuptake inhibitors
11. Octreotide

Therapeutic Considerations
1. What medication is most likely to work in this subtype?
2. What is least likely to interact with other medications or conditions?
3. What can the patient afford?
4. What medication will best fit their lifestyle and occupation?
5. Is pregnancy an issue?
“He who saves a single life, it is as if he had saved an entire world…”

Pitke Avot
The Talmud
200 C.E.

“If you save one human life, it is as if you had saved the whole of humanity.”

Sura Maida
Chapter 5 Verse 32
The Koran

“One of the essential qualities of the clinician is an interest in humanity, for the secret of the care of the patient is in caring for the patient”

Francis Weld Peabody MD
“Ancora Imparo...”  
(I am still learning...)  
Michelangelo, age 87