Pathophysiology of Syncope

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Section I: Prevalence and Impact

The Significance of Syncope

The only difference between syncope and sudden death is that in one you wake up.¹

The Significance of Syncope

- More than 1 million patients in the U.S.¹
- More than 500,000 new patients per year ²
- 1-6% of admissions ²,³
- 3% of emergency room visits per year ³

Syncope Reported Frequency

- Individuals <18 yrs 15%
- Military Population 17-46 yrs 20-25%
- Individuals 40-59 yrs* 16-19%
- Individuals >70 yrs* 23%

* during a 10-year period

500,000 new syncope patients each year ⁵
170,000 have recurrent syncope ⁶
70,000 have recurrent, infrequent, unexplained syncope ¹-⁴

Syncope:
A Symptom...Not a Diagnosis

- Self-limited loss of consciousness and postural tone
- Relatively rapid onset
- Variable warning symptoms
- Spontaneous complete recovery

Definition

Sudden and brief loss of consciousness associated with a loss of postural tone, from which recovery is spontaneous

Section II:
Etiology

Definition

Sudden and brief loss of consciousness associated with a loss of postural tone, from which recovery is spontaneous
Syncope: Etiology

<table>
<thead>
<tr>
<th>Neurally-Mediated</th>
<th>Orthostatic</th>
<th>Cardiac Arrhythmia</th>
<th>Structural Cardio-Pulmonary</th>
<th>Non-Cardiovascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasovagal</td>
<td>Drug induced</td>
<td>Bradycardia</td>
<td>Aortic Stenosis HOCM</td>
<td>Psychogenic</td>
</tr>
<tr>
<td>Carotid Sinus</td>
<td>ANS Failure</td>
<td>Tachy</td>
<td>Pulmonary Hypertension</td>
<td>Metabolic</td>
</tr>
<tr>
<td>Situational</td>
<td>Brady</td>
<td>VT</td>
<td></td>
<td>e.g. hyper-ventilation</td>
</tr>
<tr>
<td>Cough</td>
<td>VT</td>
<td></td>
<td></td>
<td>Neurological</td>
</tr>
<tr>
<td>Post-micturition</td>
<td>SVT</td>
<td></td>
<td></td>
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</tbody>
</table>

|         | 24% | 11% | 14% | 4%  | 12% |

Unknown Cause = 34%

Section III: Diagnosis and Evaluation Options

Syncope: Diagnostic Objectives

- Distinguish ‘True’ Syncope from other ‘Loss of Consciousness’ spells:
  - Seizures
  - Psychiatric disturbances
- Establish the cause of syncope with sufficient certainty to:
  - Assess prognosis confidently
  - Initiate effective preventive treatment

Initial Evaluation (Clinic/Emergency Dept.)

- Detailed history
- Physical examination
- 12-lead ECG
- Echocardiogram (as available)

Syncope Evaluation and Differential Diagnosis

History – What to Look for

- Complete Description
  - From patient and observers
- Type of Onset
- Duration of Attacks
- Posture
- Associated Symptoms
- Sequelae

Distinguishing Syncope

- Dizziness, presyncope, and vertigo
  - No LOC or loss of postural tone
- “Drop attacks”
  - Lead to falls without loss of consciousness
  - Sometimes sign of vertebrobasilar TIA (15%)
- Precipitants/Prodromal Symptoms
  - LOC precipitated by pain, exercise, micturition, defecation, or stressful event usually syncope
  - Sweating, nausea = syncope
  - Aura = Seizure
  - Disorientation/ LOC > 5 minutes usually seizure rather than syncope
### Conventional Diagnostic Methods/Yield

<table>
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<tr>
<th>Test/Procedure</th>
<th>Yield</th>
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<tr>
<td>History and Physical (including carotid sinus massage)</td>
<td>49-85%</td>
</tr>
<tr>
<td>ECG</td>
<td>2-11%</td>
</tr>
<tr>
<td>Electrophysiology Study without SHD*</td>
<td>11%</td>
</tr>
<tr>
<td>Electrophysiology Study with SHD</td>
<td>49%</td>
</tr>
<tr>
<td>Tilt Table Test (without SHD)</td>
<td>11-87%</td>
</tr>
<tr>
<td>Ambulatory ECG Monitors:</td>
<td></td>
</tr>
<tr>
<td>§ Holter</td>
<td>2%</td>
</tr>
<tr>
<td>§ External Loop Recorder (2-3 weeks duration)</td>
<td>20%</td>
</tr>
<tr>
<td>§ Insertable Loop Recorder (up to 14 months duration)</td>
<td>65-88%</td>
</tr>
<tr>
<td>Neurological †</td>
<td>0-4%</td>
</tr>
</tbody>
</table>

*  Structural Heart Disease  
†  MRI not studied


### 12-Lead ECG
- **Normal or Abnormal?**
  - Acute MI
  - Severe Sinus Bradycardia/pause
  - AV Block
  - Tachyarrhythmia (SVT, VT)
  - Preexcitation (WPW), Long QT, Brugada
- **Short sampling window (approx. 12 sec)**

### Carotid Sinus Massage
- **Site:**
  - Carotid arterial pulse just below thyroid cartilage
- **Method:**
  - Right followed by left, pause between
  - Massage, NOT occlusion
  - Duration: 5-10 sec
  - Posture – supine & erect

**Carotid Sinus Syndrome (CSS)**

**Contraindications**
- Carotid bruit, known significant carotid arterial disease, previous CVA, MI last 3 months

**Risks**
- 1 in 5000 massages complicated by TIA

### Ambulatory ECG

<table>
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<tr>
<th>Method</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
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<td>Holter (24-48 hours)</td>
<td>Useful for infrequent events</td>
</tr>
</tbody>
</table>
| Event Recorder | • Useful for infrequent events  
• Limited value in sudden LOC |
| Loop Recorder | • Useful for infrequent events  
• Implantable type more convenient (ILR) |
| Wireless (internet) Event Monitoring | In development |
Head-up Tilt Test (HUT)
- Unmasks Vasovagal syncope susceptibility
- Reproduces symptoms
- Patient learns VVS warning symptoms
- Physician is better able to give prognostic / treatment advice

Electroencephalogram
- Not a first line of testing
- Syncope from Seizures
- Abnormal in the interval between two attacks – Epilepsy
- Normal – Syncope

Unexplained Syncope Diagnosis
- History and Physical Exam
- Surface ECG
- Neurological Testing
  - Head CT Scan
  - Carotid Doppler
  - MRI
  - Skull Films
  - Brain Scan
  - EEG
- CV Syncope Workup
  - Holter
  - ELR or ILR
  - Tilt Table
  - Echo
  - EPS
- Other CV Testing
  - Angiogram
- Exercise Test
- Psychological Evaluation
- Endocrine Evaluation

Typical Cardiovascular Diagnostic Pathway

Mass Fainting at Rock Concerts
NEJM 1994;332;1721
- All were girls between 11-17 YO
- 44% reported having lost consciousness
- Many still breathing rapidly backstage during interview
- Reported combination provoking factors
  - Sleeplessness during previous night
  - Fasting since early AM while waking in line
  - Long periods of standing
  - Hyperventilation (vasoconstriction)
  - Valsalva-like pressure
- Interpretation - ROCK-CONCERT SYNCPE
  - Multifactorial pathophysiology
  - Preventive guidelines - sleep, sit, eat, keep cool, stay out of the crowd

Section IV:
Specific Conditions
Neurally-Mediated Reflex Syncope (NMS)

- Vasovagal syncope (VVS)
- Carotid sinus syndrome (CSS)
- Situational syncope
  - post-micturition
  - cough
  - swallow
  - defecation
  - blood drawing
  - etc.

NM Reflex Syncope: Pathophysiology

- Multiple triggers
- Variable contribution of vasodilatation and bradycardia

NMS – Basic Pathophysiology

![Pathophysiology Diagram]

Etiology of CSS

- Sensory nerve endings in the carotid sinus walls respond to deformation
- "Deafferentation" of neck muscles may contribute
- Increased afferent signals to brain stem
- Reflex increase in efferent vagal activity and diminution of sympathetic tone results in bradycardia and vasodilation

Carotid Sinus Hypersensitivity (CSH)

- Abnormal response to CSM
- Absence of symptoms attributable to CSS
- CSH reported frequent in ‘fallers’ (Kenny)

CSH ≠ CSS

Management Strategies for VVS

- Optimal management strategies for VVS are a source of debate
  - Patient education, reassurance, instruction
  - Fluids, salt, diet
  - Tilt Training
  - Support hose
- Drug therapies
- Pacing
  - Class II indication for VVS patients with positive HUT and cardioinhibitory or mixed reflex
Principal Causes of Orthostatic Syncope

- Drug-induced (very common)
  - diuretics
  - vasodilators
- Primary autonomic failure
  - multiple system atrophy
  - Parkinsonism
- Secondary autonomic failure
  - diabetes
  - alcohol
  - amyloid
- Alcohol
  - orthostatic intolerance apart from neuropathy

Syncope Due to Arrhythmia or Structural CV Disease: General Rules

- Often life-threatening and/or exposes patient to high risk of injury
- May be warning of critical CV disease
  - Aortic stenosis, Myocardial ischemia, Pulmonary hypertension
- Assess culprit arrhythmia / structural abnormality aggressively
- Initiate treatment promptly

Principal Causes of Syncope due to Structural Cardiovascular Disease

- Acute MI / Ischemia
  - Acquired coronary artery disease
  - Congenital coronary artery anomalies
- HOCM
- Acute aortic dissection
- Pericardial disease / tamponade
- Pulmonary embolus / pulmonary hypertension
- Valvular abnormalities
  - Aortic stenosis, Atrial myxoma

Syncope Due to Cardiac Arrhythmias

- Bradyarrhythmias
  - Sinus arrest, exit block
  - High grade or acute complete AV block
- Tachyarrhythmias
  - Atrial fibrillation / flutter with rapid ventricular rate (e.g. WPW syndrome)
  - Paroxysmal SVT or VT
  - Torsades de pointes

Rhythms During Recurrent Syncope

- Normal Sinus Rhythm: 58%
- Bradycardia: 36%
- Tachyarrhythmia: 6%

AECG: 74 yr Male, Syncope Sinus pause

From the files of DG Benditt, UM Cardiac Arrhythmia Center
Syncope: Torsades

Drug-Induced QT Prolongation

- Antiarrhythmics
  - Class IA: Quinidine, Procainamide, Disopyramide
  - Class III: Sotalol, Ibutilide, Dofetilide, Amiodarone, (NAPA)
- Antianginal Agents
  - (Bepridil)
- Psychoactive Agents
  - Phenothiazines, Antihistamines, Imipramine, Ziprasidone
- Antibiotics
  - Erythromycin, Pentamidine, Fluconazole
- Nonsedating antihistamines
  - (Terfenadine), Astemizole
- Others
  - (Cisapride), Droperidol

Treatment of Syncope Due to Bradyarrhythmia

- Class I indication for pacing using dual-chamber system wherever adequate atrial rhythm is available
- Ventricular pacing in atrial fibrillation with slow ventricular response

Treatment of Syncope Due to Tachyarrhythmia

- Atrial Tachyarrhythmias:
  - AVRT due to accessory pathway – ablate pathway
  - AVNRT – ablate AV nodal slow pathway
  - Atrial fibrillation – pacing, linear / focal ablation, ICD selected pts
  - Atrial flutter – ablation of reentrant circuit
- Ventricular Tachyarrhythmias:
  - Ventricular tachycardia – ICD or ablation where appropriate
  - Torsades de Pointes – withdraw offending Rx or ICD (long-QT Brugada)
- Drug therapy may be an alternative in many cases

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Conclusion

Syncope is a common symptom, often with dramatic consequences, which deserves thorough investigation and appropriate treatment of its cause.