Syncope

David T. Hart MBBS, FACC
Division of Cardiovascular Medicine
The Ohio State University

Syncope: A Symptom…Not a Diagnosis

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

The Significance of Syncope

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

The Significance of Syncope

- Infrequent, unexplained 38% to 47%
- Explained 53% to 62%
- 500,000 new syncope patients each year
- 170,000 have recurrent syncope
- 70,000 have recurrent, infrequent, unexplained syncope

Causes of Syncope

<table>
<thead>
<tr>
<th>Cause</th>
<th>Prevalence (Mean) %</th>
<th>Prevalence (Range) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reflex-mediated:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasovagal</td>
<td>18</td>
<td>8-37</td>
</tr>
<tr>
<td>Situational</td>
<td>5</td>
<td>1-8</td>
</tr>
<tr>
<td>Carotid Sinus</td>
<td>1</td>
<td>0-4</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>8</td>
<td>4-10</td>
</tr>
<tr>
<td>Medications</td>
<td>3</td>
<td>1-7</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>2</td>
<td>1-7</td>
</tr>
<tr>
<td>Neurological</td>
<td>10</td>
<td>3-32</td>
</tr>
<tr>
<td>Organic Heart Disease</td>
<td>4</td>
<td>1-6</td>
</tr>
<tr>
<td>Cardiac Arrhythmias</td>
<td>14</td>
<td>4-38</td>
</tr>
<tr>
<td>Unknown</td>
<td>34</td>
<td>13-41</td>
</tr>
</tbody>
</table>

Syncope Reported Frequency

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

The Significance of Syncope

- Some causes of syncope are potentially fatal
- Cardiac causes of syncope have the highest mortality rates
## Causes of Syncope-like States

- Migraine*
- Acute hypoxemia*
- Hyperventilation*
- Somatization disorder (psychogenic syncope)
- Acute intoxication (e.g., alcohol)
- Seizures
- Hypoglycemia
- Sleep disorders

* may cause 'true' syncope

## 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

## 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>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Vasovagal</td>
<td>Drug-induced</td>
<td>Brady</td>
<td>Aortic Stenosis</td>
<td>Psychogenic</td>
</tr>
<tr>
<td>Carotid Sinus</td>
<td>AV failure</td>
<td>Sinus block</td>
<td>HOCM</td>
<td>Metabolic</td>
</tr>
<tr>
<td>Situational</td>
<td>Primary</td>
<td>Tachy</td>
<td>Pulmonary Hypertension</td>
<td>e.g. hyper-ventilation</td>
</tr>
<tr>
<td>Cough</td>
<td>Secondary</td>
<td>SVT</td>
<td></td>
<td>Neurological</td>
</tr>
</tbody>
</table>

Unknown Cause = 34%

## 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

Syncope Basic Diagnostic Steps

- Detailed History & Physical
  - Document details of events
  - Assess frequency, severity
  - Obtain careful family history
- Heart disease present?
  - Physical exam
  - ECG: long QT, WPW, conduction system disease
  - Echo: LV function, valve status, HOCM
- Follow a diagnostic plan...

Unexplained Syncope Diagnosis

History and Physical Exam
- Surface ECG
- CV Syncope Workup
  - Holter
  - ELR or ILR
  - Tilt Table
  - Echo
  - EPS
- Psychological Evaluation

Endocrine Evaluation
- Other CV Testing
  - Angiogram
  - Exercise Test
  - SAECG

Conventional Diagnostic Methods/Yield

<table>
<thead>
<tr>
<th>Test/Procedure</th>
<th>Yield (based on mean time to diagnosis of 5.1 months)</th>
</tr>
</thead>
<tbody>
<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>40%*</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>65-85%*</td>
</tr>
<tr>
<td>Neurological † (Head CT Scan, Carotid Doppler)</td>
<td>0-4%</td>
</tr>
</tbody>
</table>

* Structural Heart Disease
† MRI not studied
4 Kapoor, Medicine, 1990
5 Kapoor, JAMA, 1992
6 Krahn, Circulation, 1995
7 Krahn, Cardiology Clinics, 1997.
8 Eagle K et al. The Yale J Biol and Medicine 1983; 56: 1-8
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)

Value of Event Recorder in Syncope

* Asterisk denotes event marker

Ambulatory ECG

<table>
<thead>
<tr>
<th>Method</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holter (24-48 hours)</td>
<td>Useful for infrequent events</td>
</tr>
<tr>
<td>Event Recorder</td>
<td>• Useful for infrequent events</td>
</tr>
<tr>
<td></td>
<td>• Limited value in sudden LOC</td>
</tr>
<tr>
<td>Loop Recorder</td>
<td>• Useful for infrequent events</td>
</tr>
<tr>
<td></td>
<td>• Implantable type more convenient (ILR)</td>
</tr>
<tr>
<td>Wireless (internet)</td>
<td>In development</td>
</tr>
<tr>
<td>Event Monitoring</td>
<td></td>
</tr>
</tbody>
</table>

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 Massage**

- **Outcome:**
  - ✓ 3 sec asystole and/or 50 mmHg fall in systolic blood pressure with reproduction of symptoms = 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

**Head-Up Tilt Test (HUT)**

- Unmasks VVS 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
Conventional EP Testing in Syncope

- Limited utility in syncope evaluation
- Most useful in patients with structural heart disease
  - Heart disease...........50-80%
  - No Heart disease...18-50%
- Relatively ineffective for assessing bradyarrhythmias


Diagnostic Limitations

- Difficult to correlate spontaneous events and laboratory findings
- Often must settle for an attributable cause
- Unknowns remain 20-30% ¹


EP Testing in Syncope: Useful Diagnostic Observations

- Inducible monomorphic VT
- SNRT > 3000 ms or CSRT > 600 ms
- Inducible SVT with hypotension
- HV interval ≥ 100 ms (especially in absence of inducible VT)
- Pacing induced infra-nodal block

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

Vasovagal Syncope (VVS): Clinical Pathophysiology

- Neurally Mediated Physiologic Reflex Mechanism with two Components:
  - Cardioinhibitory (HR)
  - Vasodepressor (BP)
- Both components are usually present
Prevalence of VVS

- Prevalence is poorly known
  - Various studies report 8% to 37% (mean 18%) of cases of syncope (Linzer 1997)
- In general:
  - VVS patients younger than CSS patients
  - Ages range from adolescence to elderly (median 43 years)
  - Pallor, nausea, sweating, palpitations are common
  - Amnesia for warning symptoms in older patients

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

Carotid Sinus Syndrome (CSS)

- Syncope clearly associated with carotid sinus stimulation is rare (≤1% of syncope)
- CSS may be an important cause of unexplained syncope / falls in older individuals

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
CSS and Falls in the Elderly

- 30% of people >65 yrs of age fall each year
  - Total is 9,000,000 people in USA
  - Approximately 10% of falls in elderly persons are due to syncope
- 50% of fallers have documented recurrence
- Prevalence of CSS among frequent and unexplained fallers unknown but...
  - CSH present in 23% of >50 yrs fallers presenting at ER

Richardson DA, Bexton RS, et al. Prevalence of cardioinhibitory carotid sinus hypersensitivity in patients 50 years or over presenting to the Accident and Emergency Department with "unexplained" or "recurrent" falls. PACE 1997

VVS: Pharmacologic Rx

- Salt /Volume
  - Salt tablets, ‘sport’ drinks, fludrocortisone
- Beta-adrenergic blockers
  - 1 positive controlled trial (atenolol),
  - 1 on-going RCT (POST)
- Disopyramide
- SSRIs
  - 1 controlled trial
- Vasoconstrictors (e.g., midodrine)
  - 1 negative controlled trial (etilephrine)

Treatment Options

Vasoconstrictors (e.g., midodrine)

Midodrine for Neurocardiogenic Syncope

VVS: Tilt-Training

- Objectives
  - Enhance Orthostatic Tolerance
  - Diminish Excessive Autonomic Reflex Activity
  - Reduce Syncope Susceptibility / Recurrences
- Technique
  - Prescribed Periods of Upright Posture
  - Progressive Increased Duration

VVS Pacing Trials Conclusions

- DDD pacing reduces the risk of syncope in patients with recurrent, refractory, highly-symptomatic, cardioinhibitory vasovagal syncope.

Status of Pacing in VVS

- Perception of pacing for VVS changing:
  - VVS with +HUT and cardioinhibitory response a Class IIb indication
- Recent clinical studies demonstrated benefits of pacing in select VVS patients:
  - VPS I
  - VASIS
  - SYDIT
  - VPS II –Phase I
  - ROME VVS Trial

Head-Up Tilt Test (HUT)

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

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 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

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
AECG: 74 yr Male, Syncope

Syncope: Torsades

Infra-His Block

28 yo man in the ER multiple times after falls resulting in trauma
VT: ablated and medicated

83 yo woman
Bradycardia: Pacemaker implanted
**Drug-Induced QT Prolongation**

- **Antiarrhythmics**
  - Class IA: Quinidine, Procainamide, Disopyramide
  - Class III: Sotalol, Ibutilide, Dofetilide, Amiodarone, (NAPA)
- **Antianginal Agents**
  - (Bepridil)
- **Psychoactive Agents**
  - Phenothiazines, Amitriptyline, 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 fibr – 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

**Typical Cardiovascular Diagnostic Pathway**

1. **Syncope**
   - History and Physical, ECG
   - Known SHD
   - Echo
     - EPS
     - Tilt ILR
   - No SHD
   - > 30 days; > 2 Events
     - Tilt ILR
   - < 30 days
     - Tilt Holter ELR ILR
   - Treat

• “I want to die like my father, peacefully in his sleep; not screaming like the passengers in his car”

George Burns

The End