Syncope
Mechanisms and Management
Case Study

- 20 y/o female competitive cyclist
- Dizzy when stands up quickly
- Syncope during training ride
Syncope (Greek – to interrupt)

- **Syncope** is the sudden transient loss of consciousness and postural tone with spontaneous recovery.
- **Loss of consciousness** occurs within 10 seconds of hypoperfusion of the reticular activating system in the mid brain.
Maintenance of Postural Normaltension

- **Upright posture** results in translocation of 30% of central blood volume to dependent body parts within seconds and transcapillary fluid shifts over 30 minutes further reduce blood volume by 5%.

- **Compensatory responses**
  - Muscle pump
  - Nuerovascular compensation
  - Humoral compensation
  - Local vascular
Action of the Musculovenous Pump in Lowering Venous Pressure in the Leg

Maintenance of Postural Normaltension

**Neurovascular Compensation**

- High pressure mechanoreceptors
- Low pressure mechanoreceptors
Syncope is important because….

- It is common
- Costly
- May be disabling
- May be only warning sign before sudden death
Relative Frequency of Syncope

• 15% of children before the age of 18
• 16% during 10 year period in men aged 40–59
• 19% during 10 year period in women aged 40–49
• 23% during 10 year period in elderly > 70 years old
• Recurrence in 35% in 3 years
Syncope Mortality

- Low mortality vs. high mortality
- Neurally-mediated syncope vs. syncope with a cardiac cause

Syncope: Key questions to address with initial evaluation

• Is the loss of consciousness attributable to syncope or not?

• Is heart disease present or absent?

• Are there important clinical features in the history that suggest the diagnosis?
Syncope Mimics

• Disorders without impairment of consciousness
  Falls
  Drop attacks
  Cataplexy
  Psychogenic pseudo-syncope
  Transient ischemic attacks

• Disorders with loss of consciousness
  Metabolic disorders
  Epilepsy
  Intoxications
  Vertebrobasilar transient ischemic attacks
## Differential Diagnosis of Syncope: Seizures vs Hypotension

<table>
<thead>
<tr>
<th>Observation</th>
<th>Seizure</th>
<th>Inadequate Perfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Sudden</td>
<td>More gradual</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Minutes</td>
<td>Seconds</td>
</tr>
<tr>
<td><strong>Jerks</strong></td>
<td>Frequent</td>
<td>Rare</td>
</tr>
<tr>
<td><strong>Headache</strong></td>
<td>Frequent (after)</td>
<td>Occasional (before)</td>
</tr>
<tr>
<td><strong>Confusion after</strong></td>
<td>Frequent</td>
<td>Rare</td>
</tr>
<tr>
<td><strong>Incontinence</strong></td>
<td>Frequent</td>
<td>Rare</td>
</tr>
<tr>
<td><strong>Eye deviation</strong></td>
<td>Horizontal</td>
<td>Vertical (or none)</td>
</tr>
<tr>
<td><strong>Tongue biting</strong></td>
<td>Frequent</td>
<td>Rare</td>
</tr>
<tr>
<td><strong>Prodrome</strong></td>
<td>Aura</td>
<td>Dizziness</td>
</tr>
<tr>
<td><strong>EEG</strong></td>
<td>Often abnormal</td>
<td>Usually normal</td>
</tr>
</tbody>
</table>
Causes of True Syncope

1. Neurally-Mediated
   - VVS
   - CSS
   - Situational
     - Cough
     - Post-Micturition

2. Orthostatic
   - Drug-Induced
   - ANS Failure
     - Primary
     - Secondary

3. Cardiac Arrhythmia
   - Brady
     - SN Dysfunction
     - AV Block
   - Tachy
     - VT
     - SVT
   - Long QT Syndrome

4. Structural Cardio-Pulmonary
   - Acute Myocardial Ischemia
   - Aortic Stenosis
   - HCM
   - Pulmonary Hypertension
   - Aortic Dissection

Unexplained Causes = Approximately 1/3

DG Benditt, MD. U of M Cardiac Arrhythmia Center
Causes of Syncope

<table>
<thead>
<tr>
<th>Framingham Cohort(^1) (N=727)</th>
<th>Composite Data (Linzer(^2)) (N=1,002)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cause</strong></td>
<td><strong>Prevalence Mean %</strong></td>
</tr>
<tr>
<td>Vasovagal</td>
<td>21</td>
</tr>
<tr>
<td>Orthostatic</td>
<td>9.3</td>
</tr>
<tr>
<td>Cardiac</td>
<td>10</td>
</tr>
<tr>
<td>Seizure</td>
<td>5.2</td>
</tr>
<tr>
<td>Medication</td>
<td>6.8</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>4.2</td>
</tr>
<tr>
<td>Other</td>
<td>7.8</td>
</tr>
<tr>
<td>Unknown</td>
<td>35.9</td>
</tr>
</tbody>
</table>


Causes of Syncope by Age

Younger Patient

• Vasovagal
• Situational
• Psychiatric
• Long QT*
• Brugada syndrome*
• WPW syndrome*
• RV dysplasia*
• Hypertrophic cardiomyopathy*
• Catecholaminergic VT
• Other genetic syndromes

Older Patient

• Cardiac**
  – Mechanical
  – Arrhythmic
• Orthostatic hypotension
• Drug-induced
• Neurally mediated
• Multifactorial

Underlined: benign
* Rare, not benign
** Not benign
Syncope: Key questions to address with initial evaluation

• Is the loss of consciousness attributable to syncope or not?

• Is heart disease present or absent?

• Are there important clinical features in the history that suggest the diagnosis?
Syncope: Important Historical Features

Questions about circumstances just prior to attack

• Position (supine, sitting, standing)
• Activity (rest, change in posture, during or immediately after exercise, during or immediately after urination, defecation or swallowing)
• Predisposing factors (crowded or warm place, prolonged standing post-prandial period) and of precipitating events (fear, intense pain, neck movements)

Questions about onset of the attack

• Nausea, vomiting, feeling cold, sweating, pain in chest, pain in neck, or shoulders,
Syncope: Important Historical Features

Questions about onset of the attack

- Nausea, vomiting, feeling cold, sweating, pain in chest, pain in neck, or shoulders,
Syncope: Important Historical Features

*Questions about attack (eye witness)*
- Skin color (pallor, cyanotic)
- Duration of loss of consciousness
- Movements (tonic-clonic, etc.)
- Tongue biting

*Questions about the end of the attack*
- Nausea, vomiting, diaphoresis, feeling cold, muscle aches, confusion, skin color, wounds
Syncope: Important Historical Feature

Questions about background

• Number and duration of syncope spells
• Family history of arrhythmic disease or sudden death
• Presence of cardiac disease
• Neurological disease (Parkinsons, epilepsy, narcolepsy)
• Internal history (Diabetes)
• Medications (Hypotensive, negative chronotropic and antidepressant agents)
Clinical Features Suggesting Specific Cause of Syncope

Neurally-Mediated Syncope

• Absence of cardiac disease
• Long history of syncope
• After sudden unexpected, unpleasant sensation
• Prolonged standing in crowded, hot places
• Nausea vomiting associated with syncope
• During or after a meal
• With head rotation or pressure on carotid sinus
• After exertion
Clinical Features Suggesting Specific Cause of Syncope

Syncope due to orthostatic hypotension

• After standing up
• Temporal relationship to taking a medication that can cause hypotension
• Prolonged standing
• Presence of autonomic neuropathy
• After exertion
Clinical Features Suggestion
Cause of Syncope

Cardiac Syncope

- Presence of structural heart disease
- With exertion or supine
- Preceded by palpitations
- Family history of sudden death
Initial Exam: Thorough Physical

• Vital signs
  – Heart rate
  – Orthostatic blood pressure change

• Cardiovascular exam: Is heart disease present?
  – ECG: Long QT, pre-excitation, conduction system disease
  – Echo: LV function, valve status, HCM

• Neurological exam

• Carotid sinus massage
  – Perform under clinically appropriate conditions preferably during head-up tilt test
  – Monitor both ECG and BP
Carotid Sinus Massage (CSM)

• **Method**
  – Massage, 5-10 seconds
  – Don’t occlude
  – Supine and upright posture (on tilt table)

• **Outcome**
  – 3 second asystole and/or 50 mmHg fall in systolic BP with reproduction of symptoms = Carotid Sinus Syndrome

• **Absolute contraindications**
  – Carotid bruit, known significant carotid arterial disease, previous CVA, MI last 3 months

• **Complications**
  – Primarily neurological
  – Less than 0.2% transient
Syncope: Diagnostic Testing in Hospital Strongly Recommended

- Suspected/known ‘significant’ heart disease
- ECG abnormalities suggesting potential life-threatening arrhythmic cause
- Syncope during exercise
- Severe injury or accident
- Family history of premature sudden death
## Diagnostic Methods and Yields

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Yield*</th>
</tr>
</thead>
<tbody>
<tr>
<td>History and Physical Exam</td>
<td>25-35%</td>
</tr>
<tr>
<td>ECG</td>
<td>2-11%</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td></td>
</tr>
<tr>
<td>Holter Monitoring</td>
<td>2%</td>
</tr>
<tr>
<td>External Loop Recorder</td>
<td>20%</td>
</tr>
<tr>
<td>Insertable Loop Recorder</td>
<td>43-88%</td>
</tr>
<tr>
<td><strong>Test/Procedure</strong></td>
<td></td>
</tr>
<tr>
<td>Tilt Table</td>
<td>11-87%</td>
</tr>
<tr>
<td>EP Study without SHD**</td>
<td>11%</td>
</tr>
<tr>
<td>EP Study with SHD</td>
<td>49%</td>
</tr>
</tbody>
</table>

**Structural Heart Disease**
Heart Monitoring Options

- **Event Recorders** (non-lead and loop): 7-30 Days
- **Holter Monitor**: 2 Days
- **12-Lead**: 10 Seconds
- **ILR**: Up to 14 Months

**TIME (Months)**
Insertable Loop Recorder (ILR)

The ILR is an implantable patient – and automatically – activated monitoring system that records subcutaneous ECG and is indicated for:

- Patients with clinical syndromes or situations at increased risk of cardiac arrhythmias
- Patients who experience transient symptoms that may suggest a cardiac arrhythmia
CASE: 56 year-old woman with refractory syncope accompanied by seizures.

CASE: 65 year-old man with syncope accompanied by brief retrograde amnesia.

Symptom-Rhythm Correlation with the ILR

Medtronic data on file.
Head-Up Tilt Test (HUT)

- Protocols vary
- Useful as diagnostic adjunct in atypical syncope cases
- Useful in teaching patients to recognize prodromal symptoms
- Not useful in assessing treatment
Response to Tilt Table Testing

Normal

Vasal vagal
Response to Tilt Table Testing

POTS

Dysautonomia
Indication for Tilt Table Testing

• The evaluation of recurrent syncope, or a single syncopal event accompanied by physical injury, motor vehicle accident, or in high risk setting in which clinical features suggest vasovagal

• In patients in whom dysautonomias may contribute to symptomatic hypotension

• Evaluation of recurrent exercise induced syncope in patients without structural heart disease
Conventional EP Testing in Syncope

• Greater diagnostic value in older patients or those with SHD

• Less diagnostic value in healthy patients without SHD

• Useful diagnostic observations:
  – Inducible monomorphic VT
  – SNRT > 3000 ms or CSNRT > 600 ms
  – Inducible SVT with hypotension
  – HV interval ≥ 100 ms (especially in absence of inducible VT)
  – Pacing induced infra-nodal block
Diagnostic Limitations of EPS

• Difficult to correlate spontaneous events and laboratory findings

• Positive findings\(^1\)
  – Without SHD: 6-17%
  – With SHD: 25-71%

• Less effective in assessing bradyarrhythmias than tachyarrhythmias\(^2\)

• EPS findings must be consistent with clinical history
  – Beware of false positive
“…cardiac syncope can be a harbinger of sudden death.”

- Survival with and without syncope
- 6-month mortality rate of greater than 10%
- Cardiac syncope doubled the risk of death
- Includes cardiac arrhythmias and SHD

Syncope Due to Cardiac Arrhythmias

• Bradyarrhythmias
  – Sinus arrest, exit block
  – High grade or acute complete AV block
  – Can be accompanied by vasodilatation (VVS, CSS)

• Tachyarrhythmias
  – Atrial fibrillation/flutter with rapid ventricular rate (eg, pre-excitation syndrome)
  – Paroxysmal SVT or VT
  – Torsade de pointes
Syncope Due to Structural Cardiovascular Disease: Principle Mechanisms

- Acute MI/Ischemia
  - 2° neural reflex bradycardia
  - Vasodilatation, arrhythmias, low output (rare)
- Hypertrophic cardiomyopathy
  - Limited output during exertion (increased obstruction, greater demand), arrhythmias, neural reflex
- Acute aortic dissection
  - Neural reflex mechanism, pericardial tamponade
- Pulmonary embolus/pulmonary hypertension
  - Neural reflex, inadequate flow with exertion
- Valvular abnormalities
  - Aortic stenosis – Limited output, neural reflex dilation in periphery
  - Mitral stenosis, atrial myxoma – Obstruction to adequate flow
Neurally-Mediated Reflex Syncope

- Vasovagal Syncope (VVS)
- Carotid Sinus Syndrome (CSS)
- Situational syncope
  - Post-micturition
  - Cough
  - Swallow
  - Defecation
  - Blood drawing, etc.
VVS Clinical Pathophysiology

• Neurally-mediated physiologic reflex mechanism with two components:
  1. Cardioinhibitory (↓ HR)
  2. Vasodepressor (↓ BP) despite heart beats, no significant BP generated

• Both components are usually present
Incidence

- Most common form of syncope
  - 8% to 37% (mean 18%) of syncope cases

- Depends on population sampled
  - Young without SHD, ↑ incidence
  - Older with SHD, ↓ incidence
VVS

General Treatment Measures

• Optimal treatment strategies for VVS are a source of debate

• Treatment goals
  – Acute intervention
    • Physical maneuvers, eg, crossing legs or tugging arms
    • Lowering head
    • Lying down
  – Long-term prevention
    • Tilt training
    • Education
    • Diet, fluids, salt
    • Support hose
    • Drug therapy
    • Pacing
CSS

Carotid Sinus Syndrome

- 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
- Prevalence higher than previously believed
- Carotid Sinus Hypersensitivity (CSH)
  - No symptoms
  - No treatment
CSS

Etiology

- Sensory nerve endings in the carotid sinus walls respond to deformation
- Previous neck surgery may contribute
- Increased afferent signals to brain stem
- Reflex increase in efferent vagal activity and diminution of sympathetic tone results in bradycardia and vasodilatation
SAFE PACE

Syncope And Falls in the Elderly – Pacing And Carotid Sinus Evaluation

• Objective
  – Determine whether cardiac pacing reduces falls in older adults with carotid sinus hypersensitivity

• Randomized controlled trial (N=175)
  – Adults > 50 years, non-accidental fall, positive CSM
  – Pacing (n=87) vs. No Pacing (n=88)

• Results
  – More than 1/3 of adults over 50 years presented to the Emergency Department because of a falls have CS hypersensitivity
  – With pacing, falls ↓ 70%
  – Syncopal events ↓ 53%
  – Injurious events ↓ 70%

Orthostatic Hypotension

• Etiology

• Drug-induced (very common)
  – Diuretics
  – Vasodilators

• Primary autonomic failure
  – Multiple system atrophy
  – Parkinson’s Disease
  – Postural Orthostatic Tachycardia Syndrome (POTS)

• Secondary autonomic failure
  – Diabetes
  – Alcohol
  – Amyloid
Treatment Strategies for Orthostatic Intolerance

- Patient education, injury avoidance
- Hydration
  - Fluids, salt, diet
  - Minimize caffeine/alcohol
- Sleeping with head of bed elevated
- Tilt training, leg crossing, arm pull
- Support hose
- Drug therapies
  - Fludrocortisone, midodrine, erythropoietin
- Tachy-Pacing (probably not useful)
Syncope and Driving

“I want to die peacefully in my sleep like my grandfather did, not like the screaming passengers in his car.”

George Burns
Syncope and Driving: Medical-Legal Concerns

- State of California requires physicians to report, in good faith, patients who have a physical or mental condition which, in the physician’s judgment, impairs the patient’s ability to exercise reasonable and ordinary control over a motor vehicle. The report may be made without the patient’s informed consent.

- The physician is obliged to inform the patient of the severity of the condition and that operating a motor vehicle is advised against. This informed advise should be documented in the medical record.
Syncope and Driving: Medical Legal Concerns

Examples of syncopal conditions that would prohibit driving

• Untreated syncope in patients with heart disease

• Undiagnosed recurrent syncope which occurs without prodrome and can occur while sitting
• 20 y/o female cyclist, dizzy when stands quickly, syncope during training ride
• 20 y/o female cyclist, dizzy when stands quickly, snycope during training ride

• Sitting: HR 65, BP 120/80, Standing: HR 90, BP 115/80

• EKG normal
• 20 y/o female cyclist, dizzy with standing quickly, syncope on training ride

• Sitting: HR 65, BP 120/80  Standing: HR 90, BP 115/80

• EKG normal

• Echo normal
• 20 y/o female cyclist, dizzy when stands quickly, syncope during training ride
• Sitting: HR 65, BP 120/80, Standing HR 90, BP 115/80
• EKG normal
• Echo normal
• Exercise test normal
20 y/o female cyclist
Dizzy when stands quickly, syncope during training ride

- Sitting: HR 65, BP 120/80, Standing: HR 90 BP 115/80
- EKG normal
- Echo normal
- Exercise test normal
- Tilt test abnormal
• **Diagnosis**
  
  Postural orthostatic tachycardia syndrome
  POTS

• **Treatment**
  
  hydration
  fludrocortisone
  midodrine
  welbutrin
  zoloft
  procrit
  atacand @ HS
Diagnostic Objectives

• Distinguish true syncope from syncope mimics
• Determine presence of heart disease and risk for sudden death
• Establish the cause of syncope with sufficient certainty to:
  – Assess prognosis confidently
  – Initiate effective preventive treatment
How to Evaluate Syncope

History: Patient and witnesses

Physical: Including carotid massage and ECG

- Transient or reversible cause?
  - yes
    - No work-up or chronic therapy
  - no
    - Suspected cardiac or arrhythmic cause?
      - yes
        - Admit, cardiology consult, EPS*
      - no
        - Neurocardiogenic cause? No obvious cause? No heart disease?
          - yes
            - 1st episode?
              - yes
                - Tilt table
              - no
                - Loop recorder
          - no
            - Referral

*EPS if BBB or LVEF < 40%

## Diagnostic Tests for Syncope

<table>
<thead>
<tr>
<th>Test</th>
<th>Indication</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holter Monitor</td>
<td>Frequent symptoms of palpitations or dizziness</td>
<td>Low yield with 24 hours of monitoring if symptoms are intermittent</td>
</tr>
<tr>
<td>Post-Event Recorder</td>
<td>Intermittent symptoms; patient maintains consciousness</td>
<td>Not useful for syncope without warning symptoms</td>
</tr>
<tr>
<td>Continuous-Loop Recorder</td>
<td>Intermittent or very transient symptoms; patient has little warning before symptoms occur</td>
<td>Inconvenient to use for long periods of time</td>
</tr>
<tr>
<td>Insertable Loop Recorder</td>
<td>Infrequent episodes of syncope; diagnosis cannot be made noninvasively</td>
<td>Requires invasive procedure</td>
</tr>
<tr>
<td>Signal-Averaged ECG</td>
<td>Syncope and structural heart disease</td>
<td>Low positive predictive value</td>
</tr>
<tr>
<td>Upright Tilt Testing</td>
<td>Suspected vasovagal syncope; syncope without structural heart disease</td>
<td>Inadequate reproducibility of test results</td>
</tr>
<tr>
<td>Electrophysiologic Study</td>
<td>Syncope when diagnosis cannot be made non-invasively; syncope with structural heart disease</td>
<td>Invasive; low yield when no structural heart disease</td>
</tr>
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