Syncope Case Study

38-year-old female with recurrent syncope occasionally occurring during emotional stressful times. Her physical examination and 12 lead EKG are normal.

Approach to the Patient with Syncope

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Syncope: Definition

- a syndrome in which loss of consciousness
  - relatively sudden,
  - temporary,
  - self-terminating
  - usually rapid recovery
- due to inadequate cerebral perfusion,
- most often triggered by a fall in systolic arterial pressure below 70 mmHg


Impact of Syncope on Mortality Risk

- Vasovagal Syncope has low mortality risk
  - But recurrences are a concern
- Syncope of presumed cardiac cause is associated with high mortality risk

Syncope: Causes

Neurally-Mediated Reflex
- Vasovagal Syncope (VVS)
- Drug-induced ANS Failure
- Situational
- Cough
- Post-micturition

Orthostatic
- Hypotension

Cardiac Arrhythmia
- Bradycardia
- Sinus pause/ arrest
- AV block
- Tachycardia
- VT
- Long QT syndrome

Structural Cardiac-Pulmonary
- Aortic Stenosis
- HCM
- Pulmonary Hypertension
- Aortic Dissection

Unexplained Causes = Approximately 10%


Syncope: Epidemiological Data

- 40% population, presumed syncope at least once
- 1-6% of hospital admissions
- Approx 1% of ED visits per year
- 10% of falls by elderly are believed due to syncope
- Injuries:
  - 6% major morbidity (e.g., fractures, MVA)
  - Minor injury in 29%

References:

Impact of Syncope in USA: Annual Expenditures

- Syncope evaluation and treatment > $2.4 billion
- Estimated hospital costs >$5400/hospitalization
- Treating ‘falls’ in older adults >$7 billion

References:
1. Benjamin C. Sun, MD, MPP, Jennifer A. Emond, MS, and Carlos A. Camargo, Jr., MD, DrPH. Direct medical costs of syncope-related hospitalizations in the USA. Am J Cardiol 2005;95:668-671.

Diagnostic Strategy

The Initial Evaluation: 4 Key Questions

- Did the patient suffer ‘true’ Transient Loss of Consciousness (TLOC)?
- Was TLOC due to syncope or some other cause?
- Is Heart disease present?
- Does the medical history (including observations by witnesses) suggest a specific diagnosis?

Essential Elements of the History

- Circumstances of recent event(s)
  - Eyewitness account of event
  - Symptoms at onset of event (warning symptoms)
  - Sequelae
- Concomitant disease, especially cardiac
  - Medication history
- Pertinent family history
  - Cardiac disease, Sudden death
  - Metabolic disorders
- Past medical history
  - Neurological history
  - Syncope

Essential Elements of the Physical Examination

- Vital signs
  - Heart rate, regularity
  - Orthostatic blood pressure change: symptomatic fall in systolic BP from a baseline value > 20 mmHg or diastolic BP > 10 mmHg, or a decrease in systolic BP to < 90 mmHg
- CV Exam: Is heart disease present?
  - Signs of heart failure with elevated neck veins, rales, S3 gallop, murmurs, lower extremity edema
- Neurological exam
  - Residual deficits?
- Carotid sinus massage
  - Perform under clinically appropriate conditions preferably during tilt-table test. Monitor BP
Carotid Sinus Massage (CSM)

**Indication**
- > 40 years
- Unknown syncope etiology

**Method**
- Massage, ~10 seconds, firm but do not occlude
- Supine and upright posture (on tilt-table)

**Diagnosis**
- >3 sec asystole and/or >50 mmHg fall in systolic BP
- Reproduction of symptoms (usually only occurs with CSM during upright posture)


Indications for Specific Electrocardiographic Monitoring

- In patients who have clinical or ECG features suggesting arrhythmic syncope:
  - Holter monitoring for patients with frequent syncpe or pre-syncpe (≥1 per week)
  - External loop recorders in patients who have an inter-symptom interval ≤ 4 weeks
  - Implantable loop recorder (ILR) for patients with recurrent syncpe of unknown origin, absence of high risk criteria, and high likelihood of recurrence
    - ILR should be considered to assess the contribution of bradycardia before using cardiac pacing


Adhesive Patch Electrocardiographic Monitoring

- Demonstrated improved clinical accuracy and detection of potentially malignant arrhythmias in atrial fibrillation patients compared with a 24-hour Holter Monitor in the same patients.
- Achieved both superior patient and physician satisfaction compared to 24-hour Holter.


Implantable Loop Recorder (ILR)

- An ECG monitoring system that is implanted subcutaneously
- Capable of recording, storing, and if necessary remotely transmitting ECG signals
  - Patient-activated and/or automatically-activated
  - Longevity of current ILRs up to 36 months

Selected Use Based on Initial Examination and Risk Stratification

- Head-Up Tilt Test (usually combined with CSM)
- Electrophysiology Study (EPS)
- Non-invasive Risk Stratification for Life-threatening ventricular tachyarrhythmias†
  - Signal-Averaged Electrocardiogram (SAECG)
  - Microvolt Twave alternans

† Generally exhibit high negative predictive value but low positive predictive value

Indications for Tilt Table Testing

- Unexplained single syncopal episode in high risk settings or recurrent episodes in absence of organic heart disease
- To demonstrate susceptibility to reflex syncope
- To discriminate between reflex and orthostatic syncope
- To differentiate syncope with jerking movements from epilepsy
- Evaluating patients with recurrent unexplained falls
- Evaluating patients with frequent syncpe and psychiatric disease


**Tilt-Table Testing**

- Upright posture during test decreases venous return and reduces LV filling.
- There is increased force of contraction due to increased sympathetic stimulation.
- Mechanoceptors in the ventricles respond to the increased force of contractions resulting in reflex parasympathetic discharge causing hypotension, bradycardia, or both.

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**Tilt-Table Testing**

- Of patients without diagnosis for syncope, 24-49% have positive tilt-table test alone and 60-66% have positive test with Isoproterenol or nitroglycerin.
- Controls without history of syncope have positive tests in 10-30%.
- If the clinical history is consistent with vasovagal syncope, a positive tilt-table test can be useful.

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

- Protocols vary
- Performed with or without provocative drugs
- Goals:
  - Unmask VVS susceptibility
  - Reproduce symptoms
  - Patient learns VVS warning symptoms
  - Patient more confident of diagnosis
- Not useful for predicting treatment benefit

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**Induction of VVS by Upright Posture**

**Cardioinhibitory & Vasodepressor Components**

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**Indications for Electrophysiologic Study**

- In patients with ischemic heart disease with suggested arrhythmic cause of syncope
- In patients with BBB when non-invasive tests have failed
- In patients with syncope preceded by sudden and brief palpitations when non-invasive tests have failed
- In patients with Brugada syndrome, ARVC, and HCM
- In patients with high-risk occupations

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**Electrophysiologic (EP) Testing**

- Well established technique for detecting arrhythmias but less sensitive for bradyarrhythmias. Overall diagnostic yield is 30-50%.
- Of patients with unexplained syncope:
  - 15% have inducible ventricular tachycardia
  - 15% have inducible supraventricular tachycardia
  - 20-41% have findings suggestive of bradycardia
Neurological Tests for TLOC
EEG, Head CT / MRI
- Not useful for syncope evaluation
- Imaging may be warranted if there is concern re head injury from ‘fall’
- May be useful in non-syncope TLOC patients but neurological consultation is advised prior to tests

Psychiatric Evaluation
- In recurrent syncope, 20% have a panic disorder, generalized anxiety disorder, or major depression.
- A hyperventilation maneuver (open mouth breathing for 2-3 minutes) that results in syncope is strongly associated with psychogenic syncope.


Emergency Department Decision Rules and Syncope Units
- The San Francisco Syncope Rule has sensitivity and specificity of 98% and 56% for predicting adverse 30-day outcomes.
  - High risk features (CHESS: CHF, Hematocrit<30%, abnormal EKG, Shortness of breath, Systolic BP<90mmHg)
- SEEDS trial assessing the Syncope Unit in the Emergency Department found the diagnostic yield higher c/w SOC (67% vs 10%)

Specific Conditions and Treatment

Selected Specific Conditions
- Neurally-Mediated Reflex Syncope (NMS)
  - Vasovagal, Carotid Sinus Syndrome (CSS)
- Orthostatic Hypotension
  - Autonomic dysfunction
    - Drug induced
- Cardiac Syncope
  - Structural heart disease
  - Channelopathies
    - Long QT Syndrome (idiopathic, drug-induced)
    - Brugada Syndrome

Neurally-Mediated reflex Syncope (NMS)
- Vasovagal Syncope (VVS)
- Carotid Sinus Syndrome (CSS)
- Situational Syncope
  - post-micturition
  - cough
  - swallow
  - defecation
  - blood drawing
  - etc.
**NMS: Clinical Pathophysiology**

- Neurally-mediated physiologic reflex mechanism with two components:
  - Cardioinhibitory (HR)
  - Vasodepressor (BP)
- Both components are usually present:
  - Vasodpressor may be masked in the presence of severe bradycardia.
  - Pace or pre-treat with atropine in order to observe vasodepressor component

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**VVS: Optimal Initial Treatment Strategy**

- Patient education, reassurance, instruction
- Salt/Volume
  - Increased dietary salt,
  - Increased volume intake
  - (e.g., electrolyte rich 'sport' drinks)
- Physical maneuvers
  - Standing / tilt-training
  - Muscle tensing, leg-crossing
- Support hose, Abdominal binders

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**Physical Maneuvers to Counter an Imminent Vasovagal or Orthostatic Faint**

- Schematics illustrating physical counter-manuvers designed to delay an imminent vasovagal or orthostatic faint.
- Each of these maneuvers might boost blood pressure sufficiently to delay symptoms. The objective is to "buy time" during which the affected individual can seek a safe haven.
- (A) The subject is depicted using leg-crossing with lower body muscle tensing (left) or squatting (right) to enhance blood pressure. (B) Arm-tensing is illustrated.

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**PC-Trial (Physical Counterpressure Manoeuvres Trial)**

- Physical counter-pressure maneuvers (PCM) are increasingly advocated to abort neuromediated or orthostatic faint
  - Squatting, arm-tensing, leg-crossing, and leg-crossing with lower body muscle tensing
- PC-Trial randomized 208 patients with VVS to conventional therapy (fluid/salt intake, counselling, avoidance) versus conventional therapy augmented by physical maneuvers.
  - After 18 months, the syncope burden was lower in PCM-trained patients versus control subjects (32% of PCM-trained and 51% of conventional arm patients experienced syncope recurrence)
  - PCM should be part of the treatment strategy in patients with warning symptoms

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**Randomized Trials of Pharmacologic Therapy for VVS**

- **Fludrocortisone** for the prevention of VVS (POST II)¹
  - Fludrocortisone is of no benefit in reducing episodes of moderate to severe vasovagal syncope.
- **Beta-blocker** use in VVS (POST)²
  - No benefit was found. But recent meta-analysis suggests benefit in those aged 242 years.
- **Midodrine** for syncope³
  - No efficacy. But may have benefit in orthostatic hypotension.
- **SSRI** for VVS⁴
  - Benefit with paroxetine but not observed in clinical practice.

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**Pacing / Ablation in VVS**

- Early studies were not double blind
- Pacemaker implantation may create emotional and psychological responses that modulate reflex syncope and autonomic responses⁵
- Pacing therapy is effective in some but not all. Recent ISSUE-3 study with benefit in cardioinhibitory patients⁶
- Endocardial radiofrequency catheter ablation of the cardiac vagal nervous system with good outcome in select patients⁷

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¹Sheldon RS. Canadian J Card. 2011; 27(5): S335-S336
²Sheldon RS. Circulation. 2006;113:1164-1170
³Romme JJ. Europace. 2011;13:1639-1647
⁵Kapoor W. JAMA. 2003;289:2272-2275
Carotid Sinus Syndrome (CSS)

- Syncope clearly associated with carotid sinus stimulation was thought to be rare (≤ 1% of syncope):
- Carotid Sinus Syndrome (CSS)
- CSS may be a more important cause of unexplained syncope/falls in older individuals than previously expected
- Carotid Sinus Hypersensitivity (CSH) implies positive response to carotid massage:
  - > 50 mmHg drop in systolic pressure
  - > 3 sec asystolic pause
  - Reproduction of symptoms
- CSH without symptoms is not treated

Orthostatic Hypotension: Etiology

- Drug-induced (very common)
  - Diuretics, Vasodilators
- Primary autonomic failure
  - Multiple system atrophy, Parkinsonism
- Secondary autonomic failure
  - Diabetes, Alcohol, Amyloid

Syncope Due to Structural Cardiovascular Disease

- Often life-threatening
- May be warning of critical CV disease
  - Aortic stenosis, myocardial ischemia, pulmonary hypertension, aortic dissection
- Assess culprit arrhythmia or structural abnormality aggressively
- Initiate treatment promptly
  - Specific for culprit condition

Syncope in Structural CV Disease

- Principal Mechanisms
  - Acute MI / Ischemia
    - 2nd neural reflex bradycardia - vasodilation, arrhythmias
  - HCM
    - Exertional syncope (increased obstruction, greater demand), arrhythmias, neural reflex
  - Acute aortic dissection
    - Neural reflex mechanism, pericardial tamponade
  - Pulmonary embolus/pulmonary hypertension
    - Neural reflex, inadequate flow on exertion
  - Valvular abnormalities
    - Aortic stenosis - output limitation, reflex dilatation in periphery
    - Mitral Stenosis, Atrial myxoma - obstruction to inflow

Treatment for Carotid Sinus Hypersensitivity

- Permanent pacing
  - Class I indication in patients with recurrent syncope caused by carotid sinus stimulation in the absence of any drug that depresses the sinus node or atrioventricular conduction.
  - Class IIa indication in patients with recurrent syncope without clear, provocative events and with a hypersensitive cardioinhibitory response.
- Permanent pacing is discouraged in patients with a hypersensitive cardioinhibitory response to carotid sinus stimulation in the absence of symptoms.

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 tensing
- Support hose, abdominal binders
- Drug therapies
  - Fludrocortisone, midodrine

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 (e.g., long QT syndrome)

Syncope Due to Bradyarrhythmias

- Class I indication for pacing
- Dual-chamber pacing in most cases
- Ventricular pacing in atrial fibrillation with slow ventricular response

Syncope Due to Supraventricular Tachyarrhythmias

- AVRT due to accessory pathway (e.g., WPW)
  - Ablation of pathway preferred
- AV Node Reentry (AVNRT)
  - Ablation of AV nodal slow pathway is preferred
- Atrial flutter
  - Ablate the Cavo-Tricuspid isthmus is preferred
- Atrial fibrillation
  - Drug therapy remains first-line
  - Linear/focal ablation may be a reasonable option
  - AV Node ablation with pacing remains a back-up plan

Syncope: Torsades

Treatment of Syncope Due to Bradyarrhythmia

- AV Node Reentry (AVNRT)
  - Ablation of AV nodal slow pathway is preferred
- Torsades de pointes (e.g., long QT syndrome)

Treatment of Syncope Due to Bradyarrhythmia

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  - Ablation of pathway preferred
- AV Node Reentry (AVNRT)
  - Ablation of AV nodal slow pathway is preferred
- Atrial flutter
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- Atrial fibrillation
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  - Linear/focal ablation may be a reasonable option
  - AV Node ablation with pacing remains a back-up plan

Recommendations Concerning Driving in Patients with Syncope

Ischemic or Dilated Cardiomyopathy
  - ICD therapy indicated for SCD protection, but may not prevent syncope*
  - Ablation where appropriate

Channelopathies
  - Withdraw offending drugs
  - ICD (long-QT syndrome / Brugada syndrome)

Outflow Tract Tachycardias
  - Ablation is first-line

Arrhythmogenic Dysplasia
  - ICD therapy

* Olshansky B et al, JACC 2008
Summary

- Syncope is only one of many causes of transient loss of consciousness, symptoms are fleeting, events are often unwitnessed, and there is often an excessive sense of diagnostic “urgency”
- A thorough evaluation of the cause of syncope is warranted in all patients – not just in those deemed to be at high mortality risk
- The mere presence of an abnormal finding does not constitute a “diagnosis”
- The goal in every case should be to determine the cause with sufficient confidence to provide a reliable assessment of prognosis and treatment options