Disclosures

• Paid Consultant: St. Jude, Medtronic
• Speaker: Sanofi-Aventis, Boeringher-Ingleheim
• Research Support: Medtronic, St. Jude
Objectives

- Review the differential diagnosis of syncope
- Review the diagnostic value of various tests used in syncope
- To be able to initiate a thoughtful and directed workup for the patient with syncope
- To gain an understanding of neurally mediated syncope
What is Syncope?

• A syndrome consisting of a relatively short period of temporary and self limited loss of consciousness.
The Significance of Syncope

1 National Disease and Therapeutic Index on Syncope and Collapse, ICD-9-CM 780.2, IMS America, 1997
Frequency of Syncope

- Spans all age groups
  - < 18 y/o 15%
  - 17-26 y/o 25% (military)
  - 40-59 y/o 16% (male), 19% (female)
  - Nursing home 23%

<table>
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<tr>
<th>Area of Impairment</th>
<th>Proportion Impaired</th>
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<td>Anxiety/depression</td>
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<td>Relationships with family, spouse, friends</td>
<td>28-30%\textsuperscript{2}</td>
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\textsuperscript{1} Linzer M. *J Clinical Epidemiol.* 1991;44:1037-1043.
Why do we all Hate Syncope?

- An occasional patient will have something bad
- Diagnostic workup is hard
  - History is the key diagnostic tool but no one trusts it
  - “Objective” tests are often non-diagnostic or worse
- The most common form of syncope occurs in healthy people and is often dramatic
Classification of Syncope

- Neurally mediated
- Orthostatic
- Cardiac arrhythmia
- Structural / Obstructive
- Cerebrovascular
- (Psychiatric)
- (Not Syncope)
Neurally Mediated Syncope

• This is an *active* reflex
• Vasovagal Syncope (trigger = postural stress)
• Situational Faint
  – Cough, Sneeze, Micturition, Defecation, Swallowing, Post prandial, Emotional, Post-exercise, Pain, Post-operative
• Carotid Sinus Hypersensitivity
Examples of “Vagal” Syncope
Orthostatic Syncope

• This is a *passive* process

• Primary Autonomic Failure Syndromes
  – Pure Autonomic Failure
  – Multisystem Atrophy (Shy-Drager)
  – Parkinson’s Disease
  – ? POTS

• Secondary Autonomic Failure
  – DM, drugs, Alcohol, Amyloid, MS, GBS

• Volume Depletion
Cardiac Arrhythmias

- Bradycardia
  - Sinus Node dysfunction
  - AV block
- Tachycardia
  - Structurally abnormal heart (CHF, etc)
  - Electrically abnormal heart (LQT, Brugada, etc)
Structural / Obstructive

- Valvular disease
- HOCM
- Aortic dissection
- Atrial Myxoma
- Pulmonary embolism
- Pulmonary hypertension
Cerebrovascular

- Vascular Steal Syndrome
- Vertebro-basilar insufficiency
- Basilar artery migraine
Psychiatric Diagnosis

- May account for up to 35% in referral population
- Diagnosis
  - Generalized Anxiety
  - Panic
  - Major Depression
  - EtOH
  - Conversion
- Usually with high rate of recurrence
- 60% of pts with hyperventilation syncope have an underlying psychiatric diagnosis.
Syncope vs Epilepsy

• Lampert study in 59 German med students
• 12% had tonic-clonic type movements, 80% myoclonic
  – Brief
  – After LOC
  – Not really tonic-clonic (gross flailing, random, contraction of axial muscles, non-rhythmic)
Syncope vs TIA

- **Syncope**: Transient loss of consciousness without neurological deficit
- **TIA**: Transient neurological deficit without loss of consciousness
Syncope-like States

- Migraine*
- Acute Hypoxemia*
- Hyperventilation*
- Somatization disorder (psychogenic syncope)
- Acute Intoxication (e.g., EtOH, drugs)
- Seizures
- Hypoglycemia
- Sleep disorders

* May cause ‘true’ syncope
Relative Incidence of Causes: Unselected patients presenting to the ER

Workup of Syncope

“Medicine is an art of certainty and a science of probability.”

- Sir William Osler
Diagnostic Testing in Syncope

- History & Physical Examination
  - Most valuable test
  - Diagnostic Yield: 35-40%

- Other generally useful tests
  - Echocardiogram
  - Resting ECG
  - Ambulatory ECG (Loop recorder)

- Rarely useful
  - MRI, CT, Dopplers, EEG, EP study, Treadmill

- Controversial: Tilt table test
History & Physical

Is This Syncope?
- Is there loss of consciousness?
- Is it transient & self-limited?
- Was it Intoxication, Drugs, Hypoxia or Falling asleep?
- Was there continued confusion/disorientation for >5 minutes after regaining consciousness?

Neurally Mediated
Orthostatic
Arrhythmic
Obstructive
Cerebrovascular
Psychiatric

Not Syncope
History & Physical

Neurological Findings?

- Are there focal neurological deficits on exam?
- Was there a migraine type headache?
- If no findings, you do not need MRI, CT, dopplers, EEG, etc.
Orthostatic Hypotension?

Is the patient Orthostatic?
- Not all patients will show orthostatic tachycardia

- Does the patient have any of the medical conditions predisposing to Orthostatic Hypotension?
- Are there predisposing drugs?
- Is there suggestion of dehydration?
Orthostatic Hypotension Characteristics

- Syncope after arising rapidly
- May be sudden in elderly
- Recurrent episodes or persistent pre-syncope
- May occur in elderly after large meals
- Other Manifestations of autonomic dysfunction
Neurally Mediated
Orthostatic
Arrhythmic
Obstructive
Cerebrovascular
Psychiatric
Not Syncope

Is it Obviously Vagal?

• If typical vagal episode, diagnosis can be purely clinical
• Carotid Sinus Massage in elderly can be diagnostic
History Pearls: Vagal

• Pre-event
  – Stereotypical Trigger (Postural, cough, micturition, etc)
  – Nausea, diaphoresis, feeling warm, pale

• Recovery
  – Simultaneous recovery of consciousness and orientation
  – Persistent nausea, urge to defecate, weak/lightheadedness
  – Post recovery can feel lousy for hours and faint again
  – Pallor

• Post-LOC “seizure” = NON-neurological event
  – Usually vagal. Sometimes hysterical.
### Residual Differential

- Neurally Mediated
- Orthostatic
- Arrhythmic
- Obstructive
- Cerebrovascular
- Psychiatric
- Not Syncope

### Assess Prognosis
- **Is it high risk?**
- **If NOT:**
  - Syncope will likely still recur, but sudden death is unlikely
  - Reassure patient
  - Make diagnosis clinically or by recording an ambulatory event
  - Outpatient workup
- **Echocardiogram**
Assessing prognosis: Worrisome Findings

- **Resting ECG**
  - Long QT interval
  - Heart block
  - Prior infarction
  - Bundle Branch Block

- **History**
  - During exercise (NOT after)
  - Severe ambient chest pain
  - Unheralded, Complete recovery
  - Patient looks/feels fine afterwards
  - Family Hx of premature SCD

- **Echocardiogram**
  - LV dysfunction
  - RV dysplasia
  - Aortic stenosis
  - Pulmonary hypertension
  - Myxomas, other weird stuff
Unexplained Syncope

Neurally Mediated
Orthostatic
Arrhythmic
Obstructive
Cerebrovascular
Psychiatric
Not Syncope

About 40% of cases

• Good prognosis
• Would like an ECG with event
  – 1st episode: Wait for more or loop monitor
  – Frequent episodes: Loop recorder (Holter only if daily episodes)
  – Infrequent episodes: Consider implantable event monitor
  – Consider: Tilt, Psych eval
• May remain undiagnosed…
History Pearls: Unexplained syncope

• Family history
  – Consider LQT syndromes, HCM

• Palpitations suggest:
  – Sinus tachycardia from volume depletion, hypoglycemia or vasodilation
  – Hyperventilation, psychiatric, vagal
  – PSVT (rare to occur without palpitations)
  – Sick Sinus Syndrome (A-fib then pause)
  – VT (Often occurs without palpitations)

• Psychiatric history
## Diagnostic Yield (%) of Individual Tests in Work-up of Syncope, pre-Tilt Table Testing

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<th>Author (N)</th>
<th>Clinical Setting</th>
<th>% With Recurrent Syncope</th>
<th>H&amp;P</th>
<th>ECG</th>
<th>Holter</th>
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*Prospective study

Diagnostic Tests: Provocative

- **Tilt Table Test**
  - False positive rate 10-25%
  - Should only be considered positive if clinical symptoms are reproduced
  - Tests for “empty heart” vagal episodes, not other neurally mediated syncopies. False negative rate can be high.

- **Electrophysiology Testing**
  - Yield for Bradycardia: <50%
  - Tachycardia: Unknown yield, but negative test gives a prognosis equal to patients who have similar heart disease but did not have syncope.
  - Rarely helpful in patients with normal LV, ECG
Diagnostic Tests: True Clinical

- Holter Monitor
- Ambulatory Event Recording (surface or implanted)
- Implantable Loop Recorder
Diagnostic Tests: Ambulatory ECG recording

- **Holter Monitor**
  - 4% Symptoms with arrhythmia True Positive
  - 15% Symptoms and no arrhythmia True Negative
  - 14% Arrhythmia but no symptoms Confusing
  - 65% No arrhythmia, no symptoms Non-diagnostic

- **Loop Monitor (ambulatory event monitor) x 1 month**
  - 20% Symptoms and arrhythmia True Positive
  - 27% Symptoms and no arrhythmia True Negative
  - 53% No symptoms Non-diagnostic

- Implanted loop monitor now available
Holter placed when patient had a clinical episode of atrial fibrillation
Value of Event Recorder in Syncope

* Asterisk denotes event marker

Implantable loop recorder

- Allows prolonged (14 month) recordings with long pre-event looping memory.
- Patient activated and automatic triggers
- Implantation procedure <20 minutes
56 yo woman with syncope accompanied with seizures.
Infra-Hisian AV Block: Dual chamber pacemaker

65 yo man with syncope accompanied with brief retrograde amnesia.
VT and VF: ICD and meds
Summary: Syncope

- Frequent symptom often resulting in expensive, extensive workup and much patient and physician angst.
- History is critical.
- Prognosis depends on existence of cardiac disease, regardless of actual diagnosis.
- Shotgun diagnostic approach is unrewarding.
- Therapy is diagnosis dependent.
Neurally Mediated Syncope
A detailed look
Word Jumble

- Common Faint
- Vagal syncope
- Vasovagal syncope
- Neurocardiogenic syncope
- Vasodepressor syncope
- Neurodepressor syncope
- Cardiodepressor syncope
- Situational syncope
- Micturation Syncope
- Cough Syncope
- Defecation Syncope
- Swallow Syncope
- Carotid Sinus Hypersensitivity (?)
Neurally Mediated Syncope: Common Misconceptions

- It is a fancy name for orthostatic syncope
- It is a diagnosis of exclusion
- If syncope is bad enough, it can’t be just vagal
- It only affects the young
- It’s not a “real” diagnosis
Characteristics of Neurally Mediated Syncope

• Very symptomatic, alarming, events
  – Pale, sweaty, chest pain
  – Feels like a heart attack to the patient
  – Sometimes associated with “seizure” activity
  – Patients do not believe it is benign

• Recurrent

• Young healthy patient thinks you are ignoring a very serious life-threatening problem

• Almost all tests will be negative
  – Reinforces patient’s perception that it is serious
Neurally Mediated Syncope

• Clinical sequence of events:
  – Trigger of some sort: Postural, Situational, PVC, Vasodilator
  – Variable period of nausea, epigastric discomfort, weakness, pallor, diaphoresis, lightheadedness
  – Loss of consciousness often with tonic or tonic-clonic seizure like movements (convulsive syncope)
  – Recovery of consciousness when supine
  – Persistent nausea, weakness for several minutes. Often urge to have a BM

• May recur quickly if patient tries to stand up too soon
Neurally Mediated Syncope

- **Pathophysiology**
  - **Active reflex**
  - Afferent limb can be variable
    - Endocardial stretch receptors, GI stretch receptors, dorsal motor nucleus of vagal nerve, pulmonary irritation, pain receptors, central, smooth muscle receptors
  - Efferent limb
    - Removal of all sympathetic tone
    - Profound vagal input to heart leads to asystole
Neurally Mediated Syncope: Triggers

- “Empty Heart” (endocardial stretch receptors)
  - Hypovolemia, hyperdynamic (post-PVC)
  - Emotional, sight of blood, pain
- Glossopharyngeal (dorsal motor nucleus)
- Micturation or defecation syncope (smooth muscle stretch receptors)
- Swallow Syncope (stretch receptors in esoph)
Pathophysiology of Posturally Triggered Neurally Mediated (Vagal) Syncope

Tilt Table Test for Syncope

- Used to unmask postural neurally-mediated syncope
- Measure heart rate and blood pressure in supine & 70° head-up tilt positions for 30-60 mins
- Isoproterenol infusion or Nitroglycerine pharmacological stress sometimes
- Patient often learns warning symptoms (“tilt training”)
Classification of Abnormal Responses to Tilt Table Testing

• Cardio-inhibitory (mainly bradycardia)
• Vasodepressor (marked hypotension without marked bradycardia)
• Mixed (hypotension with bradycardia)
Head-Up Tilt Test (HUT)

DG Benditt, UM Cardiac Arrhythmia Center
Implantable Loop Recording: Vagal Syncope
Use of the Tilt Table Test

- NOT all patients with neurally mediated syncope
- When patient doesn’t believe your clinical diagnosis and demands a test
- Recurrent syncope (especially with injuries)
- Failure of initial therapy
Vagal Syncope: Treatment

- Reassure
- Eliminate “Empty Heart” Trigger
  - Volume/Salt loading
  - Beta Blockers
  - Disopyramide
  - Florinef
- Blunt Efferent limb of reflex
  - Midodrine
  - Pacing
- ? Mechanism
  - Paxil
Pacing helps in unblinded trials

- Vasovagal Pacemaker Study (VPS-1)
- VASIS
VPS- I

Cumulative Risk (%)

Control (No Pacemaker)

Pacemaker

2P=0.000022

Time in Months

Number At Risk

<table>
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<tr>
<th>Number</th>
<th>C 27</th>
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<td>21</td>
<td>17</td>
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Blinded Trials: Minimal Benefit

- SYNPACE
- VPS-2
VPS-II: Phase I

Pacing conclusions

- Pacemaker implantation can help some patients with NMS.
- Pacer therapy guided by results of Tilt table testing fails to show benefit in blinded randomized trials.
- Even patients who don’t have syncope after pacing will (>90%) have pre-syncope symptoms.