Transient Loss of Consciousness (TLOC)
Transient Loss of Consciousness (TLOC) (Classification)

Underlying Mechanism Is Transient Global Cerebral Hypoperfusion.

Real or Apparent TLOC

- Syncope
  - Neurally-mediated reflex syndromes
  - Orthostatic hypotension
  - Cardiac arrhythmias
  - Structural cardiovascular disease

- Disorders Mimicking Syncope
  - With loss of consciousness, i.e. seizure disorders, concussion
  - Without loss of consciousness, psychogenic “pseudo-syncope”

Syncope
A Symptom, Not a Diagnosis

- Self-limited loss of consciousness and postural tone
- Relatively rapid onset
- Variable warning symptoms
- Spontaneous, complete, and usually prompt recovery without medical or surgical intervention

Etiology, Prevalence, Impact...
Causes of True Syncope

**Neurally-Mediated**
- VVS
- CSS
- Situational
  - Cough
  - Post-Micturition

**Orthostatic**
- Drug-Induced
- ANS Failure
  - Primary
  - Secondary

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

**Structural Cardio-Pulmonary**
- Acute MI
- Aortic Stenosis
- HCM
- Pulmonary HTN
- Aortic Dissection

Unexplained Causes = Approximately 1/3
Syncope Mimics

- Acute intoxication (e.g., alcohol)
- Seizures
- Sleep disorders
- Somatization disorder (psychogenic pseudo-syncope)
- Trauma/ concussion
- Hypoglycemia
- Hyperventilation

Impact of Syncope

- 40% will experience syncope at least once in a lifetime
- 1-6% of hospital admissions
- 1% of emergency room visits per year
- 10% of falls by elderly are due to syncope
- Major morbidity reported in 6%, i.e., fractures, motor vehicle accidents
- Minor injury in 29%, i.e., lacerations, bruises

Impact of Syncope: US Trends

Emergency Department Visits

Hospital Outpatient Visits

*Syncope and collapse (ICD-9 code: 780.2) listed as primary reason for visit. NHAMCS 2002.
Quality of Life: UK Population Norms vs. Syncope Patients

- **Mobility**: UK Population Norms: 3; Patients with Syncope: 26
- **Self-Care**: UK Population Norms: 4; Patients with Syncope: 36
- **Anxiety/Depression**: UK Population Norms: 1; Patients with Syncope: 49

Syncope Mortality

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

Syncope and Driving a Vehicle

✓ Those who drive and have recurrent syncope risk their lives and the lives of others
✓ Places considerable burden on the physician
✓ Essential to know local laws and physician responsibilities
✓ Some states – Invasion of privacy to notify motor vehicle department*
✓ Other states – Reporting is mandatory*

If the patient has sufficient warning of impending syncope Driving may be permitted
Diagnosis...
Diagnostic Objectives

✓ Distinguish true syncope from syncope mimics
✓ Determine presence of heart disease
✓ Establish the cause of syncope with sufficient certainty to:
  • Assess prognosis confidently
  • Initiate effective preventive treatment
A Diagnostic Plan is Essential

✓ **Initial Examination**
  - Detailed patient history
  - Physical exam
  - ECG
  - Supine and upright blood pressure

✓ **Monitoring**
  - Holter
  - Event
  - Insertable Loop Recorder (ILR)

✓ **Cardiac Imaging**

✓ **Special Investigations**
  - Head-up tilt test
  - Hemodynamics
  - Electrophysiology study
Diagnostic Flow Diagram for TLOC

Initial evaluation (medical history, physical examination, ECG, echo)
May require assessment in syncope management unit (SMU)

- Diagnosis 'certain' (no further testing needed)
  - 'Risk stratification' (treatment)
    - Single / rare episodes 'low risk' circumstance
      Rx education and reassurance as appropriate
    - Frequent or severe episodes or 'high risk' condition
      Treatment based on diagnosis

- Diagnosis unclear
  - 'Risk stratification' (outpatient versus in-hospital evaluation)
    - Suspected diagnosis
      Selected tests to assess suspected diagnosis
      Frequent or severe episodes
      Tilt test CSM ILR
      If negative
    - No suspected diagnosis
      No structural heart disease and normal ECG
      Single / rare episodes No further evaluation absent major lifestyle impact
      If positive
    - Structural heart disease or abnormal ECG
      Selected cardiac tests:
      - Hemodynamic or coronary
      - AECG / ILR
      - Stress test
      - EP study
Initial Exam: Detailed Patient History

- Circumstances of recent event
  - Eyewitness account of event
  - Symptoms at onset of event
  - Sequelae
  - Medications
- Circumstances of more remote events
- Concomitant disease, especially cardiac
- Pertinent family history
  - Cardiac disease
  - Sudden death
  - Metabolic disorders
- Past medical history
  - Neurological history
  - Syncope
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)

✓ Method¹
  - 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 contraindications²
  - Carotid bruit, known significant carotid arterial disease, previous CVA, MI last 3 months

✓ Complications³
  - Primarily neurological
  - Less than 0.2%
  - Usually transient

¹Kenny RA. Heart. 2000; 83:564
²Linzer M. Ann Intern Med. 1997; 126:989
Other Diagnostic Tests

- Ambulatory ECG
  - Holter monitoring
  - Event recorder
    - Intermittent vs. Loop
    - Insertable Loop Recorder (ILR)
- Head-Up Tilt (HUT)
  - Includes drug provocation (NTG, isoproterenol)
  - Carotid Sinus Massage (CSM)
- Adenosine Triphosphate Test (ATP)
- Electrophysiology Study (EPS)

## Diagnostic Assessment: Yields

<table>
<thead>
<tr>
<th></th>
<th>Yield(%)</th>
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<tbody>
<tr>
<td><strong>Initial Evaluation</strong></td>
<td></td>
</tr>
<tr>
<td>History, Physical Exam, ECG, Cardiac Massage</td>
<td>38-40</td>
</tr>
<tr>
<td><strong>Other Tests/Procedures</strong></td>
<td></td>
</tr>
<tr>
<td>Head-Up Tilt Test</td>
<td>27</td>
</tr>
<tr>
<td>External Cardiac Monitoring</td>
<td>5-13</td>
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<tr>
<td>Insertable Loop Recorder (ILR)</td>
<td>43</td>
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<tr>
<td>EP Study</td>
<td>2-5&gt;</td>
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<tr>
<td>Exercise Test</td>
<td>0.5</td>
</tr>
<tr>
<td>EEG</td>
<td>0.3-0.5</td>
</tr>
<tr>
<td>MRI</td>
<td>NA</td>
</tr>
</tbody>
</table>
Neurological Tests: Rarely Diagnostic for Syncope

- EEG, Head CT, Head MRI
- May help diagnose seizure

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

Head-Up Tilt Test: ECG Leads and Intra-Arterial Pressure Tracing
Insertable Loop Recorder (ILR)
The ILR is an implantable patient – and automatically – activated monitoring system that records subcutaneous ECG.

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
Specific Conditions and Treatment...
Specific Conditions

✓ Cardiac arrhythmia
  - Brady/ Tachy
  - Long QT syndrome
  - Torsade de pointes
  - Brugada
  - Drug-induced
✓ Structural cardio-pulmonary
✓ Neurally-mediated
  - Vasovagal Syncope (VVS)
  - Carotid Sinus Syndrome (CSS)
✓ Orthostatic
Cardiac Syncope

✓ Includes cardiac arrhythmias and SHD
✓ Often life-threatening
✓ May be warning of critical CV disease
  - Tachy and brady arrhythmias
  - Myocardial ischemia, aortic stenosis, pulmonary hypertension, aortic dissection
✓ Assess culprit arrhythmia or structural abnormality aggressively
✓ Initiate treatment promptly

Cardiac Syncope …. A Harbinger of Sudden Death

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

Syncope d/t Structural Cardiovascular Disease

- Acute MI/Ischemia
  - 2nd 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
Syncope d/t Structural Cardiovascular Disease

✓ Pulmonary embolism/ pulmonary HTN
  - 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
Syncope d/t 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
CASE: 27 year-old man presents to ER multiple times after falls resulting in trauma.
VT: Ablated and medicated.

CASE: 83 year-old woman with syncope due to bradycardia:
Pacemaker implanted.
Cardiac Rhythms During Unexplained Syncope

Arrhythmia 21% (13-32%)

Bradycardia 15% (11-21%)

Tachycardia 6% (2-11%)

Other 11%

No Recurrence 36% (31-48%)

Normal Sinus Rhythm 31% (17-44%)
Long QT Syndromes

✓ Mechanism
  - Abnormalities of sodium and/or potassium channels
  - Susceptibility to polymorphic VT (Torsade de pointes)

✓ Prevalence
  - Drug-induced forms – Common
  - Genetic forms – Relatively rare, but increasingly being recognized
  - “Concealed” forms:
    - May be common
    - Provide basis for drug-induced torsade

Syncope: Torsade de Pointes
Drug-Induced QT Prolongation

✓ Antiarrhythmics
  - Class IA ...Quinidine, Procainamide, Disopyramide
  - Class III...Sotalol, Amiodarone
✓ Psychoactive Agents
  - Phenothiazines, Amitriptyline, Imipramine, Ziprasidone
✓ Antibiotics
  - Erythromycin, Pentamidine, Fluconazole, Ciprofloxacin and its relatives
✓ Nonsedating antihistamines
  - Terfenadine*, Astemizole
✓ Others
  - Cisapride*, Droperidol, Haloperidol

...List is continuously being updated
Treatment of Long QT

✓ Suspicion and recognition are critical
✓ Emergency treatment
  • Intravenous magnesium
  • Pacing to overcome bradycardia or pauses
  • Isoproterenol to increase heart rate and shorten repolarization
  • ICD if prior SCA or strong family history
  • If drug induced:
    • Reverse bradycardia
    • Withdraw drug
    • Avoid ALL long-QT provoking agents
  • If genetic:
    • Avoid ALL long-QT provoking agents
✓ For more information visit www.longqt.org
Treatment of Syncope Due to Bradyarrhythmia

✓ Class I indication for pacing using dual chamber system wherever possible

✓ Ventricular pacing in atrial fibrillation with slow ventricular response
Treatment of Syncope Due to Tachyarrhythmia

✓ Atrial tachyarrhythmia
  - AVRT due to accessory pathway – Ablate pathway
  - AVNRT – Ablate AV nodal slow pathway
  - Atrial fib – Pacing, linear/ focal ablation for paroxysmal AF
  - Atrial flutter – Ablate the IVC-TV isthmus of the re-entrant circuit for ‘typical’ flutter

✓ Ventricular tachyarrhythmia
  - Ventricular tachycardia – ICD or ablation where appropriate
  - Torsade de pointes – Withdraw offending drug or implant ICD

✓ Drug therapy may be an alternative in many cases
Neurally-Mediated Reflex Syncope

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

Pathophysiology

Autonomic Nervous System
✓ 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
VVS
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
✓ In general:
  - VVS patients younger than CSS patients
  - Ages range from adolescence to older adults (median 43 years)
• 35% of patients report syncope recurrence during follow-up ≤3 years\(^1\)

• Positive HUT with >6 lifetime syncope episodes: recurrence risk >50% over 2 years\(^2\)

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VVS Diagnosis

✓ History and physical exam, ECG and BP
✓ Head-Up Tilt (HUT) – Protocol:
  - Fast > 2 hours
  - ECG and continuous blood pressure, supine, and upright
  - Tilt to 70°, 20 minutes
  - Isoproterenol/ Nitroglycerin if necessary
  - End point – Loss of consciousness

## 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
✓ Objectives
- Enhance orthostatic tolerance
- Diminish excessive autonomic reflex activity
- Reduce syncope susceptibility/ recurrences

✓ Technique
- Prescribed periods of upright posture against a wall
- Start with 3-5 min BID
- Increase by 5 min each week until a duration of 30 min is achieved

VVS Tilt Training: Clinical Outcomes

✓ Treatment of recurrent VVS
✓ Reybrouck, et al.*: Long-term study
  • 38 patients performed home tilt training
  • After a period of regular tilt training, 82% remained free of syncope during the follow-up period
  • However, at the 43-month follow-up, 29 patients had abandoned the therapy
  • Conclusion: The abnormal autonomic reflex activity of VVS can be remedied. Compliance may be an issue.

VVS
Tilt Training: Clinical Outcomes

✓ Foglia-Manzillo, et al.*: Short-term study

- 68 patients
  - 35 tilt training
  - 33 no treatment (control)

- Tilt table test conducted after 3 weeks
- (59%) 19 of tilt trained and 18 (60%) of controls had a positive test
- Tilt training was not effective in reducing tilt testing positivity rate
- Poor compliance in the majority of patients with recurrent VVS

VVS Pharmacologic Treatment

✓ Fludrocortisone
✓ Beta-adrenergic blockers
  • Clinical evidence suggests minimal benefit¹
✓ SSRI (Selective Serotonin Re-Uptake Inhibitor)
  • 1 small controlled trial²
✓ Vasoconstrictors
  • 1 negative controlled trial (etilefrine)³
  • 2 positive controlled trials (midodrine)⁴,⁵

²Di Girolamo E, et al. JACC. 1999; 33:1227-1230
Midodrine for VVS

The Role of Pacing as Therapy for Syncope

✓ VVS with +HUT and cardioinhibitory response: Class IIb indication for pacing

✓ Three randomized, prospective trials reported benefits of pacing in select VVS patients:
  - VPS I¹
  - VASIS²
  - SYDIT³

✓ Subsequent study results less clear
  - VPS II⁴
  - Synpace⁵
  - INVASY⁶

¹Connolly SJ. J Am Coll Cardiol. 1999;33:16-20
³Ammirati F. Circ. 2001;104:52-57
⁴Connolly S. JAMA. 2003;289:2224-2229
⁵Giada F. PACE. 2003;26:1016 (abstract)
Objective: To evaluate pacemaker therapy for severe recurrent vasovagal syncope
Randomized, prospective, single center
N=54 patients
- 27 DDD pacemaker with rate drop response
- 27 No pacemaker
Inclusion: Vasodepressor response
Primary outcome: First recurrence of syncope
Results:
- (22%) 6 with PM had recurrence vs. 19 (70%) without PM
- 84% RRR (p=0.000022)
Results: 50% with pacing ON had recurrence vs. 38% with pacing OFF
not statistically significant

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

Sensory nerve endings in the carotid sinus walls respond to deformation.

Increased afferent signals to the brain stem.

Reflex increase in efferent vagal activity.

Decrease of sympathetic tone.

BRADYCARDIA AND VASODILATATION
Falls: Incidence, Recurrence, CSH*

- Incidence > Age 65
- Recurrence
- CSH* Fallers > Age 50 in ER

*Carotid Sinus Hypersensitivity

1. 50%
2. 23%
1. 30%

2. Richardson D, et al. PACE. 1997;20:820
Orthostatic Hypotension
Etiology

✓ 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)
Diagnostic Testing in Hospital Strongly Recommended!

- Suspected/known ‘significant’ heart disease
- ECG abnormalities suggesting potential life-threatening arrhythmia
- Family history of premature sudden death
- Syncope during exercise
- Severe injury or accident

Thank You!