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**Learning Objectives:**

1. Define syncope and distinguish it from other causes for loss of consciousness
2. Describe the pathophysiology that differentiates between the 3 classifications of syncope
3. Select appropriate diagnostic tests based on features of history and exam to evaluate a patient with syncope
4. Identify high risk features that warrant inpatient evaluation in patients presenting with syncope
5. *Bonus*: Initiate management and indications for expert consultation for patients presenting syncope

**Teaching Instructions:**

Plan to spend at least 30 minutes preparing for this talk by using the Interactive Board and clicking through the graphics to become familiar with the order of the content that appears. Print out copies of the Learner’s handout so learners can take notes as you review the definition, pathophysiology, and evaluation of each type of syncope.

**Anticipated time to deliver the talk is 20 min without cases. The cases may take an additional 10-15 min.**

The talk can be presented in two ways:
1. Project the “Interactive Board” OR
2. Reproduce your own drawing of the presentation on a whiteboard.

Begin by reviewing the objectives for the session. We recommend progressing in order, though this teaching material gives you the flexibility of doing more focused teaching (e.g., skipping pathophysiology). All clickable buttons/elements are indicated by a cursor icon. Each button can act as a prompt to engage your learners.

**Objective 1: Define syncope and differentiate it from other causes for loss of consciousness (*Definition*)**

*Ask your learners to define syncope and click on “what is syncope” to reveal the answer.*

Syncope is an abrupt transient loss of consciousness, presumed from cerebral hypoperfusion, followed by rapid and spontaneous recovery.1,2 Syncope is just one diagnosis within a very broad group of disorders that cause “transient loss of consciousness” (TLOC). TLOC is characterized by 1. short duration 2. abnormal motor control 3. loss of responsiveness, and 4. amnesia for the period of LOC.2

*Ask your learners “what are some syncope mimics?” and click to reveal 3 different case scenarios. Read through each scenario and have learners guess the most likely diagnosis.*

Non-syncope causes of TLOC may include seizures, metabolic disorders (hypoglycemia, hypoxia), intoxication, concussion/ trauma, transient ischemic attacks (TIA)/ strokes, or psychogenic causes. The 3 most common “mimickers” are hypoglycemia, seizures, and TIAs/ strokes.

* *Seizure* – syncope can sometimes manifest with convulsive movements (such as myoclonus) which can be confused for an epileptic episode. Seizures can be distinguished from syncope with prolonged convulsions and marked post-ictal confusion, which are rare in syncope. Loss of bowel and bladder function or tongue biting also suggest seizure.1
* *Vertebrobasilar TIA/ stroke* – posterior circulation strokes can be associated with LOC, however, this is accompanied by focal neurologic signs and symptoms such as new onset vertigo or dysarthria.
* *Hypoglycemia* – typically, hypoglycemia generally causes impaired consciousness rather than total LOC. The duration of LOC in all metabolic causes and intoxication is generally much longer than in TLOC and spontaneous recovery does not usually occur without intervention.

**Pathophysiology review (Optional):** *The following section is a review of basic pathophysiology. The authors believe this baseline knowledge is necessary to understanding the mechanisms of different types of syncope. This section takes ~ 5 min to review.*

Cerebral Perfusion Pressure (CPP)

*Click on each of the prompts to reveal the answer.*

* Syncope is caused by decrease in global cerebral perfusion. A sudden drop in cerebral blood flow for 6-8 seconds can lead to LOC.
* Cerebral perfusion pressure (CPP) is determined by mean arterial pressure (MAP) and intracranial pressure (ICP).
* MAP is determined by cardiac output (CO) and systemic vascular resistance (SVR).
* Cardiac output, in turn, is determined by heart rate and stroke volume.
* Stroke volume is impacted by preload, afterload (SVR), and contractility.

Baroreceptor reflex

Discuss the normal pathophysiology of what happens with positional change. A derangement in any part of this pathway can lead to syncope.

1. Blood pools in the lower extremities, which decreases preload and cardiac output.
2. The decrease in cardiac output results in a decrease in MAP and thus, CPP.
3. Carotid baroreceptors sense a decrease in MAP and alter sympathetic and parasympathetic system response.
4. Increase sympathetic tone results in an increase in cardiac output SVR that ultimately help maintain a stable cerebral perfusion pressure.

**Objective 2: Describe the pathophysiology that differentiates between the 3 classifications of syncope** **(*Classification*)**

*Use the left-hand table of contents to highlight the different classifications of syncope. Click on each page to learn more about the definition, pathophysiology, and causes of syncope.*

There are 3 main classifications/ mechanisms of syncope:

1. Orthostatic hypotension (OH)
2. Reflex (or neurally mediated) syncope
3. Cardiac syncope

Concurrent medications, hypovolemia, alcohol use or pulmonary disease will make all forms of syncope more likely to occur, though typically impact OH and reflex syncope most significantly.2

Orthostatic Hypotension

**Orthostatic hypotension (OH)** occurs when there is an *insufficient* autonomic response. It is defined as:

* Drop in SBP ≥ 20
* Drop in DBP ≥10
* Drop in SBP <90 with symptoms (note this particular criterion is included in the ESC syncope guidelines but NOT the ACC/AHA guidelines)1,2,3

Recall that with position change, blood first pools in the lower extremities resulting in a drop in preload which subsequently triggers several compensatory responses. An insufficient response in any of the part of the baroreceptor response pathway will lead to orthostatic hypotension and syncope. *As you click through each of the mechanisms, highlight the pathophysiology via timed animations.*

Table 1: Mechanisms of Orthostatic Hypotension

|  |  |  |
| --- | --- | --- |
| **Mechanism of OH** | **Pathophysiology** | **Differential** |
| **Insufficient sympathetic tone** | The furthest upstream are the neurologic pathways that regulate sympathetic tone, which if unable to respond appropriately will affect all downstream compensatory mechanisms. Insufficient sympathetic tone results in a ↓ CO, HR, SVR → ↓ MAP → ↓ CPP.  | Also called “neurogenic OH”Primary autonomic failure * Pure autonomic failure
* Neurodegenerative diseases (multiple system atrophy, Parkinson’s disease)

Secondary autonomic failure* Diabetes
* Amyloidosis
* Paraneoplastic syndromes
* Spinal cord injury
 |
| **Insufficient SVR response** | Insufficient compensatory increase in SVR despite adequate sympathetic tone → ↓ MAP → ↓ CPP. | * Most commonly due to drugs (vasodilators, antidepressants). Drug-induced OH is the most common cause of OH.
* Adrenal insufficiency
 |
| **Insufficient HR response** | Insufficient compensatory increase in HR despite adequate sympathetic tone → ↓ CO → ↓ MAP → ↓ CPP. | Drugs (calcium channel blockers, beta-blockers). Drug-induced OH is the most common cause of OH. |
| **Insufficient preload** **(volume depletion)** | Insufficient preload → ↓ SV → ↓ CO → ↓ MAP → ↓ CPP. | * Volume loss (diarrhea, vomiting)
* Diuretics
* Hemorrhage
* Hypotension may be exacerbated by venous pooling:
* During exercise
* After meals
* After prolonged bedrest
 |

Information from 2018 ESC Guidelines (2).

Reflex Syncope

*Engage your learners to define reflex syncope and discuss common causes.*

In contrast to OH, **reflex syncope** occurs when there is an *inappropriate* autonomic response to a physiologic stimulus or trigger. The main causes are: 2

* Vasovagal syncope
	+ Orthostatic: prolonged standing
	+ Emotional: triggered by fear, pain, blood phobia, instrumentation
* Situational syncope – triggered by micturition, defecation, cough/sneezing, post exercise
* Carotid sinus hypersensitivity – head rotation or pressure on carotid sinus leads to inappropriate activation of sympathetic and parasympathetic nervous systems

There are two main subtypes of reflex syncope – cardioinhibitory and vasodepressive – which describe the primary hemodynamic pattern.2

* Cardioinhibitory – Bradycardia predominates. An increase in vagal tone (parasympathetic tone) → ↓ HR → ↓ CO → ↓ MAP → ↓ CPP
* Vasodepressive – Low SVR predominates. A decrease in sympathetic tone → ↓ HR, SV, CO, SVR → ↓ MAP → ↓ CPP
* It is important to note that in an actual clinical setting, patients can and often do present with a mixed subtype in which vasodilation and bradycardia occur together.

Cardiac Syncope

**Cardiac syncope** occurs because of low cardiac output leading to low MAP and consequently, CPP. Factors that impact cardiac output include HR, preload, afterload (SVR) and contractility. This talk classifies causes of cardiac syncope into these 4 primary mechanisms in order to illustrate pathophysiology. However, cardiac causes can be classified as arrhythmogenic (bradycardia or tachycardia), due to structural heart disease, or due to cardiopulmonary and great vessel pathology.2

Table 2: Mechanisms of Cardiac Syncope

|  |  |  |
| --- | --- | --- |
| **Mechanism of Cardiac Syncope** | **Pathophysiology** | **Differential** |
| **Increased afterload** | Certain structural cardiac abnormalities can result in increased afterload (SVR) → ↓ CO → ↓ MAP → ↓ CPP | * Valvular heart disease (aortic stenosis, mitral stenosis, and pulmonic stenosis)2
* Hypertrophic cardiomyopathy
 |
| **Low contractility** | Decreased contractility occurs in the setting of structural heart disease or arrythmias → ↓ CO → ↓ MAP → ↓ CPP | * Acute myocardial infarction or ischemia4
* Arrhythmias (e.g., ventricular tachycardia)
 |
| **Low HR** | Decreased HR → ↓ CO → ↓ MAP → ↓ CPP | * Bradyarrhythmia – AV block, sinus node dysfunction
* Pacemaker malfunction
 |
| **Insufficient preload**  | Insufficient left ventricular preload can occur in the setting of structural cardiopulmonary disease, or arrythmias | * PE, pulmonary hypertension
* Pericardial disease (tamponade, constrictive pericarditis)
 |

*Bonus*: A 2016 study (n=560) by Prandoni, et al. published in NEJM evaluated the prevalence of PE in patients hospitalized with syncope and found that the prevalence of PE was 17.3% in patients admitted with first episode of syncope and 3.7% in patients discharged from the ED with syncope. However, subsequent studies have shown much lower incidences.5 A 2018 study of >1.5 million patients from 4 countries found that the incidence of PE was less than 1% of all patients with syncope and in less than 3% of hospitalized patients with syncope. PE, overall, is considered a relatively uncommon cause of syncope.6

**Objective 3: Select appropriate diagnostic tests based on features of history and exam to evaluate a patient with syncope (*Evaluation – History, Testing*)**

Evaluation - History

Clinicians can distinguish syncope from TLOC in ~ 60% of cases by using detailed clinical history and physical exam.2 Key information to elicit are age and medical history (who), situation during syncopal event (where/ how), and prodromal symptoms (prodrome).

Table 3: Historical Elements of Different Causes of Syncope

|  |  |  |  |
| --- | --- | --- | --- |
|  | **OH** | **Reflex** | **Cardiac** |
| **Who** | * Generally older patients with comorbidities
* History of autonomic neuropathy or parkinsonism
 | * Can occur at all ages
* Generally healthy
* History of recurrent syncope history, usually starting <40 yo
 | * Family history of sudden death at young age
* History of structural heart disease or CAD
 |
| **Where/How** | * Occurs while or after standing, prolonged standing
* Post-prandial hypotension
* Occurs after start or change in doses of vasodepressive drugs or diuretics
 | * After prolonged standing
* During meal
* Triggered by cough, defecation, micturition
* Being in crowded or hot places
* With head rotation or carotid sinus pressure (shaving, tight collars)
 | * While supine/sitting, at rest (arrhythmogenic)
* During exertion (structural)
 |
| **Prodrome** |  | * Pallor, sweating/ diaphoresis, nausea
 | * Sudden onset palpations
* May be associated with new onset chest or abdominal pain, dyspnea
 |

Disposition of patients is determined by the presence of high-risk features, which are suggestive of cardiac syncope. Click on “what are high risk features” to reveal all the criteria. Click on “What are high risk features” to reveal features that warrant further inpatient evaluation. Orthostatic hypotension and reflex syncope generally do not require further evaluation. Differentiating cardiac syncope from other causes is critically important.

Evaluation – Testing

All patients with syncope should undergo a comprehensive physical exam with a focus on cardiac exam, orthostatic vital signs, and an ECG1. An ECG will identify high risk features that warrant further evaluation.

*Click on “what testing is not routinely helpful?”* There is low utility of routine head imaging (CT or MRI) in the absence of new neurologic findings or head injury, routine EEG in the absence of history suggestive of seizure, or routine carotid artery imaging1. Significant stenosis or occlusion of bilateral carotids and/or vertebral arteries would be necessary to lead to syncope and typically does not occur in the absence of other neurologic symptoms.

*Click on “What are high risk features” to reveal vital sign abnormalities and ECG abnormalities that warrant admission and further evaluation.* The goal of evaluation is to identify patietns with high risk features concerning cardiac syncope who would benefit from inpatient monitoring and evaluation. Table 4 summarizes high and low risk features based on history and initial evaluation.

Patients with low risk features only do not require admission, patients with high risk features should be admitted for further evaluation. Patients with neither high risk or low risk features should be considered for observation in the hospital or ED.2

Table 4: High and Low Risk Features2

|  |  |  |
| --- | --- | --- |
|  | **Low Risk** | **High Risk** |
| **PMH** | * Long history of recurrent syncope with low-risk features
* No structural heart disease
 | * Family history of sudden cardiac death
* Severe structural heart disease or prior CAD
 |
| **Event history** | * Prodrome typical of reflex syncope (light-headedness, diaphoresis, nausea)
* Clear trigger (unpleasant sight, pain, cough, micturition/defecation, head turn, shaving, collars)
* Occurs after prolonged standing or crowded/hot places
 | * New onset chest pain, shortness of breath
* Occurs during exertion or when supine
* Sudden onset palpitations
* High risk features if associated with structural heart disease (or abnormal ECG)
* Short or absent prodrome (<10 s)
* Syncope in sitting position
 |
| **Physical Exam** | Normal | * SBP <90
* Signs of GIB on presentation
* HR <40 in awake state
* Undiagnosed systolic murmur
 |
| **ECG findings** | Normal | * Acute ischemia
* AV block
* Major: 2nd degree type 2 and 3rd degree AV block
* Minor: 1st degree with long PR or 2nd degree type 1
* Bradycardia
* Major: HR <40 (either slow AF or sinus bradycardia)
* Minor: HR 40-50
* Sinus pauses > 3s while awake
* BBB, ventricular hypertrophy or Q waves
* Sustained or nonsustained VT
* Pre-excited QRS complex
* ICD/ PM malfunction
* Short or very long QTc (<340 or >460 ms)
* Brugada patterns
* Arrhythmogenic right ventricular cardiomyopathy
 |

*Click on “what additional testing can help differentiate causes of syncope?” Click on each category to reveal targeted/ specialized testing for each type of syncope.* Further diagnostic testing should be highly individualized based on the suspected cause. Not all patients with syncope necessary require labs or further cardiac testing1.

* *Orthostatic syncope* – this may be due to dehydration/ volume depletion or new medication initiation or autonomic dysfunction (neurogenic OH). BMP and CBC may be considered to help identify causes of the above (e.g., AKI may suggest volume depletion, anemia may suggest occult GI bleed).
	+ Patients with neurogenic OH often have associated weakness, fatigue, cognitive decline, and visual changes. These symptoms may be provoked or exacerbated with exertion. Patients with suspected neurogenic cause of OH should undergo further evaluation of autonomic dysfunction1.
	+ Additional physical exam maneuvers such as Valsalva can help aid in diagnosis of autonomic failure. Typically, Valsalva is associated with HR and BP increase. Absence of these hemodynamic changes is suggestive of autonomic dysfunction. The degree of hypotension with Valsalva often correlates with degree of autonomic dysfunction and symptoms.2
	+ Patients with suspected autonomic dysfunction could be referred to a cardiologist or neurologist for further evaluation of autonomic dysfunction.1
	+ *Bonus*: **Tilt table testing** (TTT) is generally associated with the diagnosis of reflex syncope but may be considered for assessment of neurogenic OH/ autonomic failure and for reproduction of delayed OH. The goal is to reproduce symptoms and characteristic hemodynamic profile.1,2
* *Reflex syncope –* generally, this is diagnosed based on history.
	+ **Carotid sinus massage** – carotid massage resulting in ventricular pause lasting >3s, AV block, or a drop in SBP >50 mmHg is suggestive of carotid sinus hypersensitivity.1,2 This is typically performed in patients >40 years old with history concerning for reflex syncope. The R and L carotid sinus are sequentially massaged in supine and upright position for 5 seconds each time. The primary complication is TIA or stroke (from dislodging carotid plaque) and is contraindicated in anyone with a carotid bruit, known carotid stenosis >70%, or recent TIA or stroke in the past 3 months1. The reported incidence is low 0.24%, but given this complication, the authors of this paper do not routinely perform carotid sinus massage.2
	+ **TTT** can be used to confirm diagnosis if initial history is unclear1,2. It can help distinguish syncope from falls or epilepsy. It can also help demonstrate a patient’s susceptibility to reflex syncope, especially vasodepressive type. Positive cardioinhibitory response predicts asystolic spontaneous syncope which has implications for treatment (specifically need for pacemaker).2
* *Cardiac* *syncope* – high risk historical or initial ECG findings suggestive of cardiac syncope should undergo further evaluation in the hospital. A cardiologist should be consulted when there is suspicion of cardiac syncope.
	+ **Cardiac monitoring** – continuous cardiac monitoring (e.g., telemetry monitoring) is indicated to help identify arrhythmogenic causes of syncope. It can be hard to make the diagnosis during the initial evaluation, especially when an arrhythmia is paroxysmal. In these cases, we often recommend ambulatory EKG monitoring. The most common devices used are listed. The choice and type of monitor should be based on frequency and nature of syncope events.

Table 5: Cardiac monitors1

|  |  |  |  |
| --- | --- | --- | --- |
| **Type of monitor** | **Duration of recording** | **Details** | **Patient indications** |
| Holter monitor | 24-72h | Continuous recording | Frequent symptoms likely to recur in 24-72h |
| Event (loop) monitor | 2-6 weeks | Patient activated for events.  | Moderate frequency + prodromal symptoms. |
| Patch monitor | 2 weeks | Continuously records with patient trigger ability.Less bulky and more comfortableOnly offers 1 lead recording | Moderate frequency symptoms + prodromal symptoms. |
| Implantable loop recorder | Years | Requires surgery, subcutaneously implanted.Triggered by patient/family  | Infrequent, unexplained syncope  |

* + Cardiac biomarkers – troponin and BNP are of unclear utility but may be considered to help identify patients who are suspected of having a cardiac cause of syncope.1,2
	+ **Echocardiography** (TTE) – should be pursued in patients with suspected structural heart disease. It can help identify aortic stenosis, hypertrophic cardiomyopathy or LV dysfunction.1,2
	+ Other imaging modalities such as CT or MRI could be considered in select patients (e.g., suspected sarcoidosis or PE).1
	+ Exercise stress testing should be considered in patients with exertional syncope.1

**Objective 5: Initiate management and indications for expert consultation for patients presenting syncope (*Management*)**

*Ask learners what the first line treatment and second line treatments are for each type of syncope. Click to reveal the answer.*

* *OH syncope* - First line intervention is fluid resuscitation, adjustment of culprit meds, and behavioral modifications (standing up slowly, increasing salt intake, compression garments).
	+ Counter pressure maneuvers, which are isometric muscle contractions including leg crossing, limb or abdominal contraction, squatting could be employed as well.2
	+ When the underlying cause is due to autonomic dysfunction, fluid resuscitation is often only a temporizing measure; these types of patients may need long-term medications to help raise blood pressure such as midodrine and fludrocortisone.
* *Reflex syncope* – Counseling and reassurance should be offered to patients with vasovagal syncope.
	+ *Vasovagal syncope* - Treatment includes counter-pressure maneuvers, which is effective in patients who have long-lasting, recognizable prodromal symptoms. Midodrine, fludrocortisone, increase in salt and fluid intake may also be considered in patients with vasovagal syncope.1 Consider withdrawing medications that may cause hypotension.1 There is conflicting data, but some patients could be considered for SSRIs (fluoxetine or paroxetine) to help prevent syncope.1
		- Consider pacemaker in some patients, specifically if they have cardioinhibitory type on TTT and frequent and unpredictable syncope.1
		- TTT is not useful to monitor response to therapy.1
	+ *Carotid sinus syndrome* – pacemakers could be considered in some patients.2
* *Cardiac* syncope - The treatment for causes of cardiac syncope is highly specialized and dependent on the underlying etiology. These patients should be referred to cardiology for further management.

**Take Home Points:**

1. The pathophysiology (global cerebral hypoperfusion) is key in defining syncope and distinguishing syncope from other causes of transient loss of consciousness.
2. The 3 main types of syncope are reflex syncope, orthostatic hypotension, and cardiac syncope.
3. Patient factors (who), situation (where/how), prodrome, and medications are key elements in distinguishing between the 3 main types of syncope.
4. Every patient with syncope should get a good history, physical exam, vital signs, and EKG; outside of those things further diagnostics and certainly treatments should be highly individualized based on the suspected cause.

**References:**

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