CASE 1: NEURO-MEDIATED SYNCOPE

A 70-years-old male patient goes to the ER aftre a syncopal episode. Pacemaker rhythm at 60 bpm, blood pressure is 100/80 mmHg, blood sugar is 95mg. pH 7.41, PO_2 87 mmHg, CO_2 34 mmHg. Brain CT scan excludes an acute cerebrovascular accident.

What is the diagnostic-therapeutic pathway?

Data
- Normal HR (60-100 bpm), low BP (120/80 mmHg), normal glucose (fasting: 70-99), normal pH (7,35-7,45), normal O2 (80-100 mmHg), slightly decreased CO2 (35-45 mmHg).
- Normal brain CT → no cerebrovascular issues (CT is done to exclude lesions, not for the diagnosis)

Diagnosis
Multifactorial evaluation (also of frailty) and intervention are recommended in older patients because more than one possible cause for syncope and unexplained fall may be present. Cognitive assessment and physical performance tests are indicated in older patients with syncope or unexplained fall (if MMSE <24: CT scan).

*[1]**THEORY***
***Syncope** is the transient loss of consciousness LOC due to cerebral hypoperfusion. It has rapid onset, short duration and spontaneous, fast and complete recovery.*
[2]Il paziente è immobile e flaccido e solitamente ha estremità fredde, un polso debole, e un respiro superficiale. A volte si verificano brevi scatti muscolari involontari, simili a convulsioni. La maggior parte delle sincopi deriva da un'insufficienza del flusso cerebrale. Alcuni casi coinvolgono un flusso adeguato, ma con un insufficiente substrato cerebrale (ossigeno, glucosio, o entrambi).
La presincope è la sensazione di testa vuota e di imminente svenimento senza perdita di coscienza. Generalmente è classificata e trattata insieme alla sincope poiché le cause sono le stesse.

DD syncope with: epileptic seizures, psychogenic syncope and rare causes (as subarachnoid hemorhage, vertebrobasilar TIA) which have no cerebral hypoperfusion.

*Syncope is classified in (1) **neurally** mediated, 18%; (2) **orthostatic**, 11%; (3) **cardiac**, 17% and (4) **unknown**, 39%.*
1. *Neurally-mediated: includes (A) Vasovagal syncope: Main trigger is orthostatic stress (after standing for long), other triggers are strong emotions and physical pain. Typical in young. Prodromes: sweating, pallor, nausea, dizziness. (B) Situational syncope: triggered by the distension of hollow viscera, which activates afferent nerves inducing syncope. Caused for ex by cough, micturition, defecation, etc. (C) Carotid sinus (CS) syndrome: trigger is the pressure at the level of the carotid sinus, at the bifurcation of the common carotid, below the jaw angle. Normal response to CSM is a transient reduction of heart rate and/or AV conduction. Hypersensitive patients lower their SBP of 50mmHg. Typical over 60yo.*
2. *Orthostatic: is a dysfunction of the autonomic NS.*

[3]Ipotensione ortostatica (posturale) è un'eccessiva caduta della pressione arteriosa (caduta sistolica > 20 mmHg o diastolica > 10 mmHg), quando si assume la posizione eretta. Sintomi: debolezza, sensazione di testa vuota, vertigini, confusione o offuscamento della vista; entro 3min dall'assunzione della stazione eretta e scompaiono rapidamente stando distesi. Alcuni pazienti sperimentano cadute, sincope, o perfino raramente convulsioni generalizzate. L'ipotensione ortostatica è un sintomo di alterata regolazione della pressione arteriosa dovuta a varie condizioni, non a una patologia specifica: primary disease of ANS (parkinson), secondary diseases (Diabetic/alcoholic neuropathy), hypovolemia (hemorrhage), drugs (vasodilators, diuretics).

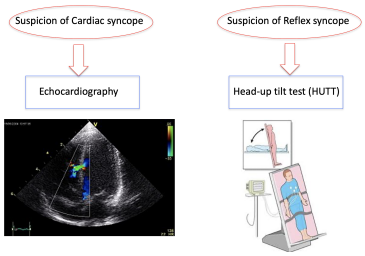
3. *Cardiac: may be due to bradyarrhythmias (AV block, sick sinus syndrome), tachyarrhythmias (VT/VF, long QT syndrome, brugada), structural heart diseases (aortic stenosis, hypertrophic cardiomyopathy), cerebrovascular disease (subclavian steal syndrome).*

[1] Slides cardiology syncope 2022
[2] https://www.msdmanuals.com/it-it/professionale/disturbi-dell-apparato-cardiovascolare/sintomatologia-delle-malattie-cardiovascolari/sincope
[3] https://www.msdmanuals.com/it-it/professionale/disturbi-dell-apparato-cardiovascolare/sintomatologia-delle-malattie-cardiovascolari/ipotensione-ortostatica?query=ipotensione%20ortostatica

Diagnosis: Anamnesis

- What kind of activity before syncope? Rest/exertion
- Any particular situation? During cough, defecation, micturition
- Any precipitating factor? Crowded place, orthostatic position for long time, fear of something, neck movement
- What happened before syncope? Nausea, vomiting, flushing
- What happened during syncope (if any wittness)? Seizures, skin colour
- What happened after syncope? Time of recovery
- Medical history? Known cv disease, familiarity for SCD, diabetes, neurologic disease

Diagnosis: 2°step



Treatment

ETIOLOGY based!!!

Aims:
1. Prevent recurrences
2. Improve quality of life

Orthostatic
- Volume expansion
- Stop hypotensive drugs
- Elastic compression
- Fludrocortisone(mineralcorticoid)
- Midodrine (a-agonist)

Carotid sinus hypersensitivity
- PMK

Reflex
- Avoid triggers
- Tilt training
- PMK

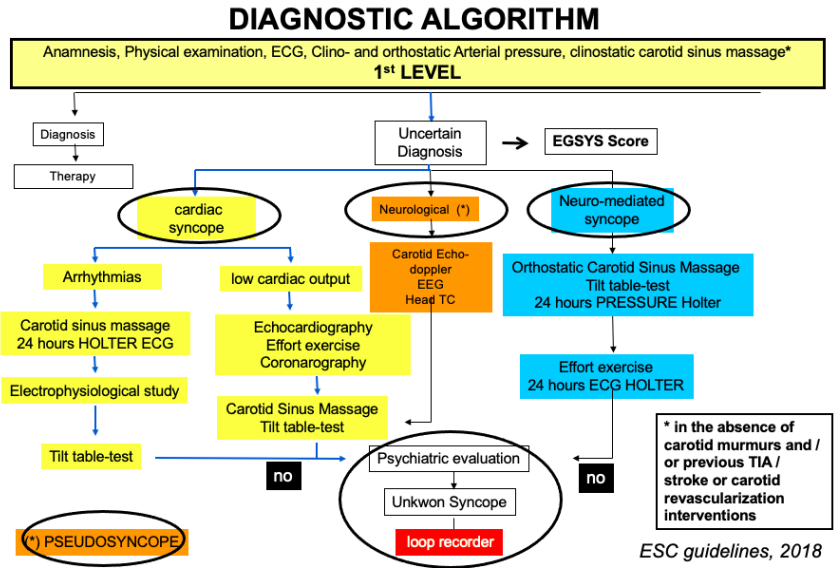
→ Physical examination + EKG. Assessment of HR and BP supine after 3 min of orthostatic position. Look for neurological or cardiovascular diseases.
Tilt test: The patient is bond to the bed (to avoid trauma) which from the supine position is tilted of 60-70° Blood pressure and EKG are registered during the whole exam.

Case
In this case, we suspect **neuro-mediated syncope** since it's the most common (66% of syncope events in the elderly) and innocent cause of syncope (caused by an overactivation of the parasympathetic system). Although, first of all, we have to exclude cardiac syncope (see algorithm) since it has a really poor prognosis and can be treated easily. It's fatal if it isn't treated.

Remarks

- All forms of syncope, but mostly reflex syncope and OH, are more likely to occur or are more severe when various factors are present: medication causing low BP (due to vasodilatation or hypovolaemia), alcohol use, volume depletion (haemorrhage, low fluid intake, diarrhoea, vomiting), pulmonary diseases causing reduction in brain oxygen supply, environmental factors (thermal stress).
- There are two main pathophysiological mechanisms in reflex syncope. "Vasodepression" refers to conditions in which insufficient sympathetic vasoconstriction results in hypotension.[1,2] "Cardioinhibition" is used when bradycardia or asystole predominates, reflecting a shift towards parasympathetic predominance. The haemodynamic pattern, i.e. cardioinhibitory, vasodepressive, or both, is independent of the trigger evoking reflex syncope. For example, micturition syncope and orthostatic VVS may equally well present as cardioinhibitory or as vasodepressor syncope
- The non-classical form of reflex syncope involves a heterogeneous group of patients. The term is used to describe reflex syncope that occurs with uncertain or apparently absent triggers and/or atypical presentation. The diagnosis of reflex syncope is probable when other causes of syncope are excluded (absence of structural heart disease) and/or symptoms are reproduced in the tilt test.[3] At present, this group also contains syncope associated with low adenosine plasma levels[4,5]
- The cardiovascular causes of orthostatic intolerance include classical OH, initial OH, delayed OH, POTS, and VVS, which in this context can be called orthostatic VVS.[6,7] Syndromes of orthostatic intolerance that may cause syncope are presented in *Web Practical Instruction section 2*.

BP = blood pressure; OH = orthostatic hypotension; POTS = postural orthostatic tachycardia syndrome; VVS = vasovagal syncope.



ESC guidelines, 2018

- Anamnesis:
  - Family history
  - History of cardiac D or diseases that cause ANS alterations (Parkinson, autonomic neuropathies).
  - HTN drugs (ACEi, BB, CCB, ARB'S → during summer, reduction of the dose or discontinuation should be considered) can trigger orthostatic hypotension, especially in polypharmacy.
  - Insulin (hypoglycemic shock is common in elderly but in this case, falls are more frequent than the loss of consciousness) → DD between syncopal and non-syncopal falls.
  - Event characteristics:

- *During an effort or supine position: suspect cardiogenic syncope*
- *Prolonged orthostatism: suspect neuro-mediated*
- *During standing or immediately after: suspect orthostatic hypotension*
- *Meal, defecation, cough, exercise: suspect situation syncope (neuro-mediated)*

- Association with: prodromal symptoms
  - *Pallor, sweating, nausea: suspect vasovagal syncope (neuro-mediated)*
  - *Tachycardia: suspect cardiogenic syncope*
- Association with jerks (seizure), neurological signs?
- Duration,
- Ask if someone witnessed: important in the elderly because history is often unreal, and a fall often hides the syncopal nature of the event
- How did the episode end? Postictal signs?
  - *1st question: was it a TLOC (transient loss of consciousness)?*
  - *2nd question: was it a syncope or something else?*

TLOC:
- *Traumatic,*
- *Not traumatic: syncope (brain hypoperfusion), epileptic seizures (excessive brain activity), psychogenic forms (conversion process), rare forms.*

• BP measurement:

Diagnostic of orthostatic hypotension if, in orthostatism, there is:
- *Reduction of SBP ≥ 20 mmHg or*
- *Reduction of DBP ≥ 10 mmHg or*
- *BP < 90 mmHg*

• Tilt-table test (enhanced with sublingual nitroglycerin)

↓ of preload in orthostatism → sympathetic activation → ↑ of HR and BP → parasympathetic activation.
We may have three different results from this test:

Type 1 – mixed	Both blood pressure (BP) and heart rate (HR) are reduced. BP reduction precedes HR reduction. HR decreases by >10%, but HR does not decrease to less than 40 beats/min (Fig. 1)
Type 2 – cardioinhibitory	Decrease in both BP and HR, and BP decrease precedes decrease in HR. Type 2A: minimum HR is less than 40 (Fig. 2), type 2B: there is asystole for 3 seconds or more (Fig. 3)
Type 3 – pure vasodepressor	BP is decreased but HR does not decrease more than 10% (Fig. 4)

- VASIS 1 (mixed response): ↓ BP and ↓ HR > 10% (≥40 bpm per > 10 sec)
- VASIS 2A (cardioinhibitory response): ↓ BP and ↓ HR with asystole ≤ 3 sec
- VASIS 2B (cardioinhibitory response): ↓ BP and ↓ HR with asystole > 3 sec = *cardiogenic*
- VASIS 3 (vasodepressive response): ↓BP and ↓HR ≤ 10%

Tilt-table test is easy and safe also in elderly.

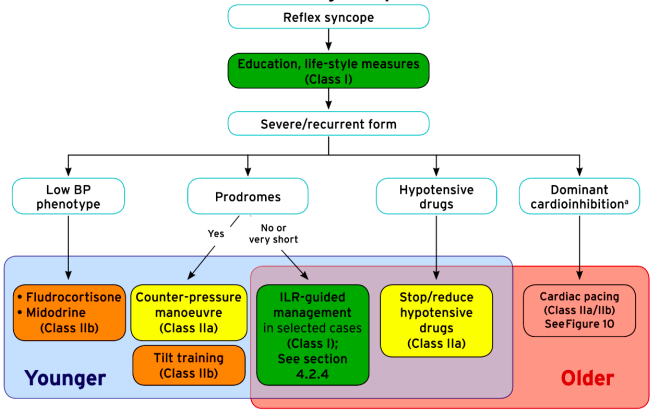
• Focus on pseudosyncope: caused by seizures and cerebrovascular events.
• Focus on psychiatric evaluation: particularly important in adult females.
• Focus on loop recorder: subcutaneously implanted ECG holter (it records for 4 years/4 years and a half), the problem is that it records only HR (not BP).

With a proper diagnosis, mortality decreases. Unexplained falls are the ones with the highest mortality.

Treatment

A person suffering from ‘‘shock’’ and hypotension should immediately be laid flat on the floor or horizontally to improve blood flow to the brain.

▪ Reflex and orthostatic syncope



Fludrocortisone is a mineralcorticoid (rises Na+ concentration and thus blood volume). Midorine is an α1-agonist, vasopressor. Physical counter pressure maneuvers (CPM) are movements that delay or prevent syncope by recruiting the skeletal muscle pump to augment cardiovascular control. Ex holding a rubber ball tight for as long as the symptoms disappear or holding tightly the two hands together and pulling them towards each other.

[4]Tilt training: prescrizione di periodi progressivamente prolungati di postura ortostatica.
*[5]The **implantable loop recorder (ILR)** is a subcutaneous electrocardiogram (ECG), a monitoring device used for diagnosis in patients with recurrent unexplained episodes of palpitations or syncope.*

Dietary advice: increase salt and water intake.
Compression stockings: to increase the preload.
Disopyramide: anti-arrhythmic drug, not frequently used. It can be used if arrhythmias + orthostatic syncope.

- Cardiac:
  - Severe aortic stenosis (the most frequent cause of low cardiac output in the elderly): surgery
  - Advanced AV block: bicameral pacemaker implantation
  - Ventricular tachycardia: cardiovertor pacemaker implantation

There is a high prevalence of short-term serious events in geriatric patients. High-risk features: structural heart disease, chronic diseases, syncope without prodromes, sinus bradycardia or sinoatrial block… These patients require early evaluation and treatment.

[4] https://www.gimsi.it/le-manovre/
[5] https://emedicine.medscape.com/article/1920236-overview