How to assess autonomic disorders without specific „autonomic“ equipment

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COI

- Honorarium/Royalties from publishers
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- Political bodies
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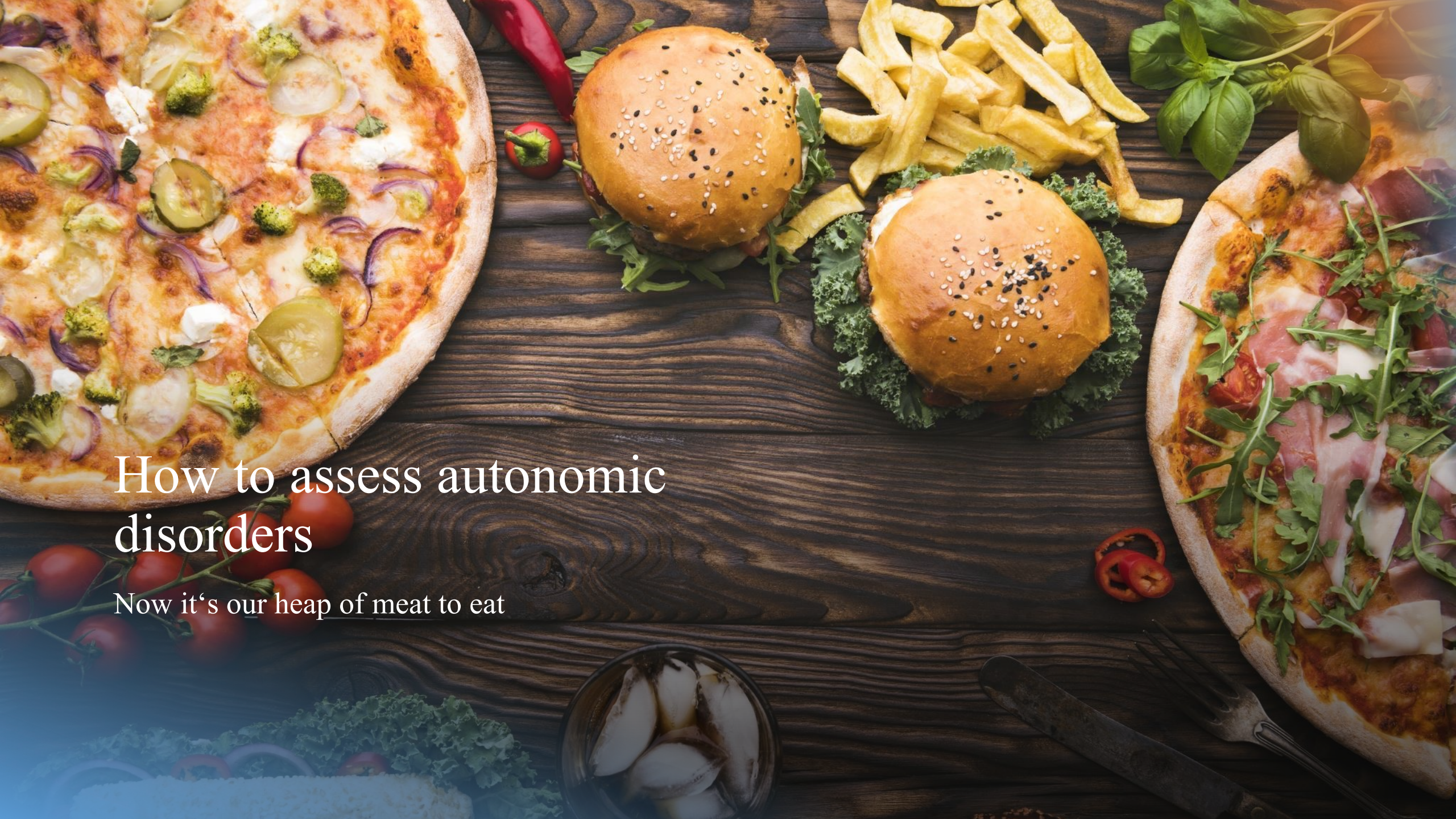
  - Austrian Neurological Society (executive board)
  - Austrian Autonomic Society – Otto Loewi Gesellschaft (executive board)
  - Austrian Alzheimer Society (executive board)

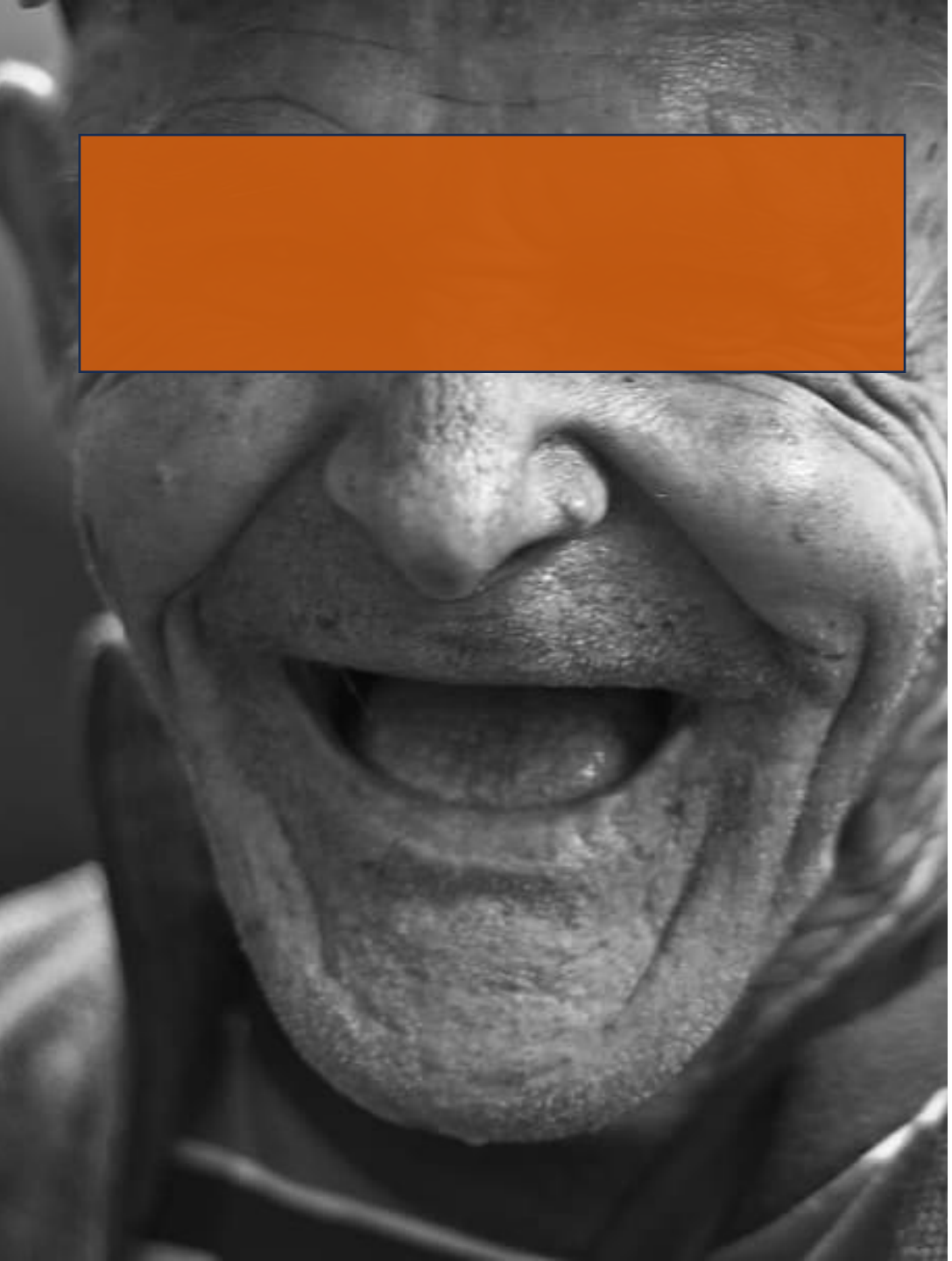


How to assess autonomic disorders

Now it‘s our heap of meat to eat

Objectives of this talk

- 2 cardinal questions to be asked in every patient
- Is it an autonomic dysfunction?
- Which differential diagnosis is likely (bedside +)?



Mr. Q

- Seen in the outpatients clinic
- I am 72 years old. I was quite lucky and was always healthy. Since two years I do have an issue. It started once every three months and now it is happening about once every two weeks. When I am on a walk or on the street and stand, eventually chat with someone I get... - well you know I get..., well you know, I feel - I don't know. I feel dizzy.
- I have lost consciousness several times in such a situation. But its not a big deal.
- Spouse: First this condition worried us but not more, but my husband does not go out anymore. He do not want to visit his friends. In fact he also does not want to visit the restaurant with me. He sits at home, and his mood gets anoying to me. … I have been present at most episodes. He starts to be a bit off, murmurs, and then is out of consciousness. .. Sometimes he leans over and it stabilizes.

Is it an autonomic dysfunction?

Or epilepsy? Or cardiogenic syncope?

Cain by Vidal, Jardin des Tuileries, Paris. Nan Palmero, commons.wikimedia.org, CC-BY-2.0

Orthostatic intolerance

Upright posture leads to symptoms

Transient loss of consciousness

Prodromi

- 2 groups
  - Cerebral and retinal hypoperfusion
  - Sympathetic and parasympathetic activity
- Prodromi are only reported if slow enough for
  - perception
  - memorizing
- Prodromi more likely in younger than older participants

Wieling W. et al., Brain, 2009

ARTICLE

Differentiating motor phenomena in tilt-induced syncope and convulsive seizures

Sharon Shmuely, MD, Prisca R. Bauer, MD, PhD, Erik W. van Zwet, PhD, J. Gert van Dijk, MD, PhD, and Roland D. Thijs, MD, PhD

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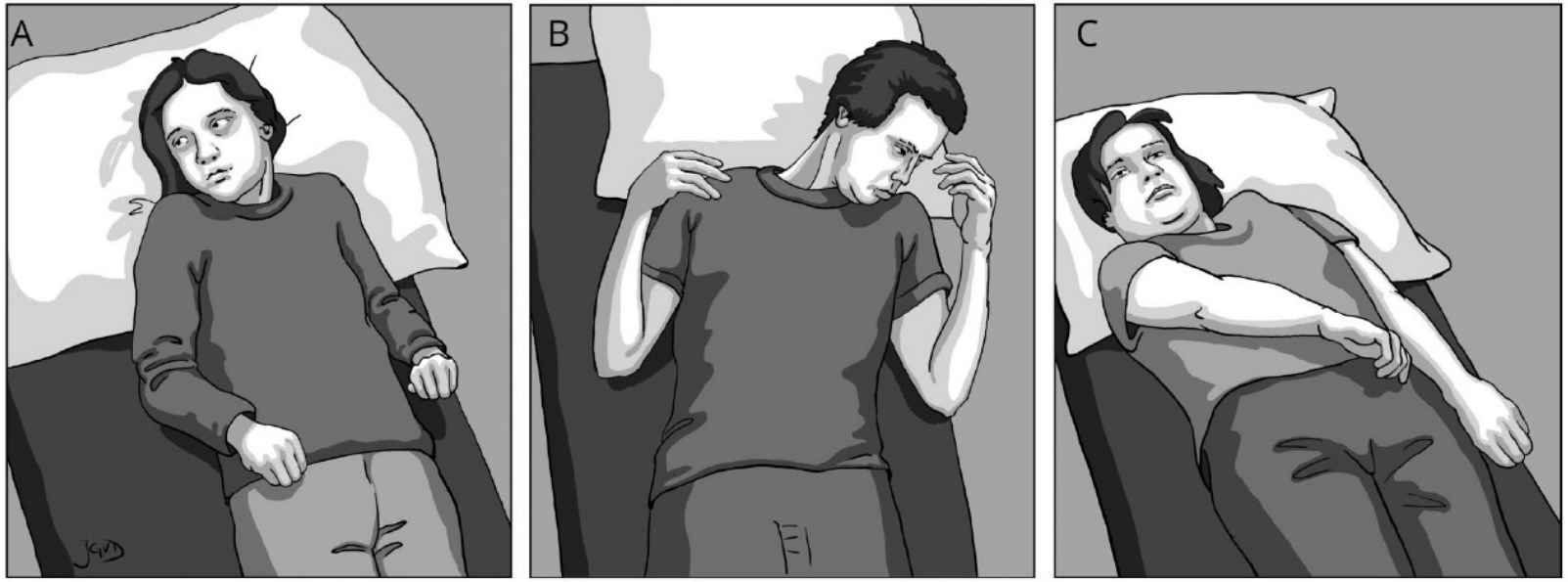


"10/20 rule"

Which differential diagnosis is likely (bedside +)?

Hemodynamic criteria

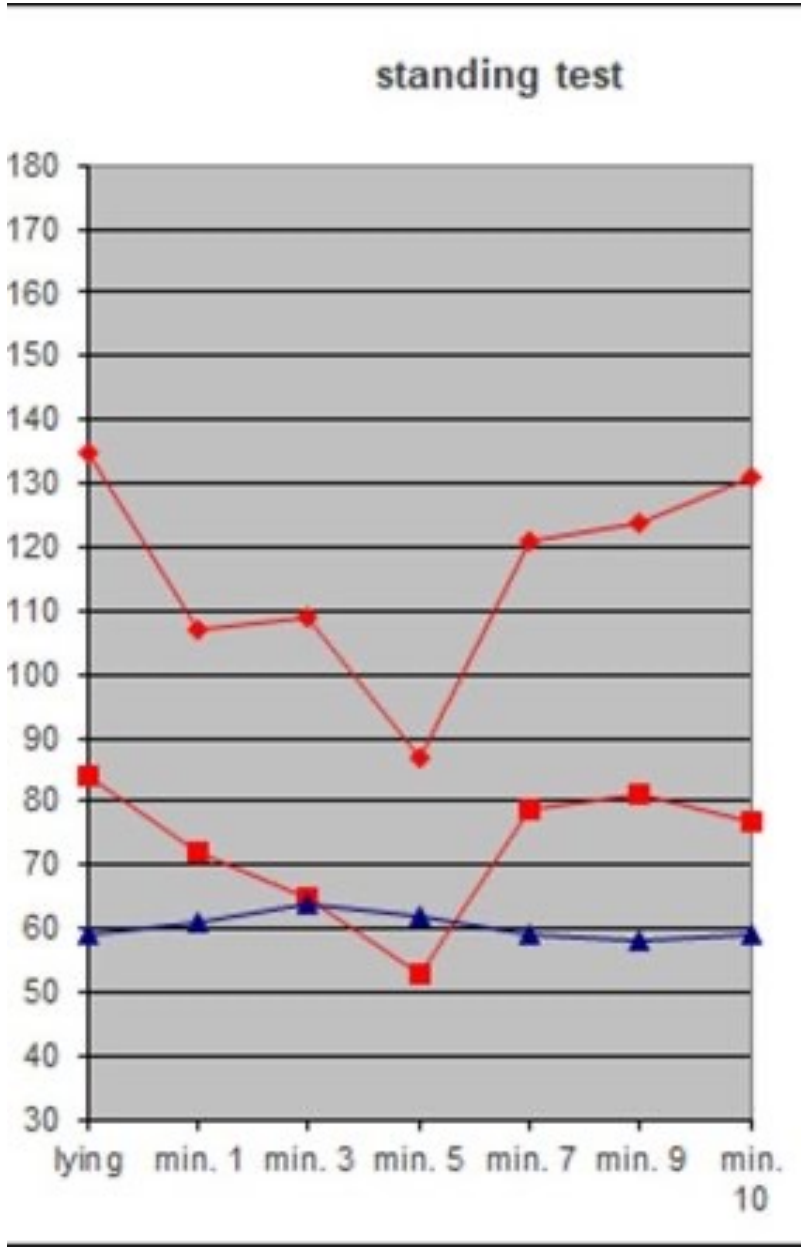
TTT/AST indication	Fall in SBP upon standing	Fall in DBP upon standing	Increase in HR upon standing	Timing
Initial OH	> 40 mmHg	> 20 mmHg	Not specified	Transient BP fall within 15 s upon standing
Classic OH[a,b]	≥ 20 mmHg[f]	≥ 10 mmHg	Not specified[c]	Sustained BP fall within 3 min standing
Delayed OH[a]	≥ 20 mmHg	≥ 10 mmHg	Not specified	Sustained BP fall > 3 min standing
POTS[d]	SBP fall not meeting OH criteria	DBP fall not meeting OH criteria	> 30 bpm[e] or > 120 bpm	Sustained HR increase within 10 min standing
Vasovagal presyncope	No formal criteria[g]	No formal criteria[g]	No formal criteria[g]	No formal criteria[g]
Delayed orthostatic BP recovery	Inability of SBP to recover to supine values within 30 s of standing. Standing SBP should be ≥ 20 mmHg lower than supine values but not meet criteria of classic or initial OH	Not meeting initial OH/ classic OH criteria	Not specified	BP fall within 30 s upon standing

AST active standing test, *classic OH* classical orthostatic hypotension, *DBP* diastolic blood pressure, *delayed OH* delayed orthostatic hypotension, *HR* heart rate, *initial OH* initial orthostatic hypotension, *POTS* postural orthostatic tachycardia syndrome, *SBP* systolic blood pressure, *TTT* tilt table test

Clinical Autonomic Research (2021) 31:369–38

Mr. Q

Standing test



First thing to look up

- Personal hit list
  1. Diuretics
  2. Antihypertensive drugs including Beta-Blocker
  3. Nitrates

nOH diagnosis at bed side

- <0,49 beats/minute per mmHg blood pressure decrease

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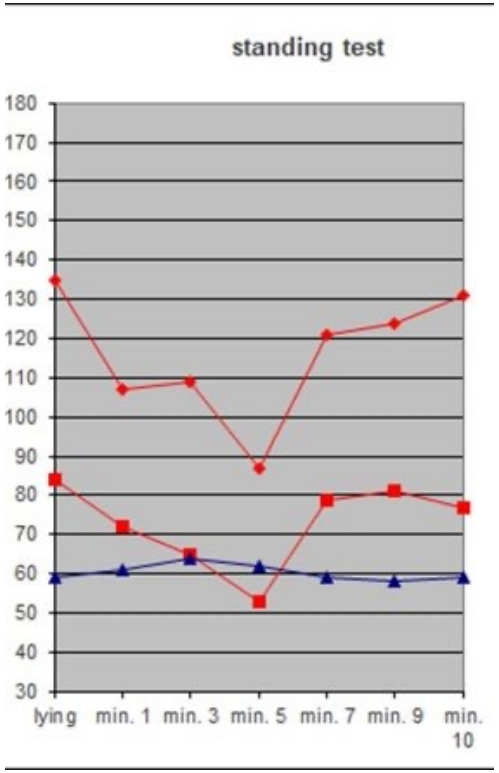
A Validated Test for Neurogenic Orthostatic Hypotension at the Bedside

Lucy Norcliffe-Kaufmann, PhD, **Jose-Alberto Palma, MD, PhD**, and **Horacio Kaufmann, MD**
Department of Neurology, Dysautonomia Center, New York University School of Medicine, New York, NY



Heart rate
59 :-> 64
Blood pressure
135 :-> 109

64-59= 5
135-109= 26

5/26= 0,19

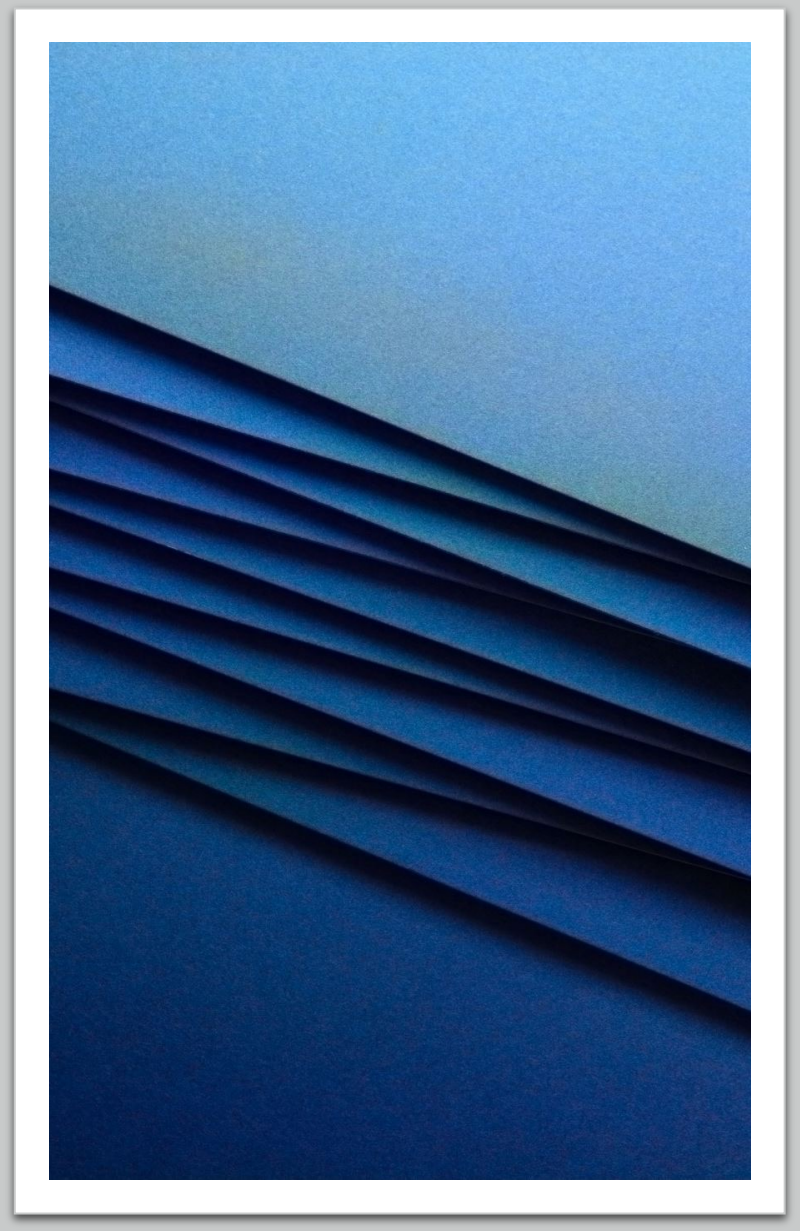
Primary neurogenic Orthostatic Hypotension (nOH)

α-synucleinopathies:

- Parkinsonian syndromes
- Dementia with lewy bodies
- Pure autonomic failure (PAF)

τ-pathies :

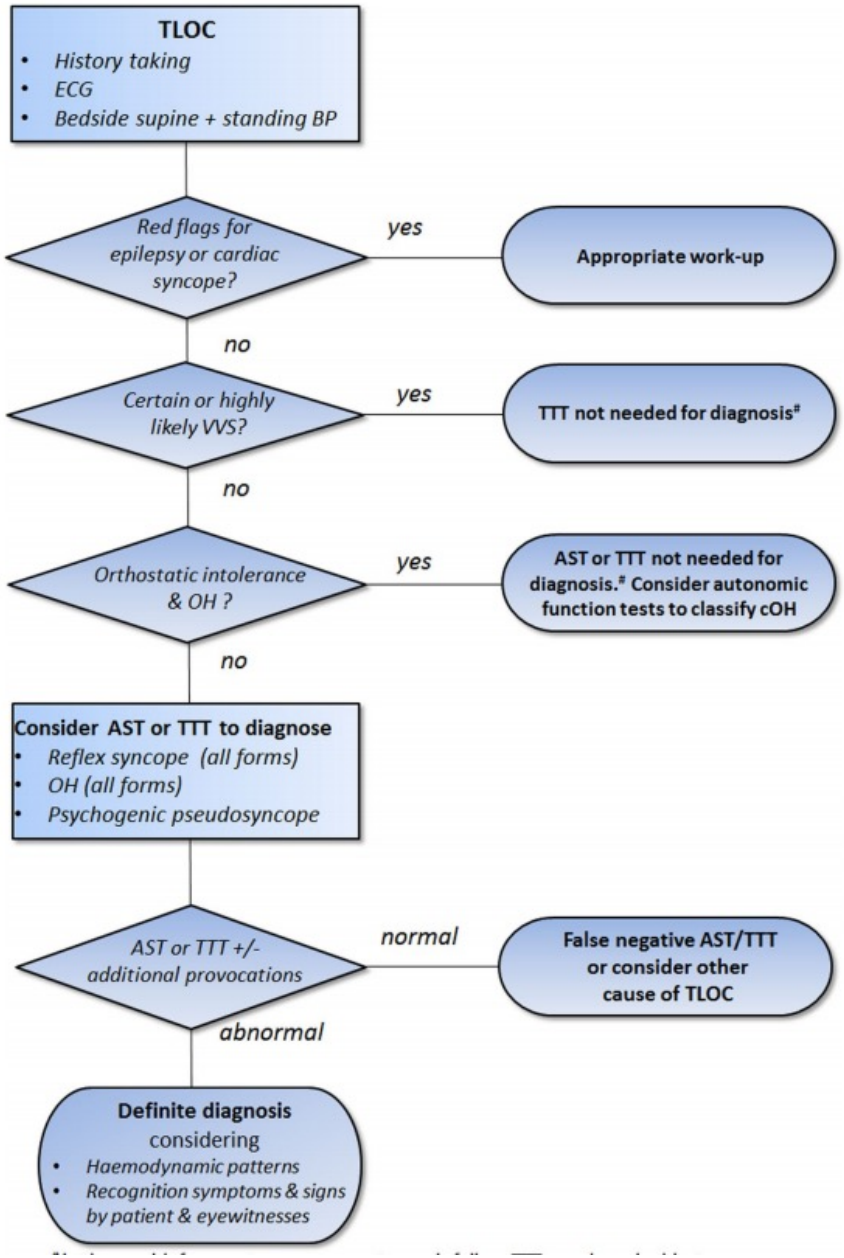
- Frontotemporal dementia (FTD)
- Progressive supranuclear palsy (PSP)



Secundary Neurogenic Orthostatic Hypotension (nOH)

- Metabolic diseases (DM, uremia)
- Immune mediated (GBS, AAG)
- Amyloidosis
- Paraneoplasia
  - α3 ganglionar AChR
  - Other ABs:

Vernino et al. 2019



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REVIEW ARTICLE

Recommendations for tilt table testing and other provocative cardiovascular autonomic tests in conditions that may cause transient loss of consciousness

Consensus statement of the European Federation of Autonomic Societies (EFAS) endorsed by the American Autonomic Society (AAS) and the European Academy of Neurology (EAN)

Roland D. Thijs[1,2] · Michele Brignole[3,4] · Cristian Falup-Pecurariu[5] · Alessandra Fanciulli[6] · Roy Freeman[7] · Pietro Guaraldi[8] · Jens Jordan[9,10,11] · Mario Habek[12] · Max Hilz[13,14] · Anne Pavy-Le Traon[15] · Iva Stankovic[16] · Walter Struhal[17] · Richard Sutton[18] · Gregor Wenning[6] · J. Gert Van Dijk[1]

Ambulatory blood pressure management

- Interpretation
  - Linking diary with blood pressure drops during the day
    - Activities during the day
    - medication
    - meals
    - WC
  - Dipping/Non-Dipping
    - Please consider overestimating the nightly blood pressure due to blood pressure drops during the day (mean values)
    - Do not interpret mean values but the absolut values
    - Degree of bed tilt plays a roll (orthostatic stress)
  - High blood pressure variability

Fanciulli, 2018

Patient that wants to dance

- 23-year-old lady comes to the outpatient clinic
- I was always sweating heavily on my palms. This started when I was about 11 or 12 years old. You know, I wanted to become a nurse. But I felt that I embarrass patients, when they are wet only because I touched them somewhere. I went to my GP back then, but he said, it's not a disease, its normal. I never really followed it up then, but I never thought it is normal. I cannot even hold a glass of champaign in my hand, it would immediately slip through.
- I became a captioner and working now for the city council. I gave up on my plan to become a nurse and like what I am doing. Its ok.
- I read online that you may be interested in things like that. To tell you the truth, I like to dance – classic dancing. I would like to do a professional course with my boyfriend, but as soon as I touch his suite, he is soaked wet wherever I touch him. He doesn’t mind, knowing that this is my issue, but I do feel embarrassed.

Forms of sweating

Thermoregulatory sweating

- Temperature control

Emotional sweating

- Social signal, in addition pheromons (controversial, since humans have only a rudamentory vomero-nasal organ)

Bedside Approach to Autonomic Disorders – eds: Struhal W, Lahrmann H, Fanciulli A, Wenning GK, 2017, Springer Wien

Thermoregulation function of sweating

target: core temperature > 37° <

lower temperature

shivering

Metabolic thermogenesis

behaviour: physical activity, environmental control

higher temperature

sweating (Sweating the most effictive means of reducing temperature in humans)

Vasomotor control

Behaviour: environmental control

History taking

History taking is the most important examination in sudomotor disorders

- Hyper- or Hypohidrosis?
  - Cave: focal hypohidrosis often reported as hyperhidrosis – compensatory thermoregulation

Triggers?

- Physical activity
- Emotional stress
- ++ environmental temperature
- Night

Focal or generalised?

Gustatory sweating?

- Normal phenomenon in spicy food
- Unilateral = pathological (parotis?)

Isolated or system disease?

Physical examination

Neurological examination

Internal examination

Looking for:

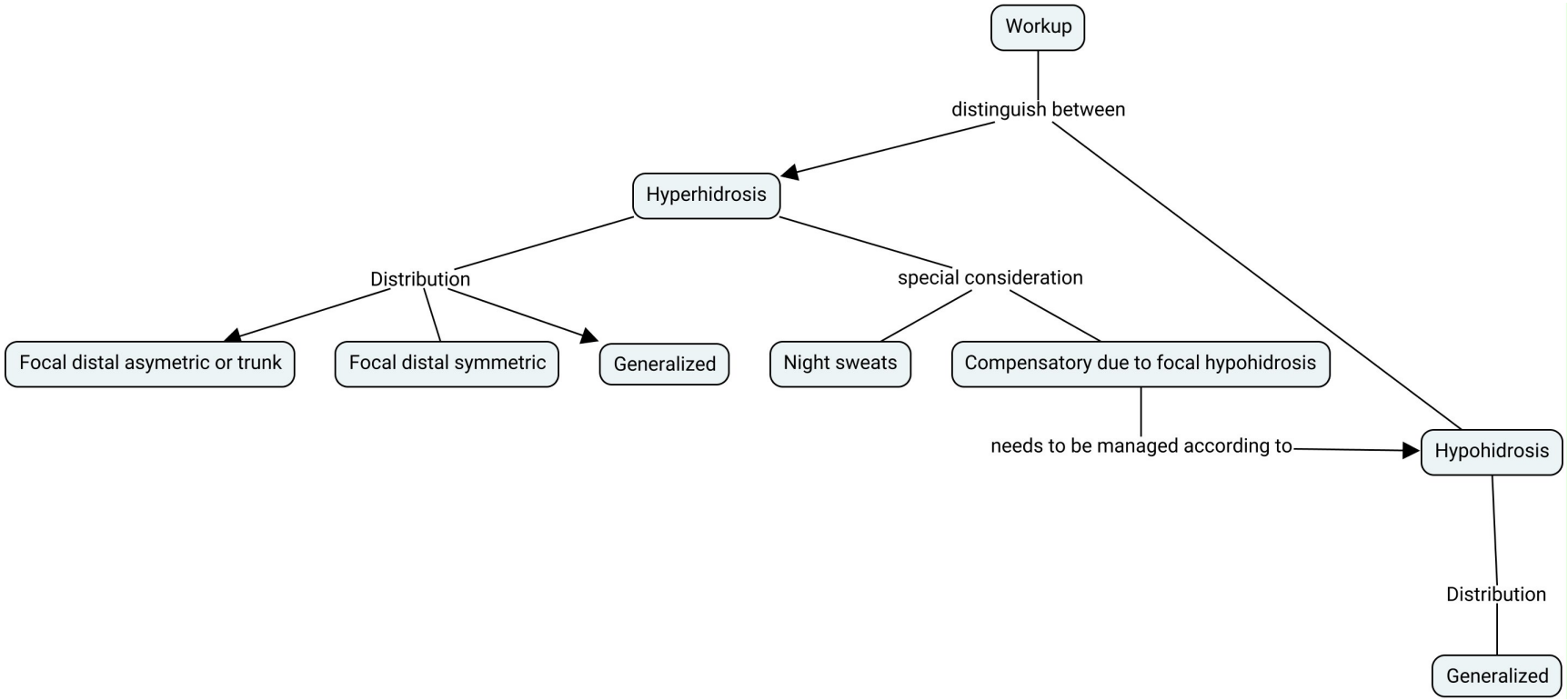
- Alphasynucleinopathy?
- Myelopathy?
- Horner‘s?
- Plexus brachialis lesion?
- Brain stem or supratenorial lesion?

Examination of sweat secretion in a conveniently temperatured environment / not interrupted / naked

- Sweat droplets? - typical areals: face, dorsal neck, axilla, palmar, planta, inguinal
- Skin discoloration?
- Topic changes?
- Skin hair?

Bedside Approach to Autonomic Disorders – eds: Struhal W, Lahrmann H, Fanciulli A, Wenning GK, 2017, Springer Wien

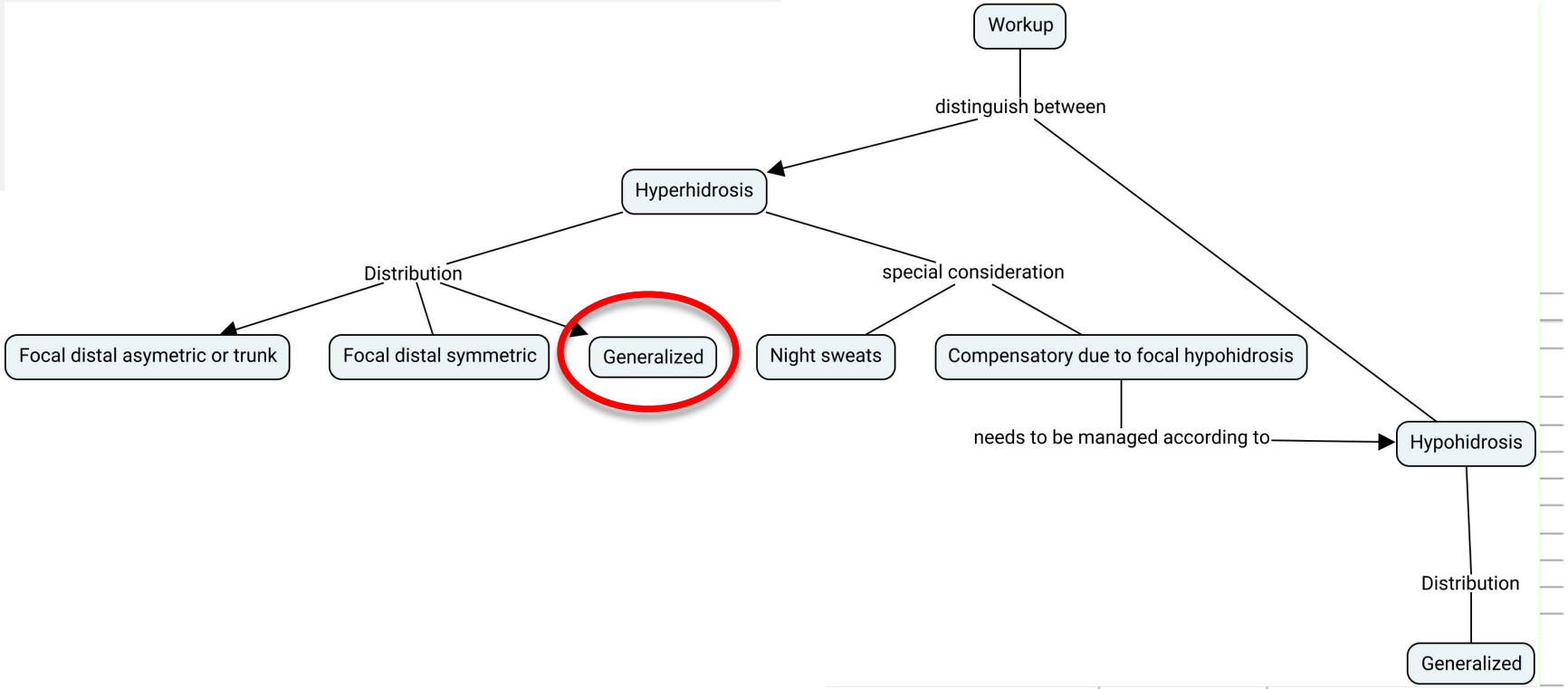
workup



Bedside Approach to Autonomic Disorders – eds: Struhal W, Lahrmann H, Fanciulli A, Wenning GK, 2017, Springer Wien

Generalised hyperhydrosis

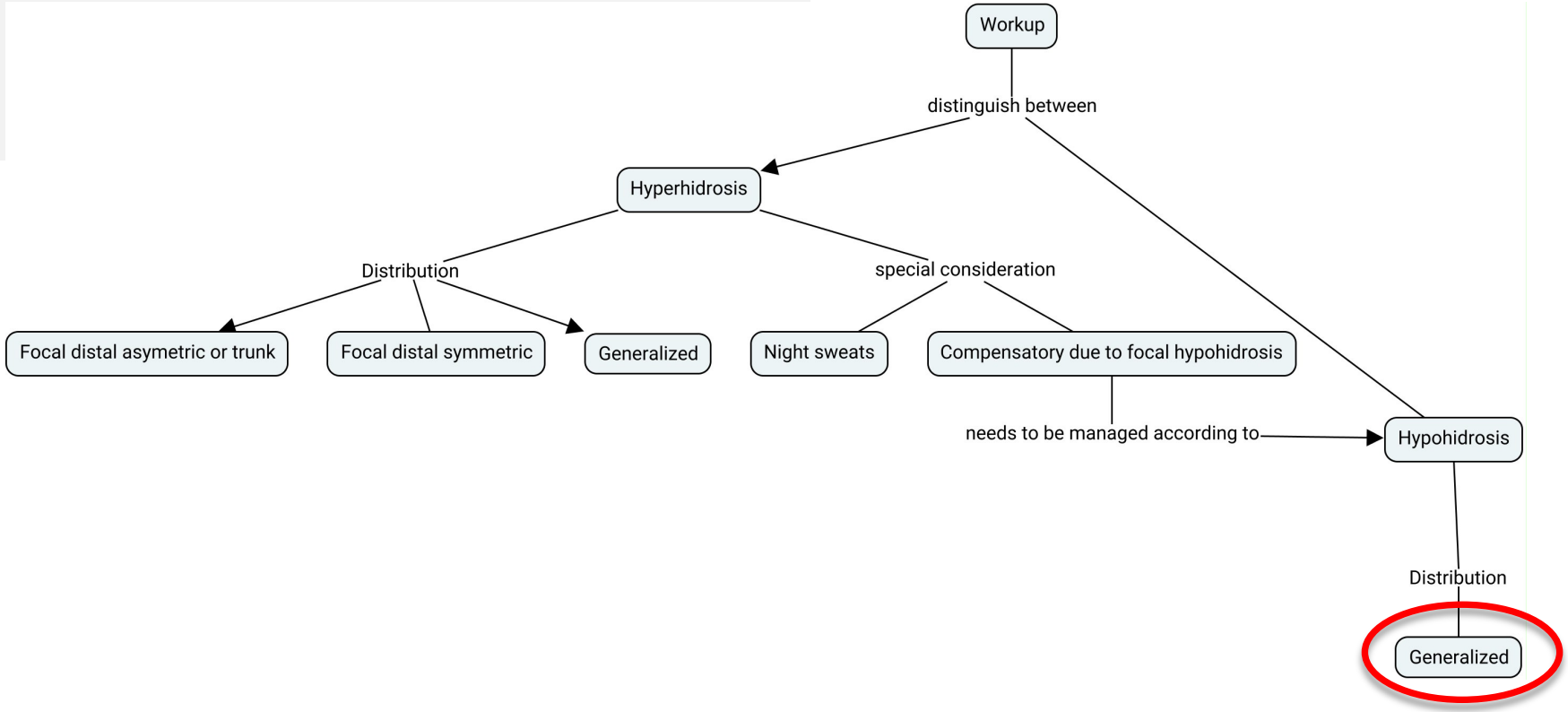
- Often systemic cause
- Most common
  - Systemic disease (e.g. thyroid disease, Diabetes mell.)
  - medication



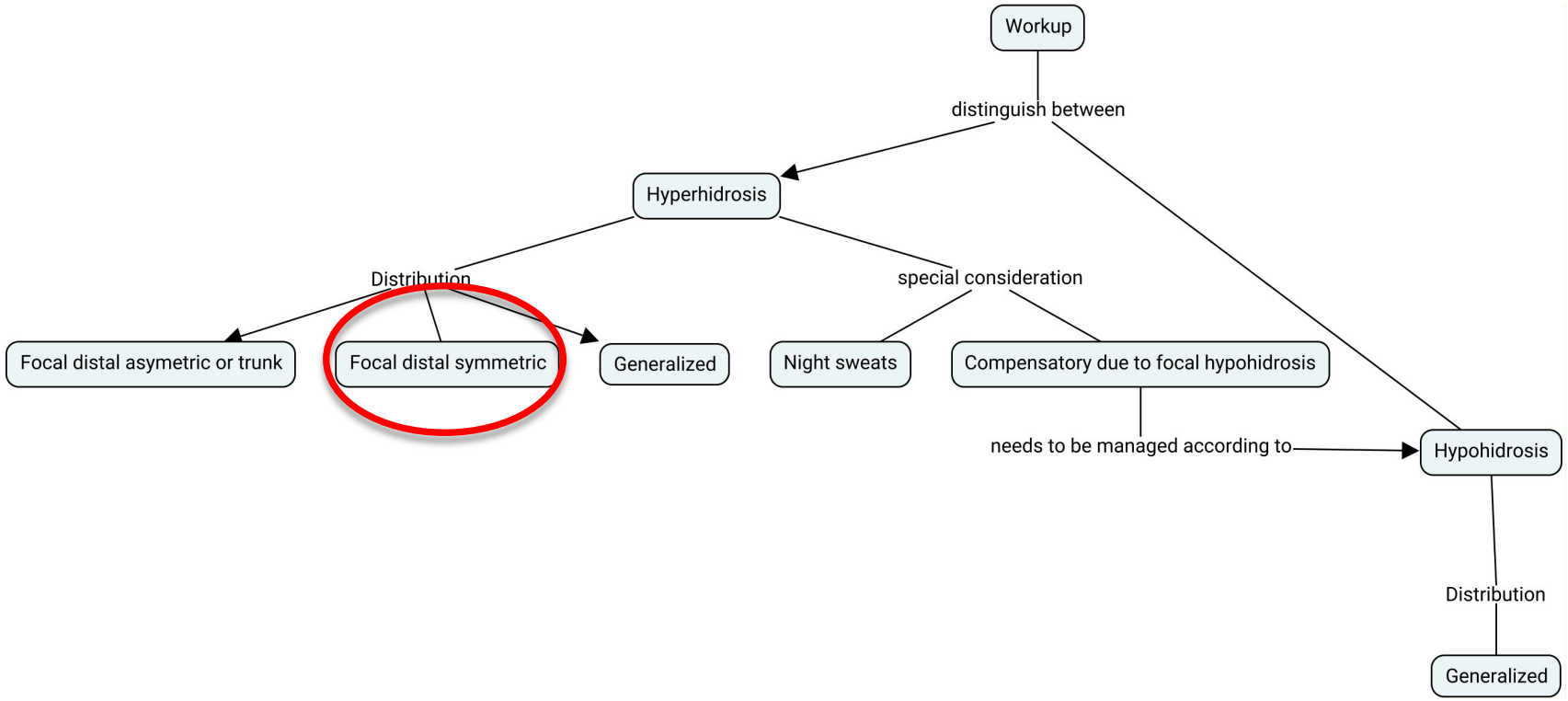
	Desipramine	
	Doxepin	
	Imipramine	

Generalised hypohidrosis

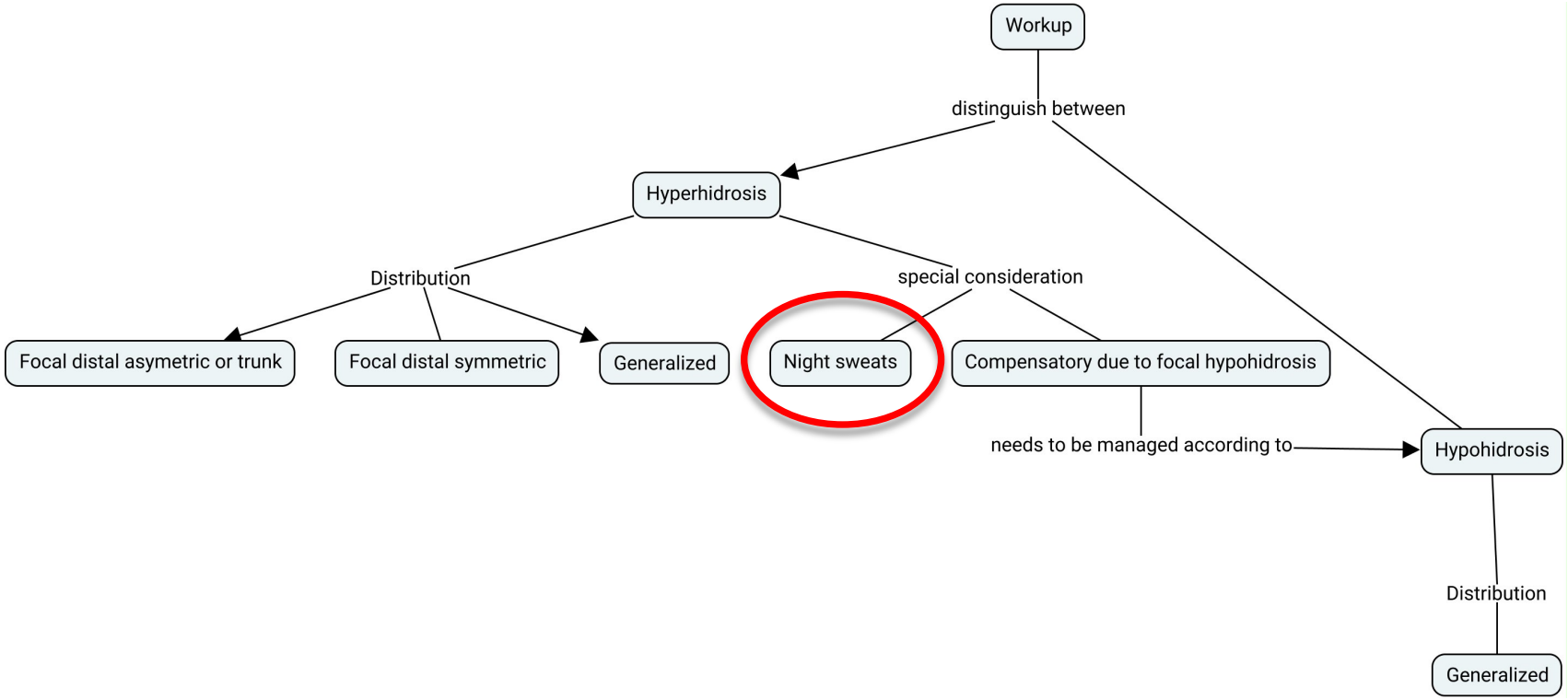
- Rare – may be life threatening



Focal distal symmetric



Night sweats



Management hypohidrosis

- Evaluate clinical relevance
- Substance induced
  - Adaptation of medicaltion and counceling of patient and care giver
- Life style modification
  - Preventing hot environments
  - Employing cool surfaces
  - Water sprays

Management hyperhidrosis

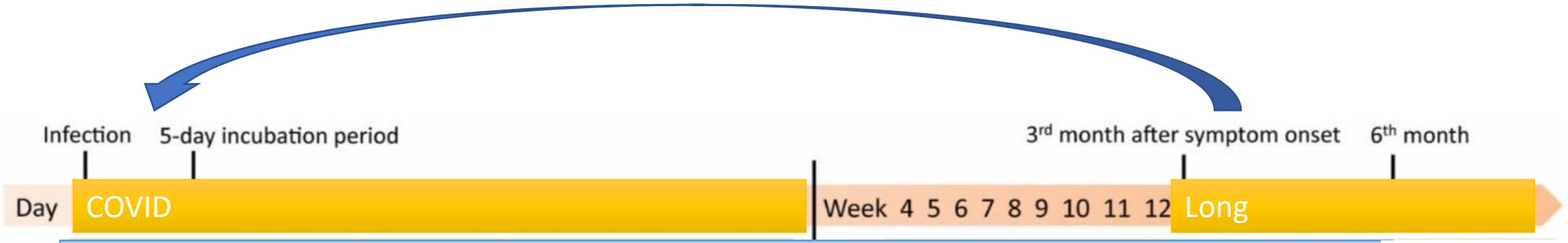
- focal
  - Aluminium chloride (often in deo sprays)
    - Often higher dosages necessary (15-25%) several times daily
    - caution: skin irritation and dysesthesia may occur
    - caution: dyscoloration of dark clothing
  - Steady current iontophoresis in palmar/plantar hypohidrosis
  - Botulinum toxin – may be efficient up to 7 months
    - caution: palmar application: paresis of small hand muscles
- Generalized – only few data available
  - anticholinergics (eg. Methanthelium bromide 2x50mg/d)
    - caution: urinary retention, obstipation, memory deficits, dry moth, reduced accomodation
  - Antidepressants – tricyclics and paroxetine
  - Beta blockers
  - Calcium channel inhibitors (eg. diltiazem)

Mrs. H

- 32 years, married, 3 kids, running a hotel, likes sports (running)
- Vacinnated once
- Beginning of August 21 after visiting a disco, SARS-CoV-2 positive, 3 days tired, headaches, fatigue, after 10 days tested negative and started working again
- End of August worsening, easily fatigued, dizzy in upright position, no appetite, „brain fog“, "I cannot make it through my day anymore"
    - Internal medicine seen first - unremarkable
    - Went online, got the impression to suffer "long-COVID" -> had recommended vegetarian diet and avoiding histamine in an online forum. Tried it, nothing improved. Was referred to us as "specialists" – again by online forum.
- Mid September first seen in September in our outpatient unit – neurologic examination remarkable

Long-COVID

- First use on twitter by Elisa Perego (italian patient)



Long-COVID
- Temporal relationship
- No entity
- Coincidence vs. causality - especially challenging during a pandemic
- Terms "post", "chronic" or "syndrome" may cause misleading associations if pathology is not understood (Infection 2021).

“Long-COVID” – surprising or new?

The result was that by the middle 1890s Russian influenza was being blamed in England for everything from the suicide rate to the general sense of malaise that marked the fin de siècle, and the image of a nation of convalescents, too debilitated to work or return to daily routines, and plagued with mysterious and erratic symptoms and chronic illnesses, had become central to the period’s medical and cultural iconography. Although H Franklin Parsons, the medical investigator for England’s Local Government Board, completed his final report on the “1889–92 epidemic” in 1893, further severe recrudescences were observed in 1893, 1895, 1898, and 1899–1900. The official end of the pandemic, therefore, did not mean the end of illness but was merely the prelude to a *longue durée* of baffling sequelae.

Mrs. H

- Next steps
  —> basic laboratory tests (exclusion of anemia, metabolic diseases)
  —> referral to psychiatry: mild depression
  —> orthostatic challenge further confirmed by HUT: POT(S)

Diagnosis and management of postural orthostatic tachycardia syndrome

Satish R. Raj MD MSCI, Artur Fedorowski MD PhD, Robert S. Sheldon MD PhD

■ Cite as: *CMAJ* 2022 March 14;194:E378-85. doi: 10.1503/cmaj.211373

Box 2: Diagnostic criteria for postural orthostatic tachycardia syndrome

All of the following criteria must be met:

- Sustained heart rate increase of ≥ 30 beats/min (or ≥ 40 beats/min if patient is aged 12–19 yr) within 10 minutes of upright posture.
- Absence of significant orthostatic hypotension (magnitude of blood pressure drop ≥ 20/10 mm Hg).
- Very frequent symptoms of orthostatic intolerance that are worse while upright, with rapid improvement upon return to a supine position. Symptoms vary between individuals, but often include lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision and fatigue.
- Symptom duration ≥ 3 months.
- Absence of other conditions that could explain sinus tachycardia (Box 3).

Box 3: Other conditions that could explain sinus tachycardia on standing[5]

- Acute hypovolemia (from dehydration or blood loss)
- Anemia
- Orthostatic hypotension
- Endocrinopathy
  - Adrenal insufficiency
  - Carcinoid tumour
  - Hyperthyroidism
  - Pheochromocytoma
- Adverse effects from medication
- Panic attacks and severe anxiety
- Prolonged or sustained bed rest
- Recreational drug effects

Personal recommendation of councelling POTS

Limited understanding on pathophysiology and common endpoint of different diseases

"This diagnosis is start of a journey, not endpoint"

- Pathophysiologic laboratory sub-definitions ("I have hyper-POTS") is interesting, but also disturbing for patients in the quest to attribute all their symptoms to POTS
- **What I personally find helpful in the journey with our patients**
  - Individual complains are the focus of management – as in other chronic diseases, try to get away from POTS as catchword
  - Not diagnosing POTS as primary diagnosis, but trying to always define the underlying condition ("Small fiber neuropathy in association with POTS" or "bilateral carotic dissection and secondary baroreceptor reflex dysfunction in association with POTS", or "Sars-COV2 infection August 2021 - postviral condition of unclear significance associated with postural orthostatic tachycardia")
- Patients and their referrers get a clearer idea, that POTS is not an entity, but a syndrome and eventually associated with a more individual, complex condition

First line

Box 4: Suggested initial approach to treatment of patient with postural orthostatic tachycardia syndrome

- Nonpharmacological treatments
  - All started at initial visit
    - Water 3 L/d
    - Salt 5 mL/d (2 tsp/d)
    - Waist-high compression garments
- Pharmacological treatments
  - May start at initial visit if symptoms are severe
    - If standing heart rate very high: propranolol 10–20 mg, 4 times per day
    - If standing heart rate very high and β-blocker is contraindicated: ivabradine 5 mg 2 times per day
    - If standing heart rate is not too high and blood pressure is low: midodrine 5 mg orally every 4 hours, 3 times per day (8 am, noon, 4 pm)

Note: tsp = teaspoon.

Pharmakologische Optionen

Table 2: Pharmacological treatments for postural orthostatic tachycardia syndrome

Drug	Dosing	Quality of evidence*	Adverse effects	Other considerations
Heart rate inhibitors				
Propranolol	10–20 mg orally up to 4 times daily	Moderate	Hypotension, bradycardia, bronchospasm	Can worsen asthma
Ivabradine	2.5–7.5 mg orally twice daily	Moderate	Visual disturbances, bradycardia	Expensive
Pyridostigmine	30–60 mg orally up to 3 times daily	Low	Increased gastric motility and cramping	
Vasoconstrictors				
Midodrine	2.5–15 mg orally 3 times daily	Moderate	Headache, scalp tingling, supine hypertension	Avoid within 4 hr of bedtime to avoid supine hypertension
Sympatholytic drugs				
Methyldopa	125–250 mg orally twice daily	Low	Hypotension, fatigue, brain fog	Start with a low dose
Clonidine	0.1–0.2 mg orally 2–3 times daily or long-acting patch	Low	Hypotension, fatigue, brain fog	Start with a low dose; withdrawal can lead to rebound tachycardia and hypertension
Blood volume expanders				
Fludrocortisone	0.1 to 0.2 mg orally per day	Low	Hypokalemia, edema, headache	Serum potassium should be monitored
Desmopressin	0.1 to 0.2 mg orally per day, as needed	Low	Hyponatremia, edema	Serum sodium should be monitored if used chronically

*We critically appraised the literature using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology.[44] We rated the quality of the evidence as high, moderate, low or very low based on the likelihood that further research would change confidence in the estimate of effect.

Long-COVID POTS

- Problem: POTS experiences focused on a very limited number of clinicians mainly in autonomic referral centers
- open questions:
  - Natural history – unclear
  - Renin-Angiotensine-Aldosterone system - open questions in relation to SARS-CoV-2
  - POTS may start with a viral diseases – this is known for decades. Is long-COVID POTS a specific phenomenon
  - Management

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REVIEW ARTICLE

Check for updates

Long-COVID postural tachycardia syndrome: an American Autonomic Society statement

Satish R. Raj[1,2] · Amy C. Arnold[2,3] · Alexandru Barboi[4] · Victoria E. Claydon[5] · Jacqueline K. Limberg[6] · Vera-Ellen M. Lucci[5] · Mohammed Numan[7] · Amanda Peltier[8] · Howard Snapper[9] · Steven Vernino[10] on behalf of the American Autonomic Society

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Mrs. H

- Venlafaxin 37,5
- relieving conversation with the patient by a neurologist specialist of my team that has also psychotherapy training
- Swift releave of symptoms severety and patient ended medication because of feeling well on her own

Summary

The most important part of any autonomic assessment is

- Diligent history taking
  - Time course
  - Domains
  - Focal/wide spread/generalized

Bed side the diagnosis may be already established

- Cardiovascular evaluation
- Sudomotor evaluation

University Diploma

European Program of Clinical Autonomic Neuroscience EPOCAN

- Language: Englisch
- Open to medical doctors
- 20 ECTS
- Blended learning

Summary

The most important part of any autonomic assessment is

- Diligent history taking
  - Time course
  - Domains
  - Focal/wide spread/generalized

Bed side the diagnosis may be already established

- Cardiovascular evaluation
  - Standing test
  - 24h Blood pressure

University Diploma

European Program of Clinical Autonomic Neuroscience EPOCAN

- Language: Englisch
- Open to medical doctors
- 20 ECTS
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