Baptist Health
HEART INSTITUTE

What's POTS and What's Not

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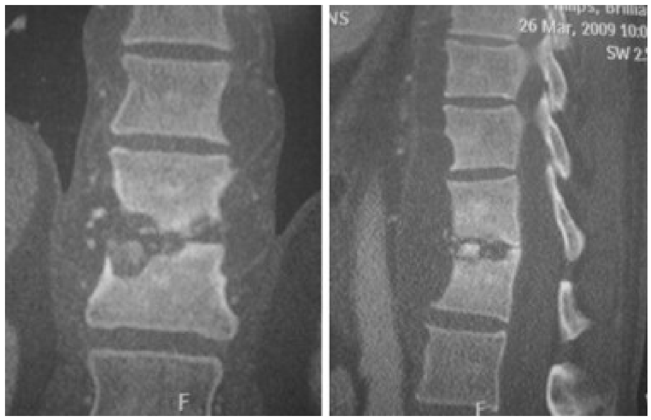
Disclosures:

CSL Behring (Research Support)
Medtronic, Inc. (Research Support)
Regeneron Pharmaceuticals, Inc. (Research Support)

This is Not



POTS Mimics

- Anemia – Iron deficiency
- Vitamin B12 deficiency
- Bedrest - Deconditioning
- Side effect of Medications – diuretics, vasodilators
- Dehydration / Moderate weight loss
- Endocrinologic Abnormalities
  - Hyperthyroidism
  - Adrenal insufficiency
  - Hypoparthyroidism
  - Hypoaldosteronism
- Diabetes Mellitus
- Connective Tissue Disease - Sjögren's syndrome, systemic lupus erythematosus
- Mitochondrial Disease

POTS Mimics

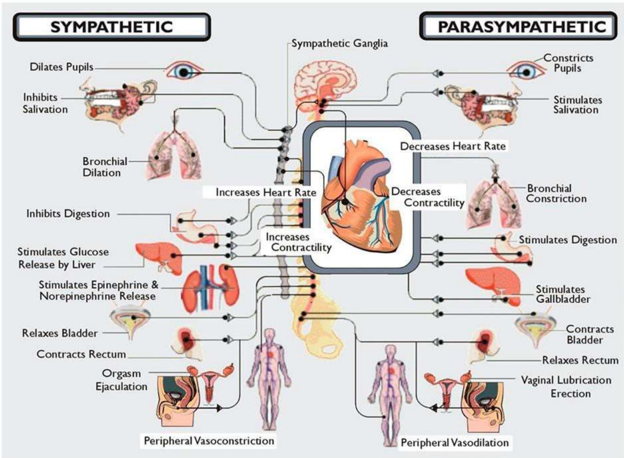
- Median Arcuate Ligament Syndrome (MALS)
- Small Fiber Neuropathy (SFN)
- Cranial Cervical Instability (CCI)
- Nutcracker Syndrome
- Mast Cell Activation (MCA)

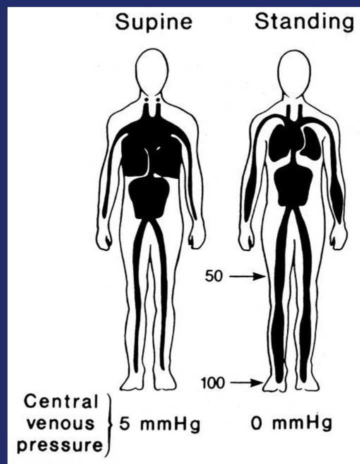
Autonomic Nervous System

<u>Autonomic</u> = not under voluntary control

Divisions

- Sympathetic
  - "fight or flight"
- Parasympathetic
  - "rest and digest"
- Enteric





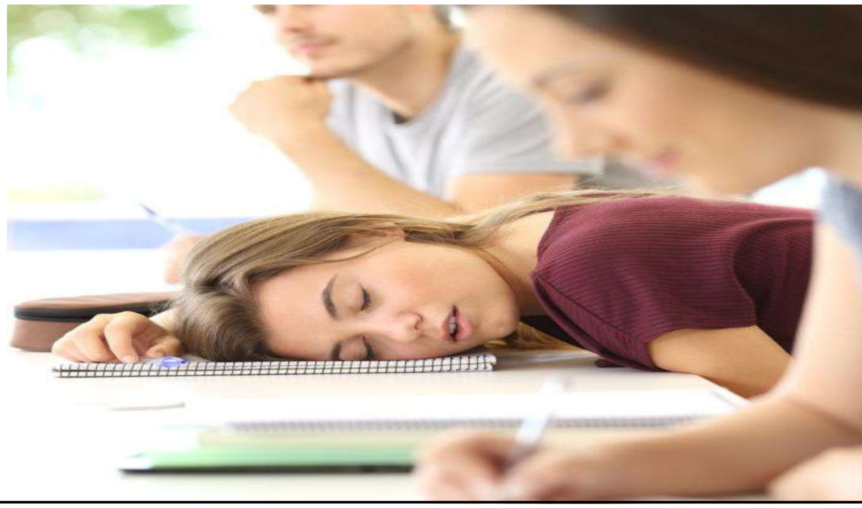
500-750 mL of blood pools in the lower half of the body on standing.

- Low PA. Clinical autonomic disorders: evaluation and management. 1993.

Symptoms of Orthostatic Intolerance

Lightheadedness	Dyspnea
Syncope	Chest discomfort
Diminished concentration	Palpitations
Headache	Tremulousness
Blurred vision	Anxiety
Fatigue	Diaphoresis
Exercise intolerance	Nausea

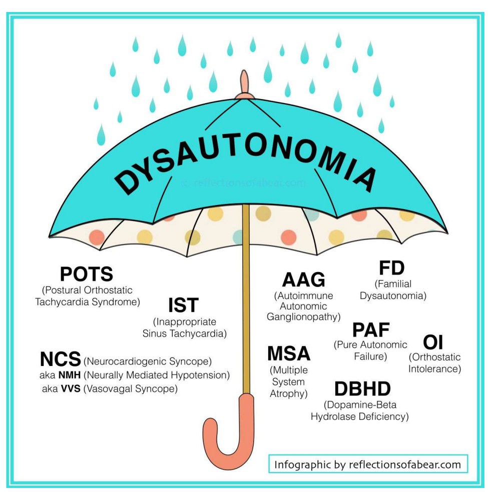
This Could Be



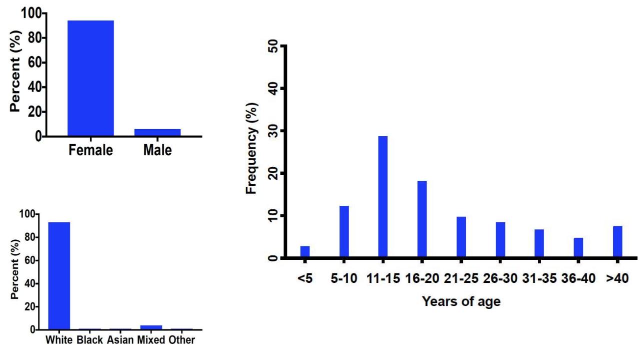
WHAT IS POTS?

Postural Orthostatic Tachycardia Syndrome

- Chronic symptoms of orthostatic intolerance
- Postural tachycardia
  - Increase of >40 bpm within 10 minutes of head up tilt (age 12- 19)
- Absence of orthostatic hypotension
  - Sustained decrease of >20/10 within 3 minutes of head up tilt/standing
- <40 beats per minute with symptoms?
  - "Chronic orthostatic intolerance"
  - Autonomic dysfunction?

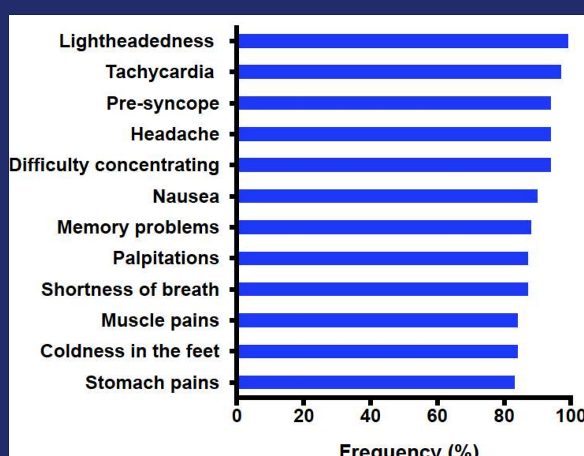


The Face of POTS



BH Shaw et al., J Intern Med. 2019 Mar 12. doi: 10.1111/joim.12895

Spectrum of Symptoms Associated with POTS



Clinical Presentation

- Dizziness, lightheadedness, weakness, blurred vision and fatigue upon standing.
- Orthostatic symptoms of palpitations, tremulousness and anxiety.
- Gastrointestinal symptoms – nausea, abdominal cramps, early satiety, bloating, constipation or diarrhea.
- Peripheral extremities – acro-cyanosis and edema when upright.

Clinical Presentation

- Intractable headaches, that are medication resistant.
- Abnormal sleep – insomnia, and frequent awakening during sleep.
- Mood disorder – panic disorder, anxiety and depression.
- Exercise intolerance.
- Cognitive dysfunction – mental "fog", ADD
- Syncope is relatively unusual.
- –Occurs in up to 40%

Clinical Evaluation

- Exam is often normal
- Heart rate variability with deep breathing (sinus arrhythmia)
- Sweating
- Pupillary light responses
- Orthostatic acrocyanosis
- Joint hypermobility

“Active stand test” is not validated for the diagnosis of POTS in adolescents

- It is in adults?
- Can detect orthostatic hypotension

No standardized protocol

- 5 minutes supine
  - HR and BP before standing
- Patient stands unassisted (no leaning), with minimal interaction
  - HR and BP at 1, 3, 5 and 10 minutes (or every minute)

Time intensive- at least 15 minutes

- Nursing or MA

Plash WB, Diedrich A, Biaggioni I, Garland EM, Paranjape SY, Black BK, Dupont WD, Raj SR. Diagnosing postural tachycardia syndrome: comparison of tilt testing compared with standing haemodynamics. Clin Sci (Lond). 2013 Jan;124(2):109-14.

Clinical Evaluation and Testing

- “Screening labs”
  - CMP (fasting)
  - CBC
  - Thyroid, adrenal function
  - Ferritin
    - 47% of 131 had low ferritin
  - Vitamin D
    - 22% of 95 had insufficiency (<20 ng/mL)

What about autonomic testing?

- When?
- Why?
- Where?

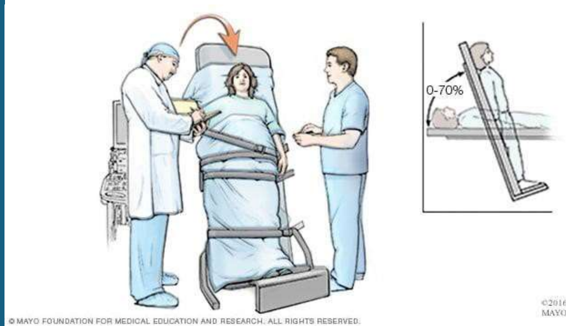
Antiel RM, Caudill JS, Burkhardt BE, Brands CK, Fischer PR. Iron insufficiency and hypovitaminosis D in adolescents with chronic fatigue and orthostatic intolerance. South Med J. 2011 Aug;104(8):609-11. doi: 10.1097/SMJ.0b013e3182246809. PMID: 21886073.

Boris JR, Moak JP. Pediatric Postural Orthostatic Tachycardia Syndrome: Where We Stand. Pediatrics. 2022 Jul 1;150(1):e2021054945.

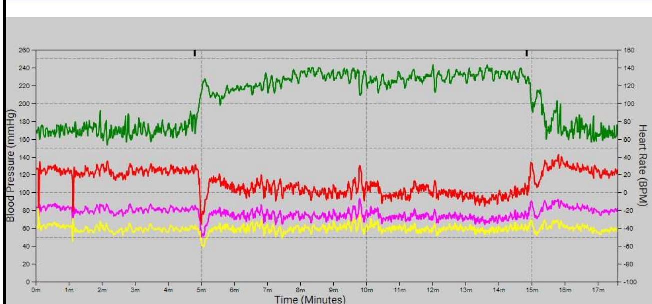
Head Up Tilt Table Testing

Autonomic reflex screening

- Sudomotor
- Cardiovagal
- Sympathetic adrenergic



Postural Orthostatic Tachycardia Syndrome

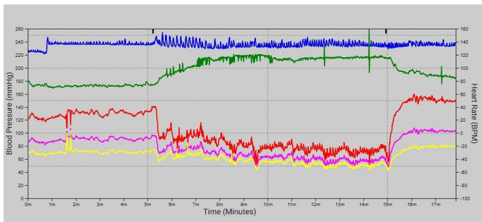


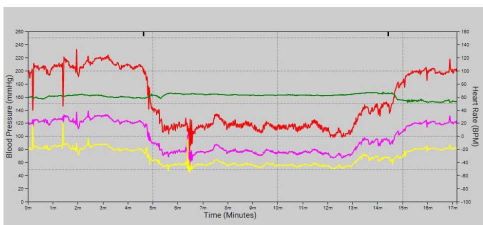
POTS

- Chronic orthostatic intolerance
- Heart rate increase of >40 beats per minute
    - In adults: >30, or absolute HR >120
- Absence of orthostatic hypotension

Stewart JM, Boris JR, Chelimsky G, et al. Pediatric Disorders of Orthostatic Intolerance. *Pediatrics.* 2018;141(1):e20171673

Orthostatic Hypotension



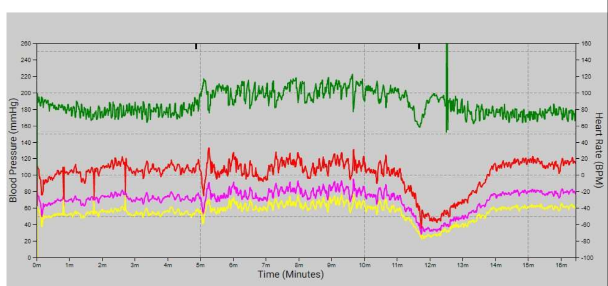


- Steady decrease in blood pressure >20/10 within 3 minutes
- Neurogenic or non- neurogenic
- Compensatory tachycardia

Stewart JM, Boris JR, Chelimsky G, et al. Pediatric Disorders of Orthostatic Intolerance. *Pediatrics.* 2018;141(1):e20171673

Vasovagal Syncope

- If intermittent/rare- this is considered normal
  - 40% lifetime occurrence
  - Average age of first faint is 15
- Cerebral hypoperfusion leads to loss of consciousness and postural tone
  - Prodrome
  - Postdrome

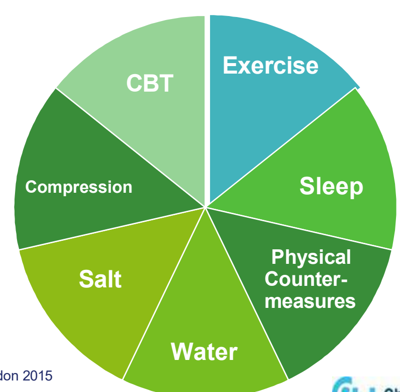


Stewart JM, Boris JR, Chelimsky G, et al. Pediatric Disorders of Orthostatic Intolerance. *Pediatrics.* 2018;141(1):e20171673

But first…

- **Remember to listen, believe, and validate your patient.**
  - "Symptoms of dysautonomias reflect real biological or chemical changes. If a clinician cannot identify the cause of a patient's symptoms, this ignorance should not lead to dismissing the patient as having a psychiatric rather than a 'real' problem"
    - - David S. Goldstein, MD PhD – Principles of Autonomic Medicine
- **Establish a therapeutic alliance.**
  - Much of the help that a provider in any specialty offers to a patient is emotional. Your nonjudgmental attitude, warmth, respect, reassurance, and willingness to listen can promote a healthy patient-doctor relationship and, in turn, that therapeutic alliance is important for the patient's compliance with your shared decision making

Non-Pharmacologic Management



Raj et al 2022, Fu et al 2018, Sheldon 2015

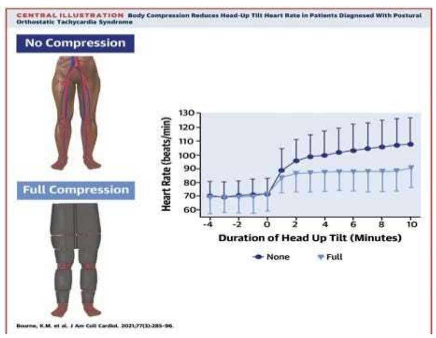
Children's Hospital of Philadelphia

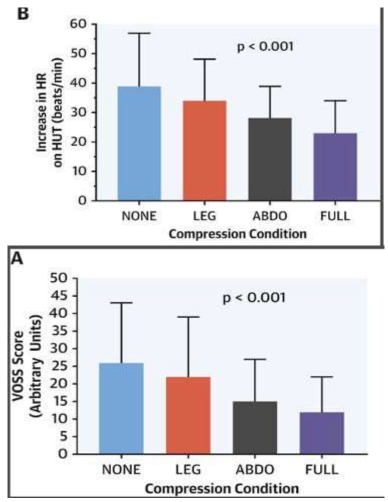
Non-Drug Therapy

Exercise and non-pharmacological interventions should be considered first-line for most patients if tolerated because they are simple, cost-effective, and have little to no side effects

Compression Garments

Why Compression?





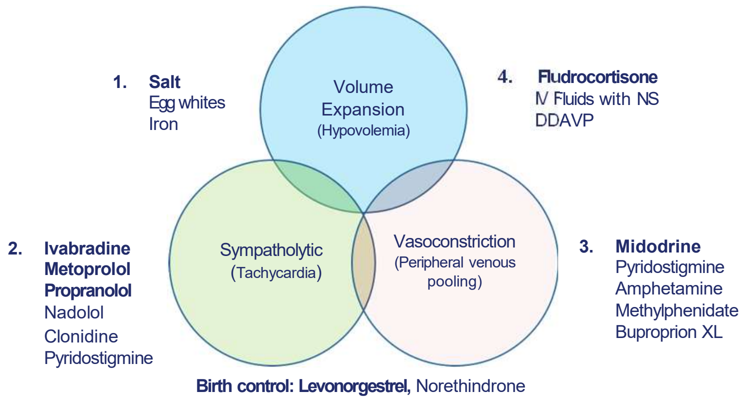
Fluids

- Daily intake goal 3-4L

Sodium

- Daily intake goal: 3-10gm

Pharmacologic Treatment



Ehlers-Danlos Syndrome

- Heterogeneous disorder of connective tissue
- Characterized by varying degrees of:
  - Skin hyperextensibility
  - Joint hypermobility
  - Cutaneous fragility
- Most forms result from mutations in genes encoding fibrillar collagens or the collagen-modifying enzymes

de Paepe A, Malfait F. The Ehlers-Danlos syndrome, a disorder with many faces. Clin Genetics 2012;82:1-11.

What type of exercise is appropriate?

Cardio training

- ↑ cardiac size and mass
- ↑ cardiac muscle strength
- Expands blood and plasma volumes
- ↑ peak oxygen uptake by 11%

Resistance Training

- Lower extremity and core training promotes skeletal (and cardiac) muscle hypertrophy
- ↑ venous blood return (Fu et al 2018)
- Improved systolic and diastolic blood pressure

BOTH ARE EQUALLY IMPORTANT!

Key Points to Remember

- Postural Tachycardia Syndrome (POTS) is a disabling disorder, representing "a common pathway" for multiple different causes.
- POTS is not a cause in and of itself. It is a **syndrome**.
- Because of the heterogeneous nature of its pathophysiology, it presents a challenge in the diagnosis and treatment.
- There currently is no treatment approach that works for everyone.
- Identify the contributing causes if possible. Often there are multiple co-morbidities.

Primary Role of PCP

- PCPs and Pediatricians are first line of defense.
  - The average pediatrician has about 20-30 POTS patients in their practice. Most are undiagnosed.
  - Its critical you believe your patients; they are usually telling you the truth.
  - Become their partner, engender a therapeutic alliance.
  - There is no accepted algorithm when it comes to drugs, so trial and error is just fine.
  - It becomes the PCP primary role to identify and apply 1st line management.
  - 50-70% get better with 1st line treatments discussed.
  - Physical Therapy is key to getting better.

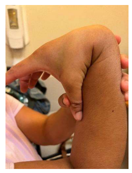
Thank You

Ehlers-Danlos Syndrome

- Because fibrillar collagen provides strength and structure to essentially all tissues and organs, EDS has widespread clinical manifestations
- Early varicose veins, easy bruising
- Easy fatigability and widespread pain common

Royce PM, Steinmann B, Superti-Furga A. The Ehlers-Danlos syndrome.
In: Connective Tissue and its Heritable Disorders. New York: Wiley-Liss, 1993: 351-407.

Beighton Score


Maneuver (1 point for each positive)	L	R	Score
Passive dorsiflexion of the fifth finger at the metacarpophalangeal joint > 90 degrees			
Passive apposition of the thumb to the flexor aspect of the forearm			
Hyperextension of the elbow > 190 degrees			
Hyperextension of the knee > 190 degrees			
Forward flexion of the trunk with the knees straight so the palms rest easily on the floor			
Beighton score (≥4 c/w hypermobility; max score=9)			

Roma M, Marden CL, De Wandele I, Francomano CA, Rowe PC. Postural tachycardia syndrome and other forms of orthostatic intolerance in EDS. Autonomic Neuroscience: Basic and Clinical 2018; 215: 89-96.

Hypermobility ≠ disease


Common EDS Subtypes (AD Transmission)

Type	Abbrev.	Genetic Basis	Protein
Classical	cEDS	COL5A1, COL1A1	Type V, I
Hypermobile	hEDS	Unknown	Unknown
Vascular	vEDS	COL3A1, COL1A1	Type III, I

Triggers of Mast Cell Activation

- Infections
- Drugs (narcotics, neuromuscular blocking agents)
- Heat
- Physical stimuli (stretch, pressure, vibration)
- Alcohol
- Exercise
- Hymenoptera stings
- Foods
- Stress

Modified from Seneviratne SL, Maitland A, Afrin L. 2017. Mast cell disorders in Ehlers–Danlos syndrome. Am J Med Genet Part C Semin Med Genet 175C:226–236.