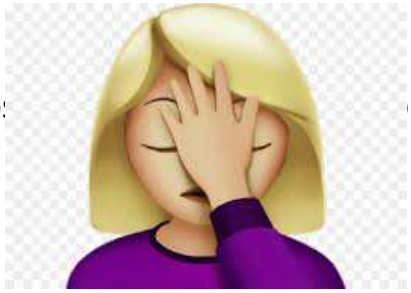
Po  me

FASU

TABLE 1. DSM-IV Codes and Categories for Somatoform Disorders and ICD-10 Equivalents

DSM-IV		ICD-10	
Code	Category	Code	Category
300.81	Somatization disorder	F45.0	Somatization disorder
300.81	Undifferentiated somatoform disorder	F45.1	Undifferentiated somatoform disorder
300.11	Conversion [illegible]order	F44.	Di[illegible]ciative [illegible]version) [illegible]ers
307.80	Pain disc[illegible]		[illegible]nt somatoform [illegible]in disorder
300.7	Hypochondriasis		Hypochondriacal [illegible]disorder
300.7	Body dysm[illegible] disor[illegible]		
300.81	Somatofo[illegible] not other[illegible] specified	F45.[illegible]	[illegible]form [illegible]onomic dysfunction
		F45.8	Other somatoform disorders
		F45.9	Somatoform disorder unspecified
		F48.0	Neurasthenia (in other neurotic disorders category)

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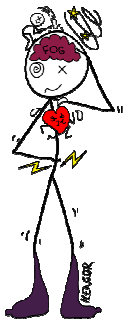
Definition



A clinical syndrome usually characterized by:

1. frequent **symptoms with standing** such as lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision, exercise intolerance & fatigue
2. an **increase in heart rate of ≥30 bpm** when moving from recumbent to standing position for more than 30 secs (or ≥40 bpm in individuals 12 to 19 years old)
3. an **absence of orthostatic hypotension** (no drop >20 mmHg drop in systolic blood pressure)

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Epidemiology & Outcome

- Prevalence reported to be 0.2% in UK
- Estimated 500,000 to 1 million in USA
- Most present between ages 15 to 25
- >75% female
- Little data on longterm outcomes
- Course varies, no known mortality, eventual improvement

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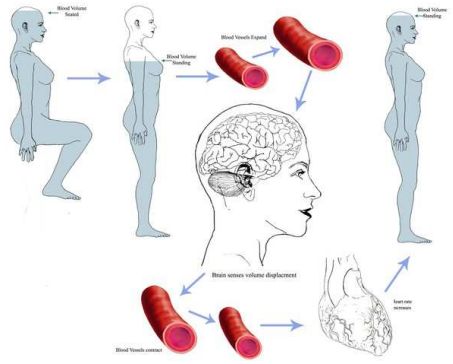

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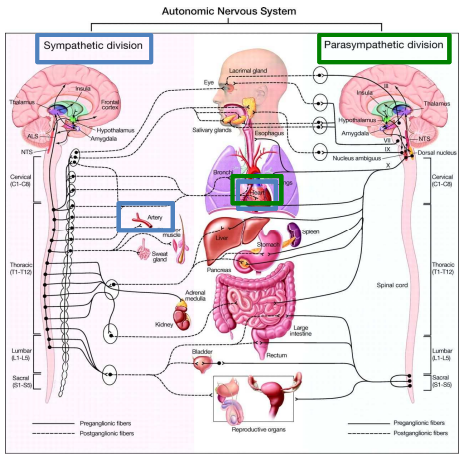
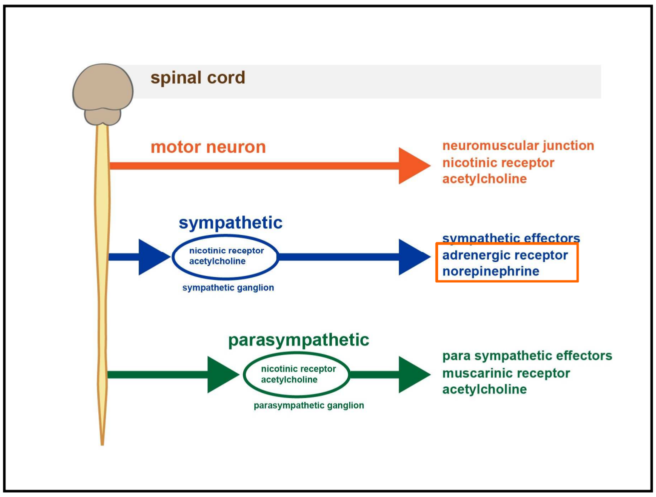
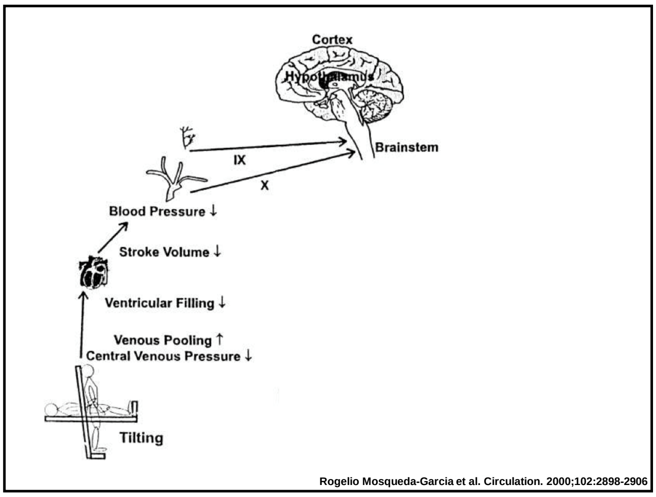
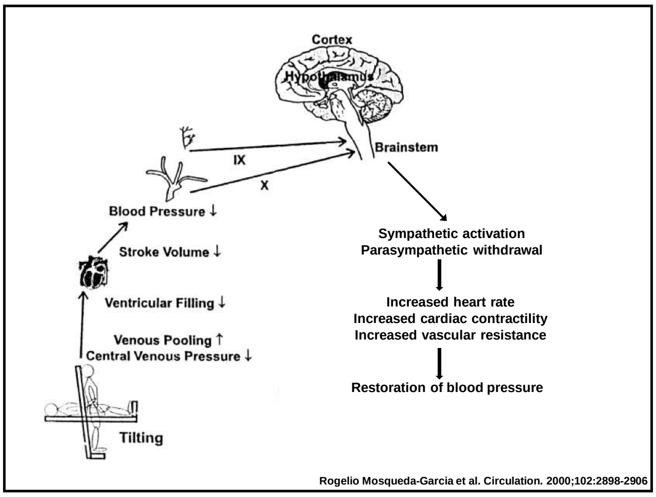
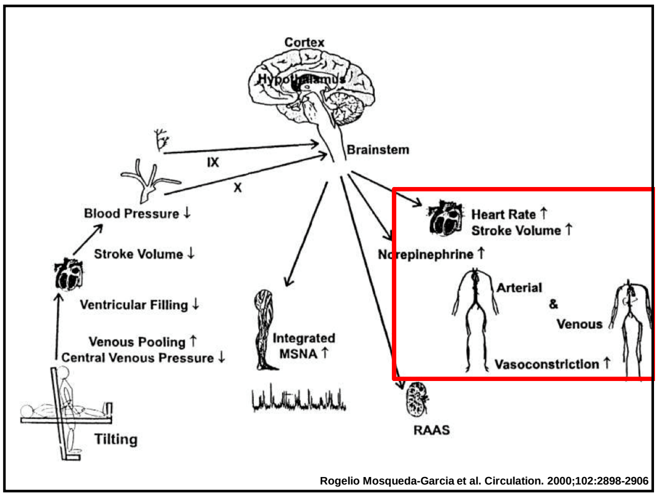
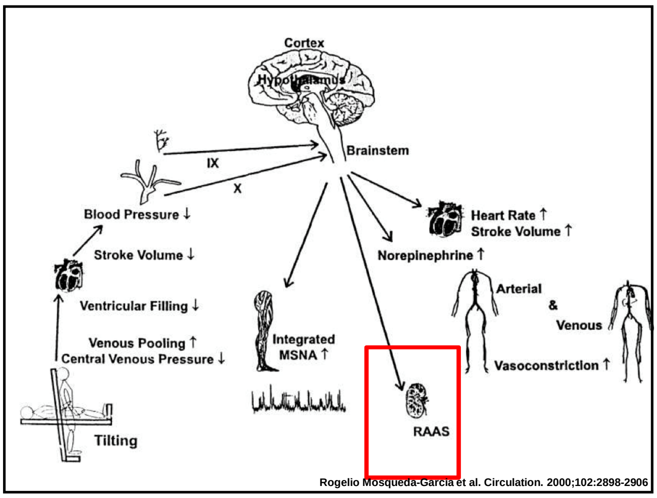



spinal cord
motor neuron
neuromuscular junction
nicotinic receptor
acetylcholine
sympathetic
nicotinic receptor
acetylcholine
sympathetic ganglion
sympathetic effectors
adrenergic receptor
norepinephrine
parasympathetic
nicotinic receptor
acetylcholine
parasympathetic ganglion
para sympathetic effectors
muscarinic receptor
acetylcholine


Cortex
Hypothalamus
Brainstem
IX
X
Blood Pressure ↓
Stroke Volume ↓
Ventricular Filling ↓
Venous Pooling ↑
Central Venous Pressure ↓
Tilting
Rogelio Mosqueda-Garcia et al. Circulation. 2000;102:2898-2906


Cortex
Hypothalamus
Brainstem
IX
X
Blood Pressure ↓
Stroke Volume ↓
Ventricular Filling ↓
Venous Pooling ↑
Central Venous Pressure ↓
Tilting
Sympathetic activation
Parasympathetic withdrawal
Increased heart rate
Increased cardiac contractility
Increased vascular resistance
Restoration of blood pressure
Rogelio Mosqueda-Garcia et al. Circulation. 2000;102:2898-2906


Cortex
Hypothalamus
Brainstem
IX
X
Blood Pressure ↓
Stroke Volume ↓
Ventricular Filling ↓
Venous Pooling ↑
Central Venous Pressure ↓
Tilting
Heart Rate ↑
Stroke Volume ↑
Norepinephrine ↑
Arterial
&
Venous
Vasoconstriction ↑
Integrated
MSNA ↑
RAAS
Rogelio Mosqueda-Garcia et al. Circulation. 2000;102:2898-2906


Cortex
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X
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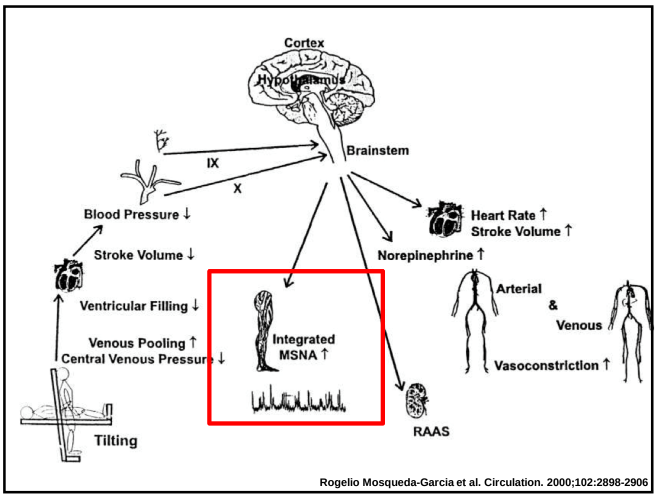
Cortex
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IX
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Blood Pressure ↓
Stroke Volume ↓
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Tilting
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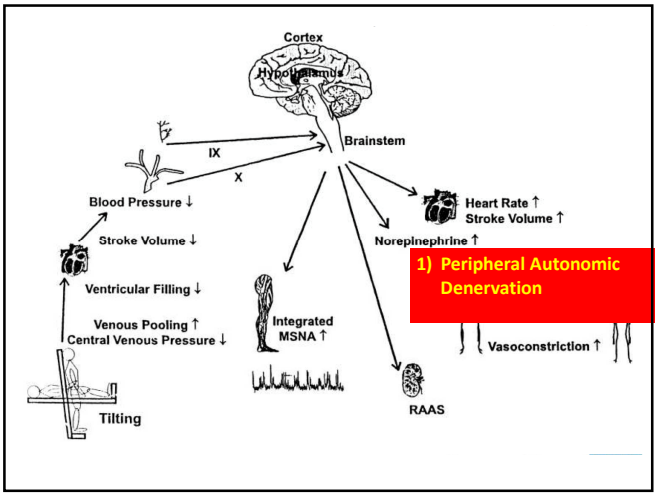
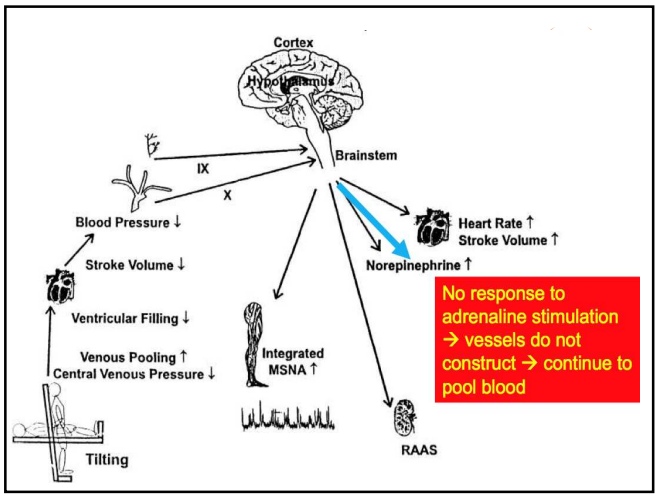
Norepinephrine ↑
Arterial
&
Venous
Vasoconstriction ↑
Integrated
MSNA ↑
RAAS
Rogelio Mosqueda-Garcia et al. Circulation. 2000;102:2898-2906

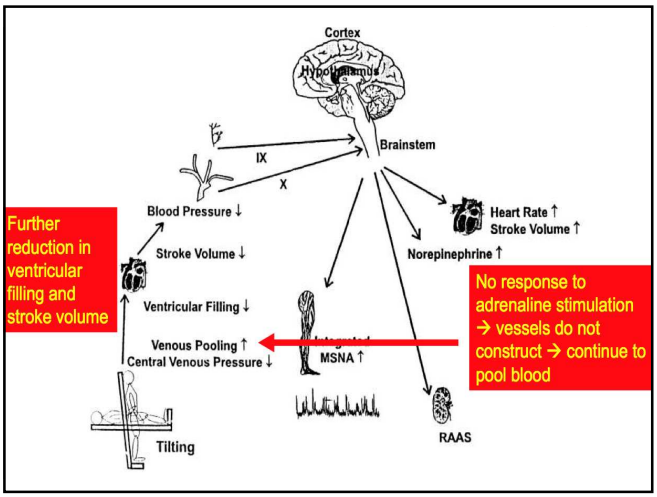
Pathophysiology

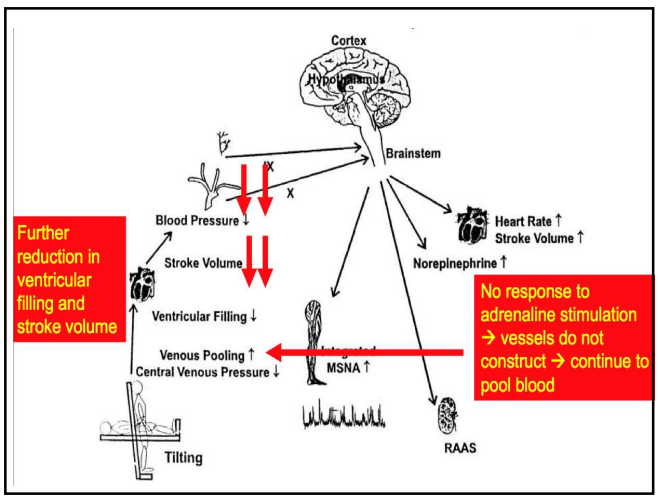
FASU

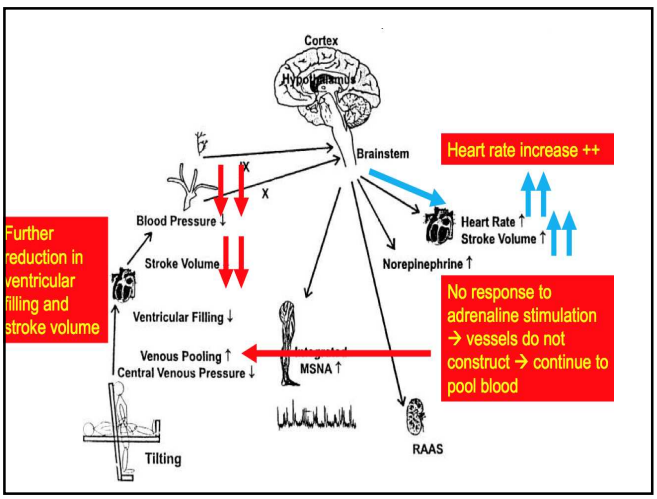
1. Peripheral autonomic denervation
2. Hypovolaemia
3. Hyperadrenergic stimulation
4. Anxiety & hypervigilence
5. Deconditioning
6. Mast cell activation syndrome

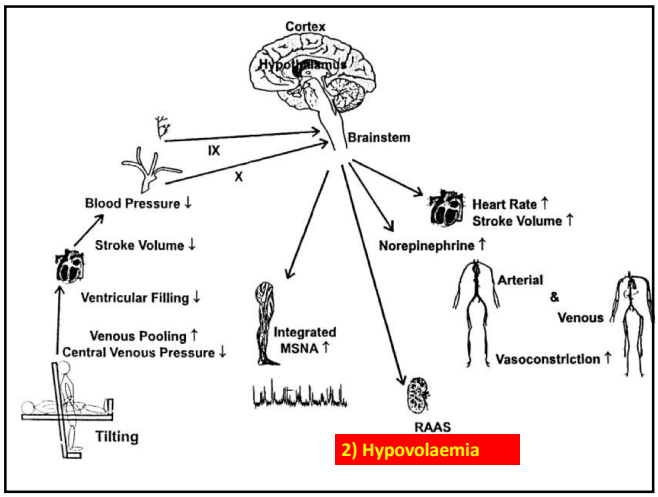


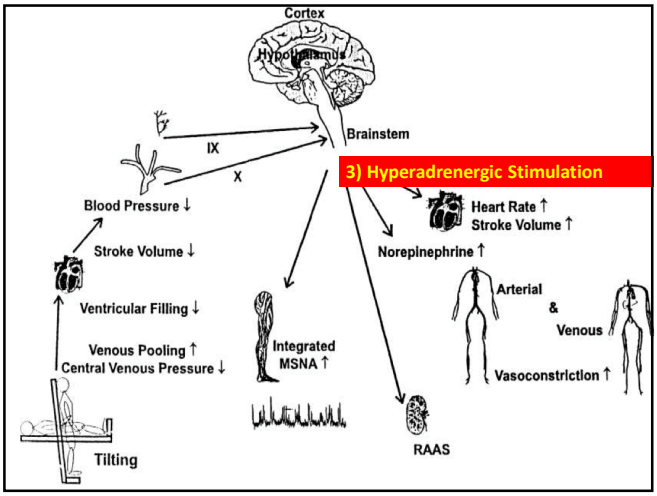


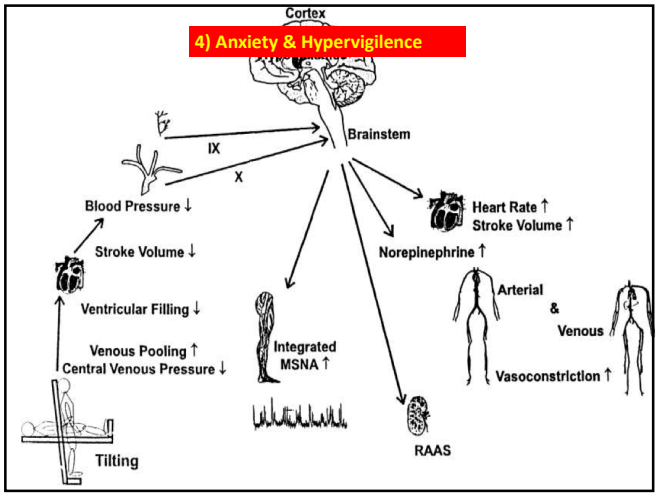












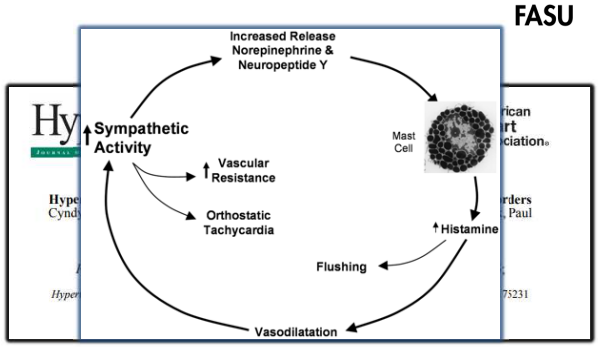
5) Deconditioning

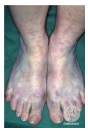
FASU

- Patients have reduced left ventricular mass, stroke volume & blood volume which improve with exercise training.
- Orthostatic symptoms induced by an initial illness can lead to overinterpretation of symptoms due to hypervigilance, which in turn leads to reduced physical activity & deconditioning.
- Unclear whether deconditioning is primary cause or secondary phenomenon.

6) Mast Cell Activation

FASU





Clinical Presentation

FASU

- Lightheadedness, weakness, blurred vision, fatigue, palpitations, tremulousness & anxiety on standing
- GI symptoms e.g. nausea, abdominal cramps, early satiety, bloating, constipation & diarrhea
- Chronic headaches, "brain fog"
- Evidence of venous pooling manifested by acrocyanosis & oedema on standing
- May have abrupt or insidious onset
- Severity variable – some profoundly incapacitated
- Many seen by cardiologists or neurologists with multiple investigations e.g. MRI brain, EEG, echo, holter etc

Believed to be associated with…

Journal of Adolescent Health 61 (2017) 577–582

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JOURNAL OF ADOLESCENT HEALTH
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Original article

Reports of Postural Orthostatic Tachycardia Syndrome After Human Papillomavirus Vaccination in the Vaccine Adverse Event Reporting System

Jorge Arana, M.D., M.P.H. [a,*], Adamma Mba-Jonas, M.D., M.P.H. [b], Christopher Jankosky, M.D., M.P.H. [b], Paige Lewis, M.S.P.H. [a], Pedro L. Moro, M.D., M.P.H. [a], Tom T. Shimabukuro, M.D., M.P.H., M.B.A. [a], and Maria Cano, M.D., M.P.H. [a]

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[b] Office of Biostatistics and Epidemiology, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration, Silver Spring, Maryland

Article history:
Keywords: Hu
Vaccine Adver

Topical Review Article

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Journal of Child Neurology
2017, Vol. 32(11) 956-965

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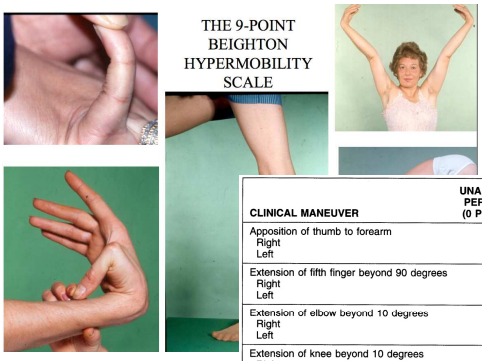
SAGE

Breann N. Butts, MD[1], Philip R. Fischer, MD[2], and Kenneth J. Mack, MD, PhD[3]

Association with Ehlers-Danlos Syndrome Type 3

- Joint Hypermobility Syndrome
- Least severe form of EDS
- Increased flexibility of joints - subluxation, dislocation or injury
- Chronic pain & other systemic symptoms e.g. fatigue, IBS
- Up to 70% patients suffer from some form of dysautonomia related symptoms
- Increase in joint laxity causing increased venous pooling with secondary hyperadrenergic state or receptor dysregulation predisposing to autonomic dysregulation has been postulated as the mechanism of association
- ?screen patients with POTS for JHS

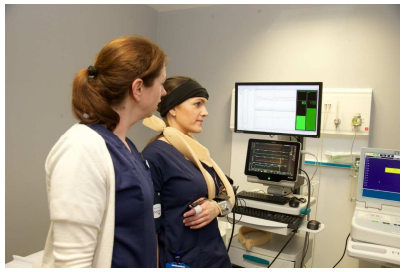


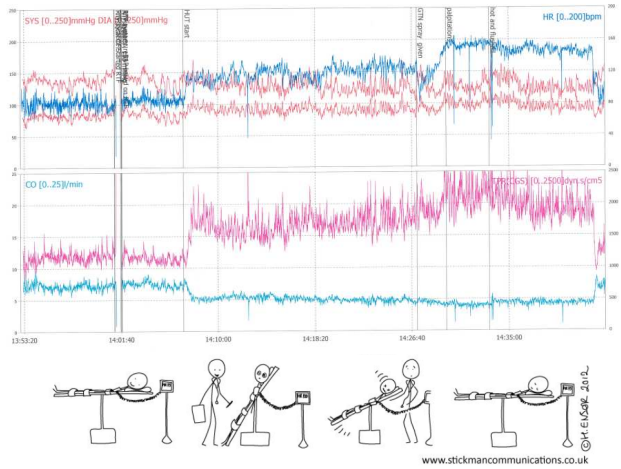
THE 9-POINT BEIGHTON HYPERMOBILITY SCALE

CLINICAL MANEUVER	UNABLE TO PERFORM (0 POINTS)	ABLE TO PERFORM (1 POINT)
Apposition of thumb to forearm Right Left	 0 0	 1 1
Extension of fifth finger beyond 90 degrees Right Left	 0 0	 1 1
Extension of elbow beyond 10 degrees Right Left	 0 0	 1 1
Extension of knee beyond 10 degrees Right Left	 0 0	 1 1
Forward flexion of trunk, legs straight, palms touching floor	0	1
Total Beighton Score (sum of points for each maneuver)	0 to 9 points	

Diagnosis

- Thorough history: chronicity, impact on ADLs, potential triggers e.g. dehydration, heat, alcohol & exercise, patient's lifestyle including diet & exercise, autonomic systems review
- Physical examination & ECG
- Haematocrit, TFTs, holter & echo sufficient to screen for potential CV or systemic aetiology
- Active Stand Test with finometry
- Head Up Tilt Table Test

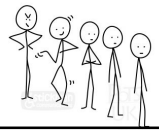




Treatment: non pharmacological

FASU

- **Withdraw medications** that may worsen POTS or OI
- Increase blood volume with enhanced **salt & fluid** intake, 10-12g/day & 2-3L/day respectively
- Reducing venous pooling with **compression garments, physical counter manouevres**
- Regular, structured, graduated & supervised **exercise program** featuring aerobic reconditioning with some resistance training
- **Education** re physiology

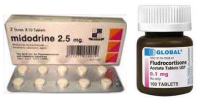


Treatment: pharmacological

FASU

Hypovolaemia:

- **Fludrocortisone**: mineralocorticoid with some glucocorticoid properties. Starting dose 100mcg, stored in fridge.
- **Midodrine**: alpha 1 agonist, vasoconstrictor. Starting dose 5mg BD. S/E: GI upset, headache, supine HTN
- IV saline: "rescue therapy"



Treatment: pharmacological

FASU

Palpitations/ Hyperadrenergic POTS

- Low-dose **propranolo**l (10-20mg TDS)
- **Ivabradine**: (2.5-7.5mg BD) anti-anginal. 3 retrospective analyses (Delle Donne et al., 2018; McDonald et al., 2011; Ruzieh et al., 2017) showed Ivabradine to be well tolerated & to decrease heart rate without impacting BP.
- **Pyridostigmine**: Acetylcholinesterase inhibitor, limited by adverse effects of diarrhea, abdominal pain & cramps, nausea, urinary symptoms
- **Clonidine** (alpha-2 agonist)/**Methyldopa**: S/E drowsiness & fatigue

Recommendations—Treatment for POTS

	Class	Level
A regular, structured, and progressive exercise program for patients with POTS can be effective.	IIa	B-R
It is reasonable to treat patients with POTS who have short-term clinical decompensations with an acute intravenous infusion of up to 2 L of saline.	IIa	C
Patients with POTS might be best managed with a multidisciplinary approach.	IIb	E
The consumption of up to 2–3 L of water and 10–12 g of NaCl daily by patients with POTS may be considered.	IIb	E
It seems reasonable to treat patients with POTS with fludrocortisone or pyridostigmine.	IIb	C
Treatment of patients with POTS with midodrine or low-dose propranolol may be considered.	IIb	B-R
It seems reasonable to treat patients with POTS who have prominent hyperadrenergic features with clonidine or alpha-methyldopa.	IIb	E
Drugs that block the norepinephrine reuptake transporter can worsen symptoms in patients with POTS and should not be administered.	III	B-R
Regular intravenous infusions of saline in patients with POTS are not recommended in the absence of evidence, and chronic or repeated intravenous cannulation is potentially harmful.	III	E
Radiofrequency sinus node modification, surgical correction of a Chiari malformation type I, and balloon dilation or stenting of the jugular vein are not recommended for routine use in patients with POTS and are potentially harmful.	III	B-NR

Future directions

FASU

- ?autoimmune basis to POTS
- Antibodies to alpha-1, beta-1, and beta-2 adrenergic receptors have been detected
- Antibodies to M1 & M2 muscarinic acetylcholine receptors also detected
- ?IVIG as a treatment for POTS

Case Study

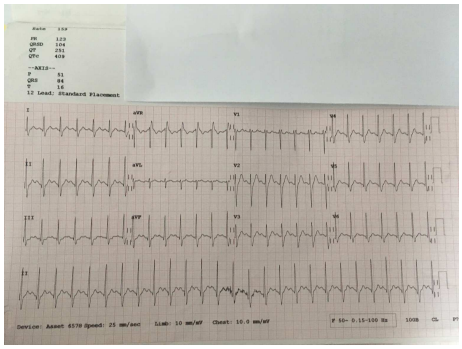
- 17 yo male presenting to AMAU April 2018
- C/O episodic palpitations for 2 months

- Associated chest pain
- Heaviness in legs
- Associated loose stools
- PMHx: Admission in Feb with pancreatitis due to alcohol binge
- Medications: Bisoprolol 2.5mg
- SHx: Student at PLC, non smoker, no C2H5OH
- FHx: nil

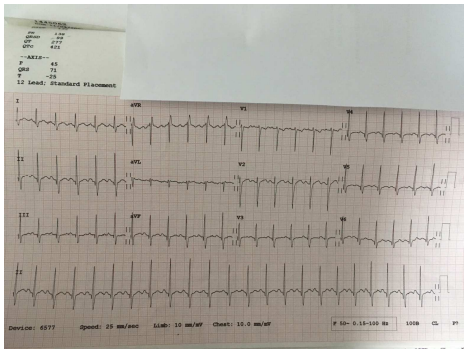
Case Study continued

- O/E: normal affect, normotensive, HR 130s
- Normal CVS, Resp, Abdo, Neuro exam
- Investigations: Bloods, CXR, Echo normal
- Telemetry HR 80s to 90s with episodic increase to 130s/140s

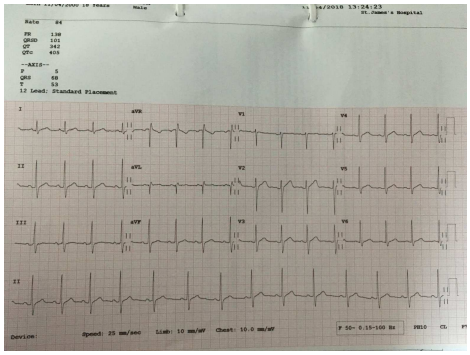
ECGs



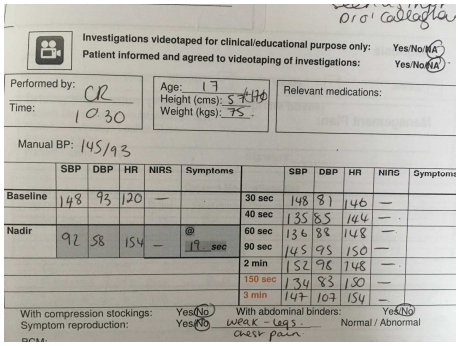
ECGs



ECGs



Active Stand



Investigations videotaped for clinical/educational purpose only: Yes/No/NA
Patient informed and agreed to videotaping of investigations: Yes/No/NA

Performed by: CR
Time: 1030

Age: 17
Height (cms): 5'4"
Weight (kgs): 75

Relevant medications:

Manual BP: 145/93

	SBP	DBP	HR	NIRS	Symptoms
Baseline	148	93	120	—	
Nadir	92	58	154	—	@ 19 sec

	SBP	DBP	HR	NIRS	Symptoms
30 sec	148	81	146	—	
40 sec	135	85	144	—	
60 sec	136	82	148	—	
90 sec	145	95	150	—	
2 min	152	98	148	—	
150 sec	134	83	150	—	
3 min	147	107	154	—	

With compression stockings: Yes/No
Symptom reproduction: Yes/No weak - legs. chest pain

With abdominal binders: Yes/No
Normal / Abnormal

Case Study Outcome

FASU

- Started Ivabradine 2.5mg BD
- Discharged home
- Titrated to 7.5mg BD in outpatient setting
- Improvement of symptoms
- 5 day R-Test decreased episodes of tachycardia
- Patient gradually weaning himself of Ivabradine
- Worsening of symptoms with episode of tonsillitis

In Summary

FASU

- Poorly understood syndrome & pathophysiological aetiology
- Definition: symptoms on standing with an increase in HR ≥30bpm & absence of orthostatic hypotension
- There can be a significant psychological overly with incapacitating symptoms
- Diagnosed with active stand/ HUTT
- Best managed with MDT input including tailored physiotherapy exercise programmes
- Remain open minded!

Practicalities

FASU

- Validate your patient
- Set realistic goals
- Provide clear & constructive advice
- Give hope

Table 2. Tips for discussing exercise

•Don't give the impression that you are blaming the patient for their exercise intolerance.
•Acknowledge that anyone who has an orthostatic disorder would have difficulty exercising.
•Suggest that you will work together to gradually improve the patient's exercise capacity.
•Explain the physiological benefits of regular exercise, particularly its ability to increase blood volume, which is important in POTS

Thank-you!

FASU