Orthostatic intolerance in EDS: More than just POTS

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Presenter Disclosure Information

Peter C. Rowe, MD

- No relationships to disclose
- Off-label uses of several drugs will be discussed

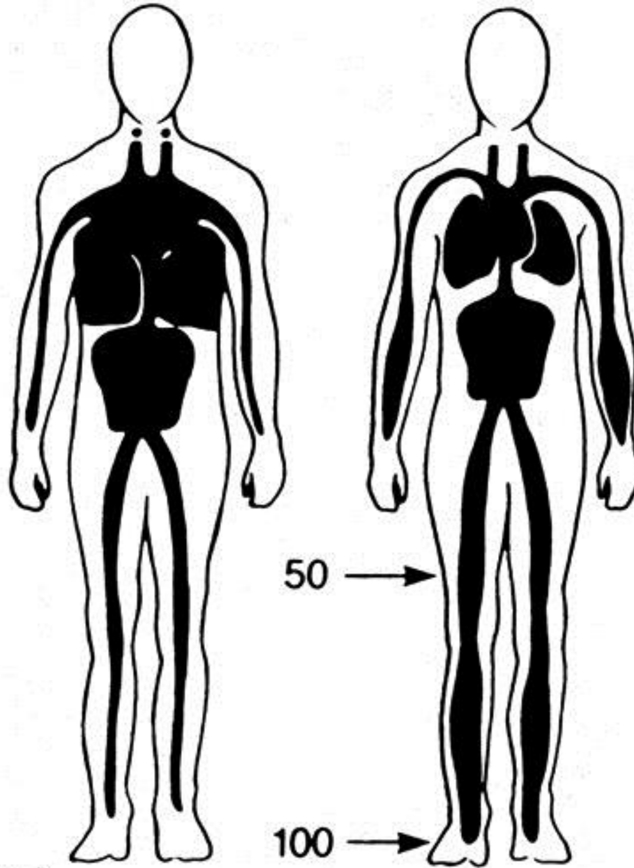
OI is more than just POTS

- Orthostatic intolerance definition
- Chronic daily OI symptoms can be associated with several circulatory patterns:
  - Low orthostatic tolerance in the absence of NMH or POTS
  - Neurally mediated hypotension (NMH)
  - Both NMH and POTS
  - Caused by other conditions

Orthostatic Intolerance

The term “orthostatic intolerance” refers to a group of clinical conditions in which symptoms worsen with assuming and maintaining quiet upright posture and improve (but are not necessarily abolished) by recumbency.

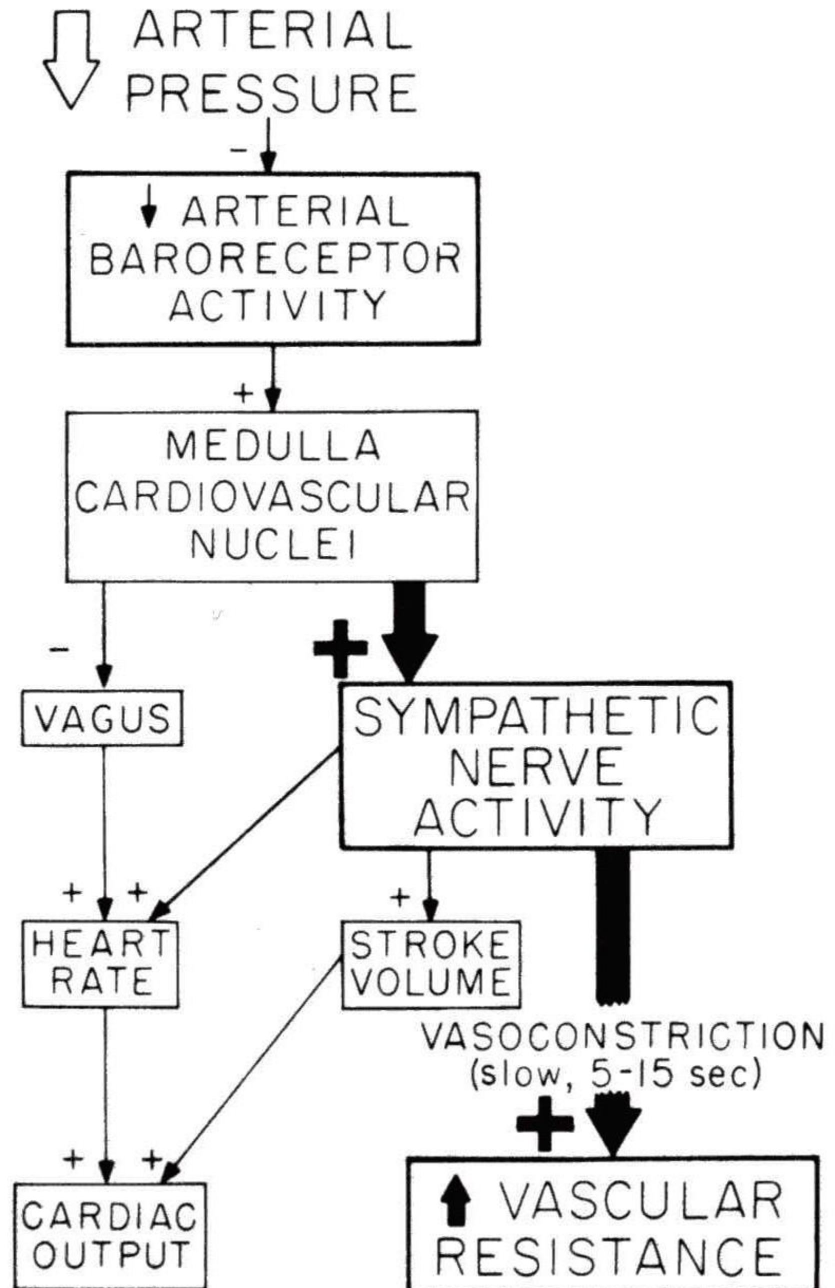
Modified from: Low PA, Sandroni P, Joyner M, Shen WK. Postural tachycardia syndrome (POTS). J Cardiovasc Electrophysiol 2009;20:352-8.



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

Low PA

Normal physiological responses to orthostatic stress



Rowell LB

Human Cardiovascular Control, 1993

Symptoms of Orthostatic Intolerance

Lightheadedness
Syncope
Diminished concentration
Headache
Blurred vision
Fatigue
Exercise intolerance

Dyspnea
Chest Discomfort
Palpitations
Tremulousness
Anxiety
Diaphoresis
Nausea

Due to reduced cerebral blood flow

- Lightheadedness
- Syncope
- Diminished concentration
- Headache
- Blurred vision
- Fatigue
- Exercise intolerance

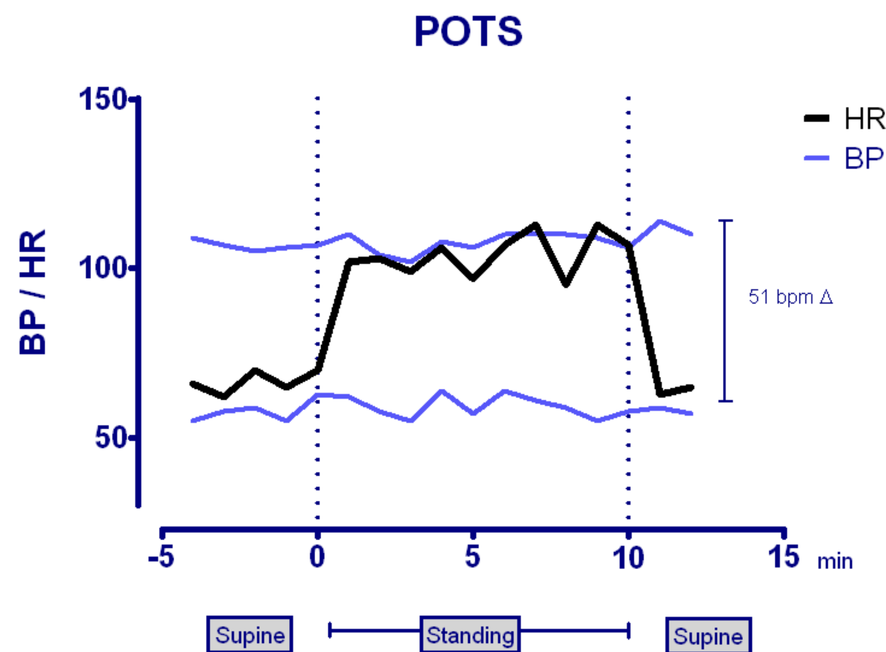
- Dyspnea
- Chest Discomfort
- Palpitations
- Tremulousness
- Anxiety
- Diaphoresis
- Nausea

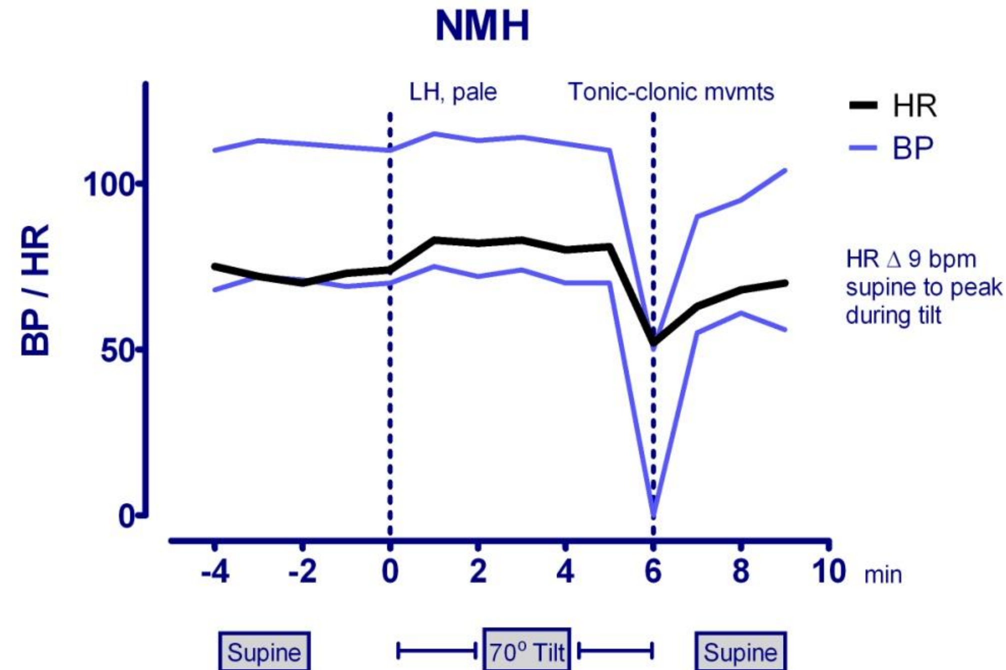
Due to 2° hyperadrenergic response

- Lightheadedness
- Syncope
- Diminished concentration
- Headache
- Blurred vision
- Fatigue
- Exercise intolerance

- Dyspnea
- Chest Discomfort
- Palpitations
- Tremulousness
- Anxiety
- Diaphoresis
- Nausea

Common forms of orthostatic intolerance





POTS: 40 bpm ↑ in HR in adolescents (30 bpm in adults) in first 10 min of standing/HUT, or HR > 120 bpm, <u>with OI symptoms</u>

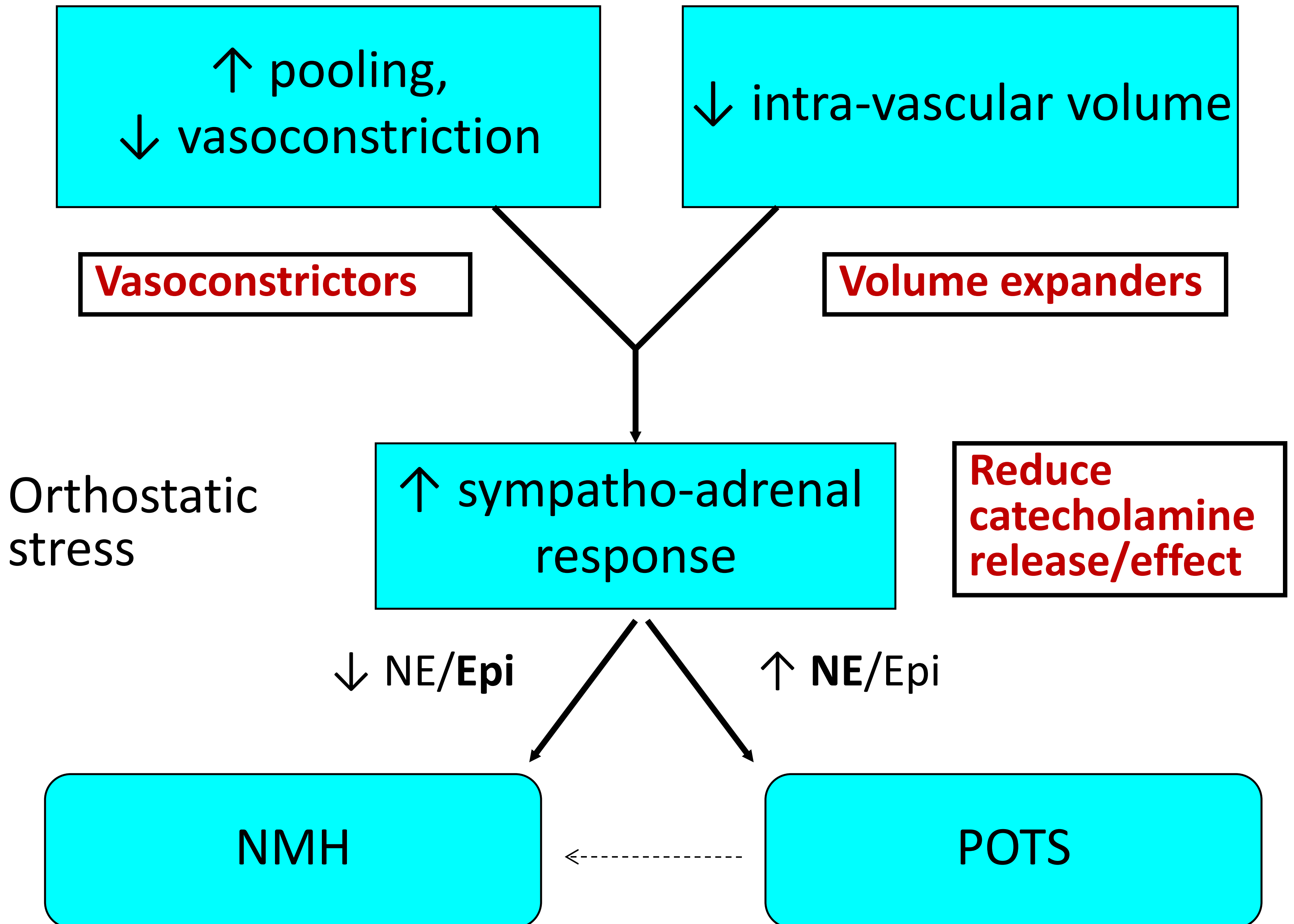
NMH: 25 mm Hg ↓ in SBP, with OI symptoms

NMH and POTS have similar chronic symptoms

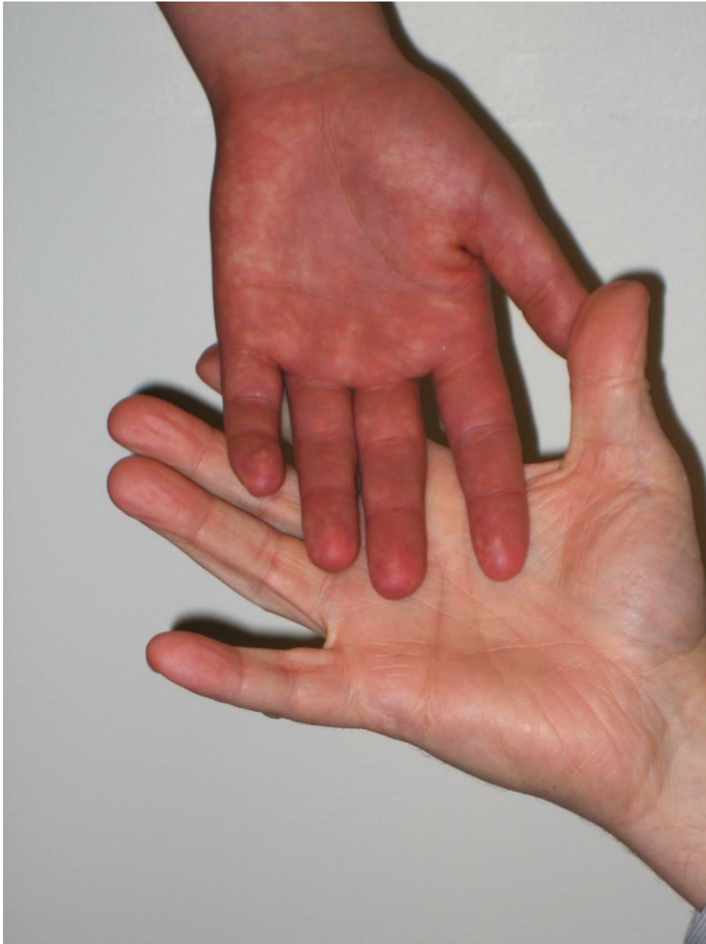
Goldstein DS, et al. Circulation 2002;106:2358

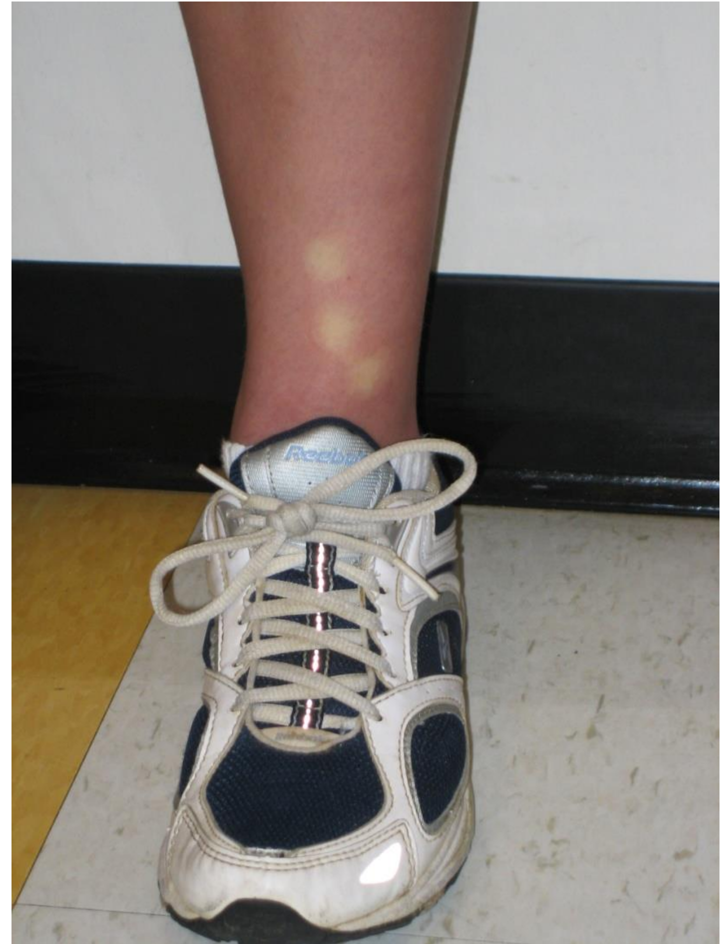
	Recurrent NMS N=36	POTS N=36
Orthostatic intolerance	28	35
Fatigue	23	28
Chest pain	17	20
Syncope	30	20
Heat intolerance	16	18
Headache	21	17
Palpitations	16	15
Exercise intolerance	11	14
Decreased concentration	18	13

NMH and POTS have some associated physiological abnormalities in common …


↑ pooling,
↓ vasoconstriction
↓ intra-vascular volume
Vasoconstrictors
Volume expanders
Orthostatic stress
↑ sympatho-adrenal response
Reduce catecholamine release/effect
↓ NE/Epi
↑ NE/Epi
NMH
POTS

Dependent acrocyanosis





Neurally Mediated Hypotension

- The most common cause of recurrent syncope
- More common in women, the young, those with low normal or low BP
- Common following infection
- Family members often affected
- Routine physical and lab tests normal
- Hypotension not detected unless orthostatic stress is prolonged
- Fatigue common for hours after syncope

OI is more than just POTS

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17 year old with fatigue

- Onset of fatigue, headaches, and joint pain at 15, associated with dysmenorrhea; Rx OCP
- 2 years after onset, after trip to endemic area, develops Lyme disease, with a 16 cm erythema migrans rash (confirmed by MD), associated with knee and hip pain.
- Rx: amoxicillin for 1 month

17 year old with fatigue

- Rash and widespread joint pain resolve
- 2 months after Lyme disease, has worse fatigue, LH, joint pain, HA, sore throat, poor concentration
- Fatigue is daily despite 7-9 hrs of sleep/night; sleep is unrefreshing. Naps after school on most days. Fatigue is worse with periods, when standing in line, after exercise.

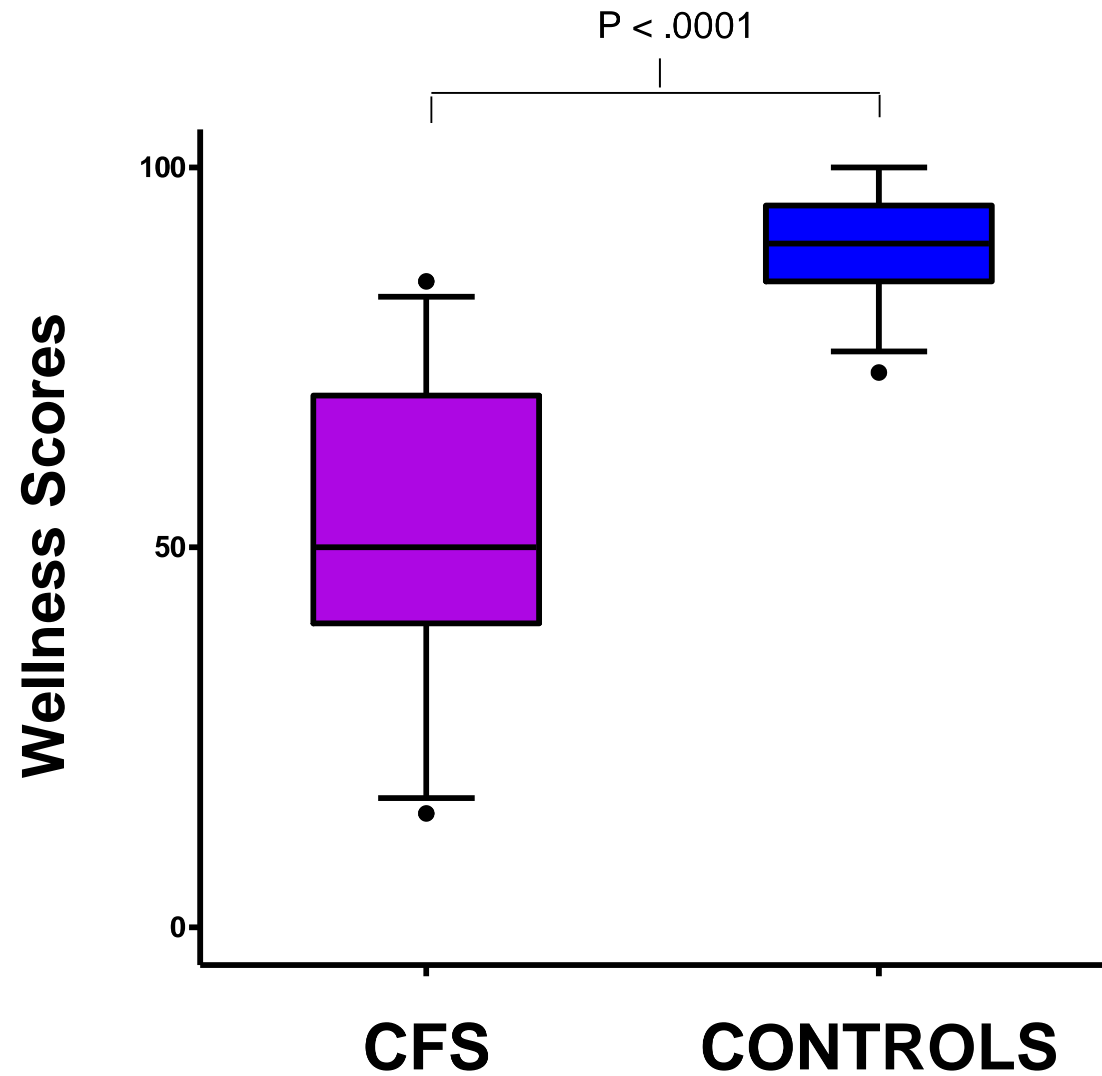
17 year old with fatigue

- Able to attend school full-time, but can’t exercise like she did before
- Headaches are bilateral, frontal and occipital, with no pounding. More common if sitting for a long time
- Low back pain with standing
- Joint pain (no swelling) in the R hip and knee
- Some R hip subluxation

17 year old with fatigue

- Zones out a lot more in class in last 3 years.
- Lightheaded when she stands, more commonly in the AM. No syncope. Fidgets a lot when standing.
- Nasal congestion, esp. in the fall
- Wellness score 70/100

Wellness Score



17 year old with fatigue: exam findings

- Nasal bogginess
- Joint hypermobility (Beighton score = 5)
- R hip tenderness with int and ext rotation
- Tender to palpation in lumbar area
- Limited straight leg raise (stretch at 36 degrees) for her degree of joint flexibility
- Standing test: LH, 38 bpm change in HR in 10 min
- Labs normal; ESR 12

Problem formulation

- Mild CFS
- Clinical dx of low orthostatic tolerance
- Hypermobile type EDS
- Postural dysfunctions/hip pain
- Dysmenorrhea and menstrual ↑ in fatigue
- Allergic rhinitis

Treatment approach

1. Explain & demystify, describe prognosis
2. Develop working hypotheses about the 1° influences on fatigue
3. Begin non-pharmacological therapies (sleep, ↑ salt/fluids, postural counter-measures, coping skills or CBT, PT and graded increases in exercise)
4. Begin pharmacological treatment as indicated, focusing on the dominant influences on symptoms (e.g., OI, sleep dysfunction, pain, HA, allergies, menstrual dysfunction, low mood, anxiety)
5. Reassess at regular intervals and repeat steps 1-4.

17 year old with fatigue: treatment

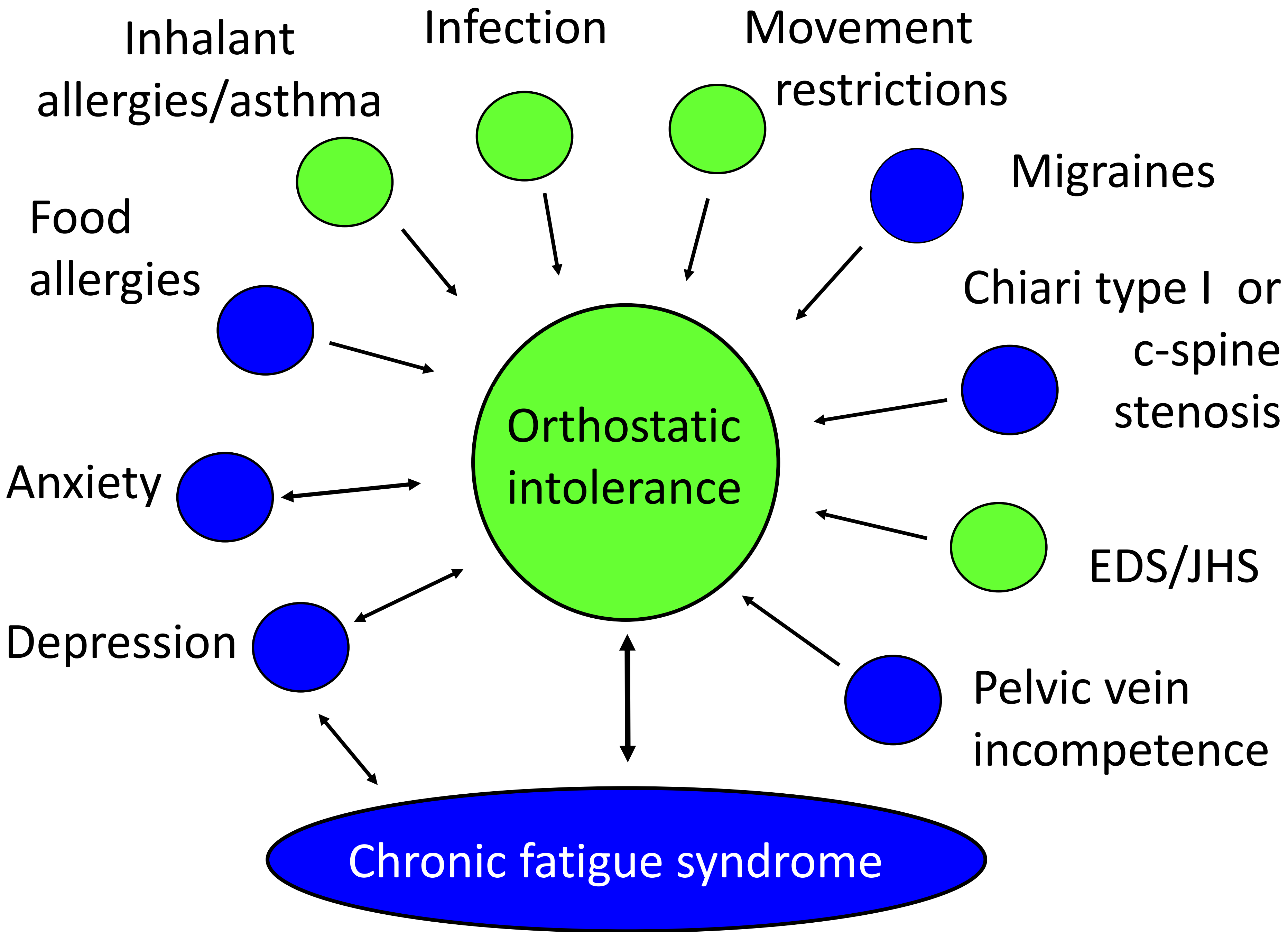
- Allergic rhinitis: antihistamine
- OI:
    - increased salt and fluids
    - postural counter-maneuvers
    - compression garments for OI
- Menstrual problems: Continuous OCP
- Manual PT for restricted movements

17 year old with fatigue: treatment

- PT identifies reduced mobility in lumbar spine, rotational abnormality in pelvis, with left hemipelvis anteriorly rotated, right side posteriorly rotated, with compensatory mechanical changes in thoracic region, including left hemi-diaphragm dysfunctions that he thinks are contributing to fatigue

17 year old with fatigue: follow-up

- At 2 month follow-up, still having OI symptoms and problems with concentration
- RX: methylphenidate ER
- 4 months: Wellness up to 82
- I year follow-up: finished 1st semester of nursing school. Walks 3-4 mi/day. Works out in gym 3 X/wk. Wellness 98/100.
- Off methylphenidate x 1 week, ↑ LH, HA, ftg.


Inhalant allergies/asthma
Infection
Movement restrictions
Migraines
Food allergies
Chiari type I or c-spine stenosis
Orthostatic intolerance
Anxiety
EDS/JHS
Depression
Pelvic vein incompetence
Chronic fatigue syndrome

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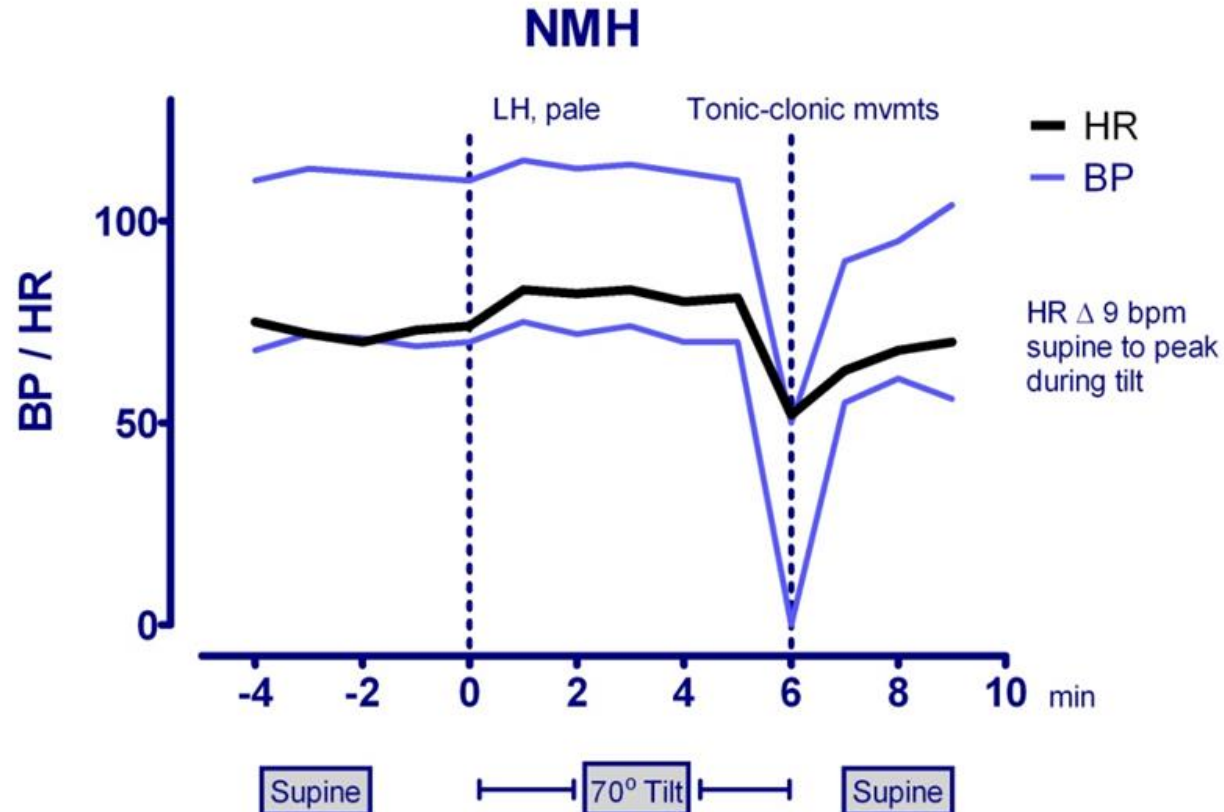
Medical student with chronic fatigue

- Onset of persistent fatigue, unrefreshing sleep, exercise intolerance, myalgias, cognitive difficulties at entry to SOM
- PMH: Syncope since age 11; usually twice a yr, often after standing or after showers
- Frequent knee dislocations, 4 spontaneous pneumothoraces

Medical student with chronic fatigue

- In medical school, much more lightheaded, now 2 episodes of presyncope/week, LH several times/day
- Worse fatigue after syncopal episodes
- Symptoms thought due to atypical depression, although mood reported as OK. Worse syncope on sertraline 150 mg/day.
- Had to repeat year 1

Medical student with chronic fatigue



(Joint and skin laxity noted by EP lab staff)

Medical student with chronic fatigue

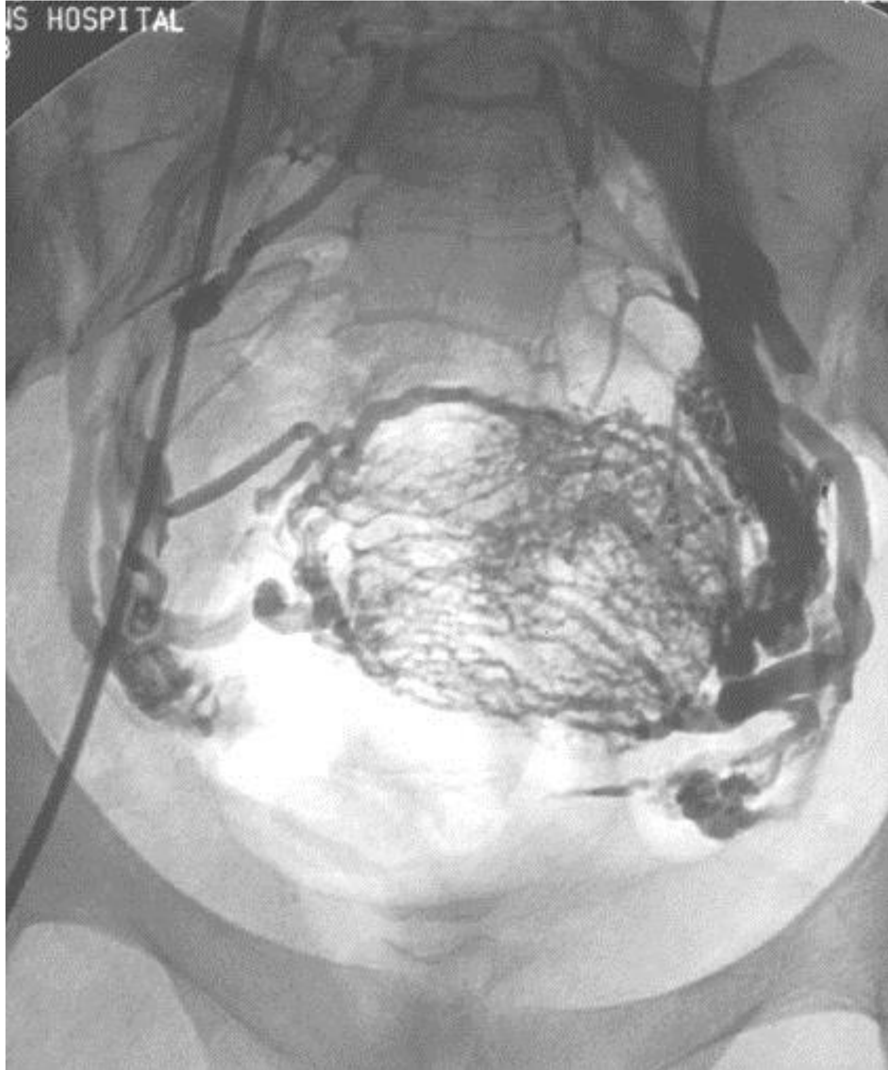
- Syncope resolved with increased salt, fluids, midodrine
- Echo: aortic root normal, mild MVP
- Dx: Ehlers-Danlos syndrome
- Persistent non-cyclic pelvic heaviness and low back pain with standing; concerned about ability to tolerate surgical clerkship

Pelvic Congestion Syndrome

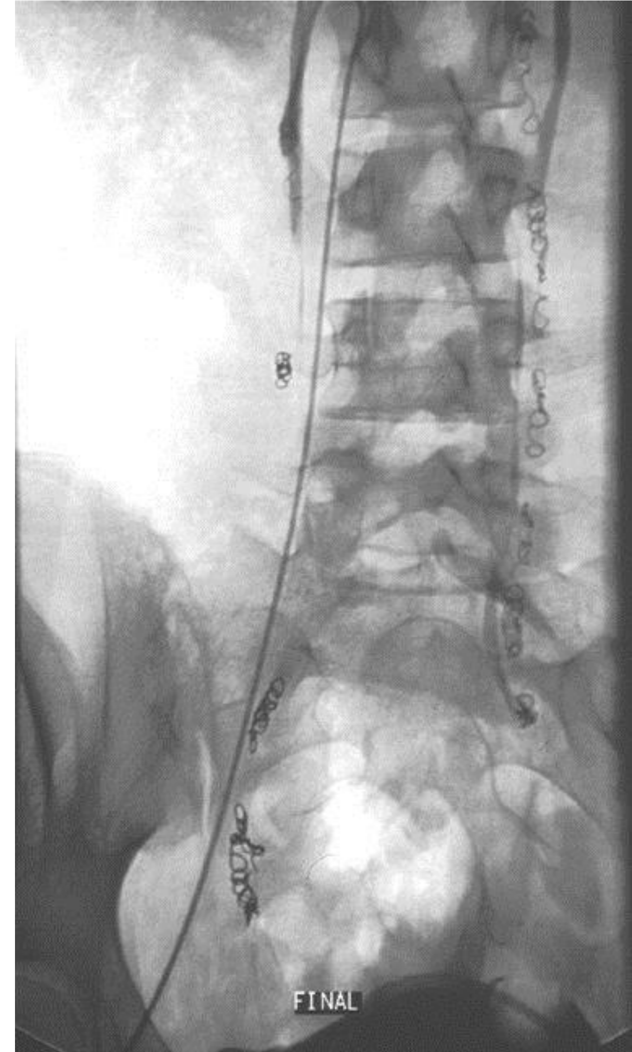
Venbrux AC, Lambert DL. Curr Opin Ob Gyn 1999; 11:395

- Pelvic heaviness or pain with long periods of standing
- Worse at end of the day, during menses
- Associated symptoms: fatigue, dyspareunia, bladder urgency
- Strong association with varicose ovarian veins
- 89% have > 80% relief after embolization of ovarian vein varicosities

Pre



Post



Medical student with chronic fatigue

- Improved pelvic pain and orthostatic symptoms after embolization of ovarian vein varices
- No further syncope
- Now able to stand for 7 hrs during surgical clerkship
- Wants to be a surgeon

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15 yr old with fatigue, LH, brain fog

Separation anxiety at school entrance (age 6-7)

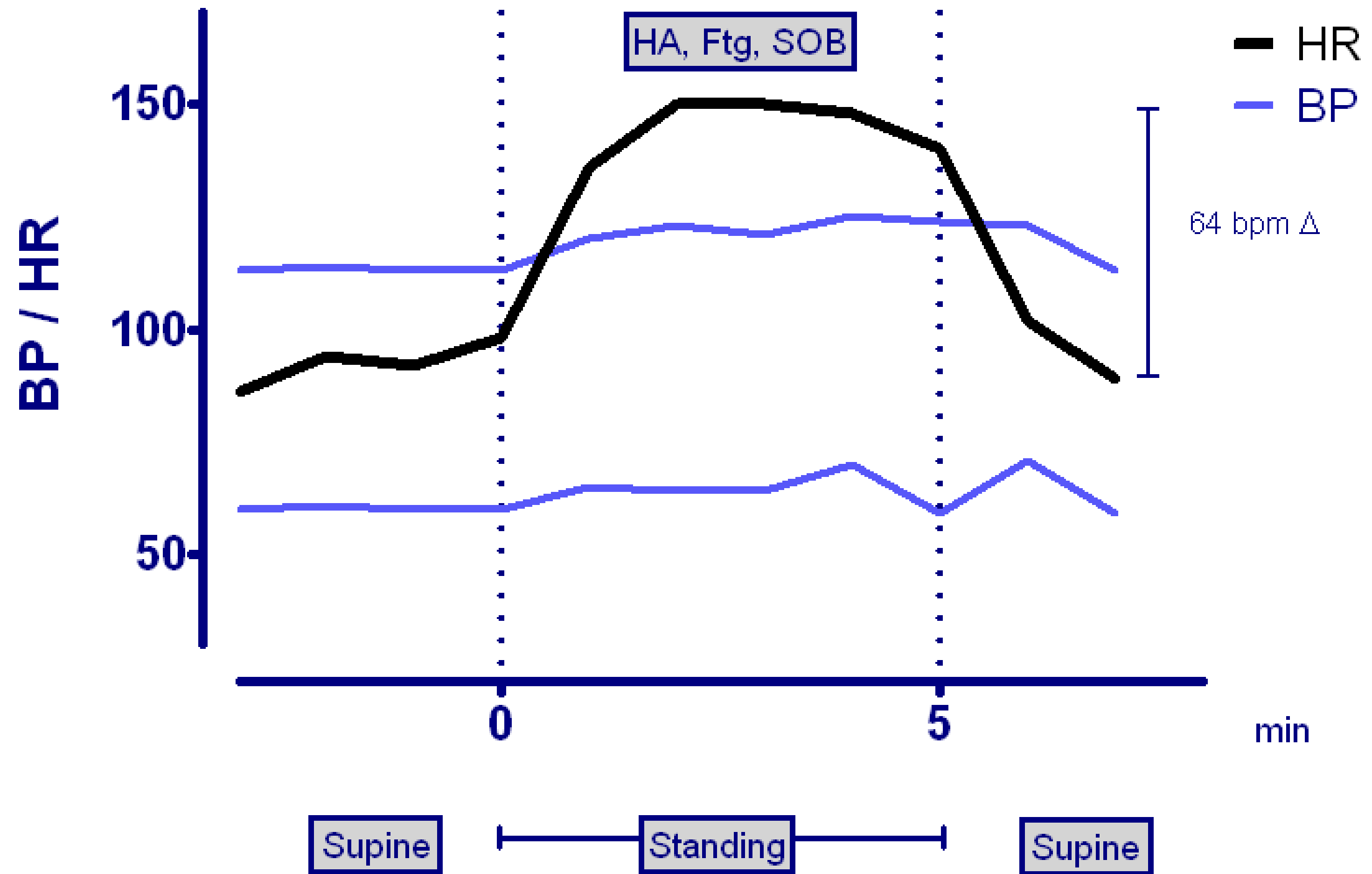
Age 12: after a GI virus, develops fatigue, LH, tachycardia, cognitive problems, myalgias, rare HA.

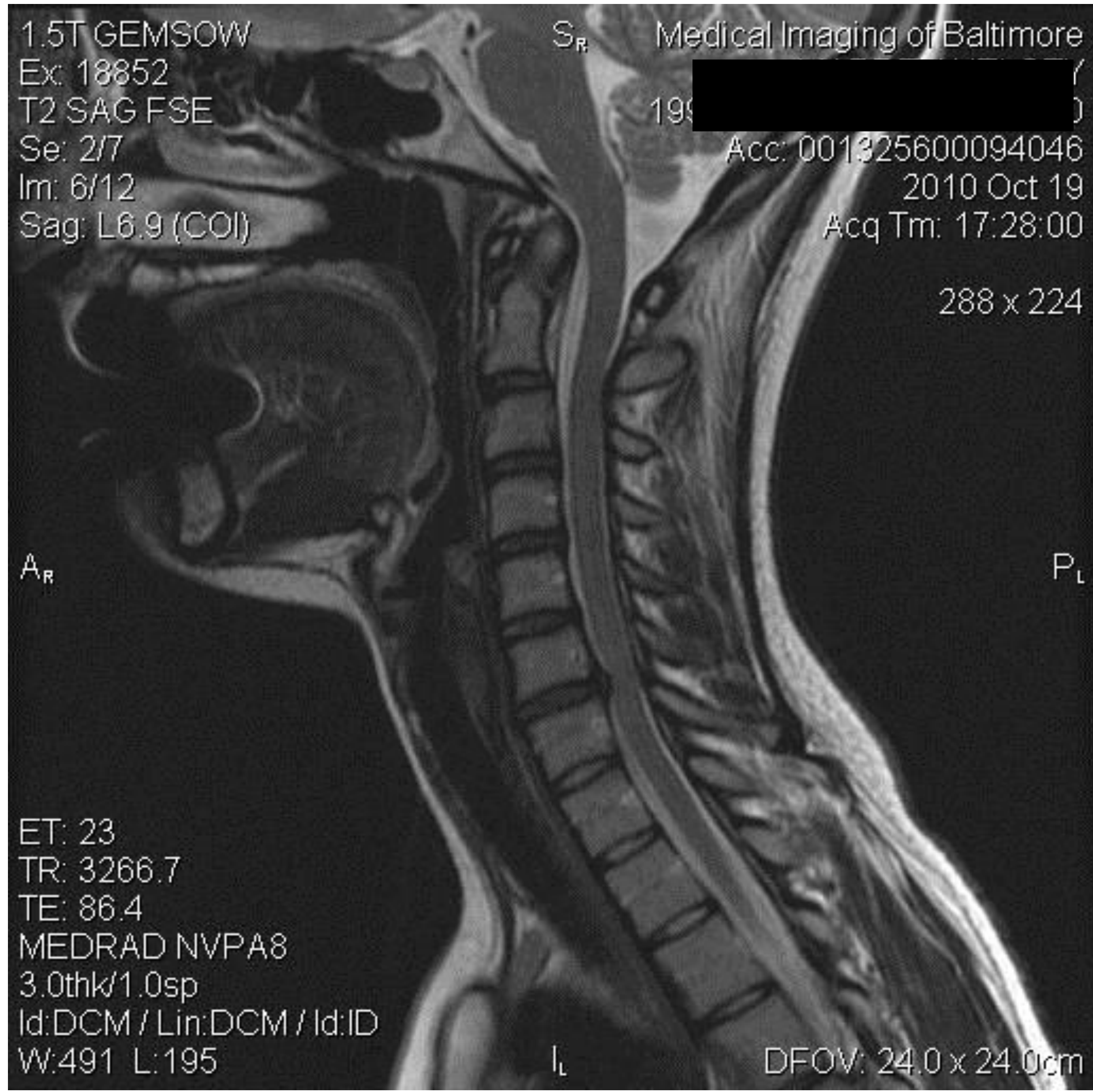
By 15, part-time schooling. Unable to attend after 10th grade due to fatigue, anxiety, LH, brain fog.

Minimal change in 5 yrs to many OI and anxiety meds

Age 19: neuro exam shows intermittently positive Hoffman sign

FH: mother has congenital cervical stenosis, 2 fusions at 34 and 43 yrs for degenerative discs, TOS surg x2


POTS
HA, Ftg, SOB
HR
BP
150
100
50
BP / HR
64 bpm Δ
0
5
min
Supine
Standing
Supine


1.5T GEMSOW
Ex: 18852
T2 SAG FSE
Se: 2/7
Im: 6/12
Sag: L6.9 (COI)
S
Medical Imaging of Baltimore
Acc: 001325600094046
2010 Oct 19
Acq Tm: 17:28:00
288 x 224
A
P
ET: 23
TR: 3266.7
TE: 86.4
MEDRAD NVPA8
3.0thk/1.0sp
Id:DCM / Lin:DCM / Id:ID
W:491 L:195
I
DFOV: 24.0 x 24.0cm

Course

- Elects to undergo conservative disc replacement at site of disc bulge at C 5-6
- Within 2 months, working as dog walker & vet tech
- Gradually able to exercise more, marked reduction in anxiety, tachycardia, LH; part-time univ. classes
- After 6 months, summer job in Colorado at dude ranch: arises at 6 AM to saddle horses, leads campers on horseback ride, cooks, active until late evening
- LTFU: full-time college student, part-time retail job, weekend wedding photographer 12 hrs/day

Orthostatic intolerance and chronic fatigue syndrome associated with Ehlers-Danlos syndrome

Peter C. Rowe, MD, Diana F. Barron, MS, Hugh Calkins, MD, Irene H. Maumenee, MD, Patrick Y. Tong, MD, PhD, and Michael T. Geraghty, MB, MRCPI

Of 100 adolescents seen in the CFS clinic at JHH over a 1 year period, we identified 12 subjects with EDS ($P < .01$, binomial test)

6 classical-type, 6 hypermobile-type EDS

11 females, 1 male

J Pediatr 1999;135:494-9

EDS In CFS Patients With Orthostatic Intolerance

5 had at least 3 episodes of syncope

7 had lightheadedness, but no syncope

NMH in 9/12, POTS in 10/12

Rowe PC, Barron DF, Calkins H, Maumanee IH, Tong PY, Geraghty MT. J Pediatr 1999;135:494-9

Conclusions

- Orthostatic intolerance symptoms are similar in those with NMH and POTS
- Both disorders are commonly present in individuals with EDS
- Low orthostatic tolerance can be present in those without POTS on a brief standing test
- NMH and POTS are not mutually exclusive
- It is important to look for other contributors to fatigue and orthostatic symptoms, especially if symptoms are not improving as anticipated

// ACKNOWLEDGEMENTS

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- Sunshine Natural Wellbeing Foundation (endowed Chair)
- Volunteer RA Colleen Marden
- Summer students (John Fan, Alli Johns, Marissa Flaherty, Jocelyn Ray, Samantha Jasion, Erica Cranston)
- Many families and patients:
  - Special thanks to the following:

    Boies, Bowen, Caldwell, Cornell, Kelly, Kiely, McFerron, Newbrand, Smith
  - Megan Lauver, Hannah Vogel