POTS in Pregnancy

Pregnancy Care ECHO
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Disclosures

- No financial disclosures relevant to this presentation.
- Medications discussed in the care of autonomic disorders are largely non-FDA approved.

Objectives

- How does POTS present?
  - Case illustration → presentation, definitions and diagnosis
- How do I use laboratory testing to assist with diagnosis?
  - Case illustration → Differential diagnosis
- What are first line therapies for POTS?
  - Case illustration → management
- What do I tell my patient with POTS who wants to become pregnant?
  - Case illustration → counselling and case planning

Case #1 Intro

32 year old G2P2001 woman s/p IVF for PCOS related infertility presented with 3 weeks of new onset symptoms associated with progesterone injections:

- **Near-syncope, feverishness, palpitations, SOB/chest tightness**
- No change after switch to progesterone gel

PMHx: anx/depr, asthma, IBS, Hashimoto's thyroiditis, pre-eclampsia/HTN with prior pregnancies

Sx persistent after d/c progesterone at 11 weeks, also developed:

- **Profound activity intolerance**/fatigue
- **Debilitating lightheadedness (worse with heat) with standing**
- Couldn't drive, care for other 2 kids

Orthostatic Intolerance (OI)

Source:https://en.wikipedia.org/wiki/Syncope_(medicine)#/media/File:Pietro_Longhi_027.jpg

- **Clinical** definition:
  - symptoms worsen upon assuming/maintaining upright posture + ameliorated by recumbency
- **Physiological** definitions:
  - **Postural tachycardia** (= increase of HR with standing)
  - **Blood pressure instability** (e.g. oscillations, neurally mediated hypotension)
  - **Delayed** variants
- Associated with various forms of syncope

Differential Diagnosis of Orthostatic Intolerance/Tachycardia:

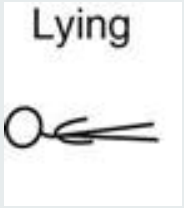
- **Endocrine**: thyroid, adrenal, pheochromocytoma
- **Cardiac**: inappropriate sinus tachycardia of pregnancy, tachyarrhythmia, orthostatic hypotension
- **Heme**: severe anemia
- **Other**: prolonged bedrest/deconditioning, chronic fatigue syndrome
- **Medications** which can aggravate orthostatic intolerance: ACE-I, high doses of α- and β-blockers/CCB, diuretics, vasodilators, MAOI, TCA's and phenothiazines
- **Neurological**: autonomic neuropathies (e.g. diabetic, autoimmune) or failure (rare)

Case #1 Exam

- **Cardiac** exam: normal
  - Holter monitor for 24hrs normal
  - TTE 2/2017: EF 64%, nml valves
- **Endocrine** exam: non-diagnostic

- Bedside VS – laying and standing (1 min):

BP 131/79, HR 74



BP 127/84, HR 101

Normal Physiology in Pregnancy

- ↑ in **blood volume** in early 1st trimester, through 3rd trimester
- **Cardiac output** ↑ in 1st/2nd trimesters
  - varied in 3rd (position dependent)
  - then ↓ postpartum
- Normal ↓ in BP due to peripheral vasodilatation, mediated by:
  - ↓ sensitivity to vasoconstrictors (angiotensin, NE)
  - ↑ production of vasodilators (NO, prostacyclin)
  - Modest increase in HR may also be observed

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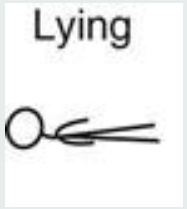


BP 127/84, HR 101

Postural Tachycardia Syndrome (PoTS)=

Increase in HR > 30 bmp or HR > 120 bpm

+ typical symptoms

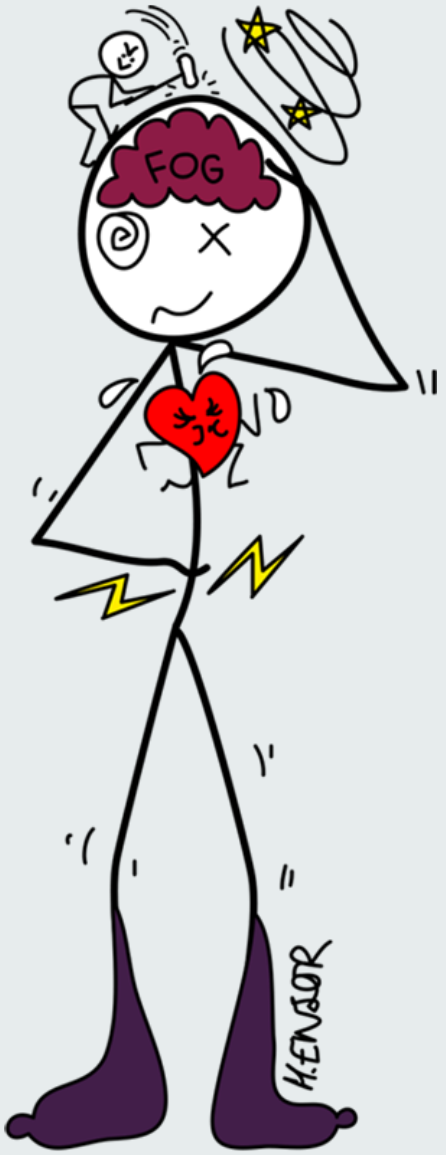
After 10 minutes for of upright posture

(absence of orthostatic hypotension)

Postural Tachycardia Syndrome (PoTS)

- **Idiopathic** (not explained by another disorder)
  - Chronic, recurrent, disabling symptoms with upright posture (often >6 months)
  - Must exclude other causes of orthostatic intolerance

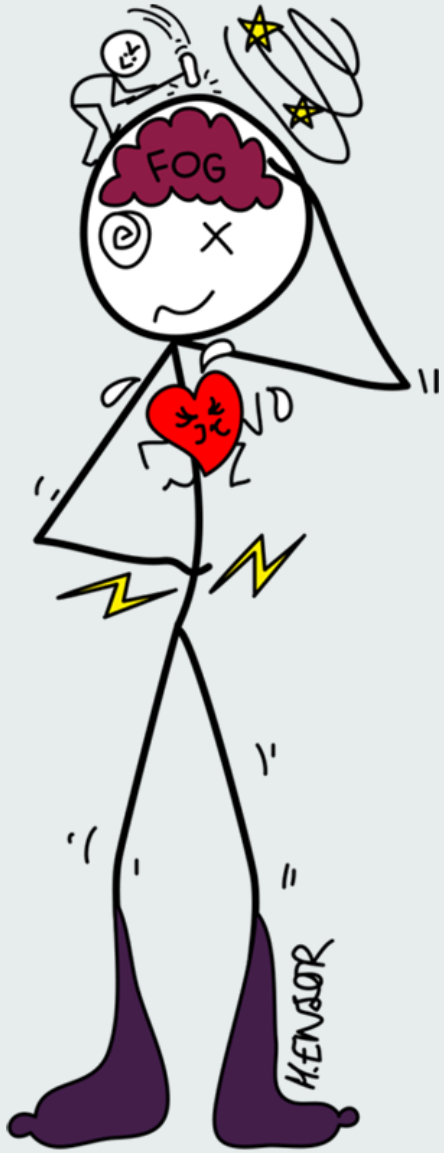
- Hypotheses: "final common pathway" for multiple overlapping pathophysiologies:
  - Limited **sympathetic neuropathy** affecting the lower body → impaired constriction → **venous pooling**
  - **Elevated sympathetic tone** → excessive **excitation**



References: Benarroch, 2012. Mayo Clin Proc. Garland et al. 2015, Curr Neurol Neurosci Rep. Image: http://www.potsuk.org/

Postural Tachycardia Syndrome

- Young (usually under 40 yo), F>M (5:1)
- Onset:
  - Post-viral or other infection/illness
  - Post-surgical
  - Post-traumatic
  - Insidious
- Worsened by:
  - Heat
  - Eating
  - Prolonged standing
  - Deconditioning/dehydration



References: Benarroch, 2012. Mayo Clin Proc. Garland et al. 2015, Curr Neurol Neurosci Rep. Image: http://www.potsuk.org/

Case #1 Continued..

32 year old G2P2001 woman s/p IVF for PCOS related infertility with continued symptoms, now at 18 weeks:

- Wheelchair bound outside of home
- Crawls around home to prevent severe lightheadedness/palpitations
- **Visual disturbances, headaches + tingling in extremities**

Due to severity and persistence → **neurological** consultation

- Neuro exam normal
- Autonomic testing ordered…

Autonomic Testing Laboratory

Opened Jan 2015

Imaging and Clinical
Neuroscience (INC) Center
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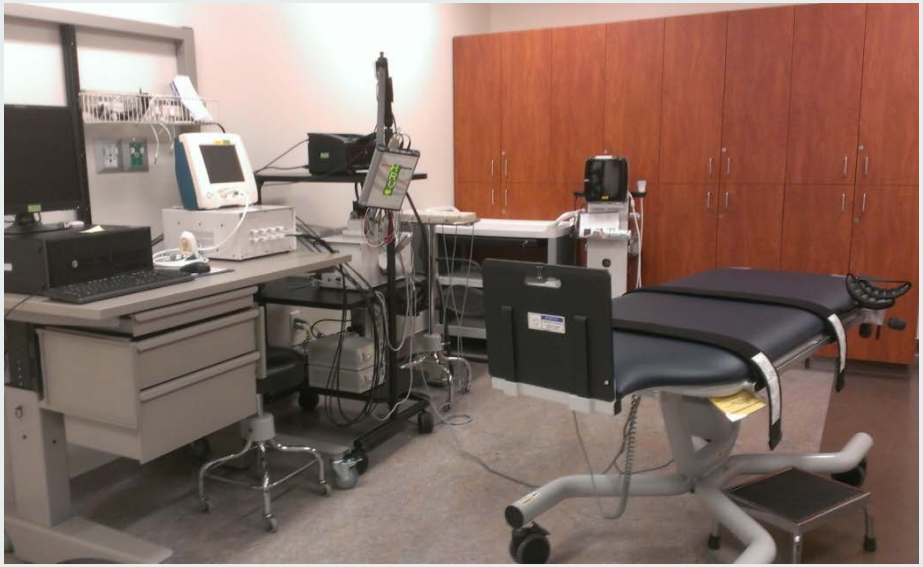


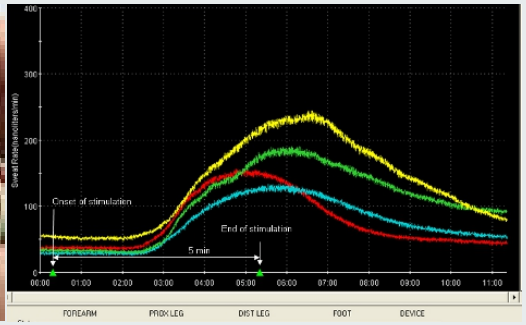
Standardized protocol/
laboratory setting

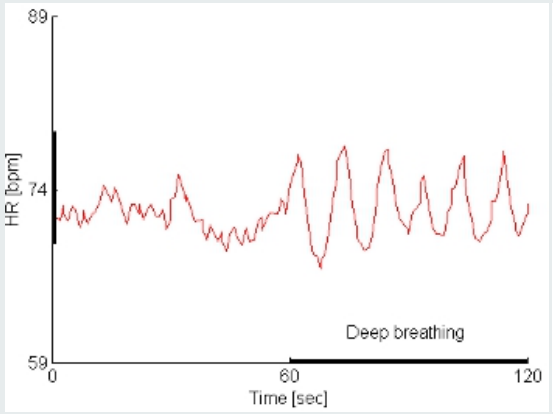
- Test Battery Selected for:
  - Non-invasive
  - Reproducible
  - Tolerability
- Normative values (age/sex)

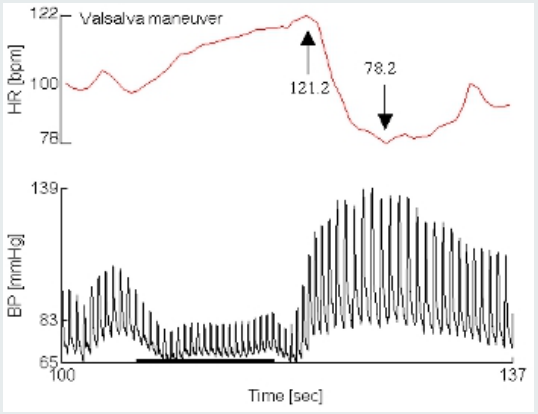
Autonomic Nervous System Testing

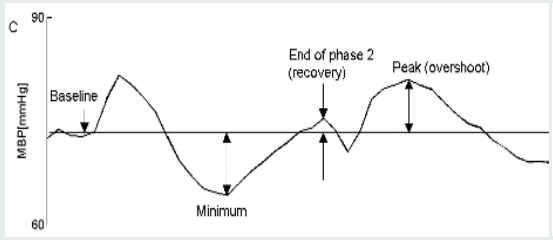
Standardized battery:

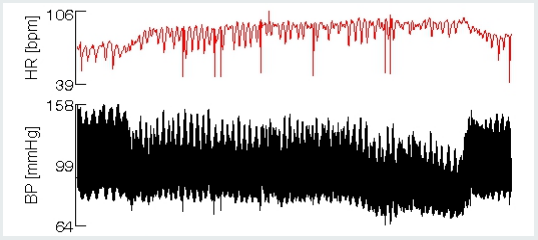
- Q-SWEAT
  - post-ganglionic sudomotor (**sweat**)
- Cardiovagal (**parasympathetic**)
  - **HR** changes with deep breathing
  - Valsalva ratio – **HR**
- Cardiovascular adrenergic (**sympathetic**)
  - Valsalva – **BP** changes
  - Orthostatic Challenge Test – **BP/HR** changes
    - Tilt-table testing NOT done in pregnancy











Source: Novak, P. Quantitative Autonomic Testing. *J. Vis. Exp.* (53), e2502, doi:10.3791/2502 (2011).

Case testing

Standing orthostatic challenge test →
increased headache, dizziness and lightheadedness upon standing

Increased BP oscillations

+

Excessive increase in HR

Case #1 Continued..

32 year old G2P2001 woman s/p IVF for PCOS related infertility with continued symptoms, now at 18 weeks

- First line management:
  - **Hydration**
  - Judicious **electrolyte** intake
    - **conservative sodium intake given HTN
    - **use of potassium and magnesium as alternative electrolytes stressed
  - **Compression** garment options
  - Recumbent **exercise** guidelines

- Referred to **high-risk OB** for co-management with **medication** initiation

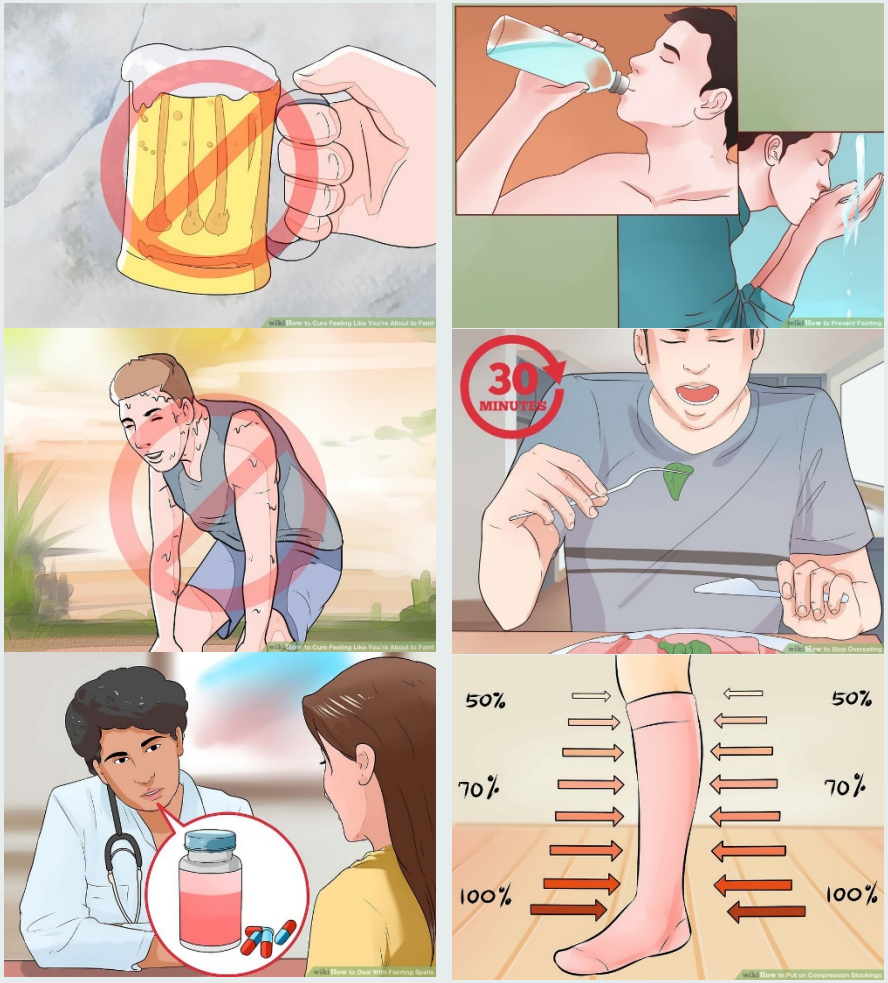
Management of Orthostatic Intolerance

DO's

- Increase **daily electrolytes** + **fluids** (2L)
  - Fluid boluses (8-16 oz cold H2O), transiently increase BP
  - Stay cool (layers)
- Judicious electrolyte use, including **salt** (goal 3-5 g/d)
- Reduce stress/get more sleep
- Address contributors:
  - **Medications** - Review/Stop
  - Treat **anemia/iron deficiency**
  - **Check blood sugar**

Image source: http://www.wikihow.com/Overcome-Dizziness
http://www.wikihow.com/Prevent-Fainting

Management of Orthostatic Intolerance

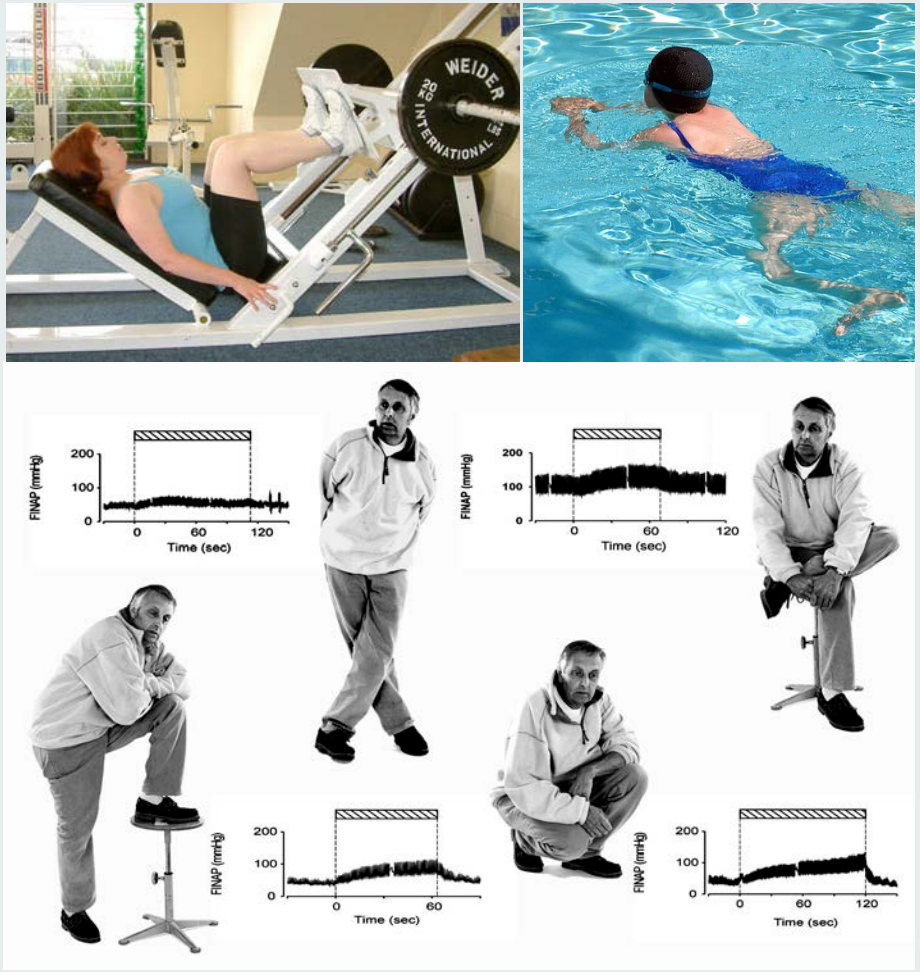


Avoid

- Triggers:
  - Excessive exertion in heat (cooling vests useful)
  - Large meals or eating too quickly
- Starting management with medications alone
  - **Combine** with fluids + salt + compression stockings

Management of Orthostatic Intolerance

- **Graduated Exercise Program**
  - To increase muscle tone
  - Promote venous return
- **Aerobic**: **recumbent → → upright**
  - Beginning 5-10 min, goal 30 min
  - 3 days/week
  - Intervals
- **Weight Training**: **Core/Lower extremity**
  - Leg press, toe press, leg extension, leg curl
  - Low resistance, 2 sets of 8-15 reps
  - 2-3 times/week
- **Compression** garments
  - abdominal binders (belly band)
  - thigh high stockings
- **Prevent syncope**
  - Avoid triggers
  - Physical counter maneuvers



Sources: https://commons.wikimedia.org/wiki/File:LegPressMachineExercise.JPG https://commons.wikimedia.org/wiki/Swimming#/media/File:Swimming.breaststroke.arp.750pix.jpg. Bennaroch. Continuum Lifelong Learning Neurol 2007;13(6):33–49.

Pharmacologic Treatment

** successful application in pregnancy without adverse maternal/fetal outcomes

not well studied in pregnancy

~ Currently no clinical guidelines for the use of medication to treat POTS in pregnancy~

- **Sympatholysis**
  - **Propranolol** (category C) ** Proposed as "first line" due to pregnancy/lactation profile
  - Alpha-2 agonist – Clonidine (category C)
- **Vasoconstriction**
  - Alpha-1 agonist – **Midodrine** (category C) **
- Expand **plasma volume** – mineralcorticoids
  - Fludrocortisone (category C) **
  - Desmopressin (pregnancy B)
- Modulate **central sympathetic control**
  - SSRI/SNRI - duloxetine (category C) and venlafaxine (category C) may help fatigue/anxiety in particular
- In patients with severe and disabling symptoms AND have failed above:
  - trial of intermittent **IV hydration with NS** may reduce sx/improve QOL ##

References: 1) Ruzieh and Grubb. Auton Neurosci. 2018 Feb 16. 2) Morgan et al. Auton Neurosci. 2018 May 9.

Case #2

- 20 year old G0P0 with PMH of POTS presents for pre-conception counseling.
  - Current management: florinef, propranolol, fluids/salt, compression

- **What to Expect**:
  - ?Possibly more hyperemesis gravidarum
    - up to 59%, related to comorbid migraine?
  - During pregnancy, the degree of cardiovascular adaption is highly variable:
    - 2/3 experience improvement/stable symptoms in the 2nd/3rd trimester
    - 1/3 experience worsening throughout pregnancy
  - No increase in maternal or fetal related complications
  - Fall and syncope precautions should be employed in all patients.
    - IF frequent falls → partial bedrest recommended to avoid traumatic injury

References: 1) Ruzieh and Grubb. Auton Neurosci. 2018 Feb 16. 2) Morgan et al. Auton Neurosci. 2018 May 9.

Delivery/Post-Partum Considerations

- Vaginal or CS can both be carried out successfully without complications
  - Mode of delivery should be based on obstetric complications, not POTS
- Choice of general vs. regional vs no anesthesia → decision should not be influenced by the diagnosis of POTS
  - Monitor VS per routine, for those who experience hypotension as needed →
    - fluid loading with IVF
    - use of vasopressors (phenylephrine ** favored over epinepherine)
  - Early initiation of pain relief may reduce the risk of hemodynamic instability during labor
  - Tachycardia should be evaluated per routine (e.g. PE, hydration, pain, etc)
- Post-partum
  - 6 months: ½ report stable/improved symptoms, ½ report worsening of symptoms
  - 1 year: 40% unchanged, 10% further improved, 50% worsened
- Ehlers-Danlos syndrome (EDS) is common associated diagnosis
  - Higher risk for maternal and fetal complications
  - Prolonged bleeding and wound healing

References: 1) Ruzieh and Grubb. Auton Neurosci. 2018 Feb 16. 2) Morgan et al. Auton Neurosci. 2018 May 9.

Take Home

- Exclude other caused/contributors
- First-line tx: fluids, electrolytes, compression
- Variable impact of normal pregnancy physiology on course

Thank you

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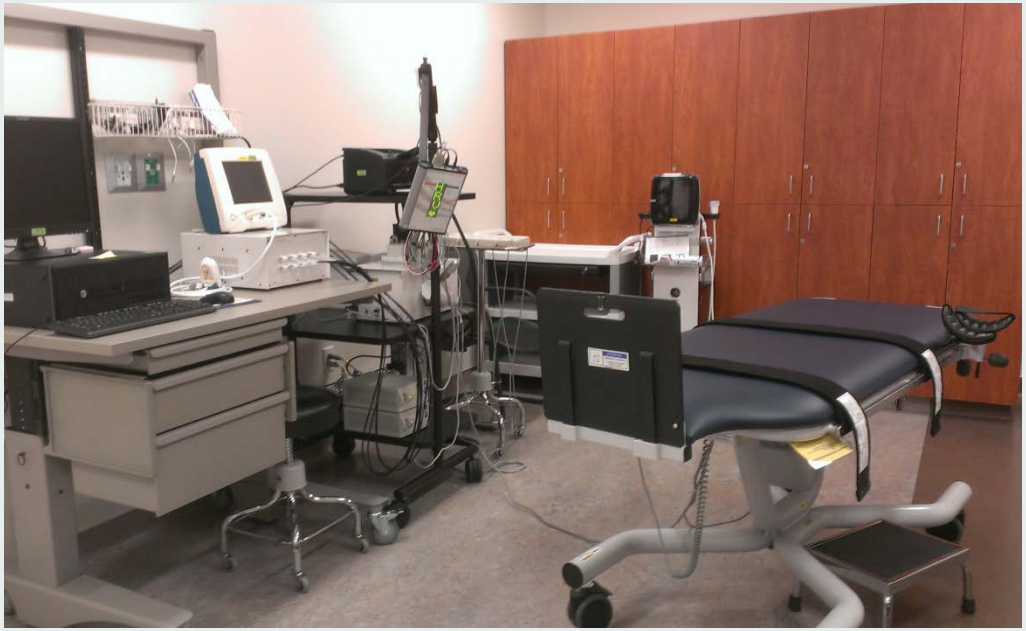

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- Ben Caler – lab technician

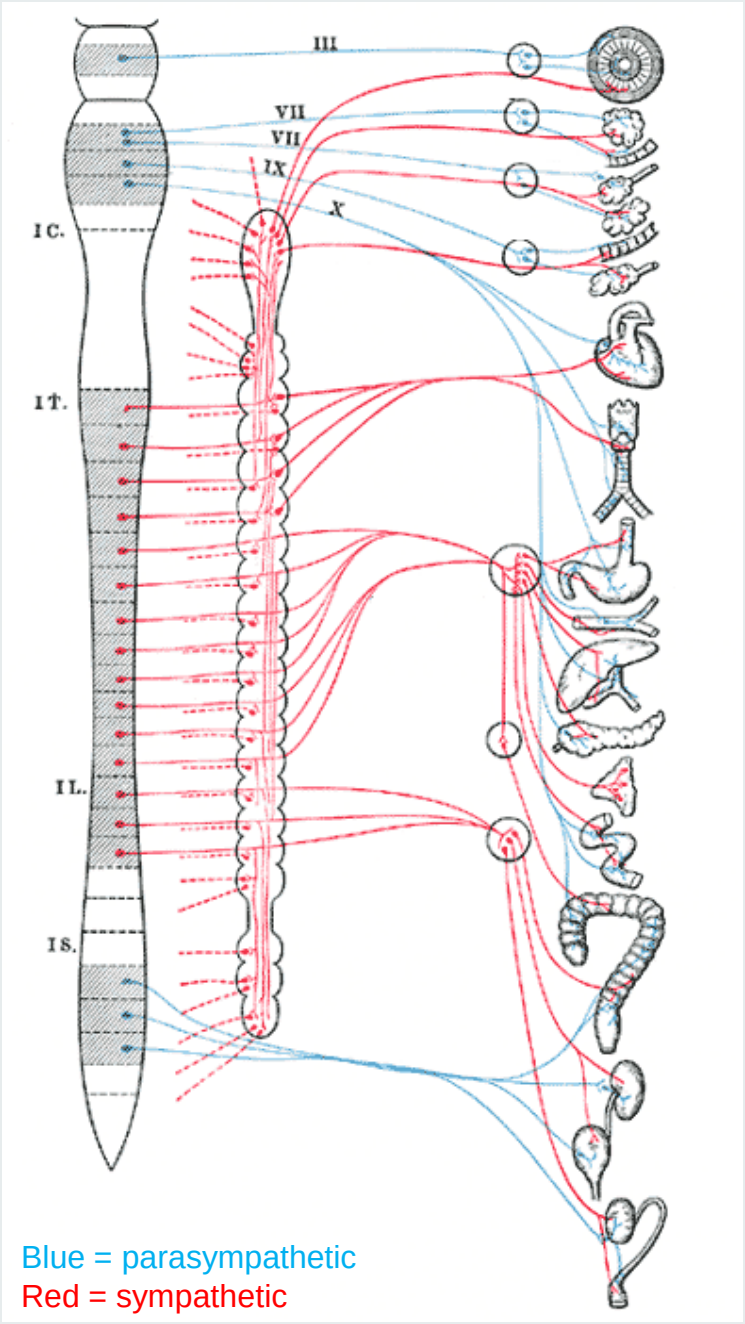
- **Support**:
- University of Utah, Department of Neurology
- School of Medicine, Office of Academic Development
- University of Utah Headache Physiology Laboratory

Additional Notes

- POTS is more common in women of child-bearing age
- A small number of previous studies have shown links between POTS and gynecological disorders.
  - Peggs et al. (2012) assessed the gynecological history and menstrual cycle lightheadedness of POTS patients compared to healthy controls
    - found significantly higher rates of amenorrhea, lightheadedness in all phases of the menstrual cycle and particularly in the follicular phase, dysfunctional uterine bleeding, endometriosis, galactorrhea, uterine fibroids, and ovarian cysts
  - A retrospective study by Blitshteyn et al. (2012) reported higher rates of miscarriage (59.9%) compared to the general population (31%)

Autonomic nervous system (ANS)

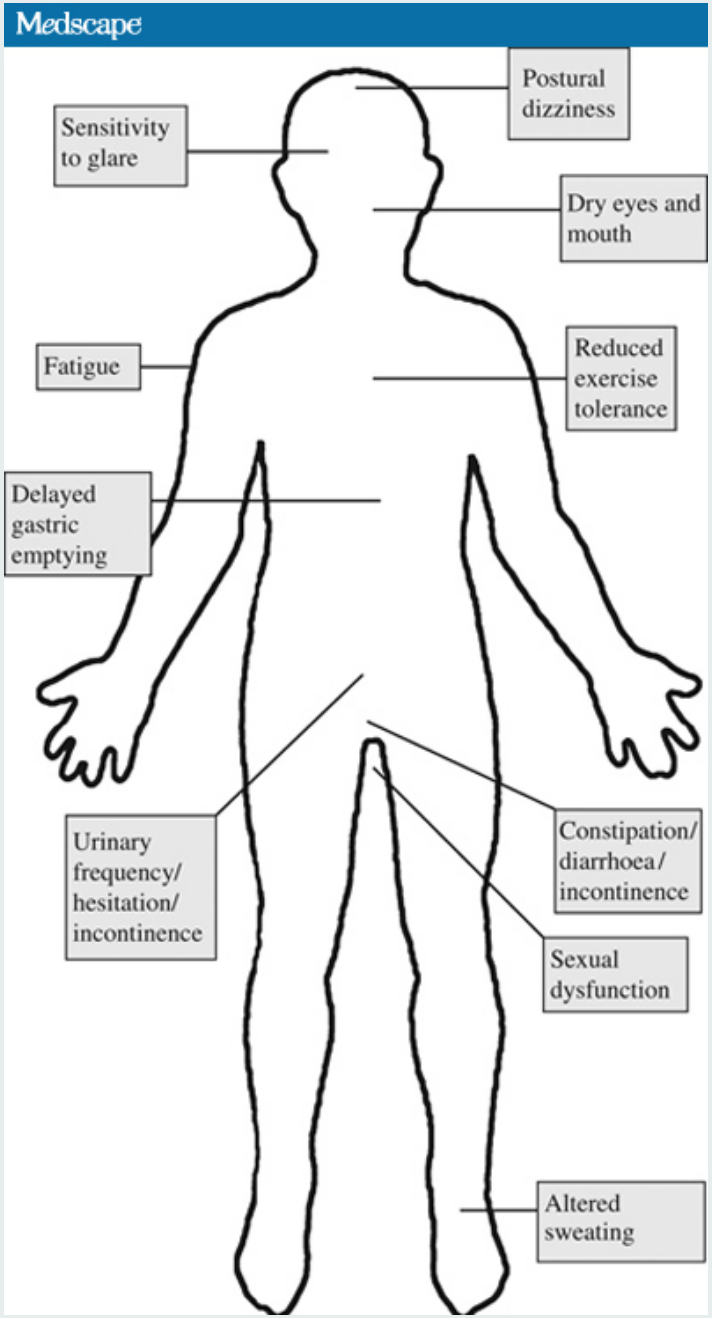
- **Integrative network** for maintaining **homeostasis**
  - 2 structurally/pharmacologically different branches
- Coordinates **visceral** function:
  - Cardiorespiratory
  - Vascular
  - Visceral: urogenital, digestive
- Interacts with **metabolic** systems:
  - Renin-Angiotensin
  - Blood sugar
  - pH
  - Reproductive behavior
  - Motor behaviors
  - Endocrine



Source: https://commons.wikimedia.org/wiki/File:Gray839.png

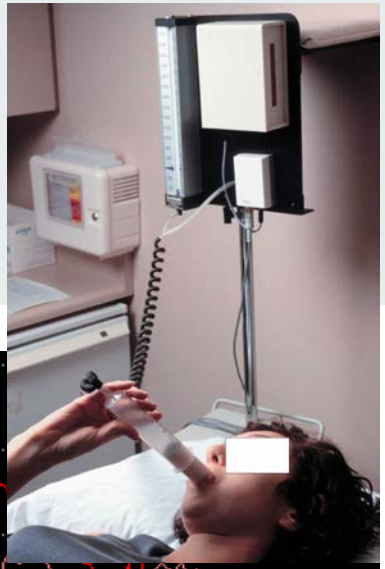
Autonomic symptoms

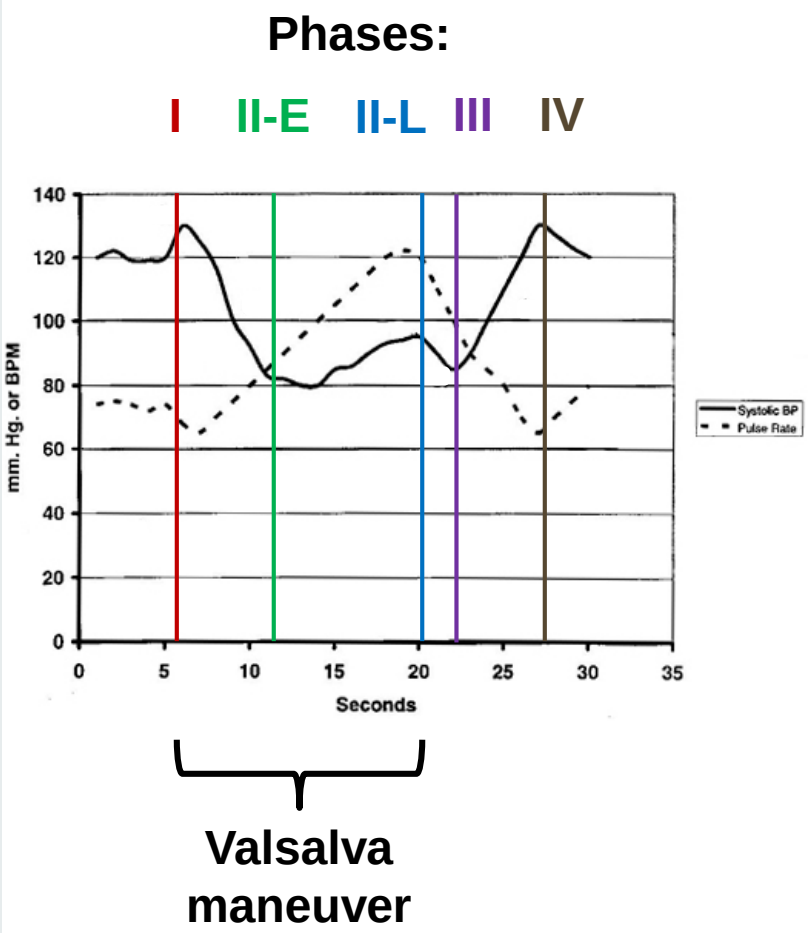
- Coordinated activation due to exercise/stress/emotion
  - e.g. BP maintenance, thermoregulation
- Sympathetic – diffuse
- Parasympathetic – organ specific

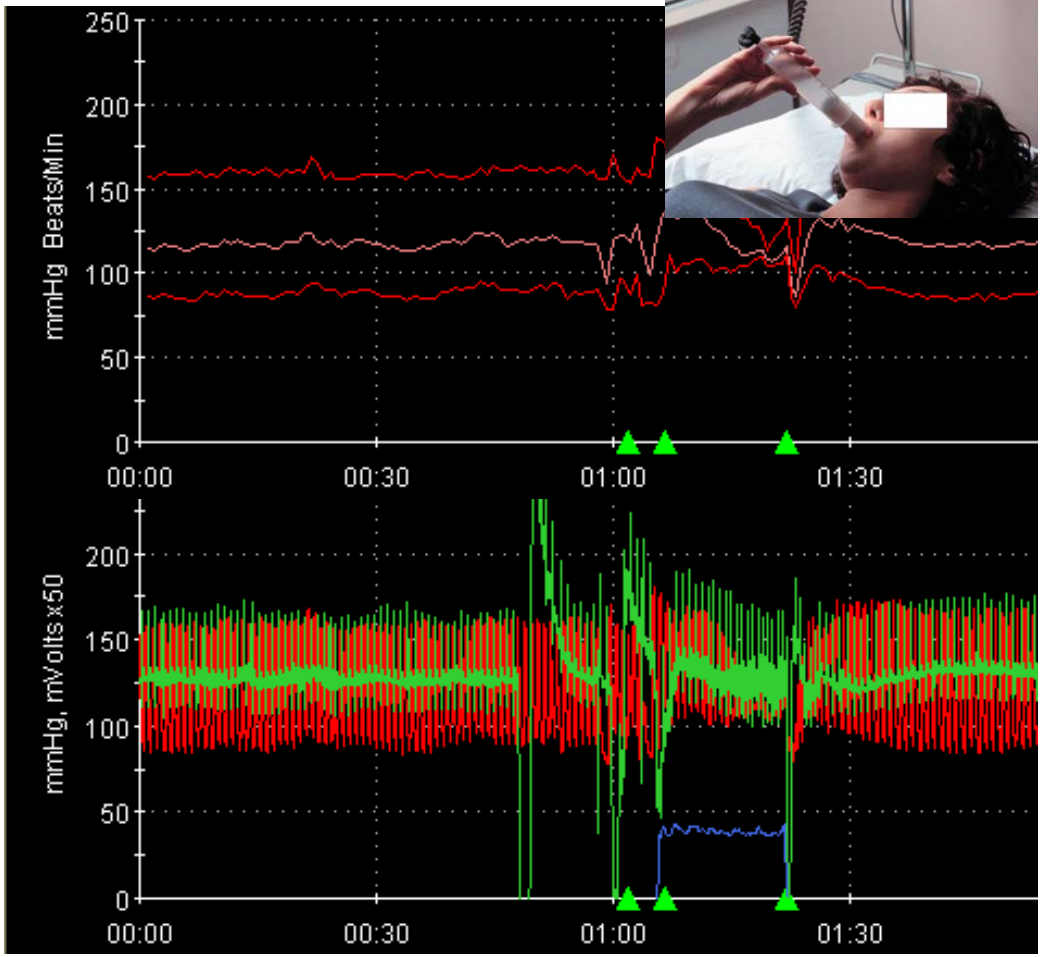


Source: http://www.medscape.com/viewarticle/706971_6

Valsalva maneuver: BP and HR changes

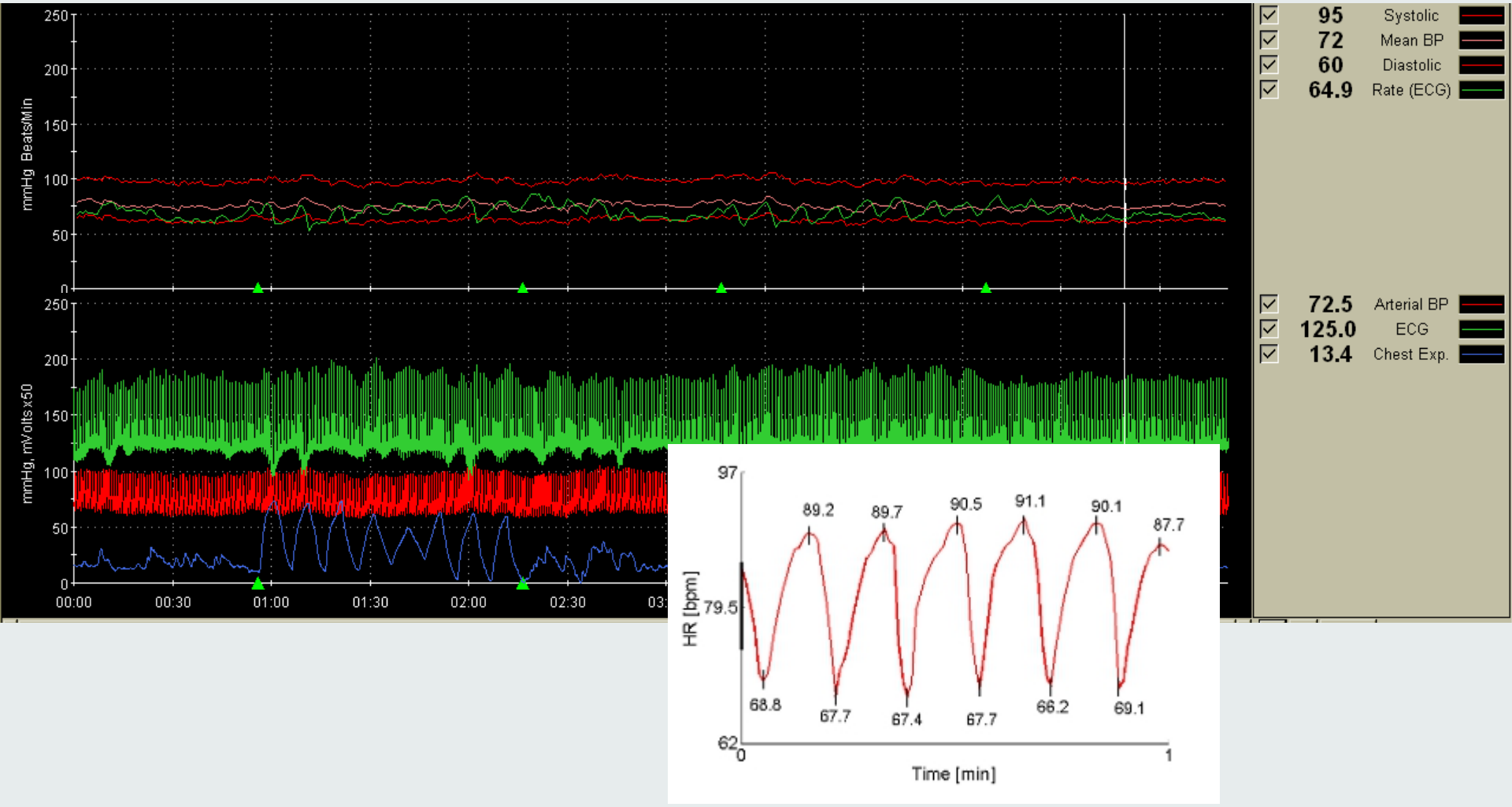




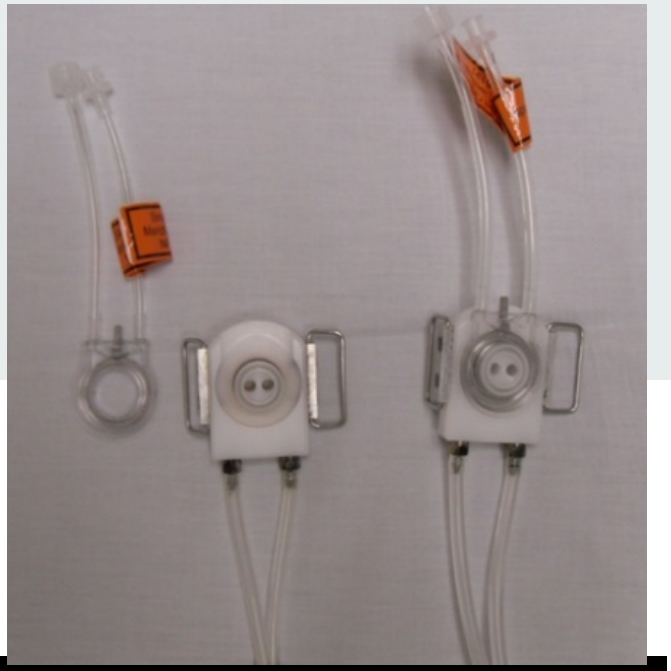


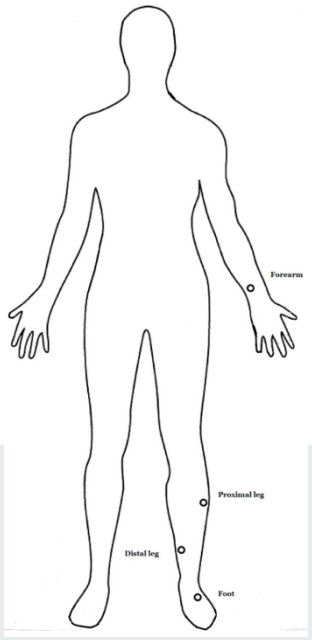
http://en.wikipedia.org/wiki/File:Valsalva3.jpg

Heart rate response to deep breathing

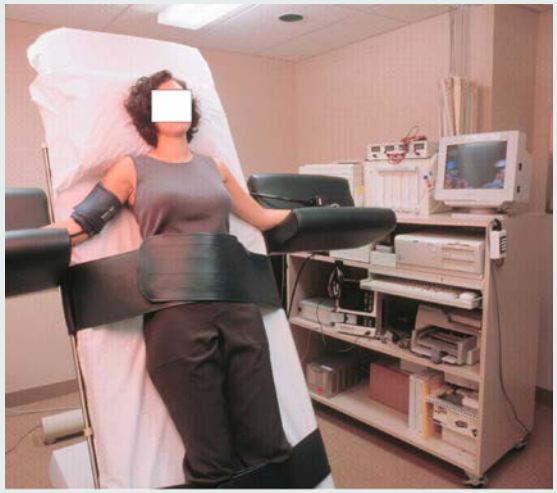


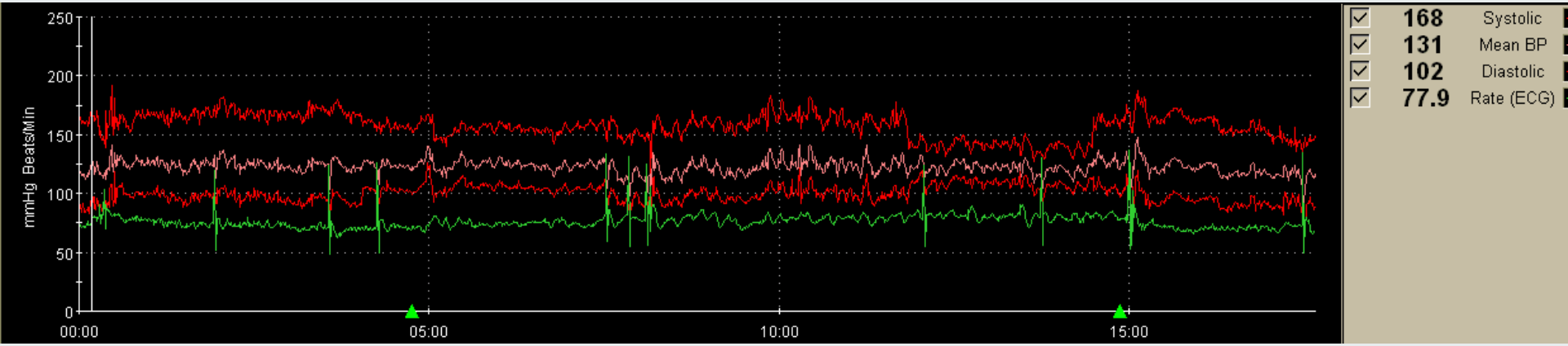
QSWEAT/QSART: Postganglionic sudomotor



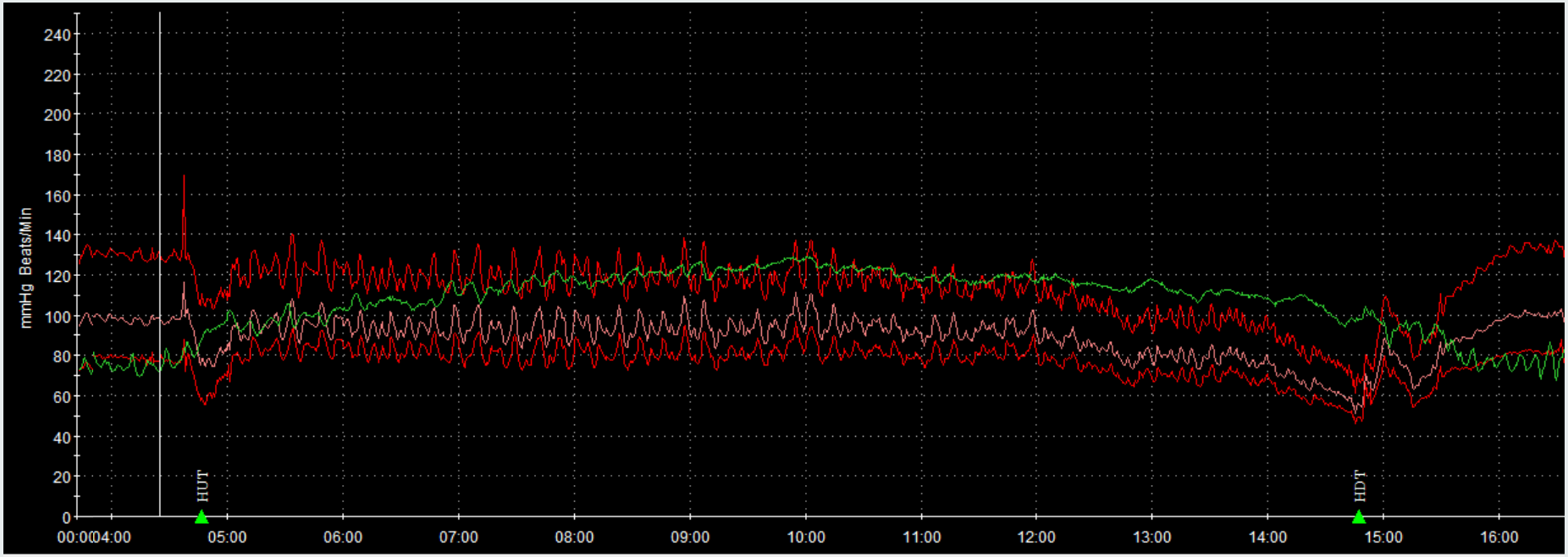


Tilt-table testing (70 degrees): BP and HR responses





HR and BP response to head-up tilt



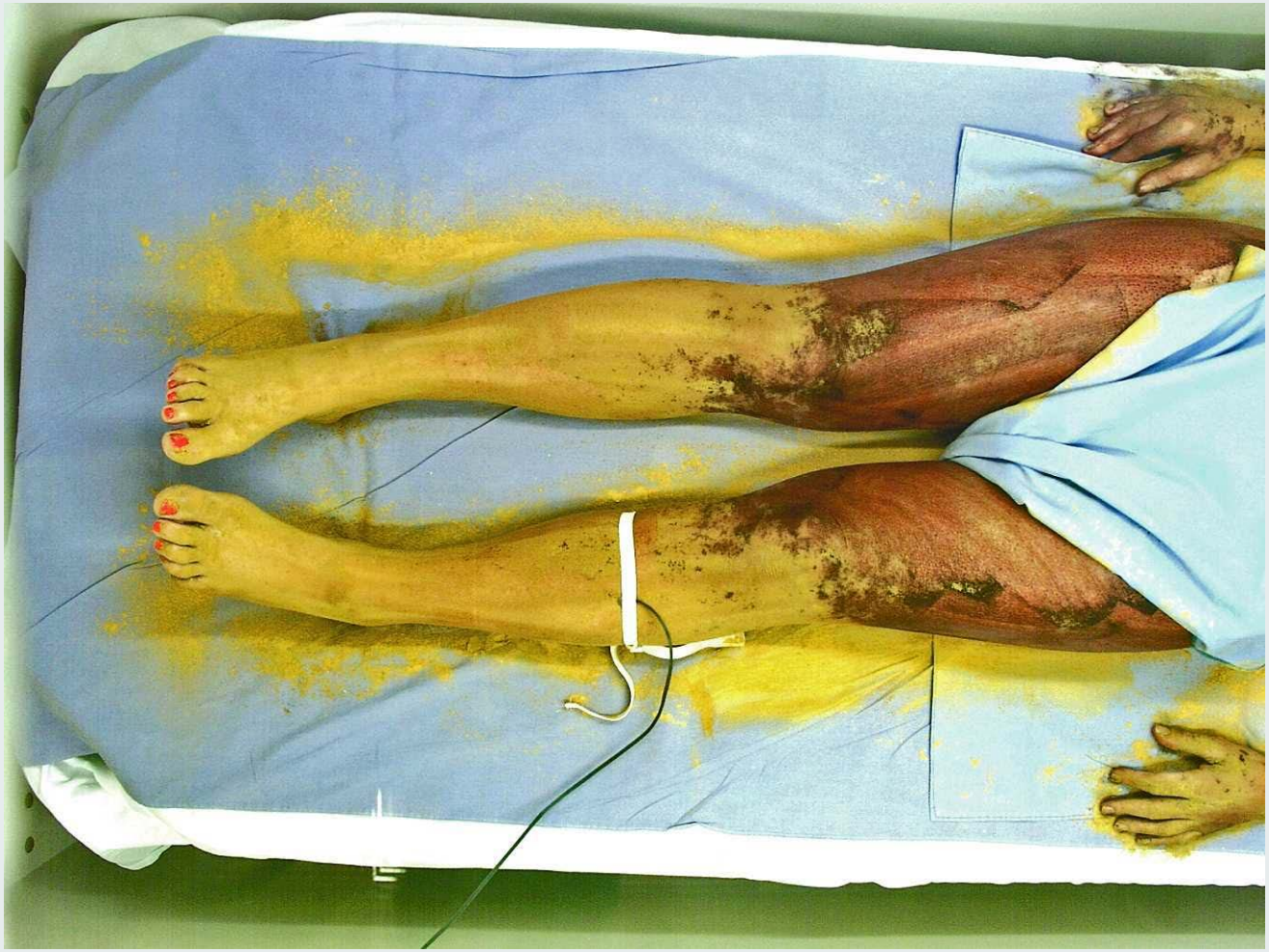
Increased BP oscillations

+

Excessive increase in HR

Near-syncope

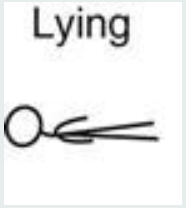
Not available…



Case #1

Vital signs at bedside:

BP 130/80, HR 80



BP 112/70, HR 87

BP 100/65, HR 95

Orthostatic Hypotension (OH) =

sustained decrease SBP > 20 mm Hg or DBP > 10mm Hg

(May be accompanied by increase in HR)

Neurally Mediated Hypotension (NMH) =

decrease SBP > 25 mm Hg

+ preceded by symptoms

Without associated increase in HR (may decrease)