

What do we mean by Orthostatic Intolerance (OI)?

(orthostasis = standing)

(OI= Can't tolerate standing)



Hard to Define but I know it when I see it?

Pediatric Group Definitions

Orthostatic Intolerance

The presence of one or more symptoms, e. g., lightheadedness, dizziness, nausea, breathlessness, and vision change, linked specifically to assuming or maintaining upright posture, and symptoms abate once supine

No mention of etiology; All Symptoms; Include Balance, Positional Vertigo, Postural Headache, Musculoskeletal Diseases?

Chronic Orthostatic Intolerance

On-going Orthostatic Intolerance for at least 3 months with functional impairment

POTS

Chronic Orthostatic Intolerance with excessive postural tachycardia (at least 40 bpm change within 10 minutes on standardized passive tilt testing) in the absence of an alternative explanation.

A physiological response or a disease? If disease then if a specific cause is found (e.g. Addison's Disease) it is no longer called POTS.

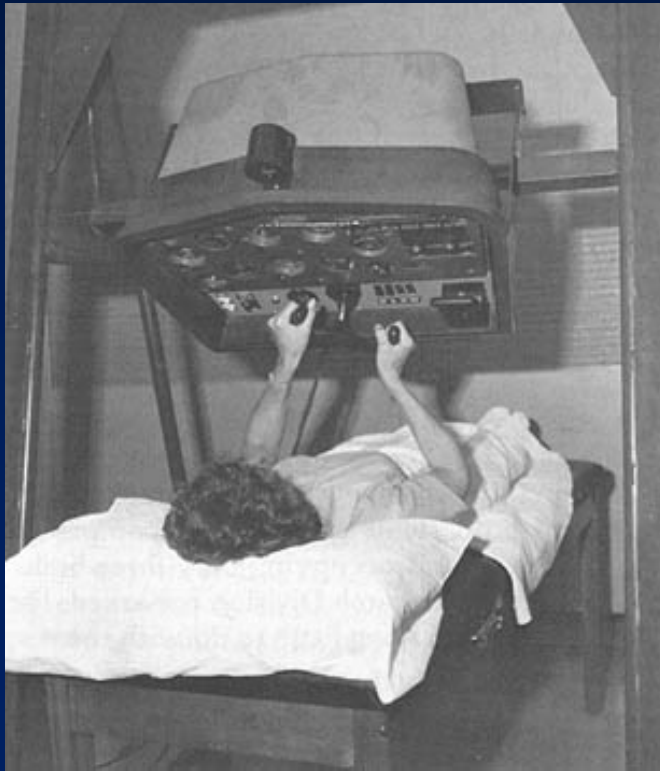
Consequence of Upright Stance But that's how we are designed

Gravitational Blood Distribution in Man and Beast

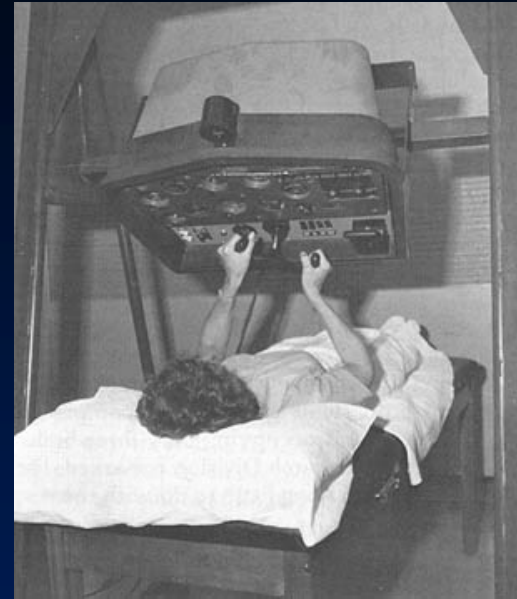


But Gravitational Deconditioning Occurs when Arteries, Veins, Heart and Viscera are at the same level

- **Bed Rest (simulated microgravity)**
- **True Microgravity**



Gravitational Deconditioning



- Reduced blood volume
- Different Regional blood volume redistribution
- Reduction in the response to norepinephrine/MSNA (and other pressors)
- Cardiovascular remodeling

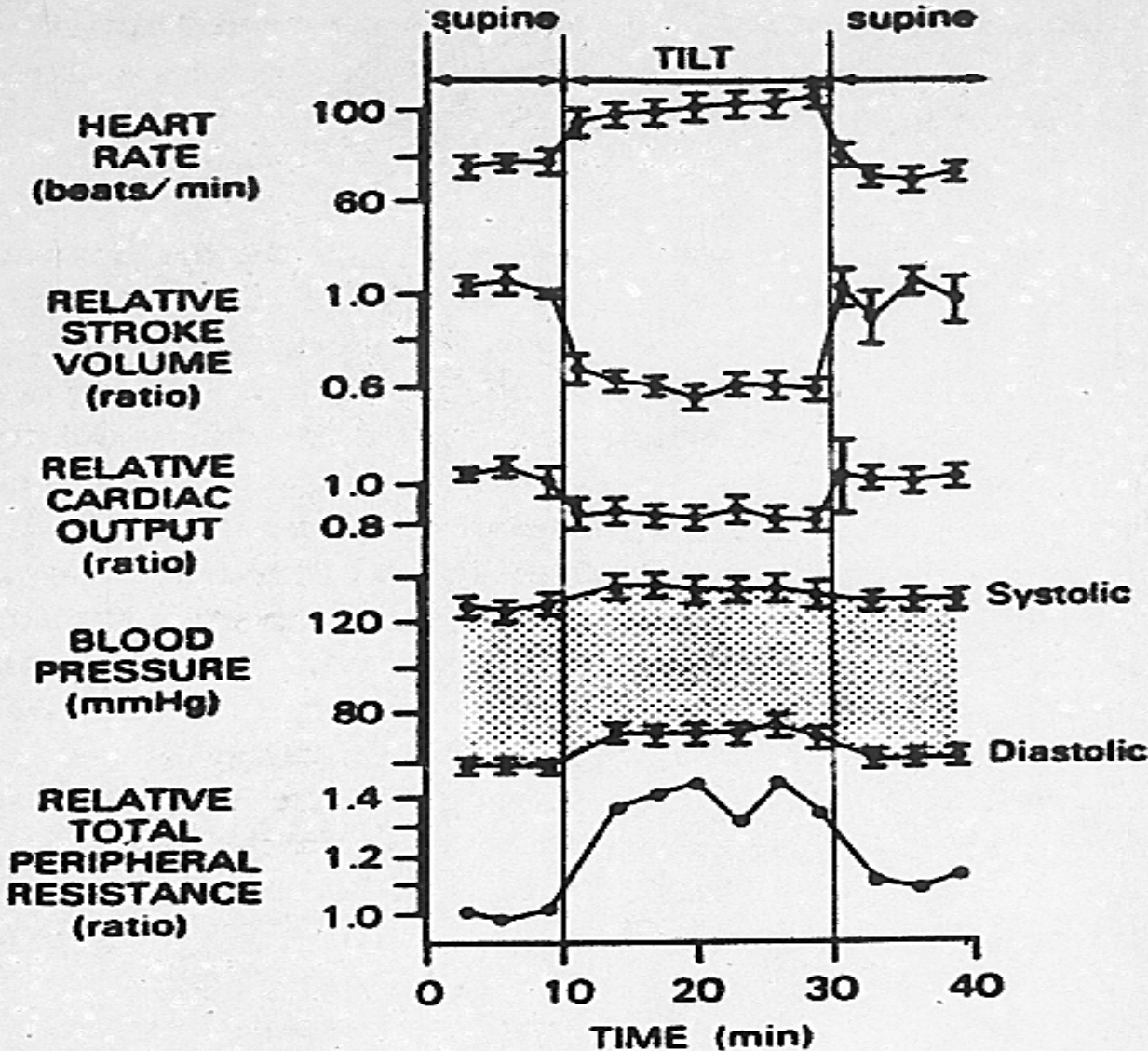
Circulatory Specializations for Orthostasis

- Physical forces (muscle/abd –resp pump)
- Vascular structure and Blood volume
- Vascular regulation of O₂ Delivery
 - Rapid
 - ANS–Sympathetic/Parasymp
 - Myogenic
 - Flow Mediated
 - Slower
 - Setting the tonic milieu –NO/Ang
 - autocrine, paracrine, endocrine
 - Metabolic
 - Gene expression -> Epigenetics

Most of OI=

Abnormalities in
adrenergic regulation
and the modulation of
adrenergic
vasoconstriction in
humans

Normal Circulatory Response to Orthostasis



Why should this be?

Why not design for full compensation to gravity?

Orthostatic Intolerance: defined by inability to tolerate the upright posture relieved by recumbence

- Loss of Consciousness
 - Lightheadedness-Dizziness
 - Neurocognitive Deficit
 - Headache
 - Fatigue – worst post-ictal
- Orthostatic Hypotension/Hypertension
 - Weakness – peripheral malperfusion?
 - Nausea/abdominal pain
 - Sweating, tremulousness
 - Exercise Intolerance

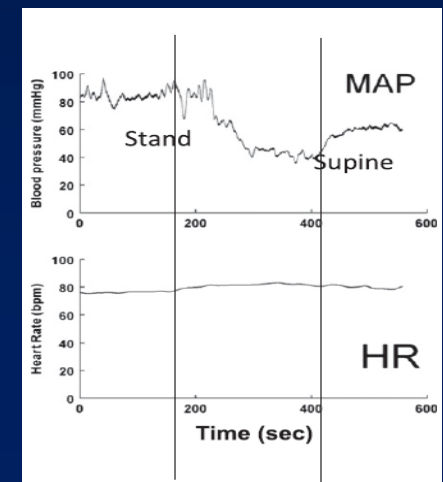
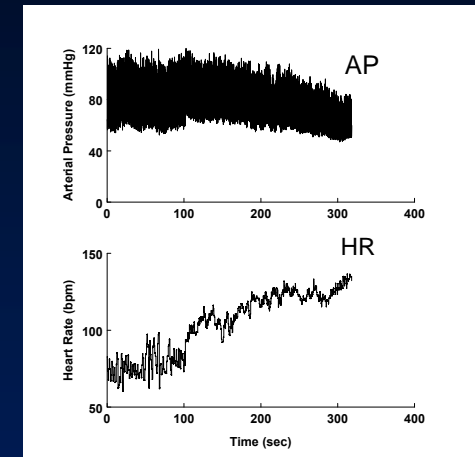
cerebral perfusion abnormalities despite cerebral autoregulation

↓↑ Adrenergic vasoconstriction

Parasympathetic ↓↑

Orthostatic Hypotension (OH) is Easy to Understand

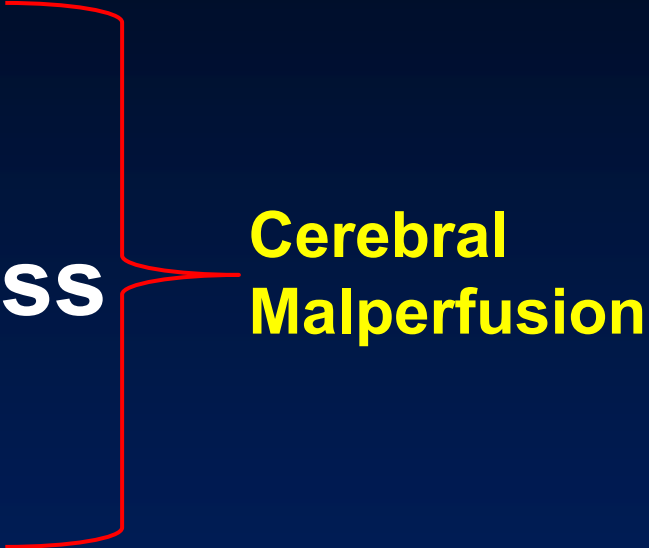
- Blood pressure falls sufficiently to impair brain blood flow
- Non-neurogenic OH
 - Hypovolemia or Forced Vasodilation
- Neurogenic OH
 - Autonomic vasoconstrictor failure due to inadequate release of norepinephrine from sympathetic vasomotor neurons.



OI without OH – POTS and Presyncope

Why can't we tolerate the upright position?

- **Loss of Consciousness**
- **Lightheadedness-Dizziness**
- **Neurocognitive Loss**



**Cerebral
Malperfusion**

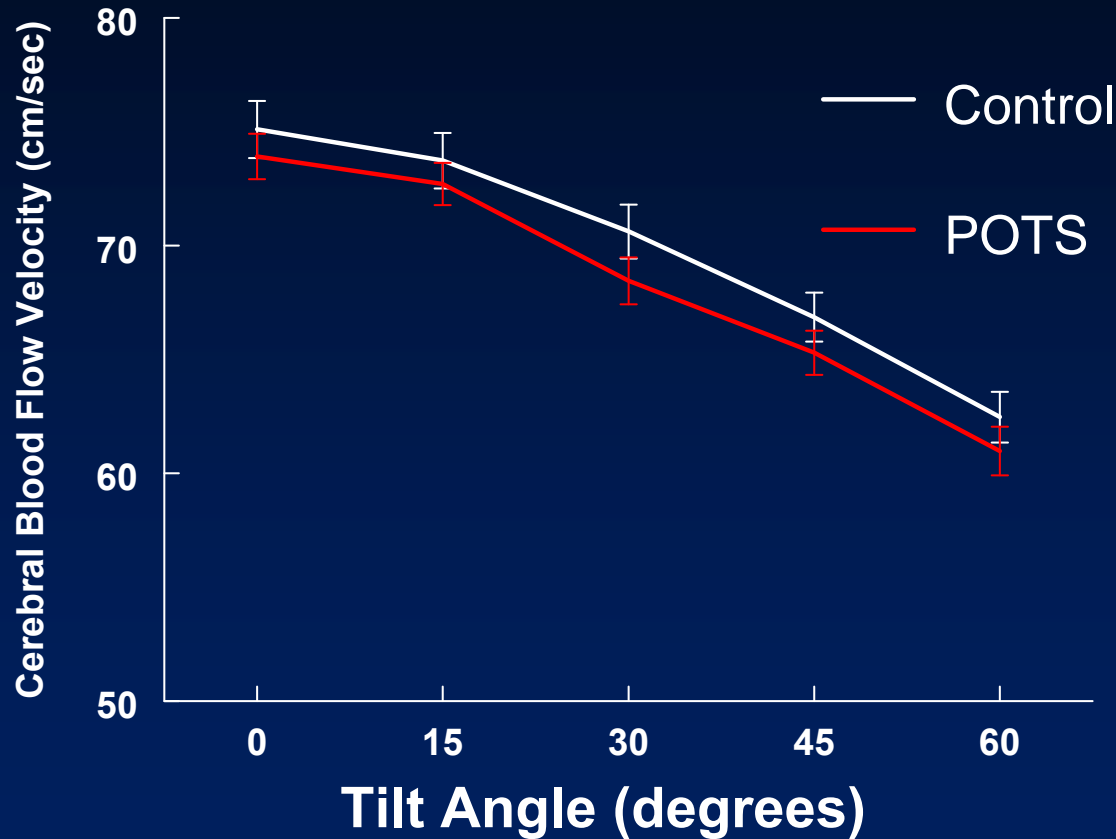
Decreased Cerebral Blood Flow?

Molteni et al J. Biomed. Opt. 17(5), 056005 (May 04, 2012).



Incremental Tilt

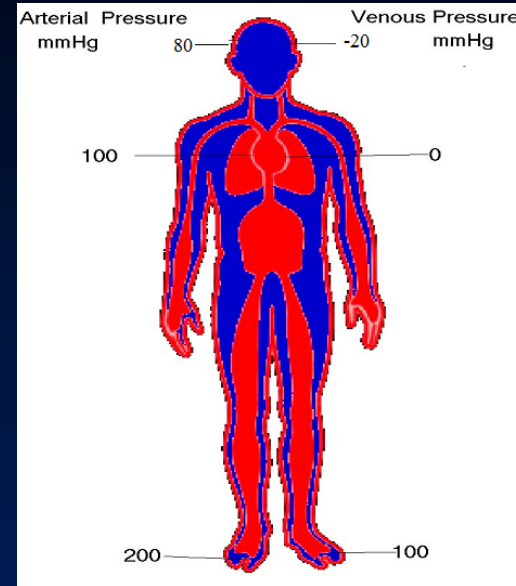
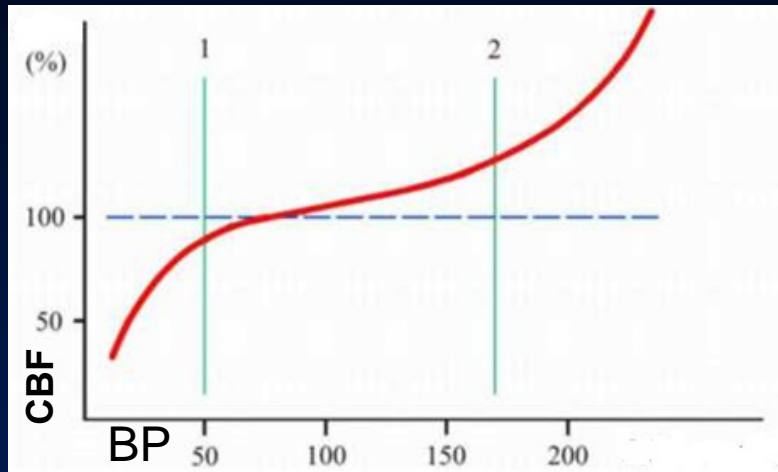
Mean Cerebral Blood Flow Decreased Equally in POTS and Controls



This should not be happening!

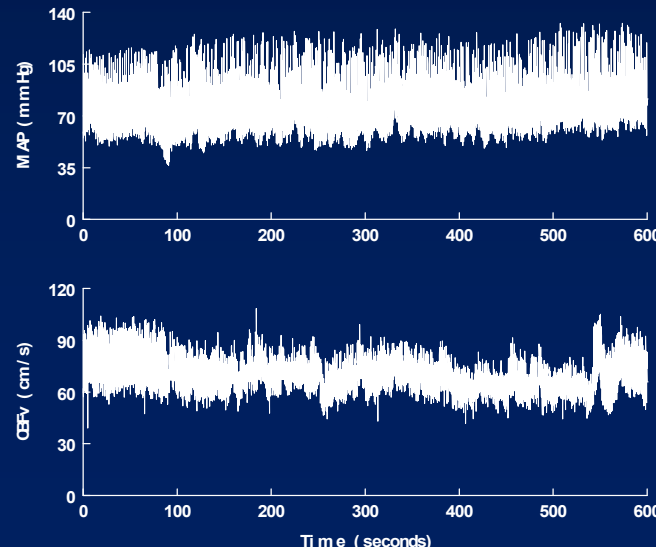
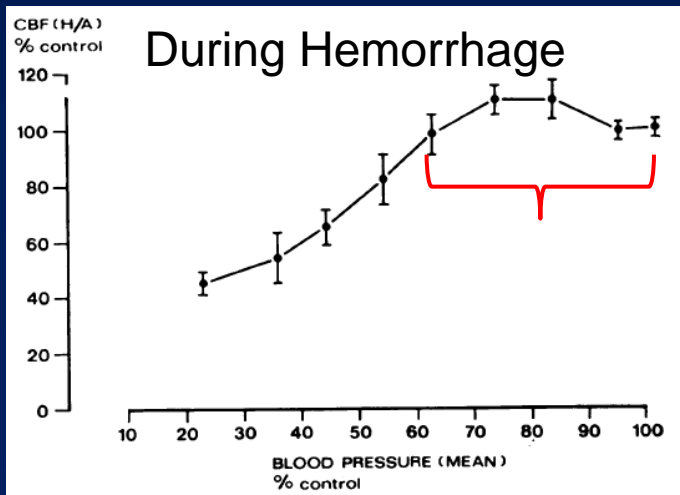
Cerebral Autoregulation

CBF is independent of changes in blood pressure over a wide range of pressure during hypotension



**But not
when
Standing**

!



During Tilt
in healthy
volunteer

