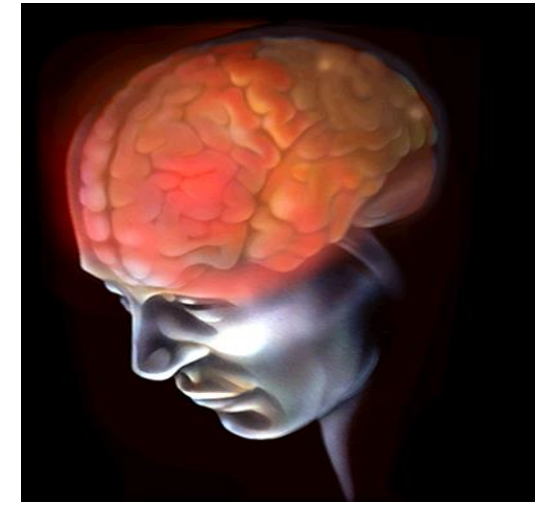
Mechanisms of Headache in Intracranial Hypotension

Stephen D Silberstein, MD

Jefferson Headache Center

Thomas Jefferson University Hospital

Philadelphia, PA



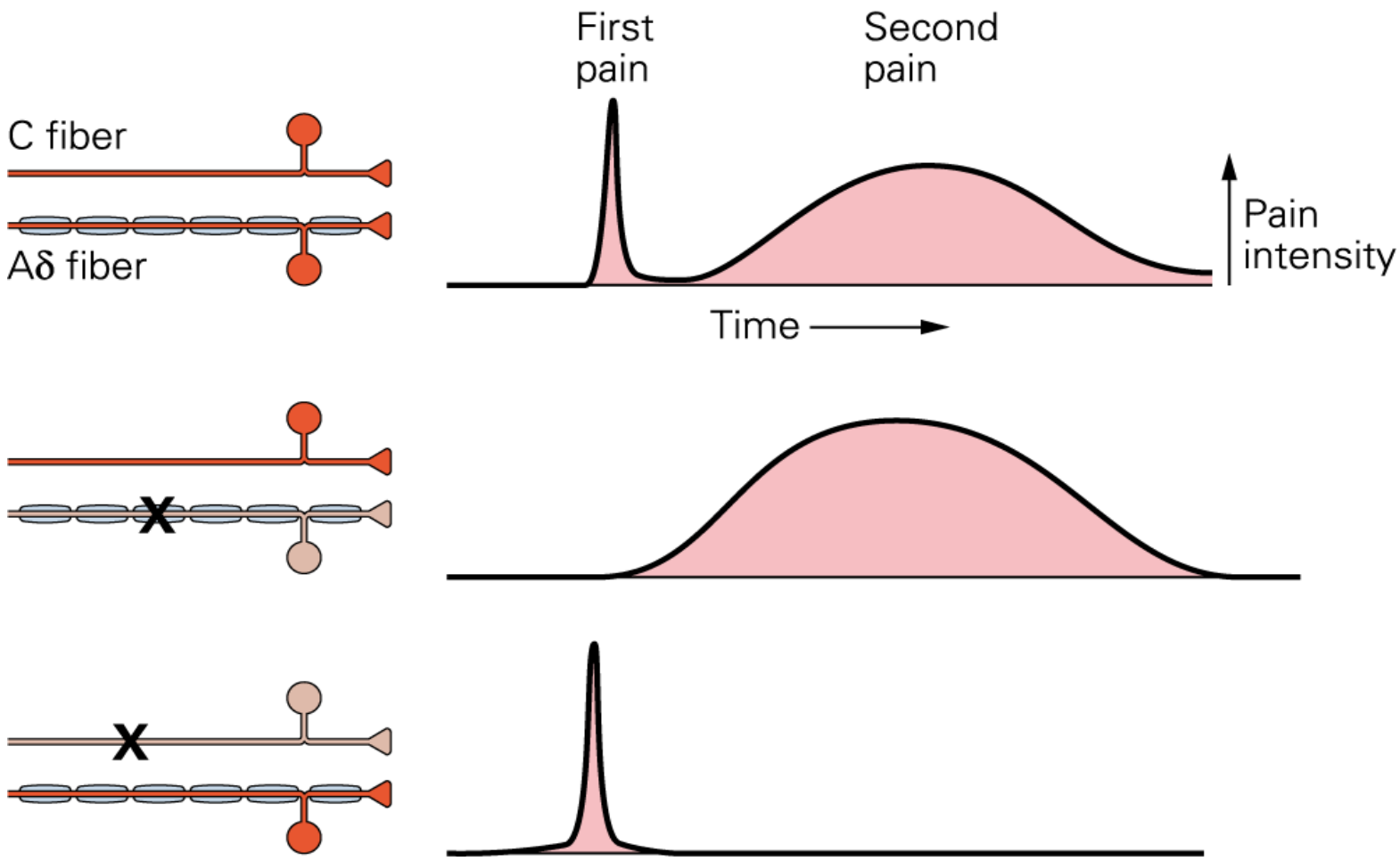
Overview

- What are the different pain fibers?
- Which are involved in pain transmission?
- What role does sensitization play in pain and headache?
- What causes headache?
- What causes low CSF pressure?
- What causes low CSF pressure headache?
  - Increased compliance?
    - HIP drift?

Sensory Nerve Fibers

Fiber type	Myelinated	Conduction velocity (meters/sec)	Sensory Information	Neurotransmitters
A-β	Yes	30-100	Touch, vibration	EAA (NPY, GAL, CCK, SP, following activation or injury)
A-δ	Yes	12-30	Initial sharp pain, touch, pressure	EAA
C	**No**	0.5-2	Dull pain, temperature	Glutamate, **SP**, **CGRP**, NKA

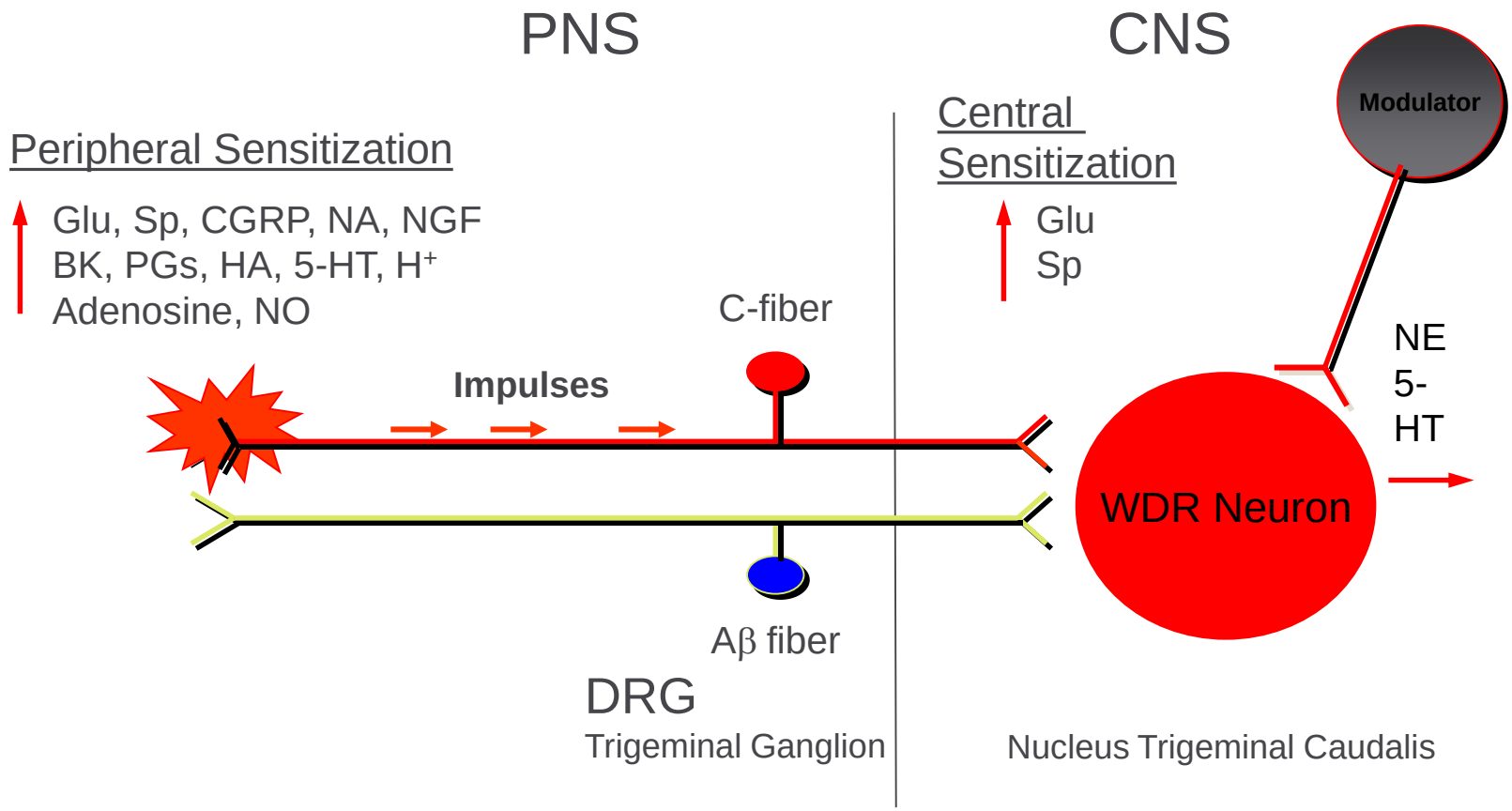
Acute Pain



Sensitization

- Increased responsiveness to stimuli
  - **Hyperalgesia**: Increase in pain sensitivity
  - **Allodynia:** Nonpainful stimuli now painful
- Peripheral sensitization
  - Increased sensitivity of nociceptive receptor
- Central sensitization
  - Increased spontaneous neuronal discharge
  - Expanded nociceptive receptive fields

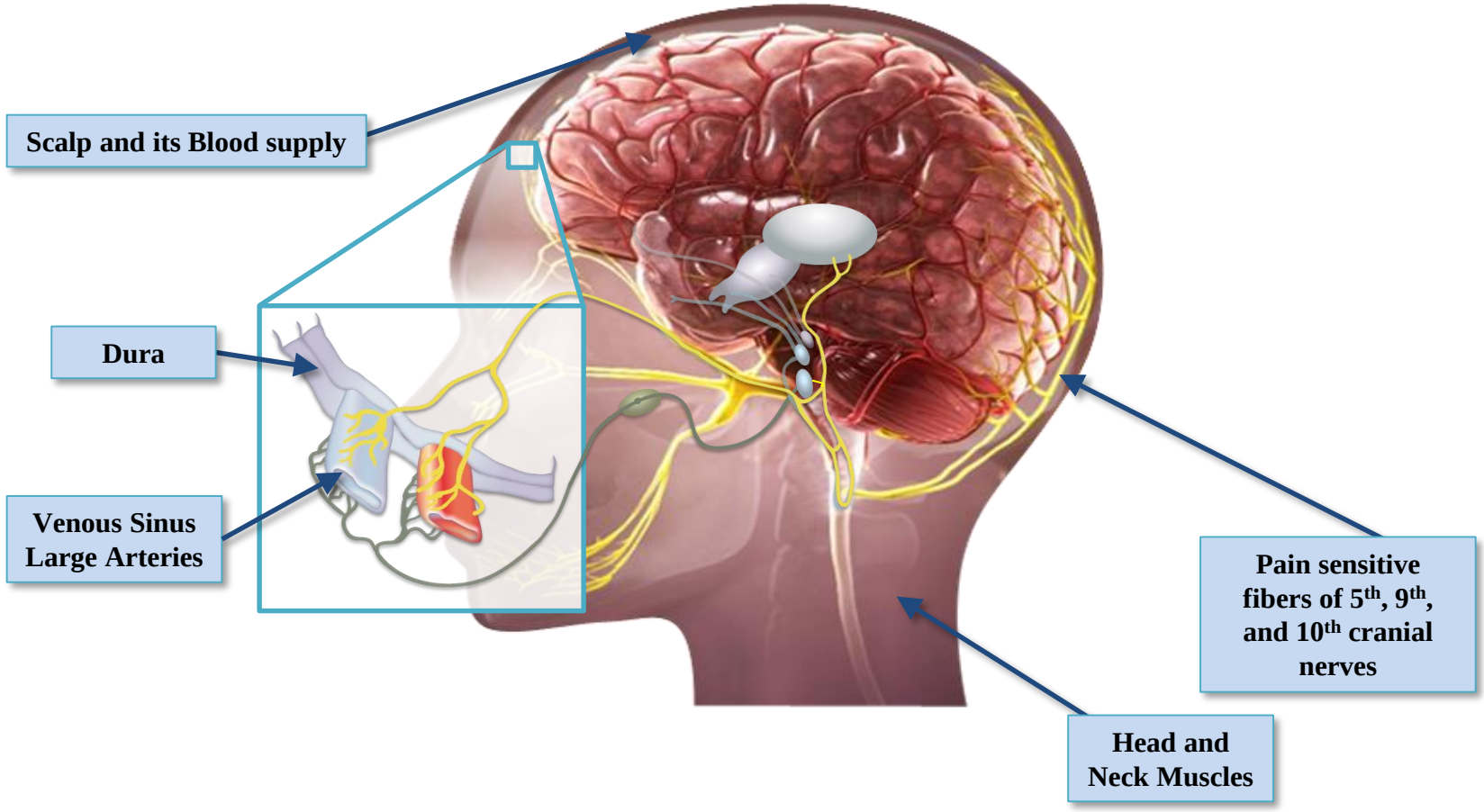
Sensitization



What Causes Headaches?

1. Traction, tension, or displacement of pain-sensitive structures
2. Distention/dilation of intracranial arteries, **veins or venous sinuses**
3. Inflammation of pain-sensitive structures
4. Obstruction of CSF pathways
5. Primary central pain: involvement of pain-modulating systems

Anatomy of Headache Pain
Pain Sensitive Cranial Structures



Intracranial Hypotension

- Normal pressure:

  70 to 200 (250?) mm H_2O

- Intracranial hypotension/hypovolemia
  - Symptoms with pressures < 70 mm H_2O
    - At times pressure not measurable
    - At times pressure normal
  - Most common cause LP

Intracranial Hypotension: Causes

A. LP: diagnostic, myelography and spinal anesthesia

B. Traumatic: head or back trauma (± CSF leak)

C. Postoperative: craniotomy, spinal surgery, postpneumonectomy

D. Malfunctioning CSF shunt

E. Spontaneous CSF leak

F. Systemic illness: dehydration, diabetic coma, hyperpnea, meningoencephalitis, uremia, severe systemic infection

Intracranial Hypotension Headache Mechanisms

1. Downward brain displacement due to loss of **CSF buoyancy**?
   – Could cause traction on pain-sensitive structures (esp. dura)
2. Intracranial CSF volume loss
   – Can cause compensatory dilation pain-sensitive intracranial venous structures

But Headache aggravated by jugular compression

- Increases intracranial pressure and venous dilatation
- Headache not caused by intracranial hypotension alone

Headache Mechanisms: Buoyancy Loss

- CSF cushions the brain
  - Does loss ↓ upward buoyant force and cause brain sag when patient is erect?
  - Sag increases tension on veins that anchor brain to dural venous sinuses
- But no evidence to support this
  - Despite CSF loss, brain remains surrounded by fluid, so no decrease in upward buoyant force

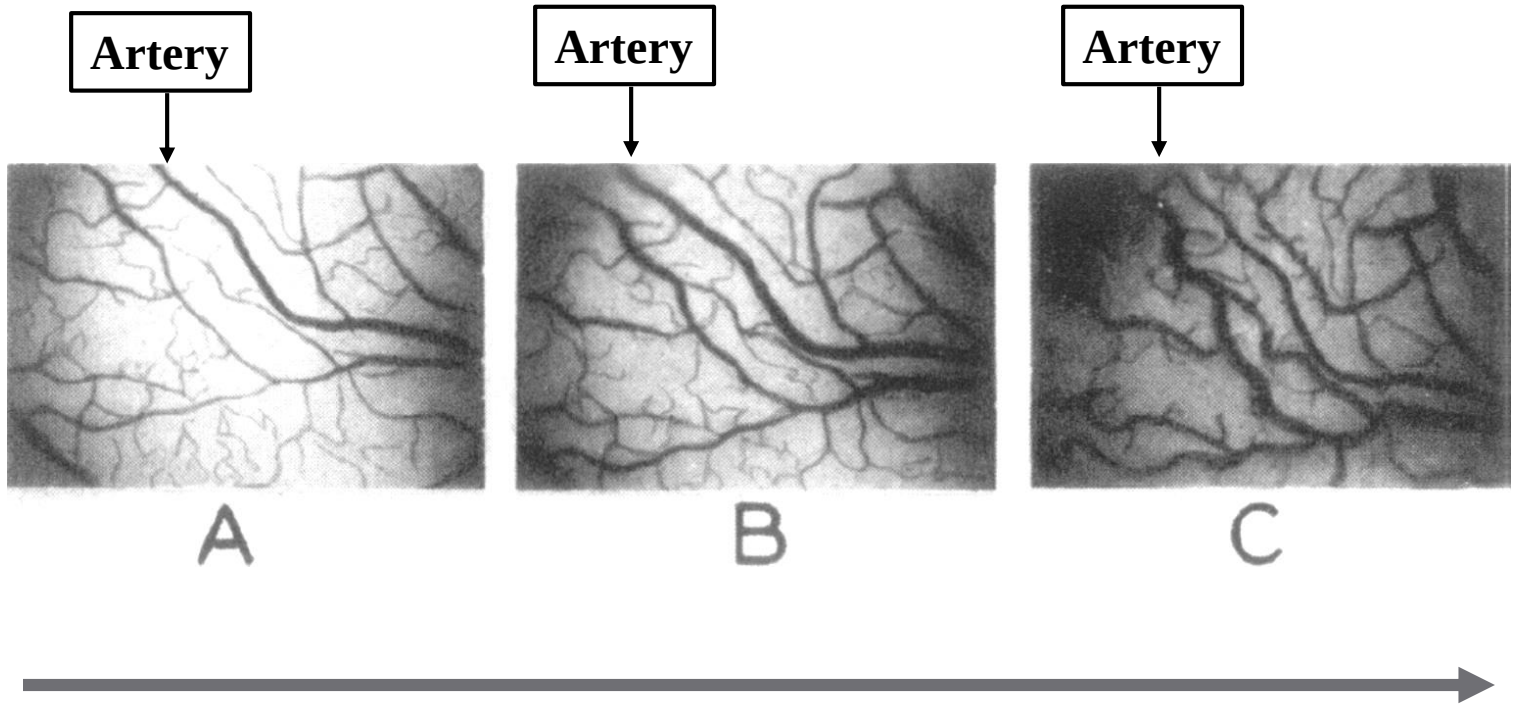
Levine DN, Rapalino O. The pathophysiology of lumbar puncture headache. J Neurol Sci 2001;192:1–8.

Headache Mechanisms: Monroe-Kellie hypothesis

- Sum of brain, CSF, and ***intracranial*** blood volume constant
  - ↓ in one causes ↑ in one or both of remaining two.
- CSF loss → ↓ CSF pressure but not venous pressure
  - Pressure difference causes veins to dilate
    - More dilatation in upright posture
- Dilatation of pain sensitive intracranial venous structures
  - → orthostatic headache
- Evidence:
  - Pial veins of anesthetized cat dilate with CSF removal
  - Jugular venous compression increases headache intensity
  - Acute venous sinuses distension produces pain

Forbes HS, Nason GI. Vascular responses to hypertonic solutions and withdrawal of CSF
Arch Neurol Psychiatry 1935;34:533–47.

Pial Vessels Dilate as CSF Pressure Decreases



Forbes HS, Nason GI. Vascular responses to hypertonic solutions and withdrawal of CSF
Arch Neurol Psychiatry 1935;34:533–47.

Intracranial Hypotension or Intracranial Hypovolemia or Neither?

CSF Pressure

- Orthostatic headache can occur with normal pressure
- No correlation between CSF pressure and headache
- Jugular compression raises pressure and worsens headache

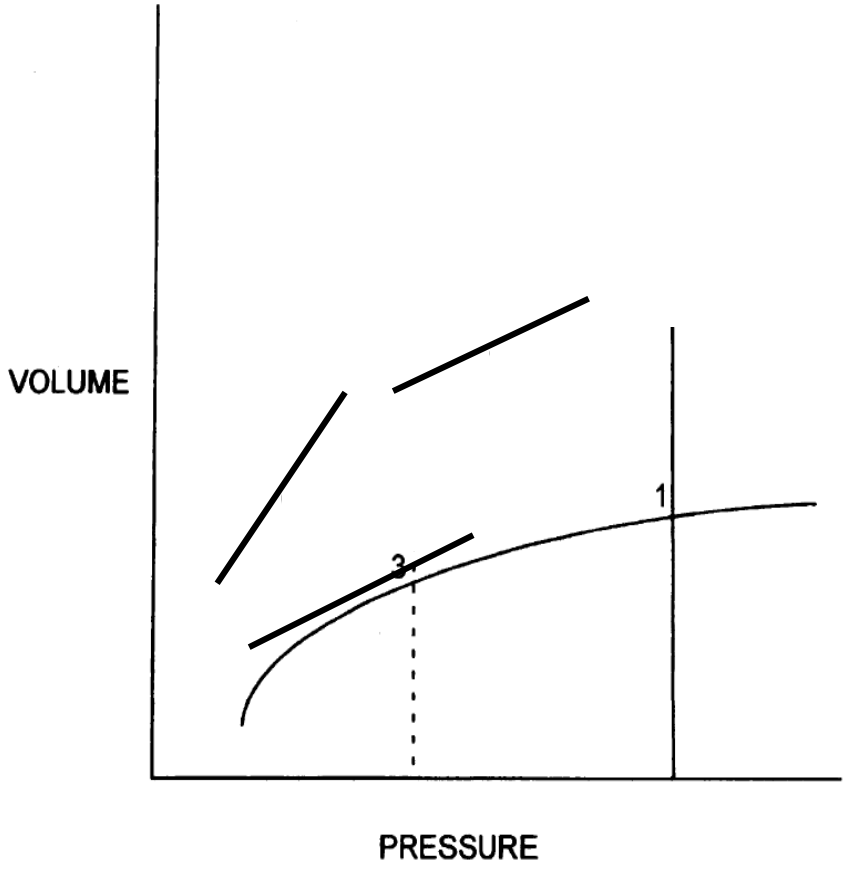
CSF Volume

- Loss correlates to post-LP headache

Craniospinal Elasticity (Compliance)

- Altered distribution due to spinal loss of CSF

Pressure Volume Curves and Compliance

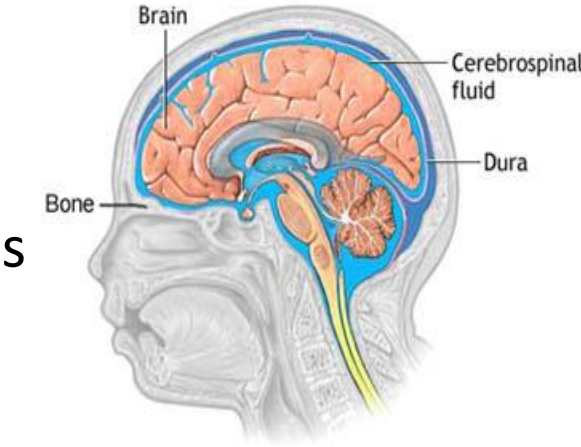


- — volume - pressure curve (less compliant)
- ---- pressure-volume curve (more compliant)
- Distensibility: slope of volume–pressure curve.
  - ↑ Compliance →↑ Distensibility
  - ↓ pressure→ ↑ Compliance

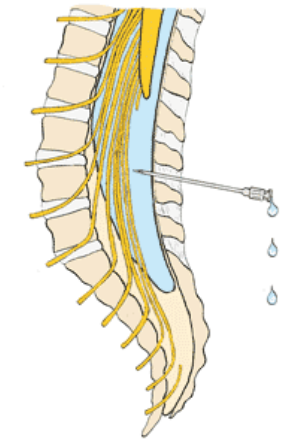
Compliance of Membranes Enclosing CSF

Different throughout system

- Rostral component (covered by rigid skull)
  - Depends upon compressibility of intracranial venous and capillary vessels



- Caudal component
  - Depends on degree of filling of spinal dural sac
- Increased lumbar compliance (more give) causes **HIP** to be displaced caudally



Levine DN, Rapalino O. The pathophysiology of lumbar puncture headache. J Neurol Sci 2001;192:1–8.

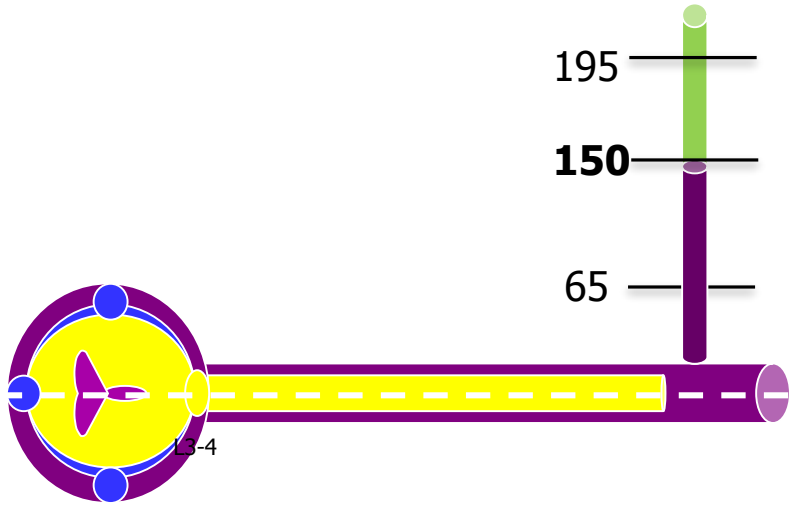
Hydrostatic Indifferent Point (HIP)

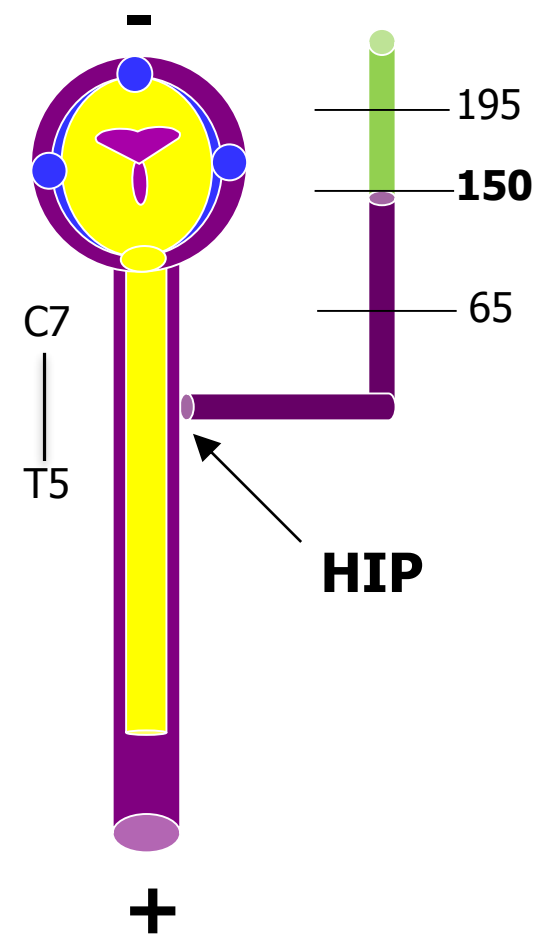
- Point were upright CSF pressure = CSF recumbent pressure
  - Normally between C7 and T5
- CSF leak may increase lumbar compliance (more give)
  - Increased lumbar compliance shifts HIP downward
  - Independent of decreased CSF volume or opening pressure
- Upright ICP more negative: equals distance HIP displaced
  - Decrease in addition to that resulting from loss of filling pressure
- Change in lumbar compliance alone (without CSF leak) could cause orthostatic headache

Levine DN, Rapalino O. The pathophysiology of lumbar puncture headache. J Neurol Sci 2001;192:1–8.

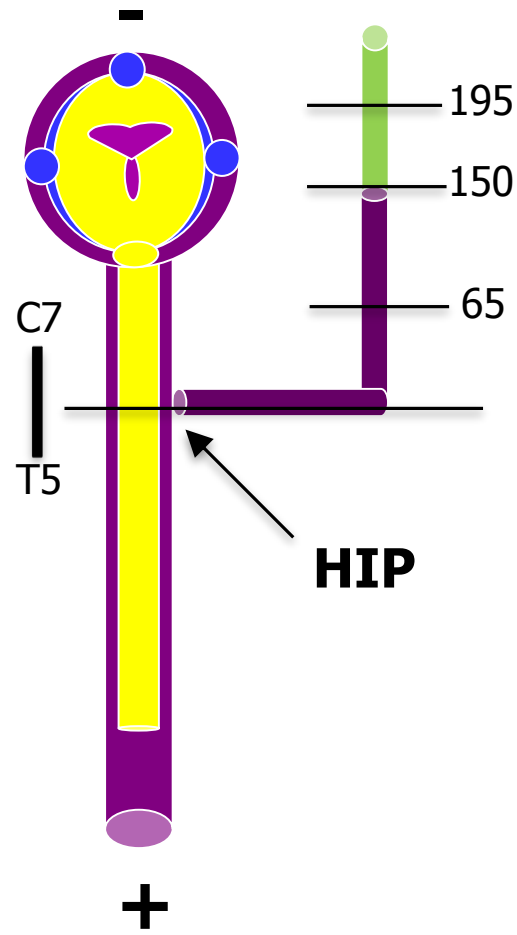
Hydrostatic Indifferent Point

Located along upright CSF axis where CSF pressure = supine CSF opening pressure

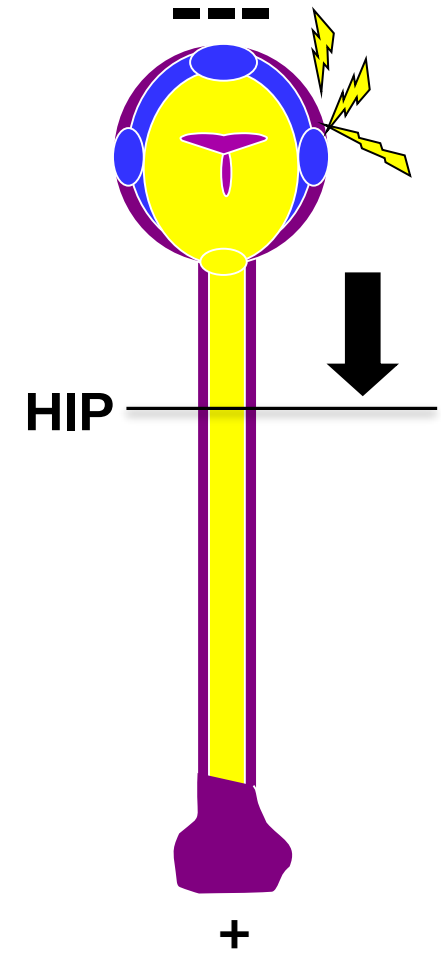




Levine DN, Rapalino O. The pathophysiology of lumbar puncture headache. J Neurol Sci 2001;192:1-8.



Normal



Increased compliance of lower CSF space

Levine DN, Rapalino O. The pathophysiology of lumbar puncture headache. J Neurol Sci 2001;192:1–8.

CSF Leak: Increased Caudal Compliance of CSF Space Relative To Cranial End

- **Lumbar dural sac compliance increases with CSF leak**
  - Causes caudal HIP displacement
  - Upright ICP more negative equal to distance HIP displaced
  - Decrease in addition to that due to loss of filling pressure
- **Cranial compliance decreases with CSF leak**
  - Cerebral veins normally slightly collapsed, because CSF pressure exceeds dural sinuses pressure
  - ↓ CSF pressure → venous engorgement
    - Walls become stiffer and less compressible

Levine DN, Rapalino O. The pathophysiology of lumbar puncture headache. J Neurol Sci 2001;192:1–8.

CSF Leak and Dural Compliance

Lumbar dura usually resists stretch

– Limits distensibility of caudal CSF space

1. **Large holes** increase lumbar compliance by

– Exposing CSF to more compliant epidural space

- Epidural veins, epidural fat, and paravertebral soft tissue

2. **↓ filling pressure** increases lumbar compliance

– Lumbar dural sac collapses and becomes more compliant

- Creates space to accommodate CSF when patient upright

Levine DN, Rapalino O. The pathophysiology of lumbar puncture headache. J Neurol Sci 2001;192:1–8.

Does CSF Rhinorrhea Produce Headache?

Rostral CSF leak displaces HIP less than that due to LP

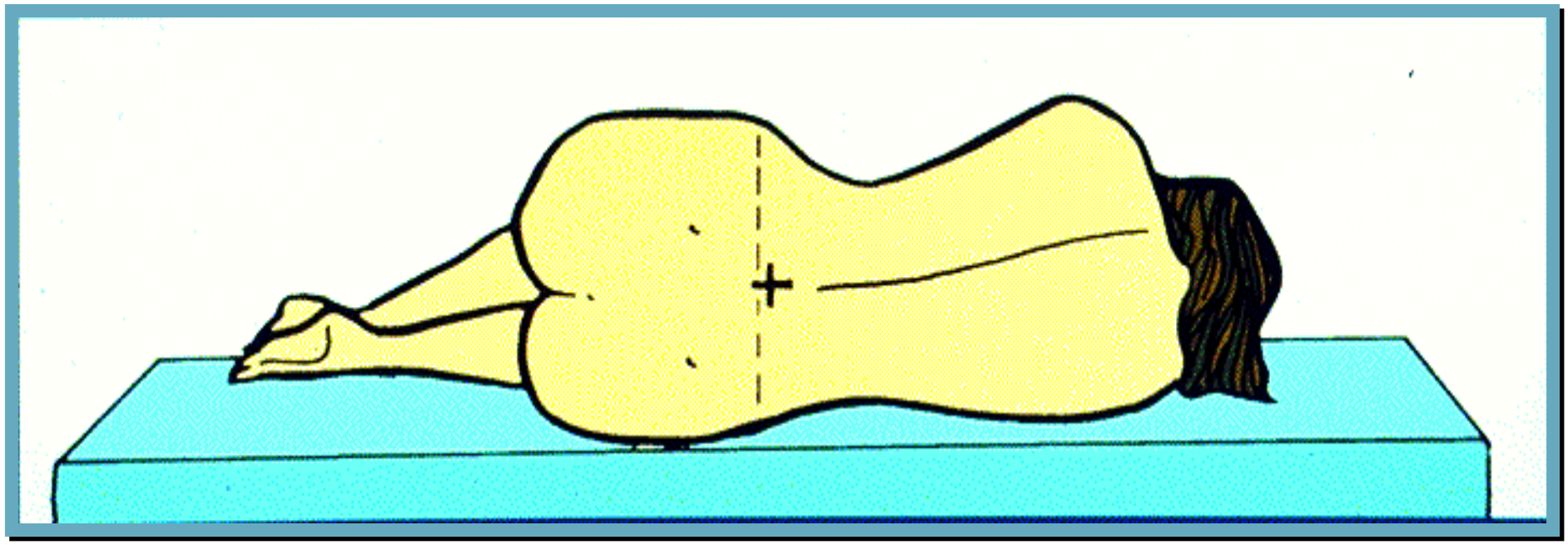
- Only 9cm caudally

WHY?

- Increased **rostral CSF space** should move HIP rostrally
- But ↓ filling pressure →↑ **caudal dural sac** compliance
  - Overcomes effects of rostral anatomic change.
  - **Thus rostral leaks may not lower HIP enough to cause headache**

Magnaes B. Body position and cerebrospinal fluid pressure J Neurosurg 1976;44:698–705.

Lumbar Puncture



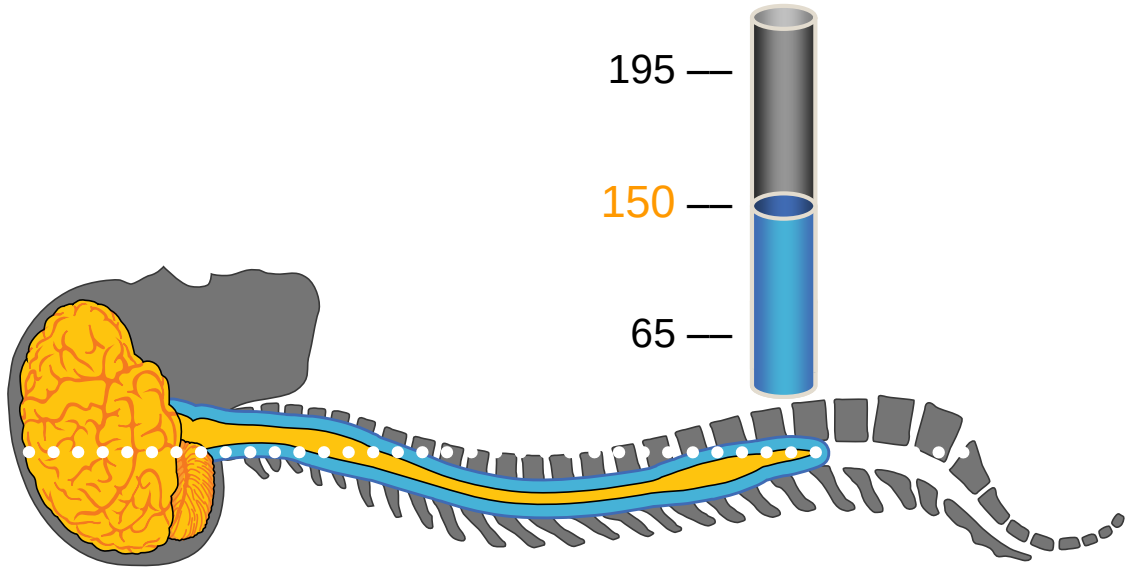
LP Causes Caudal Displacement of HIP

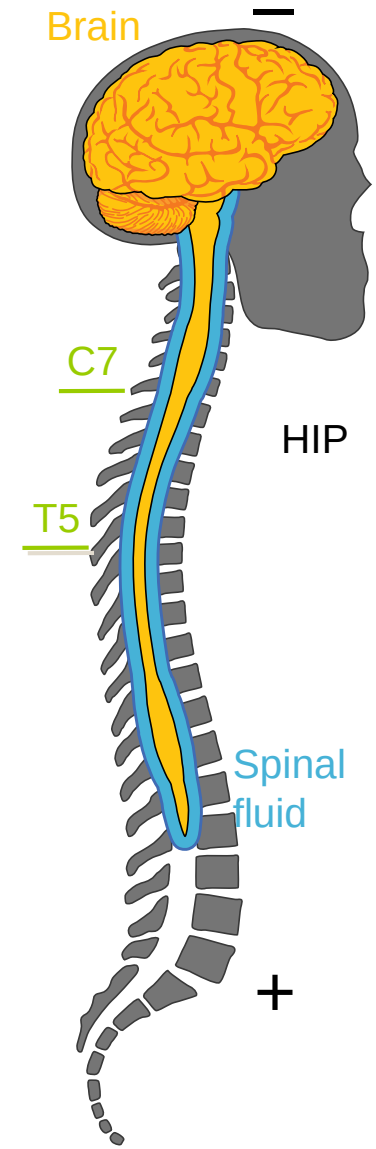
- **Initial** CSF pressure: 18 cm recumbent and 53 cm sitting
  - HIP **35** cm (53-18)
- **Post LP** CSF pressure: 5.5 cm recumbent and 28 cm sitting
  - HIP now **22.5** cm (28-5.5)
    - HIP displaced 12.5 cm (35- 22.5) caudally
- **Filling pressure ↓** 12.5 cm (18 -5.5)
- **ICP ↓** 12.5 cm recumbent, but **↓** 25 cm (12.5+12.5) upright
- **Standing → marked ↑ in transmural venous pressure**
  - Intracranial veins distend acutely
    - More distension due to loss of filling pressure
- ***Acute orthostatic venous distention causes orthostatic headache***

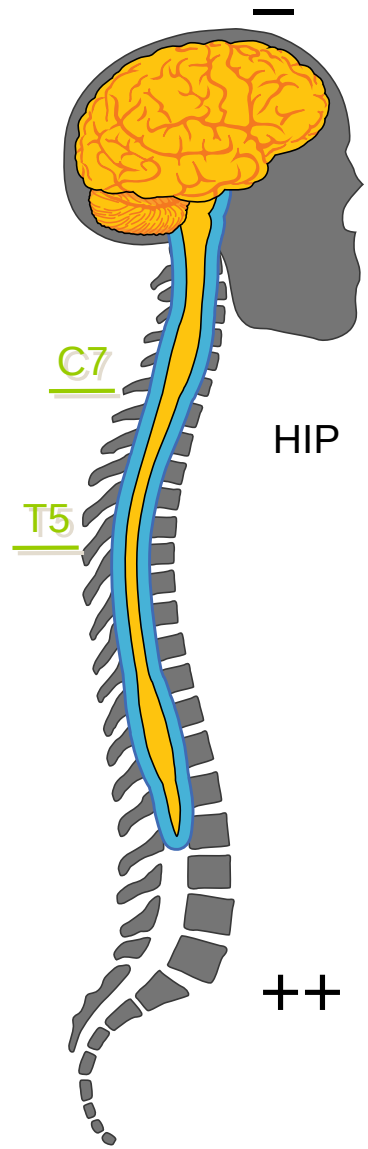
Nelson MO. Postpuncture headaches Arch Dermatol Syph 1930;21: 615–27.

Hydrostatic Indifferent Point

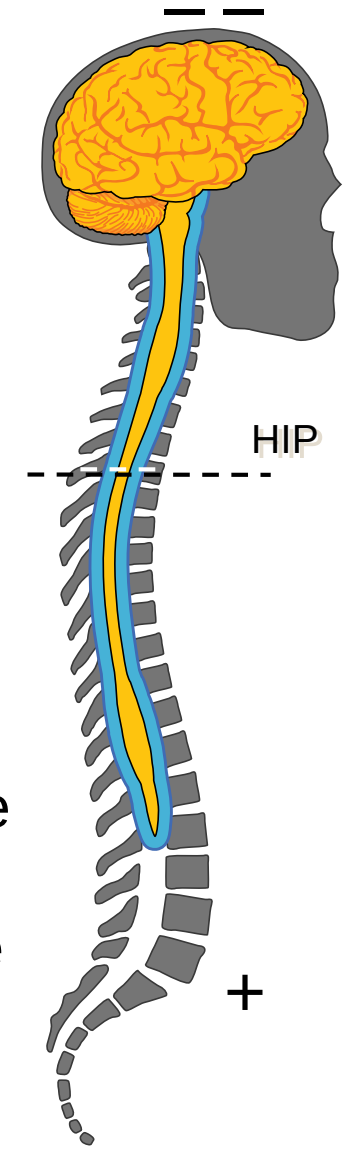
Location along the upright CSF axis where CSF pressure = supine CSF opening pressure





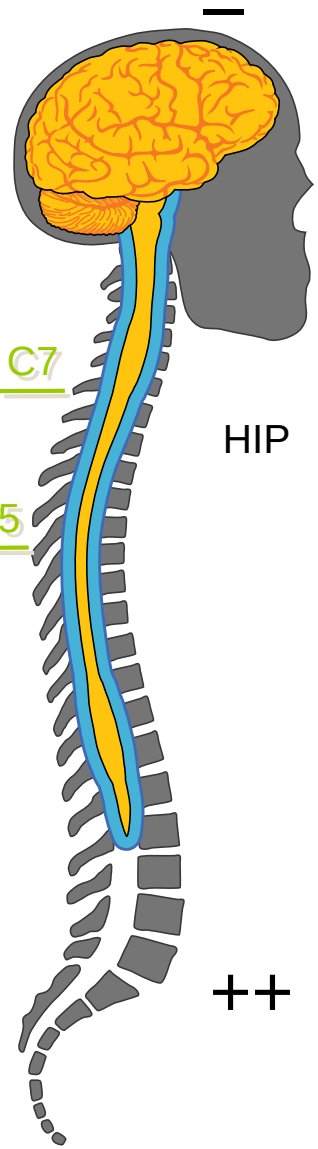


Normal

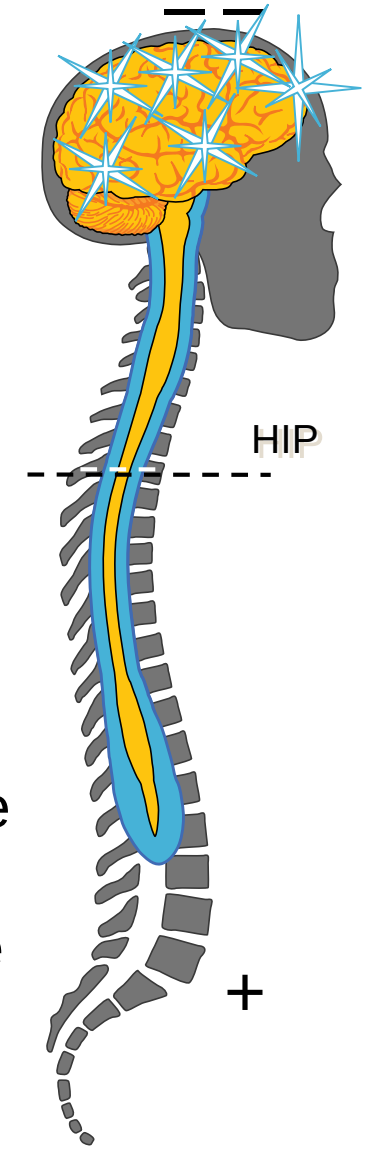


Increased compliance of lower CSF space

Back Replay



Normal



Increased compliance of lower CSF space

Back Replay

Spinal CSF Compartments: Cervical

- Cervical subarachnoid space differs from lumbar
  - Lumbar CSF space collapses but cervical CSF space expands with Valsalva maneuver
  - Opposite may occur in LPH
- Caudal HIP displacement
  - Cervical CSF pressure decreases
  - Cervical dura collapses but cervical epidural veins dilate
- Cervical dura compliance ↓
  - But does not overcome caudal HIP displacement from ↑ lumbar compliance

Spinal CSF Compartments : Cervical

- Standing: CSF from cervical and intracranial compartments move into more compliant lumbar sac
- Cervical dura partially collapses with compensatory acute distension of cervical **epidural veins**
  - Can cause orthostatic posterior cervical pain
  - **Intracranial veins** dilate causing orthostatic headache
- Young children and older adults: have stiffer caudal space
  - Less increase in caudal compliance with dural tear
    - HIP displaced less and post LP headache less common

Intracranial Hypotension Headache: Conclusion

- **Cause:** abnormal distribution of craniospinal elasticity
- ↑ lumbar compliance → HIP to move caudally → **more** intracranial hypotension and venous dilation in erect position
- **Can explain:** orthostatic character of headache
  - Spinal not cranial leakage produces headache
  - Imperfect correlation between CSF pressure and headache
  - Near absence in very young and elderly due to ↑ epidural space stiffness at these ages