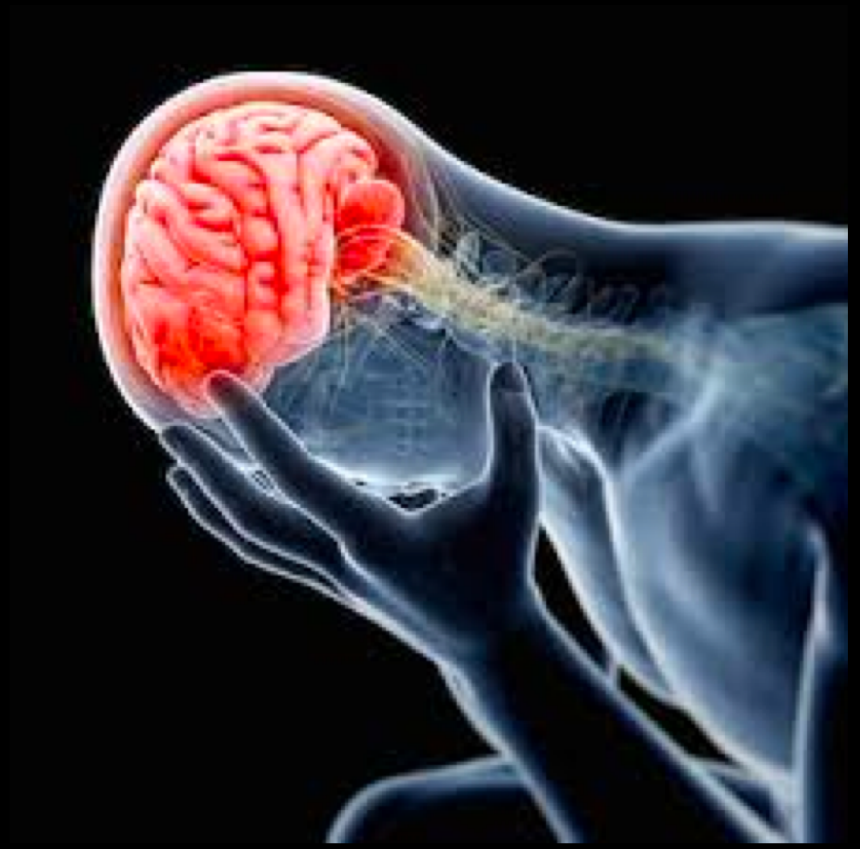
Cerebrospinal Fluid



gives me a headache…

What is CSF?

- What is it made of?
- Where is it made?
- Where does it go?

What does CSF do?

CSF Dynamics

- Anesthetic Effects
- Other pharmacologic effects

CSF Composition

- Clear aqueous solution
- 150 mL
  - Ventricles = 25 mL (20% of total CSF)
  - Subarachnoid Space = 125 mL (80%) of total CSF volume)
- Compared to Plasma:
  - Higher Na^+ Cl^- Mg^{2+}
  - Lower Glucose, Protein, Amino Acid, Uric Acid, K^+, bicarbonate, Ca^{2+} and Phosphorous

Composition of CSF

Substance	Plasma	CSF
Na^+ (mEq/l)	145.0	150.0
K^+	4.8	2.9
Ca^{++}	5.2	2.3
Mg^{++}	1.7	2.3
Cl^-	108.0	130.0
HCO_3^-	27.4	21.0
Lactate	7.9	2.6
PO_4^{---}	1.8	0.5
Protein	7000.0	20.0
Glucose	95.0	60.0

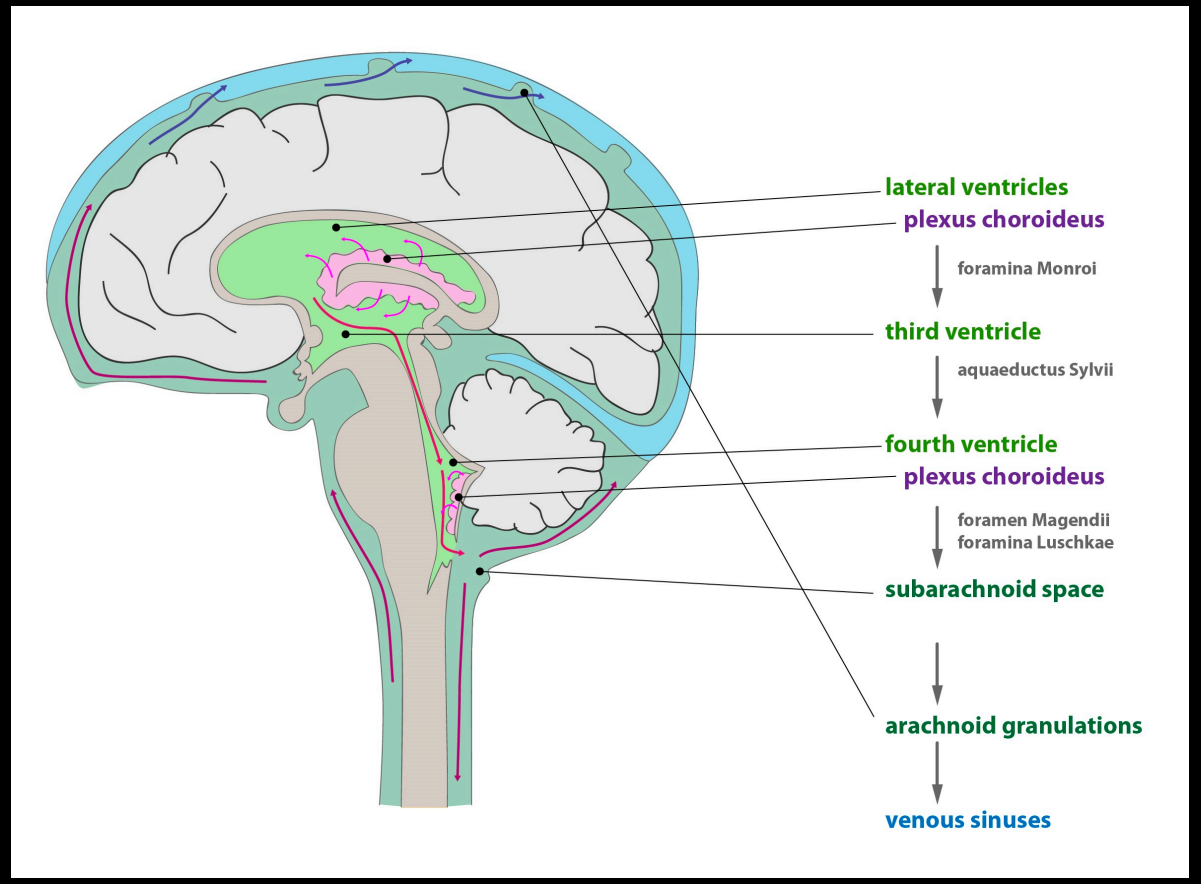
(protein and glucose expressed as mg/100 ml)

Protein

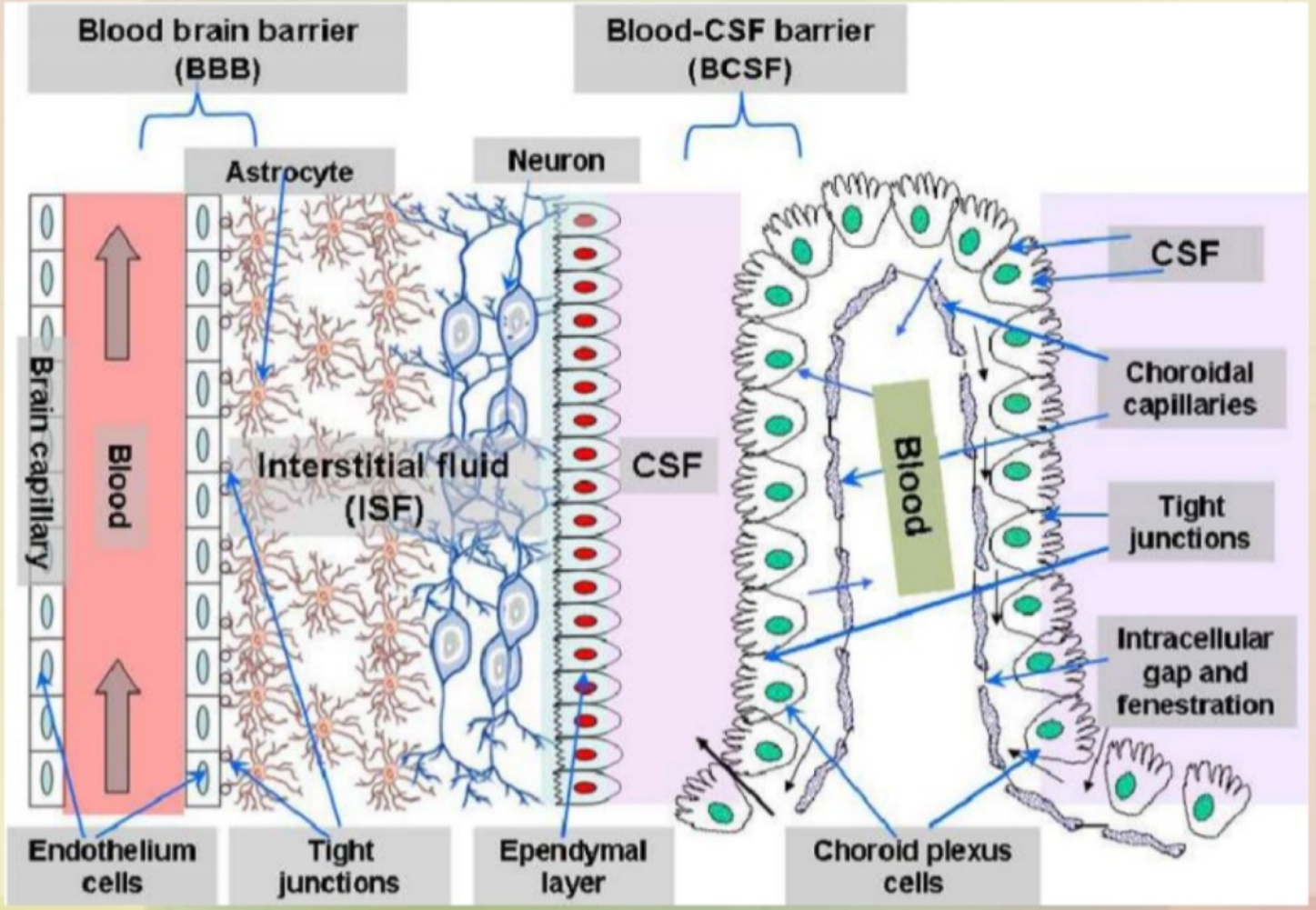
- CSF protein concentrations are normally 0.5% or less of the respective plasma or serum concentrations
- Permeability of blood-CSF barrier to albumin increases with age

CSF Formation

- Synthesized by two processes
  - Secretion from the choroid plexus and ventricular ependyma (50-70%)
  - Ultrafiltration of blood plasma through choroidal capillaries
- Rate of CSF Formation 0.35 mL/min = ***500-600 ml/day***
- Turnover for total CSF Volume ~ 6hrs (4 times/day)



Blood CSF barrier



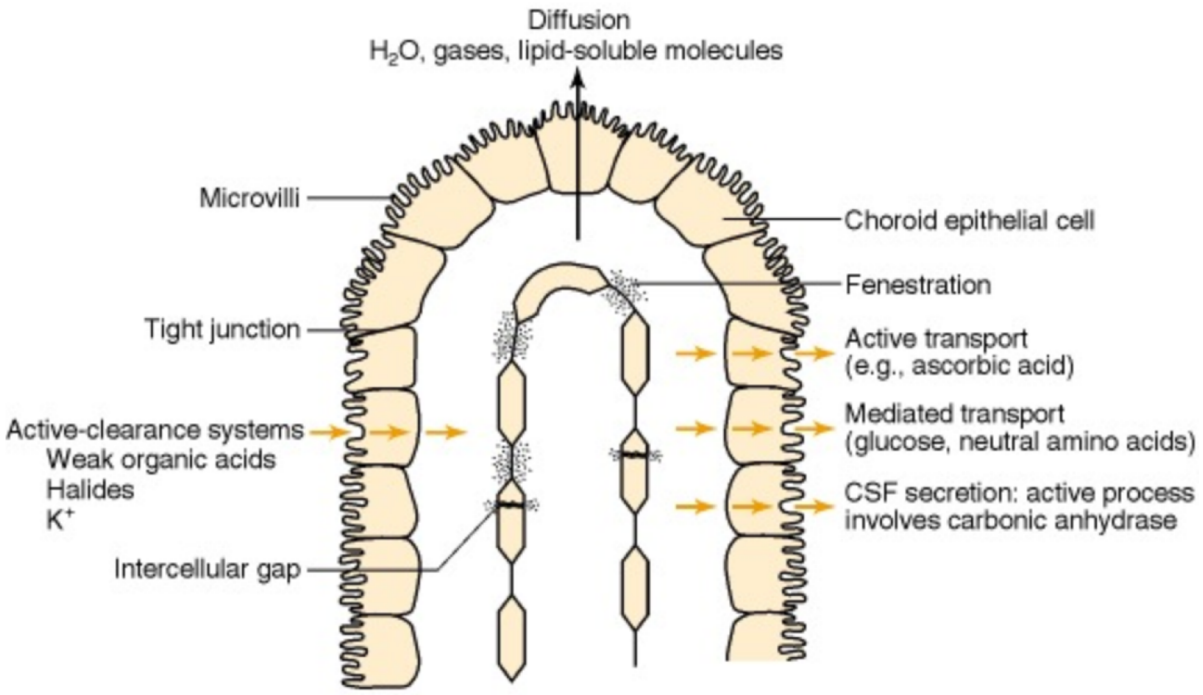
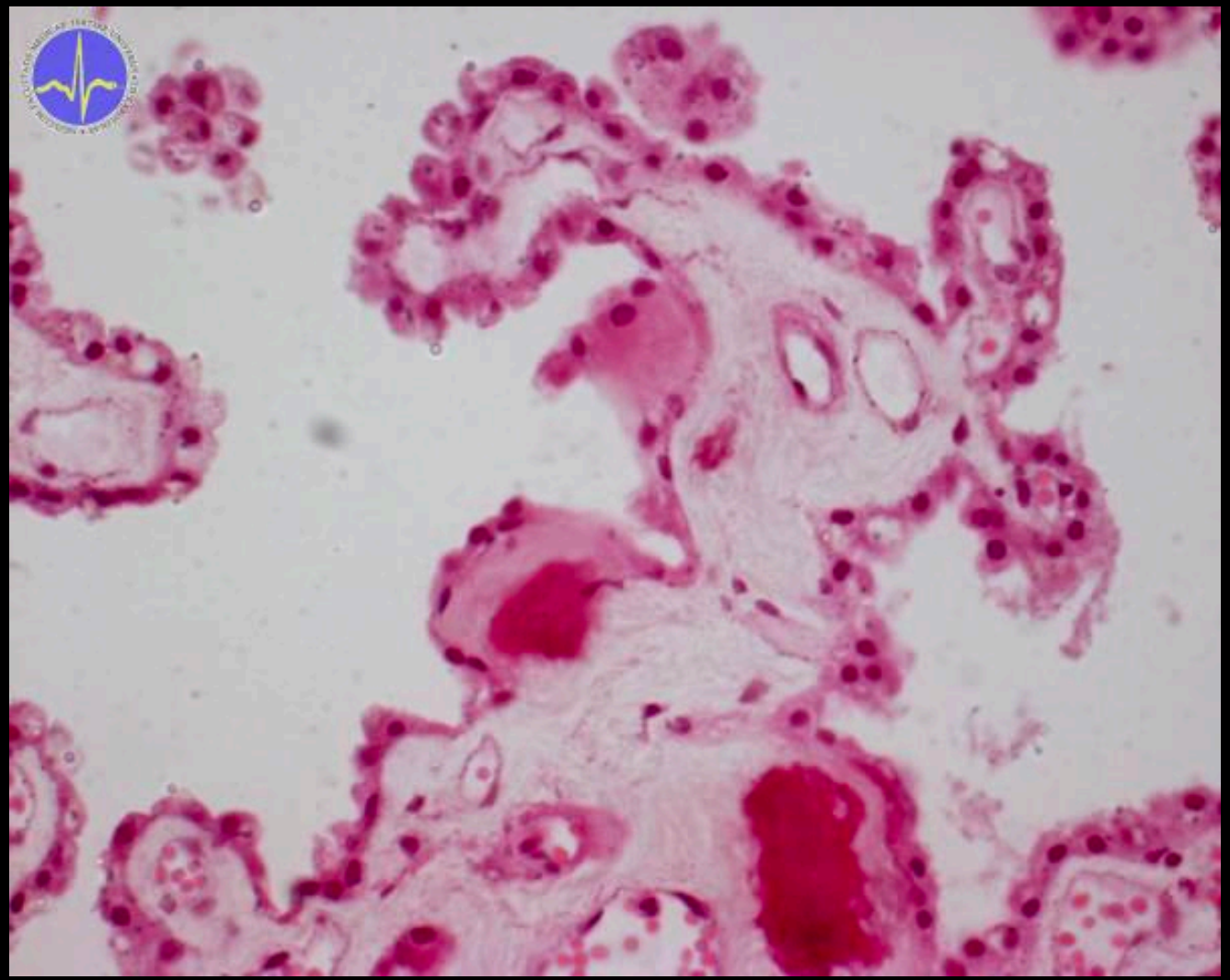


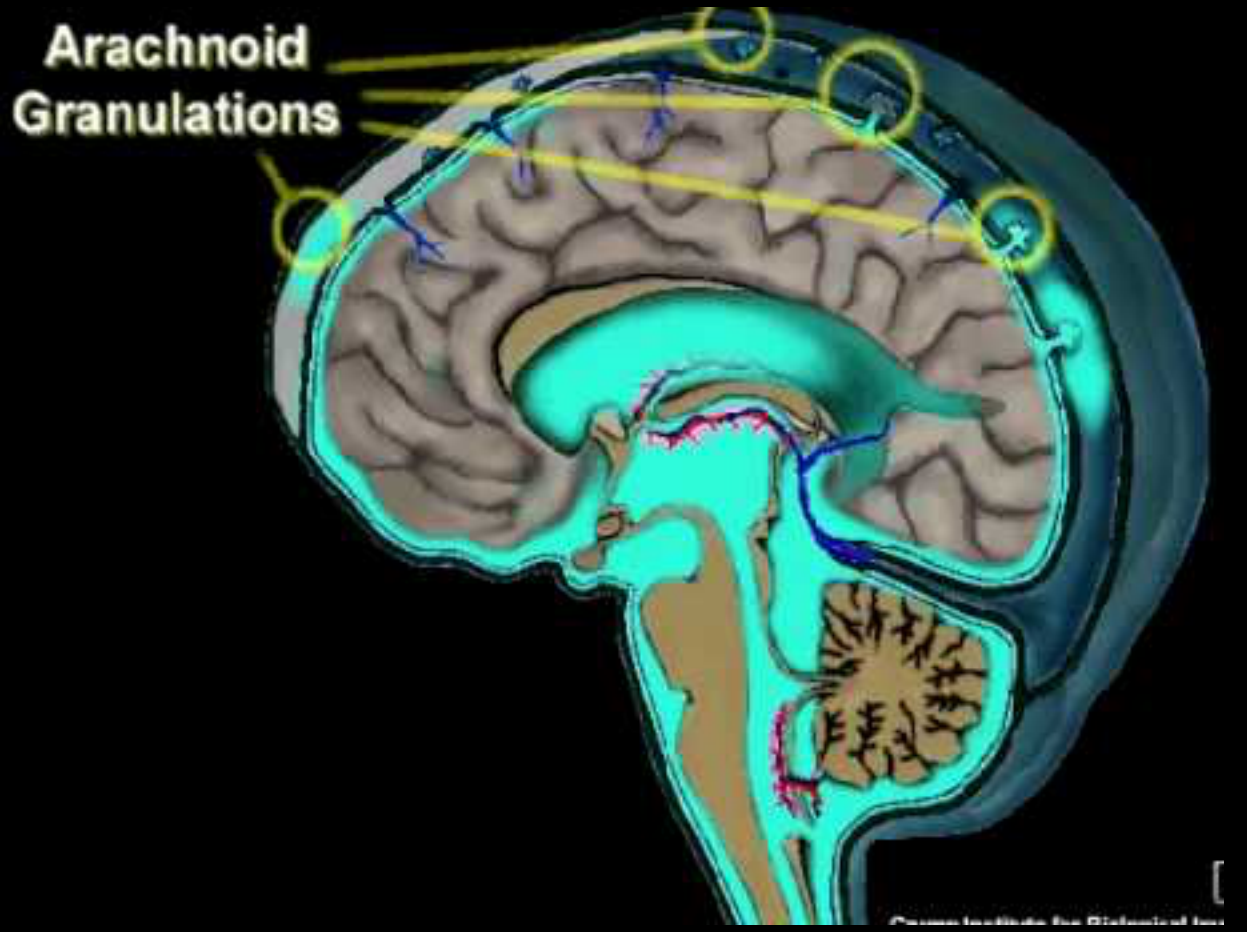
Figure 32-5

Blood—CSF barrier. The capillaries in the choroid plexus differ from those of the brain in that there is free movement of molecules across the endothelial cell through fenestrations and intercellular gaps. The blood—CSF barrier is at the choroid plexus epithelial cells, which are joined together by tight junctions. Microvilli are present on the CSF-facing surface. These greatly increase the surface area of the apical membrane and may aid in fluid secretion. Diffusion, facilitated diffusion and active transport into CSF, as well as active transport of metabolites from CSF to blood, have been demonstrated in the choroid plexus.

Choroid Plexus



CSF Circulation

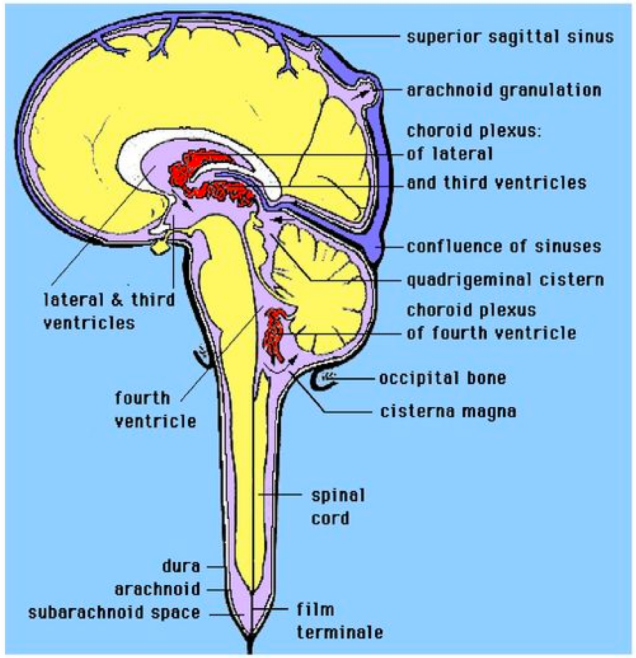


Cerebrospinal fluid circulates through the ventricles, over the surface of the brain, and is absorbed at the arachnoid villi and at the cranial and spinal nerve root sheaths

Go

- **lateral ventricles-->** foramen of Monro— >
- **third ventricle** --> aqueduct of Sylvius -->
- **fourth ventricle** --> foramina of Magendie and Luschka -->
- **subarachnoid space over brain and spinal cord** -->
- **reabsorption into venous sinus blood via arachnoid granulations**

CSF Circulation



Dual-outflow system for CSF to reach the blood circulation:

-Venous blood through arachnoid projections

-Lymphatic system

Respiration: A New Mechanism for CSF Circulation?

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Review of Dreha-Kulaczewski et al.

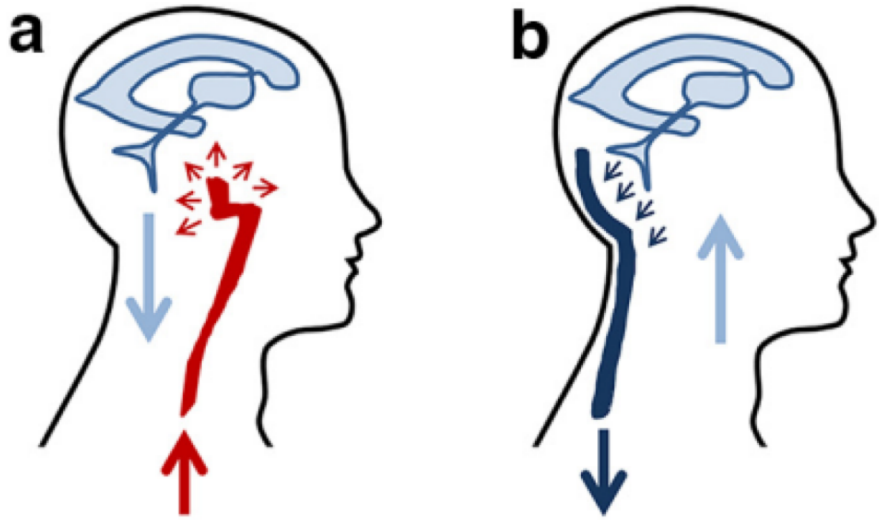


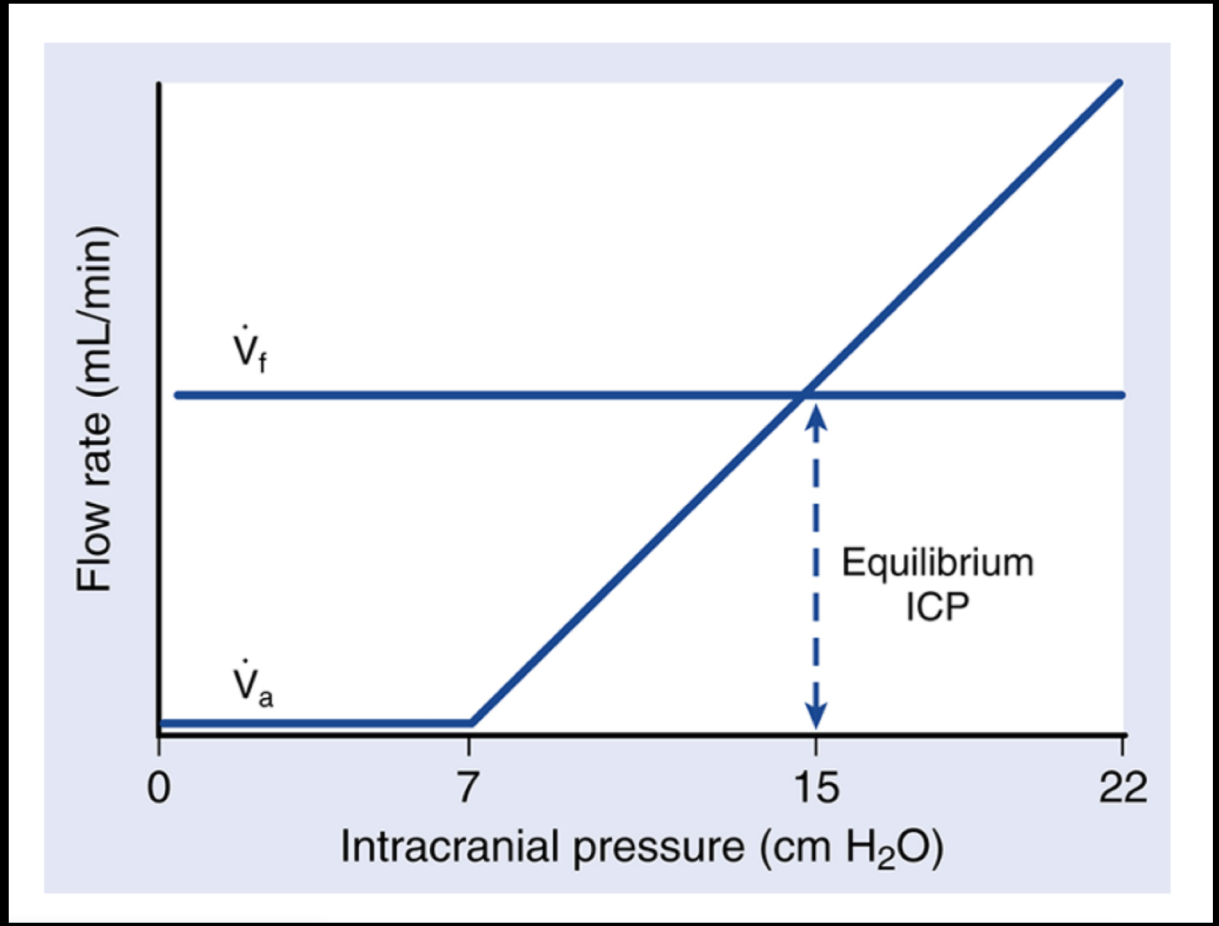
Figure 1. The two models for CSF flow. ***a***, In the classical view (O'Connell, 1943), the arrival of the arterial pulse wave (red) into the skull causes a temporary pressure increase in the incompressible intracranial compartment, resulting in CSF outflow (light blue) into the spinal canal. ***b***, In the model proposed by Dreha-Kulaczewski et al. (2017), the negative venous pressure (dark blue) produced during inspiration causes a temporary pressure decrease in the intracranial compartment, resulting in CSF flow into the head.

CSF Function

- Excretory function, brain itself has no lymphatic structures
- Intracerebral transport -- transport of hypothalamic releasing factors from cells of origin to cells in the median eminence
- Ionic homeostasis
- Protection – cushions the brain
  - Low specific gravity of CSF (1.007) relative to that of brain tissue (1.040) reduces effective mass (1400gm → 47 gm)
  - Dampens movement

CSF Dynamics

- Rate of CSF formation not affected by increased ICP
- Rate of reabsorption is affected by increased ICP
- When volume of intracranial blood or for example, tumor, increases, CSF volume contracts through translocation of intracranial CSF to the spinal subarachnoid space and reabsorption of CSF



Anesthetic Effects of CSF Production and Reabsorption

	MAP	CBF	CPP	ICP	$CMRo_2$	SSEP Amplitude Latency	CSF Production	CSF Absorption
Inhaled Agents								
Halothane	↓↓	↑↑↑	↑↑	↑↑	↓↓	↓↑	↑↓	↑↓
Isoflurane	↓↓	↑	↑↑	↑	↓↓↓	↓↑	↓↑	↑
Sevoflurane	↓↓	↑	↑	Ø–↑	↓↓↓	↓↑	↑	↓
Desflurane	↓↓	↑	↑	↑	↓	↓↑	↓↑	↑
N_2O	Ø–↓	↑–↑↑	↓	↑–↑↑	↓↑	↓Ø–↑	↓↑	↓↑
IV Agents								
Thiopental	↓↓	↓↓↓	↑↑↑	↓↓↓	↓↓↓	↓↑	↓↑	↑
Propofol	↓↓↓	↓↓↓	↑↑	↓↓	↓↓↓	↑↑	↓↑	↑
Etomidate	Ø–↓	↓↓↓	↑↑	↓↓↓	↓↓↓	↑↑	↓↑	↑
Ketamine	↑↑	↑↑↑	↓	↑↑↑	↑	↑Ø	↓↑	↓
Benzodiazepine	Ø–↓	↓↓	↑	Ø	↓↓	↓Ø–↑		↑
Opioids	Ø–↓	↓	↓↑	Ø–↓	↓	↓↑	↓↑	↑

CBF, Cerebral blood flow; *CMR,* cerebral metabolic rate; *CPP,* cerebral perfusion pressure; *CSF,* cerebrospinal fluid; *ICP,* in cranial pressure; *MAP,* mean arterial pressure; *SSEP,* somatosensory evoked potential; ↑, increased; ↓, decreased; Ø, none.

TABLE 3–3 Effects of Inhaled Anesthetics on Cerebrospinal Fluid (CSF) Dynamics

Inhaled Anesthetic	V_f	R_a	Predicted Effect on Intracranial Pressure
Desflurane	0,+,a	0	0,+,a
Enflurane:			
Low concentration	0	+	+
High concentration	+	0	+
Halothane	−	+	+
Isoflurane:			
Low concentration	0	0,+,b	0,+,b
High concentration	0	−	−
Nitrous oxide	0	0	0
Sevoflurane	−	+	?

R_a, Resistance to reabsorption of CSF; V_f, rate of CSF formation; +, increase; 0, no change; −, decrease; a, effect occurs only during hypocapnia combined with increased CSF pressure, and under such conditions treatment with furosemide (but not mannitol, dexamethasone, or fentanyl) decreases ; b, effect depends on dose; ?, uncertain.

TABLE 3–4 Effects of Sedative-Hypnotics and Antagonist Drugs on Cerebrospinal Fluid (CSF) Dynamics

Sedative-Hypnotic	V_f	R_a	Predicted Effect on Intracranial Pressure
Etomidate:			
Low dose	0	0	0
High dose	−	0, −,a	−
Midazolam*:			
Low dose	0	+, 0, a	+, 0, a
High dose	−	0, +, a	−, ?, a
Pentobarbital	0	0	0
Propofol	0	0	0
Thiopental:			
Low dose	0	+, 0, a	+, 0, a
High dose	−	0, −, a	−
Antagonists			
Flumazenil:			
Low dose	0	0	0
High dose	0	−	−

R_a, Resistance to reabsorption of CSF; V_f, rate of CSF formation; +, increase; 0, no change; −, decrease; a, effect depends on dose; ?, uncertain.

TABLE 3–5 Effects of Opioids and Other Anesthetics on Cerebrospinal (CSF) Dynamics

	V_f	R_a	Predicted Effect on Intracranial Pressure
Opioids			
Alfentanil:			
Low dose	0	–	–
High dose	0	0	0
Fentanyl:			
Low dose	0	–	–
High dose	–	0, +	–, ?
Sufentanil:			
Low dose	0	–	–
High dose	0	+, 0	+, 0
Other Anesthetics			
Cocaine	0	0	0
Ketamine	0	+	+
Lidocaine	0, –, a	0	0, –, a

R_a, Resistance to reabsorption of CSF; V_f, rate of CSF formation; +, increase; 0, no change; –, decrease; a, effect depends on dose; ?, uncertain.

Other Pharmacologic Effects

- **Furosemide**
  - Reduces CSF formation by reducing Chloride transport
  - Pulls water out of CSF and concentrates it
  - Does not decrease rate of CSF formation
  - One study reported that furosemide augmented mannitol-induced increase in plasma osmolality

- **Mannitol**
  - Does not cross the BBB (at least initially)
  - Acutely increases circulating blood volume, decreases blood viscosity
  - Then reduces cerebral parenchymal water by acting as an osmotic diuretic; increases plasma osmolality causing water to move from brain into blood
    - Reduces brain water content and ICP

- **Acetazolamide**
  - Decreases rate of CSF formation
  - Carbonic anhydrase found in the choroid plexus and neuroglial cells
  - Carbonic anhydrase is a crucial enzyme needed in the production of cerebrospinal fluid. When this enzyme is suppressed, production of CSF decreases, which also lowers intracranial pressure.