CEREBROSPINAL FLUID- ANATOMY, PHYSIOLOGY AND DYNAMICS

OUTLINE

- CSF SPACES
- CSF FORMATION – CIRCULATION – REABSORPTION
- METHODS OF DETERMINING Vf AND Ra
- EFFECTS OF DRUGS
- ALTERATION IN CSF DYNAMICS IN PATHOLOGY

ANATOMY OF CSF SPACES

CSF is clear, colourless liquid that is formed in brain and circulates through macroscopic & microscopic spaces that are in continuity.

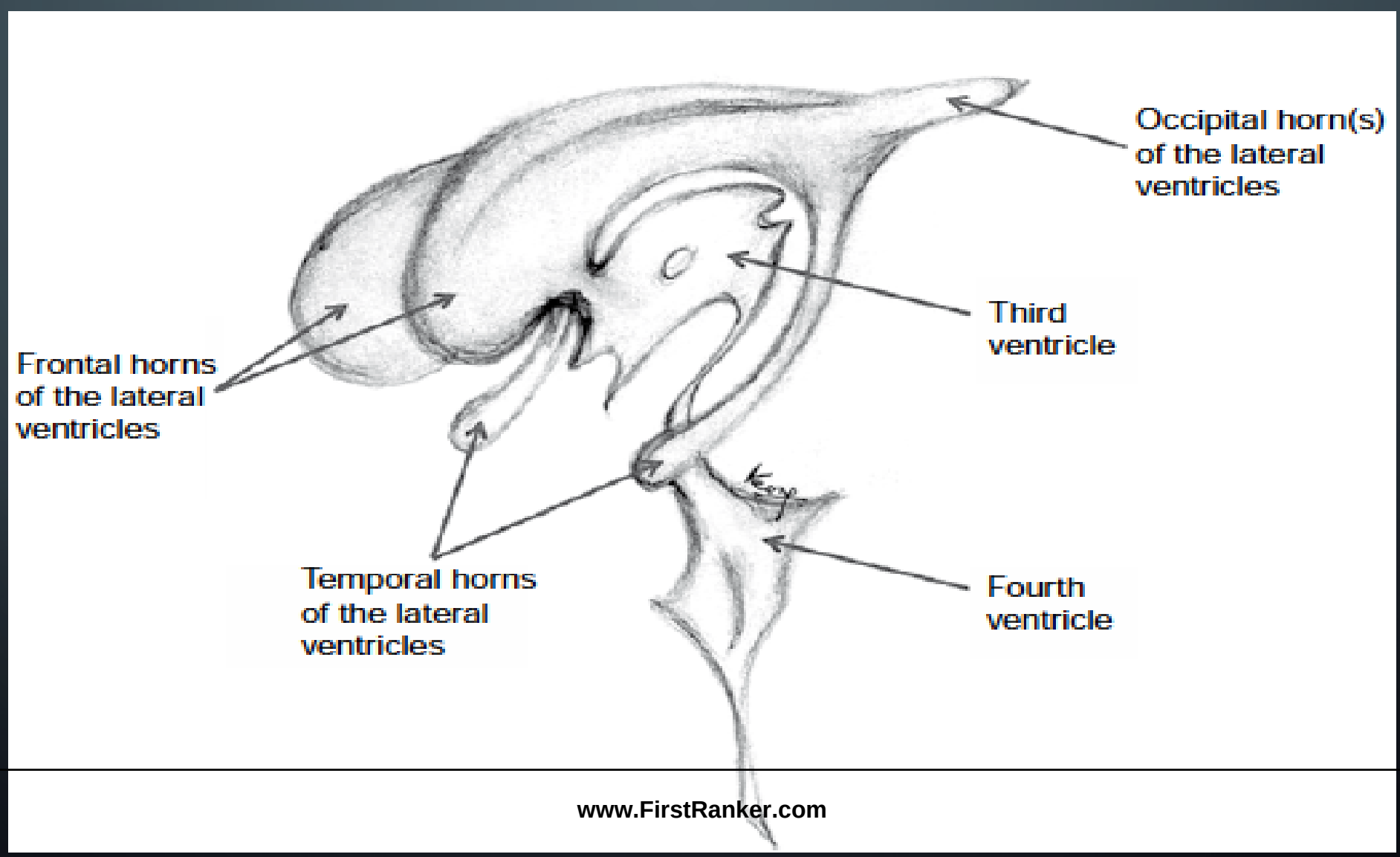
Macroscopic spaces (140-150ml)**:**

- Two lateral ventricles
- Third ventricle
- Aqueduct of sylvius
- Fourth ventricle
- Central canal of spinal cord

Microscopic spaces:

- Brain and spinal cord ECF space (300-350 ml)

THREE DIMENSIONAL SHAPE OF THE VENTRICULAR SYSTEM



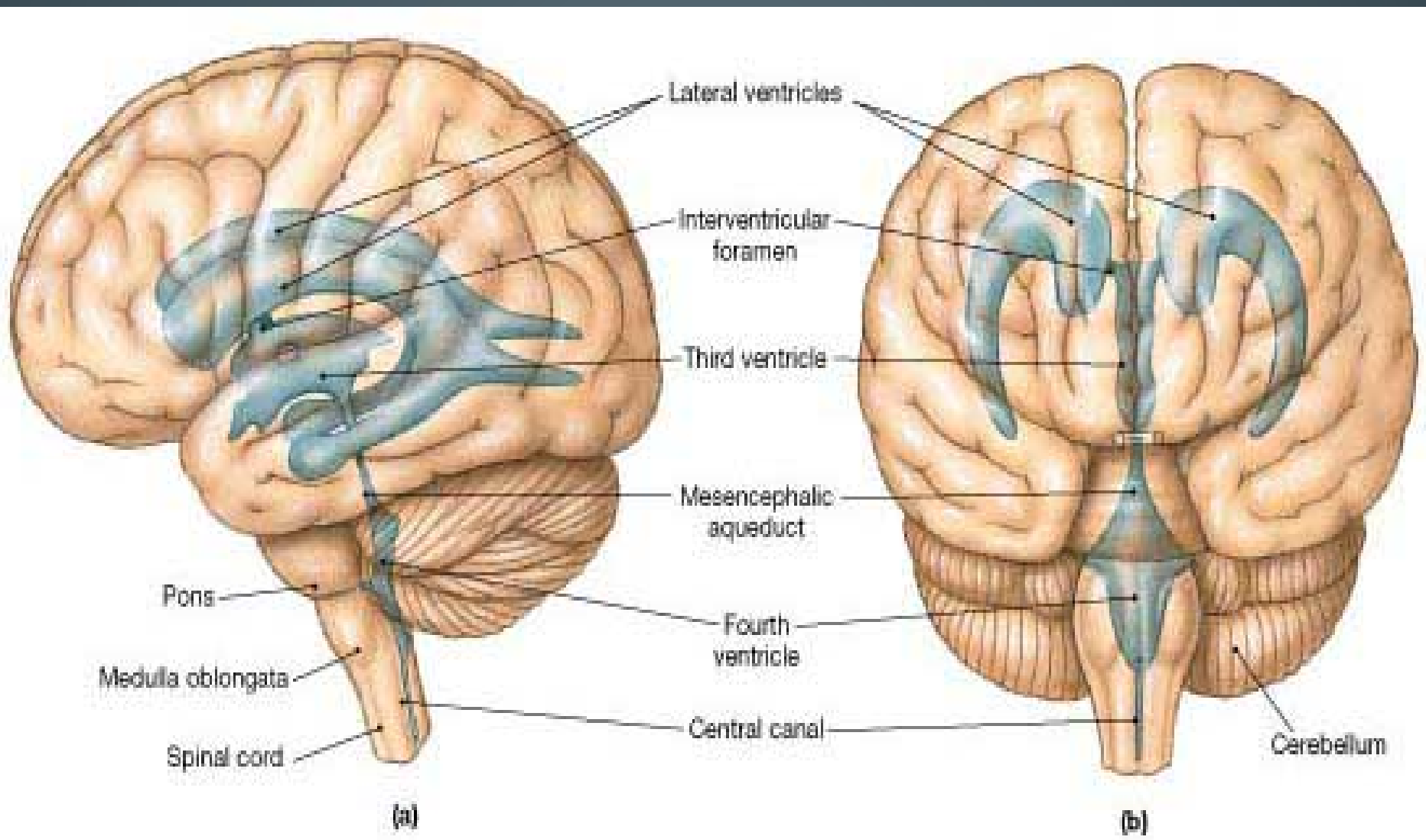
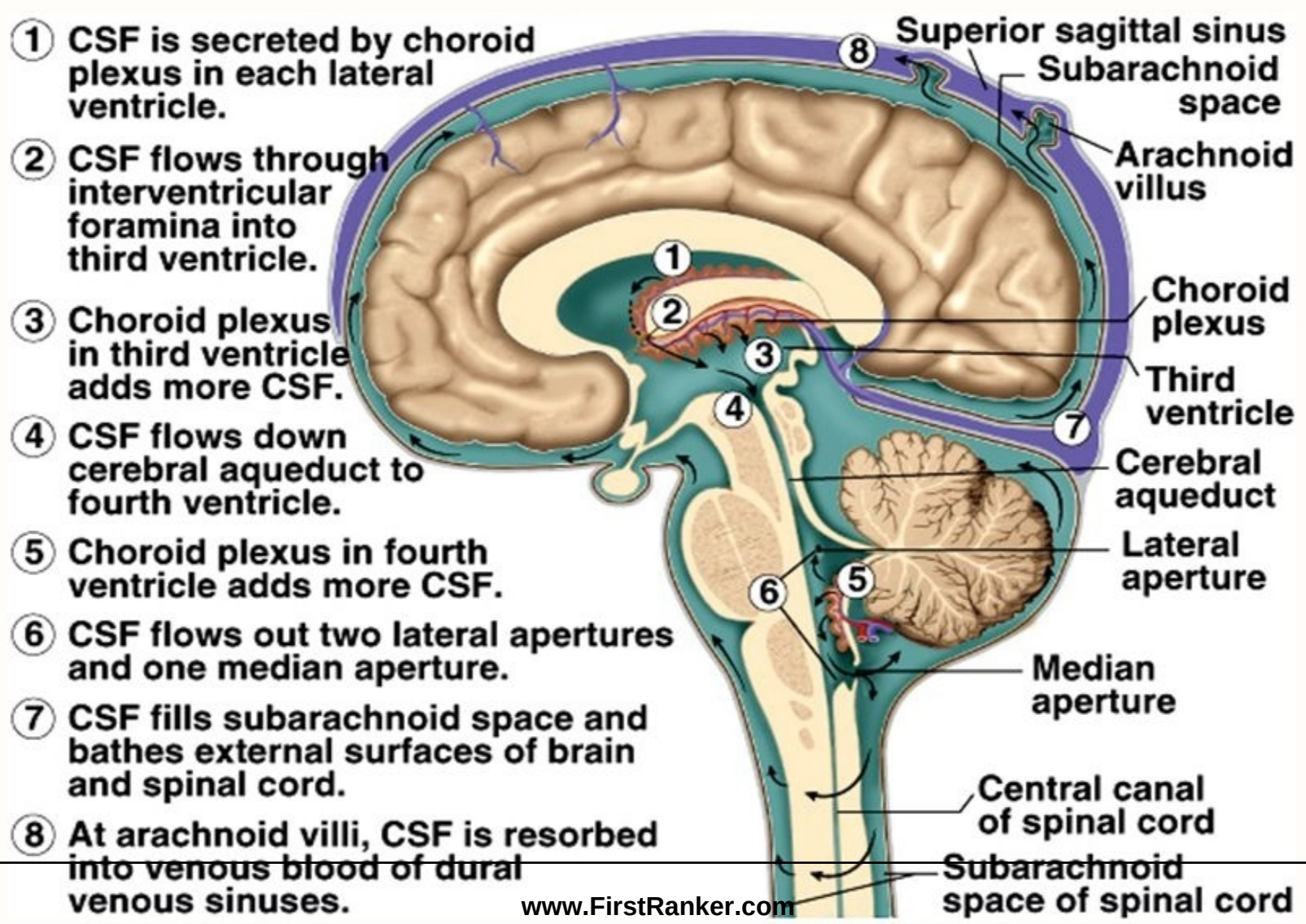


FIGURE 14-3 Ventricles of the Brain. Orientation and extent of the ventricles as they would appear if the brain were transparent. **(a)** Lateral view. **(b)** Anterior view, showing the relationships among the lateral ventricles and the third ventricle.

Flow of Cerebrospinal Fluid



PROPERTIES OF CSF

Table 3–1 Cerebrospinal Fluid (CSF) Pressure and Volume in Humans

	Range*
CSF pressure (mm Hg):	
Children	3.0-7.5
Adults	4.5-13.5
CSF volume (mL):	
Infants	40-60
Young children	60-100
Older children	80-120
Adults	100-160

COMPOSITION

Table 3–2 Composition of Cerebrospinal Fluid (CSF) and Plasma in Humans

Feature or Component	Mean CSF Value or Concentration*	Mean Plasma Value or Concentration*
Specific gravity	1.007	1.025
Osmolality (mOsm/kg H_2O)	289	289
pH	7.31	7.41
P_{CO_2} (mm Hg)	50.5	41.1
Sodium (mEq/L)	141	140
Potassium (mEq/L)	2.9	4.6
Calcium (mEq/L)	2.5	5.0
Magnesium (mEq/L)	2.4	1.7
Chloride (mEq/L)	124	101
Bicarbonate (mEq/L)	21	23
Glucose (mg/100 mL)	61	92
Protein (mg/100 mL):	28	7000
Albumin	23	4430
Globulin	5	2270
Fibrinogen	0	300

- Na content peaks at 8:00 am & 6:00 pm
- Relationship between Na concentration and migraine has been proposed as peaks correspond to migraine attacks

.. Harrington MG,Salomon RM, et al. Cerebrospinal fluid sodium rhythms. Cerebrospinal fluid Res 2010

COMPOSITION

- Varies according to sampling site
- Altered during neuroendoscopy

Na,Cl,Mg

Glucose, Protiens, AA, K ,

HCO3, Ca, Phosphate, Uric acid

FORMATION OF CSF

3 Sites:

- Choroid plexus (50 – 70 %)
- Ependymal surfaces of ventricles
- Perivascular spaces

- Rate (Vf) →0.35-0.40 ml/min
  500-600 ml/day
- Turnover time- 5-7 hrs (4 times/day)
- 40%-70%→ enters macroscopic spaces via CP
- 30%-60% → enters across ependyma and pia
- **Recent studies – Bidirectional fluid exchange at BBB far exceeds CP csf formation**

  - Brinker T.,et al. A new look at cerebrospinal fluid circulation. Fluids Barriers CNS. 2014;11:10-15

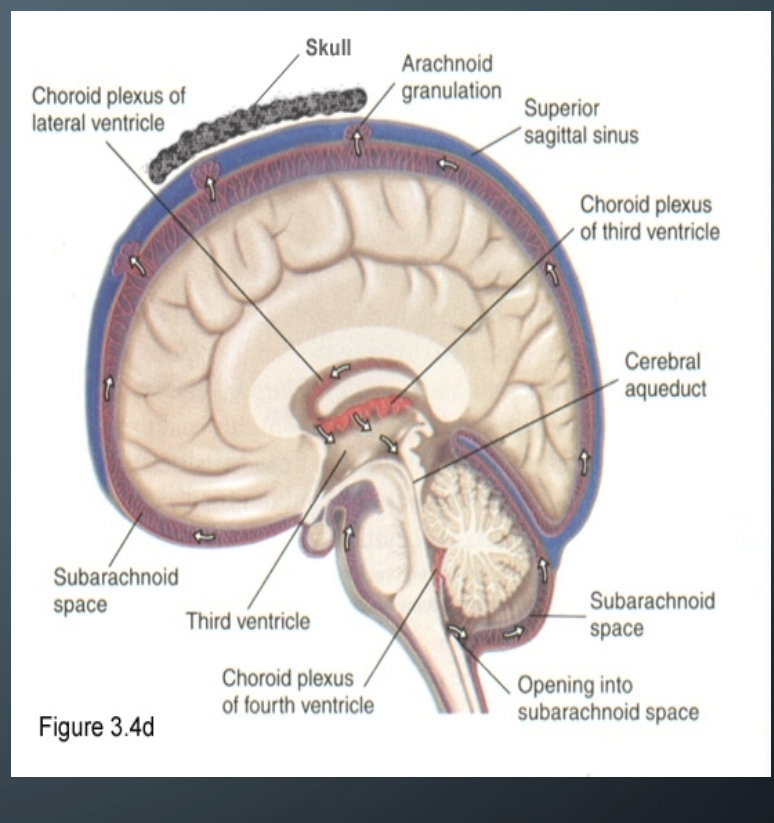


Figure 3.4d

Brinker *et al. Fluids and Barriers of the CNS* 2014, **11**:10
http://www.fluidsbarrierscns.com/content/11/1/10

FLUIDS AND BARRIERS OF THE CNS

REVIEW Open Access

A new look at cerebrospinal fluid circulation

Thomas Brinker*, Edward Stopa, John Morrison and Petra Klinge

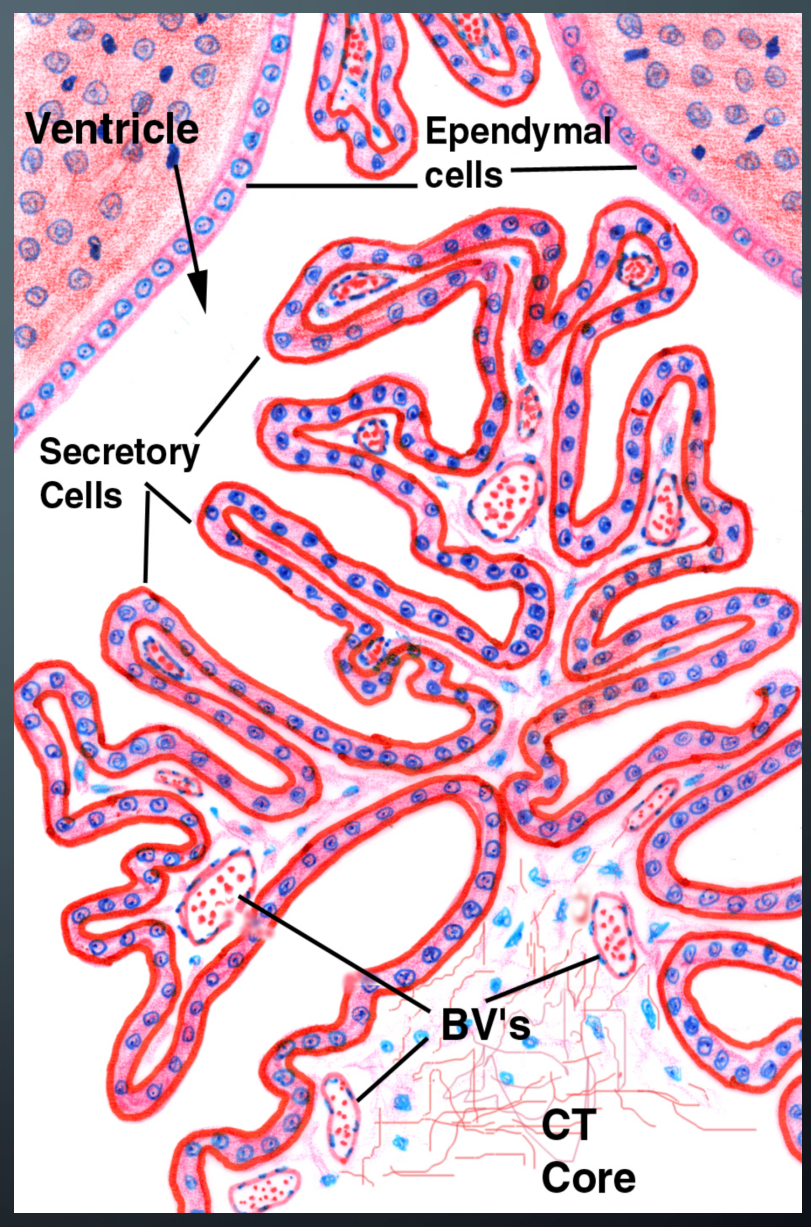
Abstract

According to the traditional understanding of cerebrospinal fluid (CSF) physiology, the majority of CSF is produced by the choroid plexus, circulates through the ventricles, the cisterns, and the subarachnoid space to be absorbed into the blood by the arachnoid villi. This review surveys key developments leading to the traditional concept. Challenging this concept are novel insights utilizing molecular and cellular biology as well as neuroimaging, which indicate that CSF physiology may be much more complex than previously believed. The CSF circulation comprises not only a directed flow of CSF, but in addition a pulsatile to and fro movement throughout the entire brain with local fluid exchange between blood, interstitial fluid, and CSF. Astrocytes, aquaporins, and other membrane transporters are key elements in brain water and CSF homeostasis. A continuous bidirectional fluid exchange at the blood brain barrier produces flow rates, which exceed the choroidal CSF production rate by far. The CSF circulation around blood vessels penetrating from the subarachnoid space into the Virchow Robin spaces provides both a drainage pathway for the clearance of waste molecules from the brain and a site for the interaction of the systemic immune system with that of the brain. Important physiological functions, for example the regeneration of the brain during sleep, may depend on CSF circulation.

Keywords: Cerebrospinal fluid circulation, Astrocyte, Aquaporin, Blood brain barrier, Virchow Robin space

CHOROID PLEXUS

It is a cauliflower like growth of blood vessels covered by a thin layer of epithelial cells.



It is made of 3 layers:

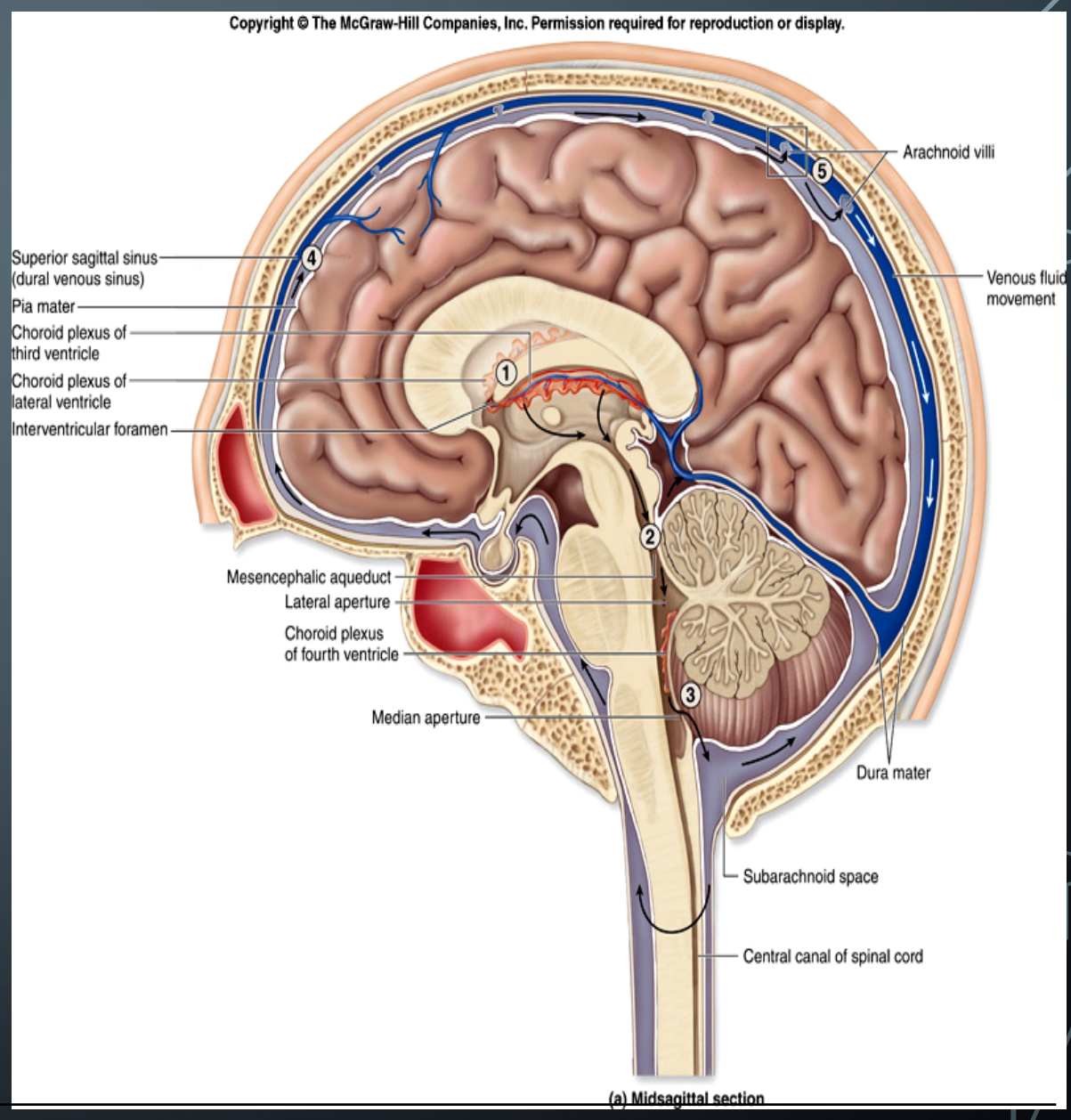
- fenestrated capillary endothelium
- extra cellular matrix
- epithelial cells

Choroid plexus projects into:

- Temporal horn of lateral ventricle
- Post. Part of 3rd ventricle
- Roof of 4th ventricle

Blood supply: ant. & post choroidal artery (lateral & 3rd ventricle) and supr cerebeller and PICA (temporal horn & 4th ventricle)

Nerve supply : branches of Vagus, Glossopharyngeal & Sympathetic N.

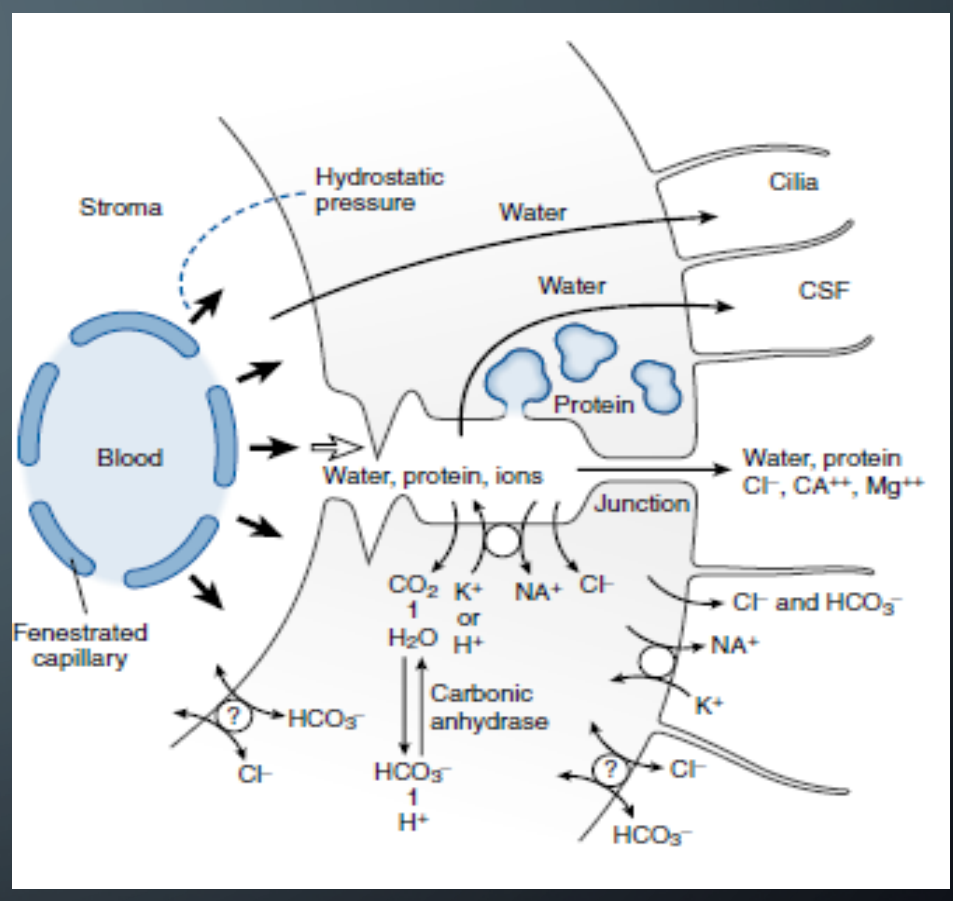


CSF FORMATION AT CHOROID PLEXUS

Blood entering CP capillaries filtered →form protein rich fluid similar to ISF in CP stroma

Hydrostatic pressure & bulk flow →enter cleft between epithelial cells

stromal fluid transported across CP epithelium- Ultrafiltration & secretion



ATP dependent membrane pump transport Na across luminal surface to macroscopic spaces in exchange for K & H.
Water moves from stroma into CSF by conc gradient by ionic pump.

CSF FORMATION AT EXTRA CHOROIDAL SITES

- Derived from ECF & cerebral capillaries across BBB
- Oxidation of glucose (into H2O & CO2) by brain [60%].
- Ultrafiltration from cerebral capillaries[40%]

TIGHT JUNCTIONS

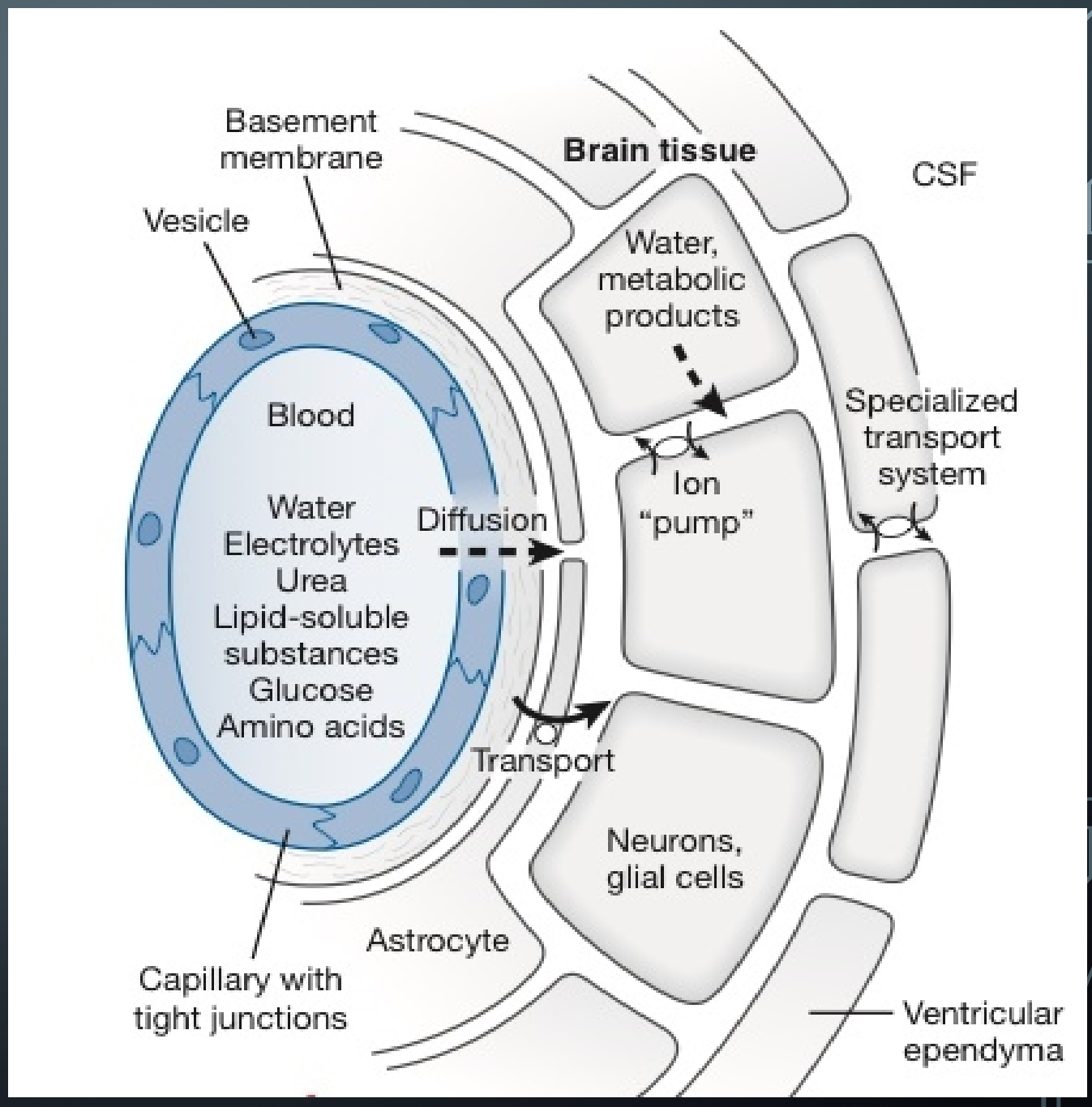
In blood-ECF interface

Glucose /electrolyte/water/AA/lipid soluble material→ Pass

Large polar/protein→ Stop

Glucose rich and protein poor fluid diffuse through ECF space toward macroscopic spaces

- Water and other constituent of plasma crosses **Blood brain Barrier** into the brain ECF space by diffusion or transport.
- Water and cellular metabolites added to the ECF from neurons and glial cells.



MOVEMENT OF GLUCOSE & PROTEIN

- CSF glucose conc. is approx. 60% of that in blood
- Ratio remains constant till 270 -360mg/dl blood glucose
- Glucose enters CSF -Facilitated transport & follows saturable kinetics (i.e rate depends on serum glucose conc.)
- Protein entry in CSF limited – conc. is 0.5% or less of serum conc.
- Protein in CSF transported with CSF & cleared from csf space to dural venous sinuses by
- "Sink effect" – flowing CSF keeps CSF & brain protein conc. Low.

EFFECT OF INCREASED ICP ON CSF FORMATION

Relation between Vf and ICP/CPP

- ↑ICP
- Vf

- ↓CPP
- Vf

➢As long as CPP remain > 70mm of Hg, increase of ICP[upto 20mm of Hg] has no major impact on Vf (rate of CSF formation).

➢When CPP is significantly lowered <70 mmHg→CBF↓ and CPBF ↓, Vf ↓

CIRCULATION OF CSF

- Hydrostatic pressure of CSF formation→15 cmH20 produce CSF flow.
- Cilia of ependymal cell→ generate current to propel CSF toward 4th ventricle & its foramina into subarachnoid space.
- Respiration variations
- Vascular pulsation of cerebral arteries , CP

} Additional CSF movement

- 15cm H20 CSF pressure of formation
- 9 cm H20 superior sagittal sinus pressure

6 cm of pressure gradient across arachnoid villi → Suction pump effect

Reabsorption – arachnoid villi (SSS) & spinal dural sinusoids in dorsal nerve roots.

REABSORPTION

- CSF pass from Subarachnoid spaces → via Arachnoid villi & granulation → into venous blood.
- Arachnoid villi or granulations are protrusion of the arachnoid cells from subarachnoid space into & through wall of venous sinuses
- **Arachnoid villi are located:**
- **Intracranial-** Superior Sagittal sinus (85-90% reabsorbed)
- **Spinal -** dural sinusoids on dorsal nerve root (10-15%)

DETERMINANTS OF REABSORPTION

- **Normal intracranial pressure:**
- Endothelium covering the villus acts as a CSF- blood barrier
- Rate of pass of CSF– 1.Trans villus hydrostatic pressure gradient
  (CSF pressure – venous sinus pressure)
  2.Pressure sensitive resistance to CSF outflow at arachnoid villi

CSF passes through endothelium via: 1. Pinocytotic vesicles
2. Transcellular openings

DETERMINANTS OF REABSORPTION

- **Increased intracranial pressure:**
- Rate of reabsorption of CSF (Va)→ ↑ if pressure gradient across villus↑
- Resistance to reabsorption of CSF(Ra)→ remains normal upto a CSF pressure of 30 cm of H20; above this it is decreased.

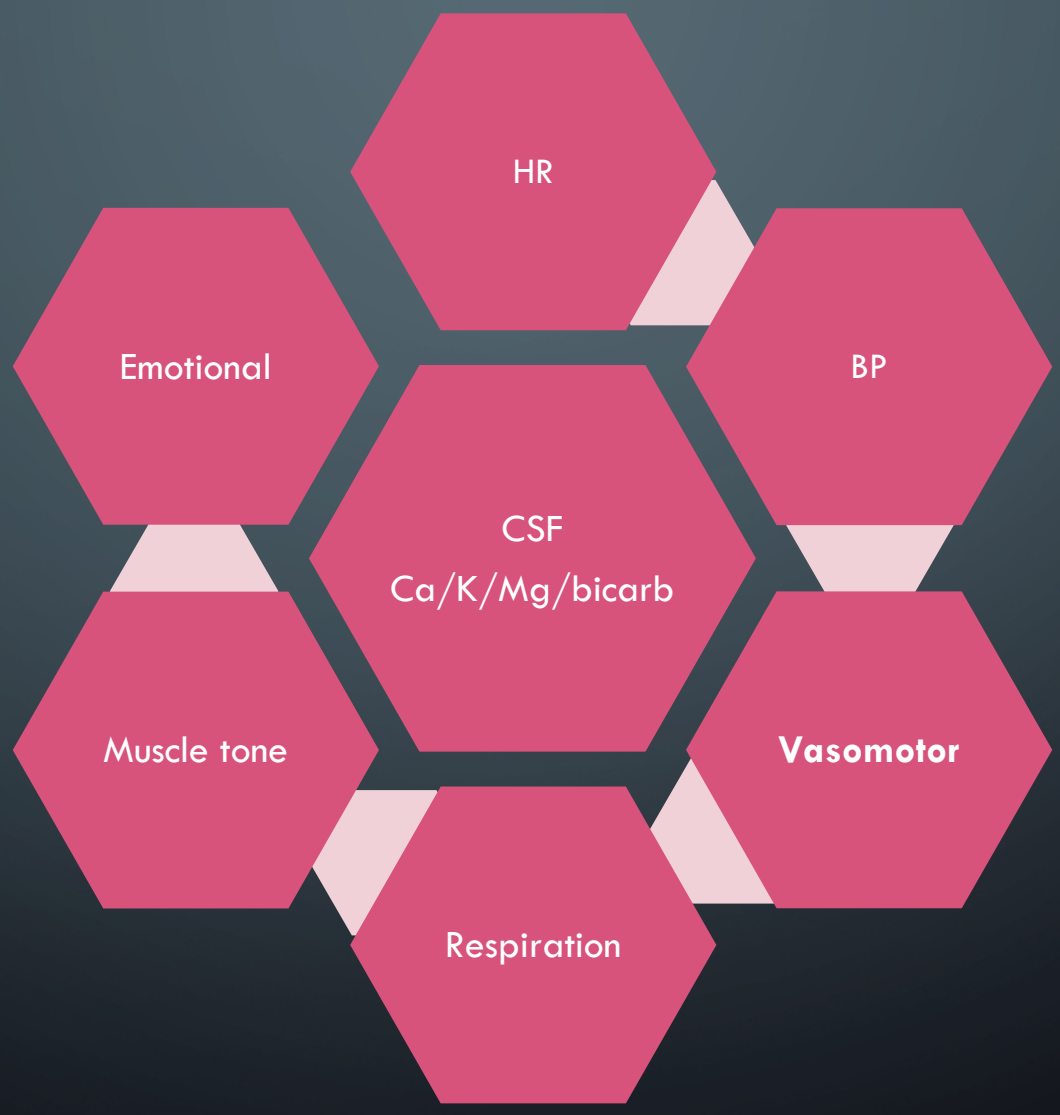
FUNCTION OF CSF

- Protection, Support, Nutrition
- The low Specific gravity of CSF (1.007) relative to that of the brain (1.040) reduces the effective mass of a 1400g brain to only 47 g.
- Stable supply of nutrients, primarily glucose(active transport); also vitamins/ eicosanoids/monosaccharides/neutral & basic amino acids/monocarboxylic acid (specialized pump mechanism).

CONTROL OF CHEMICAL ENVIRONMENT

- Exchange between neural tissue & CSF occurs readily by diffusion
- (because distance b/w CSF and any brain area is max 15 mm & ISF spaces of brain and spinal cord is continuous with macroscopic CSF spaces.)
- **Acid-base characteristics of CSF influence:-**
- Respiration
- CBF, CBF-AR
- Cerebral metabolism

CONTROL OF CHEMICAL ENVIRONMENT



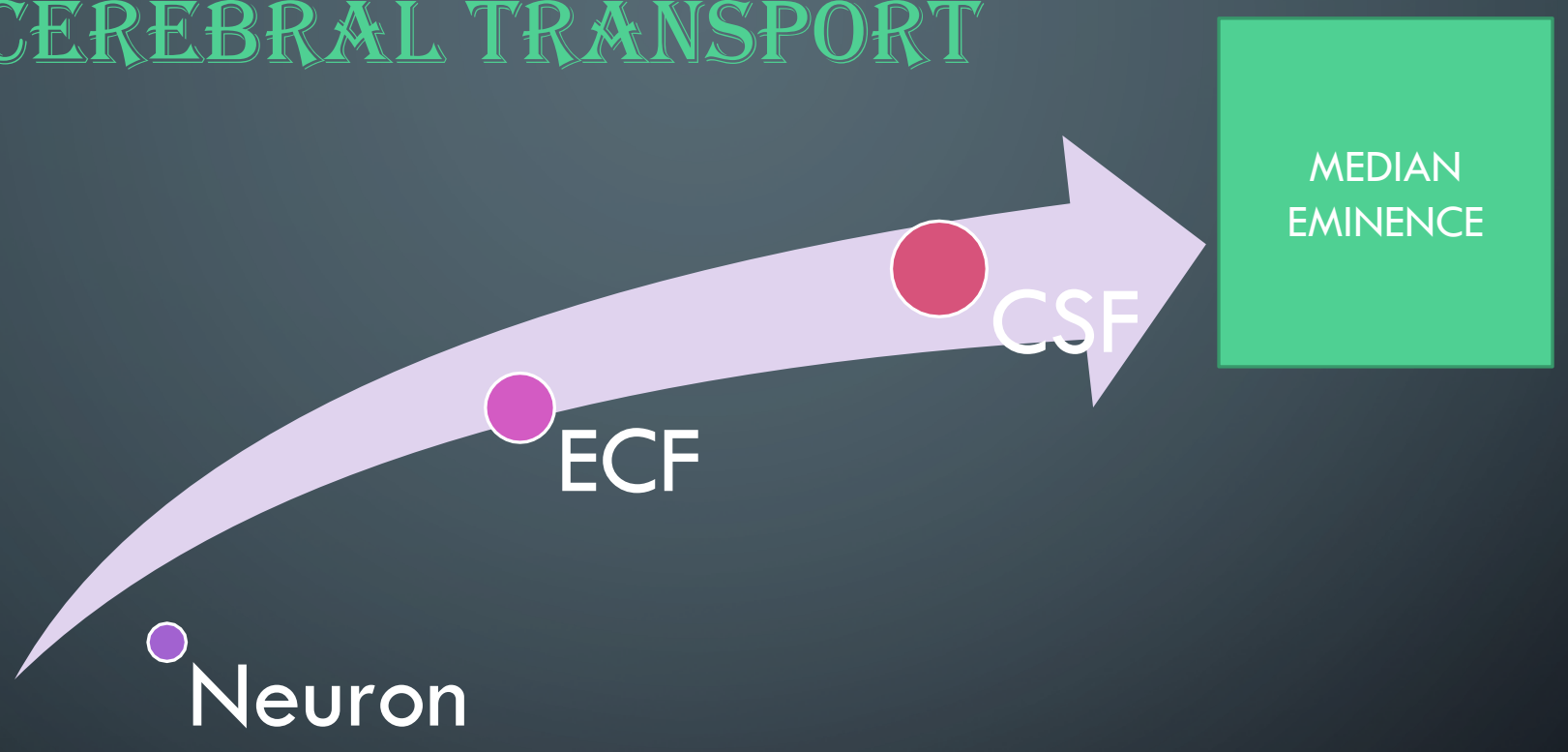
CONTROL OF CHEMICAL ENVIRONMENT

Primary pumps (active transport)	• K/HCO3 • Ca/Mg
Secondary pumps (passive transport)	• H+ • Cl-

EXCRETION

- Removes metabolic products, unwanted drugs
- BBB excludes out toxic, large , polar and lipid insoluble drug, humoral agents etc.

INTRACEREBRAL TRANSPORT



Neurohormonal releasing factor formed in hypothalamus

METHODS OF DETERMINING CSF FORMATION RATE & RESISTANCE TO CSF ABSORPTION

- Ventriculocisternal perfusion
- Manometric infusion
- Volume injection or withdrawal

VENTRICULOCISTERNAL PERFUSION

- EXPERIMENTAL ANIMALS:
- 1st described in 1960 by Heisey and Pappenheimer.
- Cannula is placed in one/ both lateral ventricles & in cisterna magna.
- Labelled mock CSF infused into the ventricle & mixed sample of labelled and native CSF collected from cisterna magna.
- Conc. Of labelled CSF in outflow sample is measured & time of sample collection noted.
- Vf, Va, Ra is measured using formulas.

IN HUMANS:

- Outflow catheter is placed in lumbar subarachnoid(SA) space and ventricular & spinal CSF pressure closely monitored.

MANOMETRIC INFUSION

- **IN EXPERIMENTAL ANIMAL :**
- Described by Maffeo and Mann in 1970.
- A manometric infusion device inserted into spinal or supracortical SA space.
- Mock CSF infused into SA space, CSF pressure is measured at same site of infusion.

- IN HUMANS:
- No. of infusion is reduced & infusion rate are limited to 0.01 - 0.1ml/sec.
- Infusion is restricted to 20-60 secs.
- Infusion discontinued at CSF pressure of 60-70 cm H2O or rapid rise of CSF pressure.

VOLUME INFUSION OR WITHDRAWAL

- IN EXPERIMENTAL ANIMALS
- Described by Marmarou and Miller in mid 1970.
- Ventricular/spinal SA catheter inserted to permit injection or withdrawal of CSF & measurement of CSF pressure change that accompanies injection or withdrawal.

IN HUMANS:

- Previous two methods are less commonly used due to hazards associated with prolonged infusion of mock CSF.
- Advantages:
- In case of raised ICP- withdrawal of CSF is therapeutic
- Calculate Vf, Ra, compliance (C)
- Risk of infection is minimum(closed system)
- Test can be use for repeated testing.

- **ANAESTHETIC AND DRUG INDUCED CHANGES IN CSF FORMATION RATE (VF) AND RESISTANCE TO CSF ABSORPTION (RA)**

INHALED ANESTHETICS

ENFLURANE	Vf	Ra	ICP
LOW[0.9%-1.8%]	0	+	+
HIGH[2.65& 3.5 end expired]	+ (40%)	0	+

ENFLURANE INCREASES METABOLISM

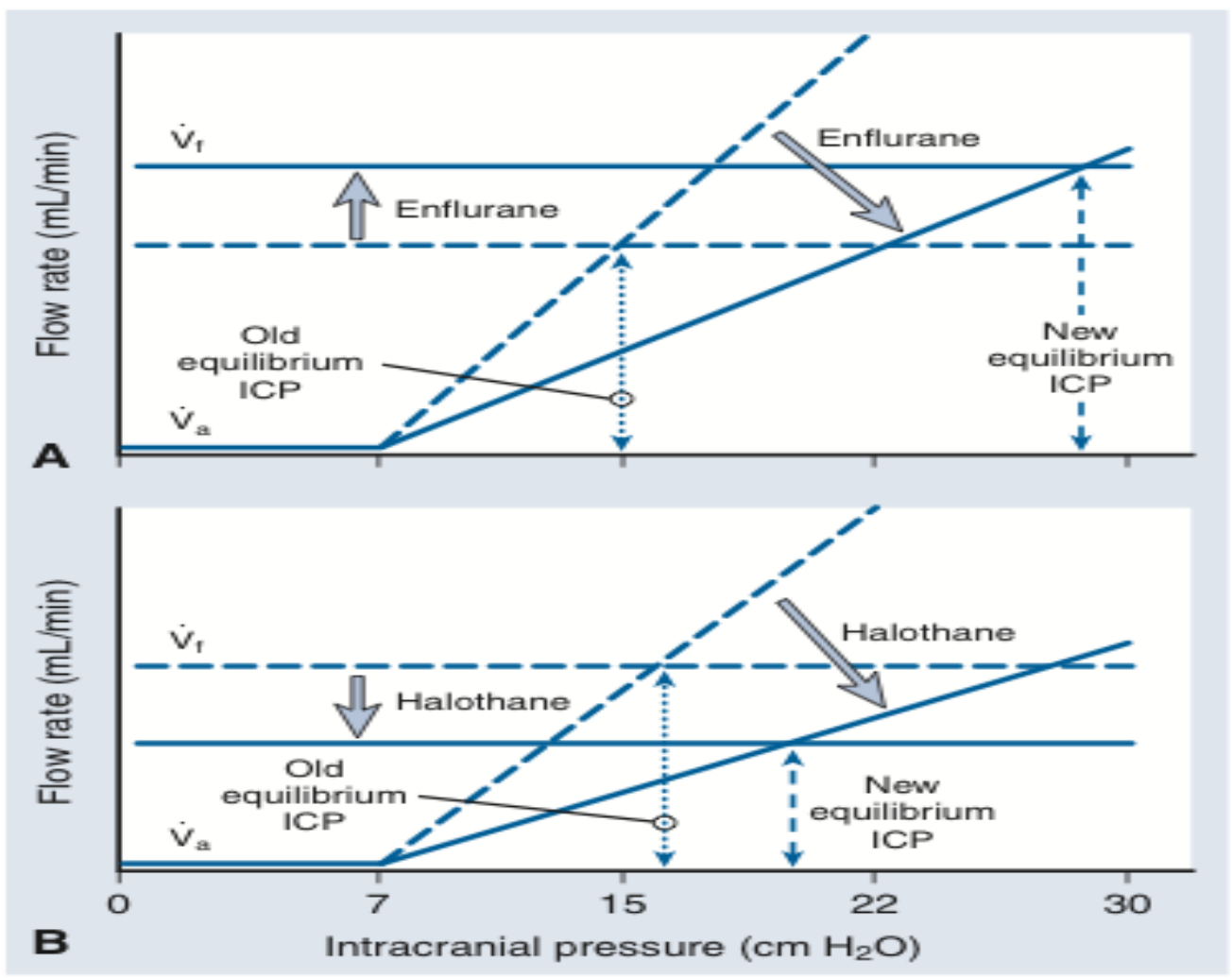


Fig. 3.7 **A,** Enflurane at intermediate concentrations increases both the rate of cerebrospinal fluid (CSF) formation ($\dot{V}_f$) ("elevating" the slope of $\dot{V}_f$ plotted against intracranial pressure [ICP]) and resistance to CSF reabsorption (R_a) ("flattening" the $\dot{V}_a$ /ICP slope). **B,** Halothane decreases $\dot{V}_f$ ("lowering" the $\dot{V}_f$ /ICP slope) and increases R_a. With both anesthetics, $\dot{V}_f$ equals $\dot{V}_a$ at increased ICP. *(From Cucchiara RF, Michenfelder JD [eds]: Clinical Neuroanesthesia. New York, Churchill Livingstone, 1990.)*

INHALED ANESTHETICS

HALOTHANE	Vf	Ra	ICP
1 MAC	--	+	+

INCREASES GLUCOSE TRANSPORT INTO BRAIN
INCREASES Na/Cl/H2O/ALBUMIN TRANSPORT INTO CSF
HALOTHANE INDUCED STIMULATION OF VASOPRESSIN RECEPTORS→DECREASE Vf

INHALED ANESTHETICS

ISOFLURANE	Vf	Ra	ICP
LOW[0.6]	0	0	0
[1.1%]	0	+	+
HIGH[1.7-2.2]	0	--	--

INHALED ANESTHETICS

SEVOFLURANE	Vf	Ra	ICP
1 MAC	--	+	?

INHALED ANESTHETICS

DESFLURANE	Vf	Ra	ICP
HYPOCAPNIA & ↑ CSF PRESSURE (0.5 & 1 MAC)	0	+	+
OTHER SITUATI0NS	0	0	0

INHALED ANESTHETICS

NITROUS OXIDE	Vf	Ra	ICP
66%	0	0	0

DECREASES BRAIN GLUCOSE INFLUX AND EFFLUX

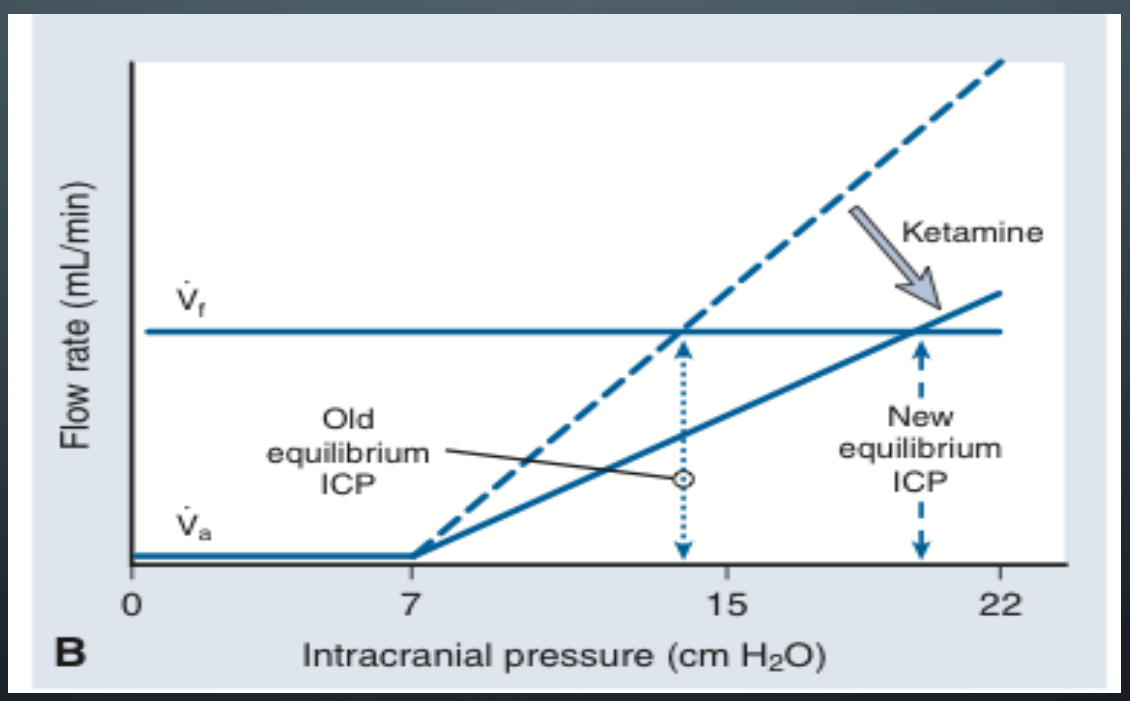
Table 3–3 Effects of Inhaled Anesthetics on Cerebrospinal Fluid (CSF) Dynamics

Inhaled Anesthetic	$\dot{V}_f$	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; $\dot{V}_f$, 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 $\dot{V}_f$; b, effect depends on dose; ?, uncertain.

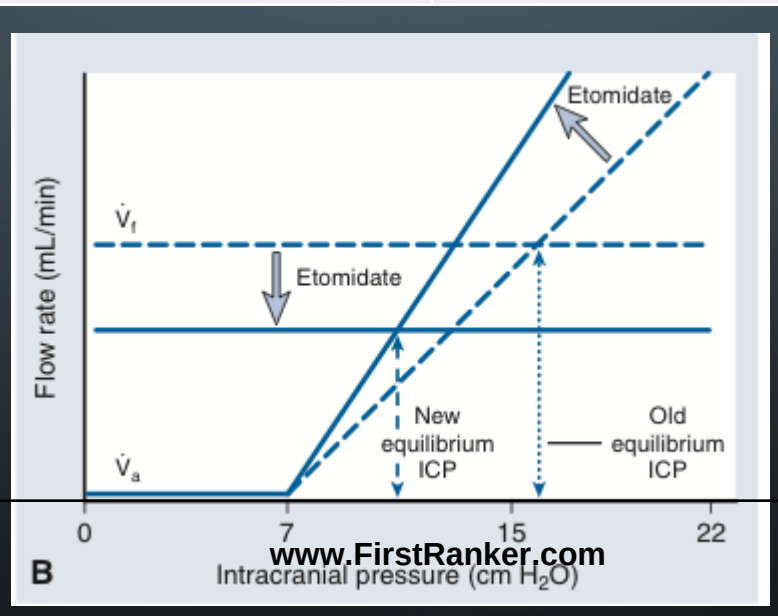
I.V. ANESTHETICS

KETAMINE	Vf	Ra	ICP
40mg/kg/hr	0	+	+



I.V. ANESTHETICS

ETOMIDATE	Vf	Ra	ICP
Low dose .86mg/kg	0	0	0
High dose	--	--	--



I.V. ANESTHETICS

PROPOFOL	Vf	Ra	ICP
6mg/kg →12,24, & 48 mg/kg/hr	0	0	0

PENTOBARBITAL	Vf	Ra	ICP
40mg/kg	0	0	0

I.V. ANESTHETICS

THIOPENTAL	Vf	Ra	ICP
LOW (6mg/kg F/B 6-12mg/kg/hr)	0	+/0	+/0
HIGH (18-24mg/kg/hr)	--	--	--

I.V. ANESTHETICS (SEDATIVES & HYPNOTICS)

MIDAZOLAM	Vf	Ra	ICP
LOW (1.6mg/kg fb 0.5mg/kg/hr)	0	+	+
INTERMEDIATE (1-1.5 mg/kg/hr)	0	0	0
HIGH (2mg/kg/hr)	--	+	--/?

FLUMAZENIL	Vf	Ra	ICP
LOW (0.0025 mg/kg)	0	0	0
HIGH (0.16 mg/kg)	0	--	

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

Sedative-Hypnotic	$\dot{V}_f$	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; $\dot{V}_f$, rate of CSF formation; +, increase; 0, no change; –, decrease; a, effect depends on dose; ?, uncertain.

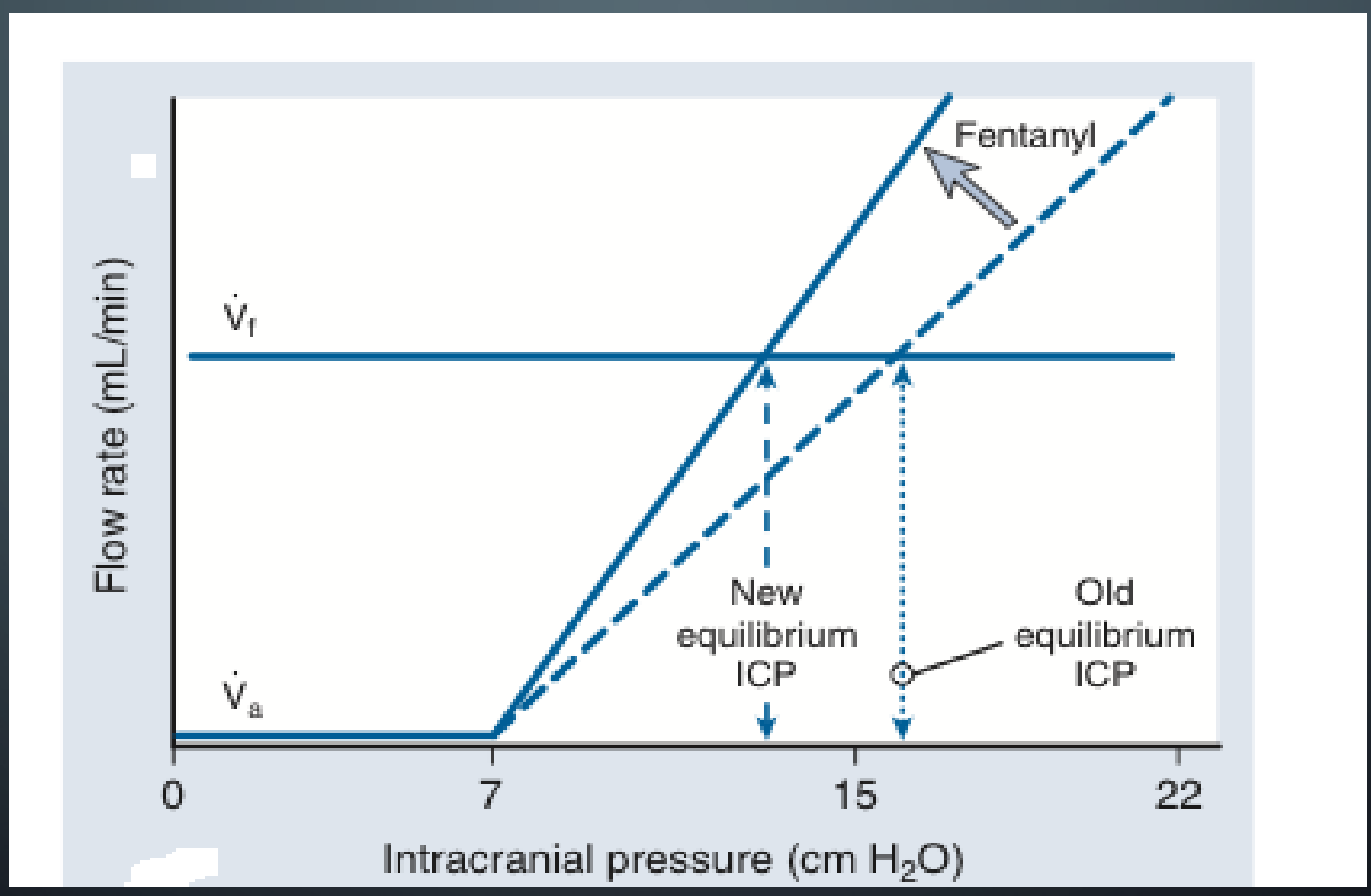
*Partial reversal with flumazenil causes CSF dynamics similar to that with lowest dose of midazolam, and complete reversal with flumazenil causes CSF dynamics similar to that with pre-midazolam (control) values.

I.V. ANESTHETICS (OPIOIDS)

FENTANYL	Vf	Ra	ICP
LOW DOSE	0	--	--
HIGH DOSE	--	0/+	--/?

SUFENTANYL	Vf	Ra	ICP
LOW DOSE	0	--	--
HIGH DOSE	0	+/0	+/0

AIFENTANYL	Vf	Ra	ICP
LOW DOSE	0	--	--
HIGH DOSE	0	0	0



I.V. ANESTHETICS

LIDOCAINE	Vf	Ra	ICP
0.5mg/kg 1µg/kg/min	--	0	0/+

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

	$\dot{V}_f$	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; $\dot{V}_f$, rate of CSF formation; +, increase; 0, no change; –, decrease; a, effect depends on dose; ?, uncertain.

CRUX OF VF AND RA

- Vf increases →
- High dose Enflurane

- Ra increases →
- Halothane (1MAC)
- DES(hypocapnia + increase csf pressure)
- Low dose enflurane
- Sevo (1 MAC)
- Midazolam(low dose)
- Ketamine

Both Vf & Ra ↓ Fentanyl , Etomidate

I.V DRUGS

- IV acetaminophen moves readily and attains peak conc. in an hour in CSF→ rapid central analgesia and antipyretic effect
- Ibuprofen : peak at 30-40 min

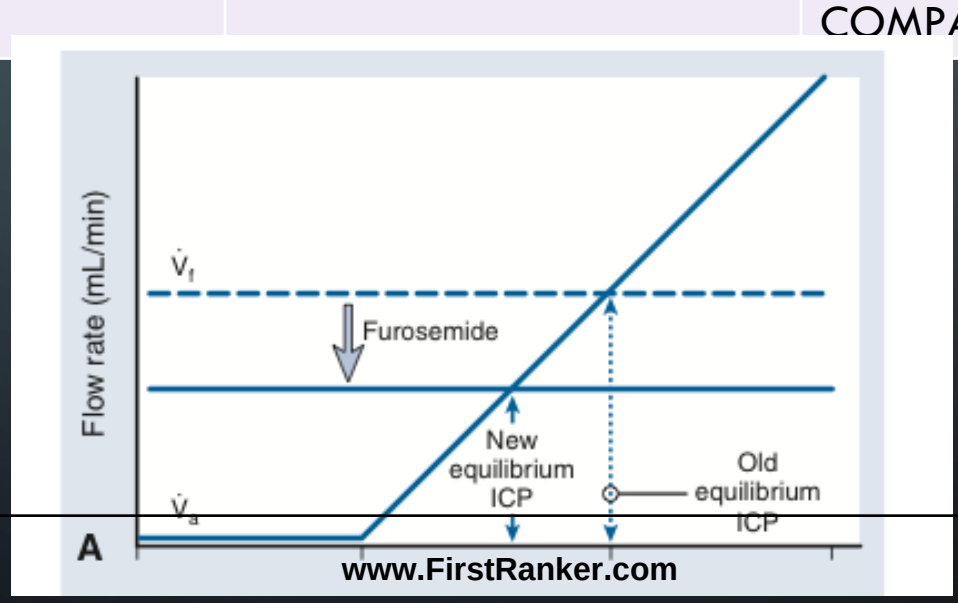
DIURETICS

	Vf	MECHANISM
ACETAZOLAMIDE	-- BY 50%	INHIBITION OF CA INDIRECT ACTION ON ION TRANSPORT(VIA HCO3) CONSTRICTS CP ARTERIOLES & DECREASE CPBF
METHAZOLAMIDE		

ACETAZOLAMIDE +OUABAIN →↓ Vf BY 95%= ADDITIVE

DIURETICS

	Vf	MECHANISM
FUROSEMIDE	--	DECREASE Na+ OR Cl- TRANSPORT
MANNITOL	--	DECREASE CP OUTPUT AND ECF FLOW FROM BRAIN TO CSF COMPARTMENT



OTHERS

DRUG	Vf	MECHANISM
DIGOXIN,OUABAIN	--	INHIBIT NA-K PUMP OF CP
THEOPHYLLIN	+	PHOSPHODIESTERASE INHIBITOR →↑CAMP→STIMULATE CP NA-K PUMP
VASSOPRESSIN	--	CONSTRICTS CP BLOOD VESSELS
3% HYPER TONIC SALINE	--	↓OSMOLALITY GRADIENT FOR MOVEMENT OF FLUID PLASMA→CP OR BRAIN TISSUE OR CSF
DINITROPHENOL	--	UNCOUPLE OXIDATIVE PHOSPHORYLATION
ANP	--	CGMP

MUSCLE RELAXANT

RELAXANTV	Vf	Ra
SCOLINE, VECURONIUM INFUSION	0	0

STEROIDS

- Decrese Ra
- MethylPrednisolone/prednisolone/cortisone/dexamethasone
- **Probable mechanism** :
  - Improved CSF flow in SA spaces/ A.villi
  - Reversal of metabolically induced changes in structure of villi, action at CP
- Dexamethasone→↓ Vf by 50%(inhibition of Na-K ATPase)

ALTERATION IN VARIOUS PATHOLOGY

- Intracranial volume changes
- Volume of intracranial blood/gas/tissue ↑→CSF volume↓

•Mechanism: Translocation into spinal spaces
- increased reabsorption

- Volume of intracranial blood/gas/tissue ↓ →CSF volume ↑

•Mechanism: Cephalad translocation
- Decreased reabsorption

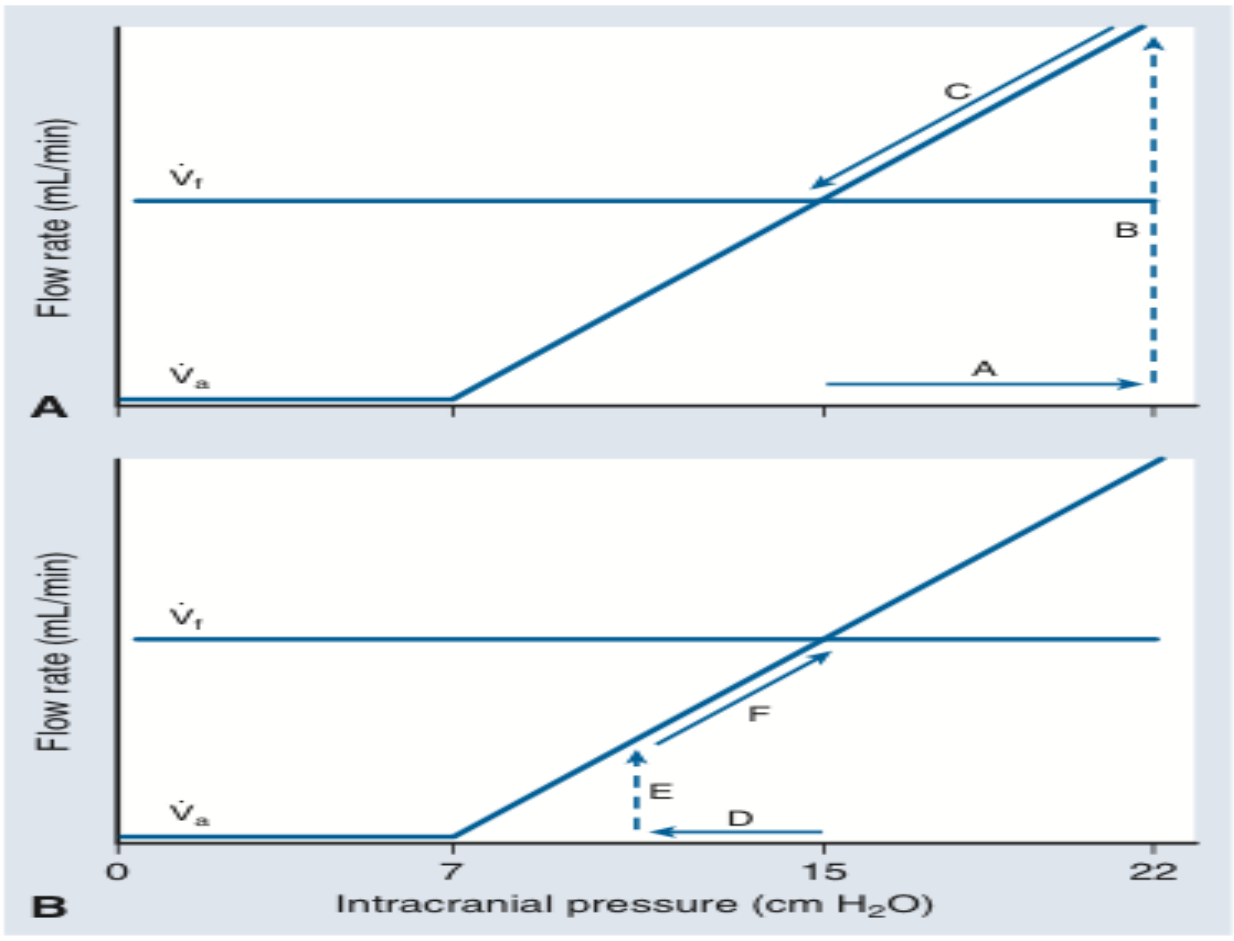


Fig. 3.10 Plots of cerebrospinal fluid (CSF) formation ($\dot{V}_f$) versus intracranial pressure (ICP) and rate of CSF reabsorption ($\dot{V}_a$) versus ICP show how CSF volume alters to offset alterations in intracranial volume, thereby minimizing ICP changes. **A,** Increase in intracranial volume raises ICP. **(A)** At higher ICP, $\dot{V}_a$ exceeds $\dot{V}_f$, **(B)** so CSF volume decreases. As CSF volume decreases, ICP decreases **(C)** until $\dot{V}_f$ equals $\dot{V}_a$. If $\dot{V}_f$ and the resistance to CSF reabsorption (Ra) are not altered, ICP returns to "normal." **B**, Decrease in intracranial volume decreases ICP **(D)**. At decreased ICP, $\dot{V}_a$ **(E)** is less than $\dot{V}_f$, so CSF volume increases. As CSF volume increases, ICP increases **(F)** until $\dot{V}_f$ equals $\dot{V}_a$. If $\dot{V}_f$ and R_a are not altered, ICP returns to "normal." *(From Cucchiara RF, Michenfelder JD [eds]: Clinical Neuroanesthesia. New York, Churchill Livingstone, 1990.)*

ACUTE SAH

- Increases ICP
- Intrathecal injection: Whole blood, plasma, diasylate of plasma, serum & saline--- Va & Ra values measured by Manometric method
- Whole blood and plasma raised ICP and caused a 3 to 10 fold rise in Ra respectively
- Fibrin deposits within villi

CHRONIC CHANGES AFTER SAH

- Extensive fibrosis of villi → leptomeningeal scarring → functional narrowing or blockage of CSF outflow tracts →[Ra is increased]→hydrocephalus

BACTERIAL MENINGITIS

- Animal study with → S.pnemoniae, E coli
- ICP & Ra increased in both
- Even with antibiotic Ra remained high for 2 weeks post Rx
- Methyl prednisolone ↓ed Ra to a value that was intermediate between control and infected.

PSEUDOTUMOR CEREBRI

- Increased ICP → Increased 1.Ra, 2.Vf, 3. greater water movement into brain 4 . CBF & CBV, 5 glial or cellular edema .
- Impaired reabsorption is the principal cause
- Prednisone decreases Ra

HEAD INJURY

Ra increased and Vf within normal limits in 75% patients.

20% of the raised ICP derived from changes in Ra /Vf.

IN SUMMARY

- CSF plays a key role in brain well being
- Vf changes : changes ICP
- Ra changes: Changes ICP, alters pressure buffering capacity of brain
- In raised ICP, Anesthetics induced changes in Vf & Ra significantly alter the effectiveness of treatments employed to reduce ICP.