Blood-Brain Barrier

Keiv Holding

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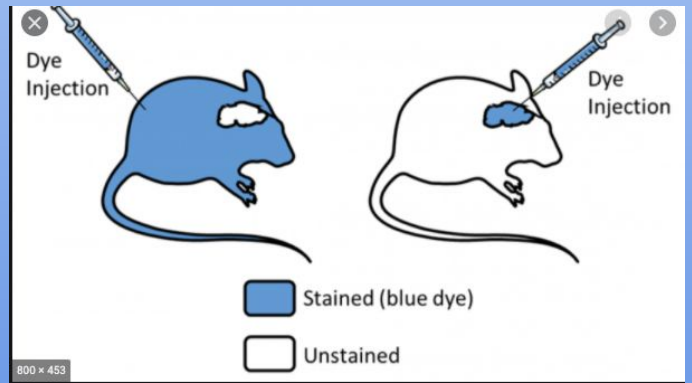
  - What is it?
  - Function?
  - Structure / Layers?
  - What can(‘t) pass through it?
- Circumventricular Organs (CVOs)
  - What is it?
  - Parts?
  - Purpose?
- Cerebrospinal fluid
  - What is it?
  - Synthesis / Reabsorption
  - Structure / Layers?
  - Function?

BBB

How was the BBB discovered?

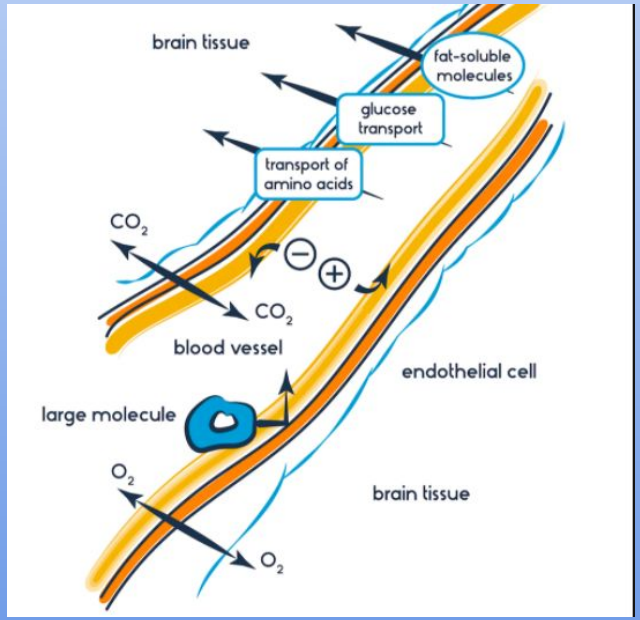
- Interesting!

- In the 1880s, Paul Ehrlich discovered that there was some sort of barrier when he injected a blue dye into the circulatory system of animals and noticed that every tissue besides the nervous system was stained blue.

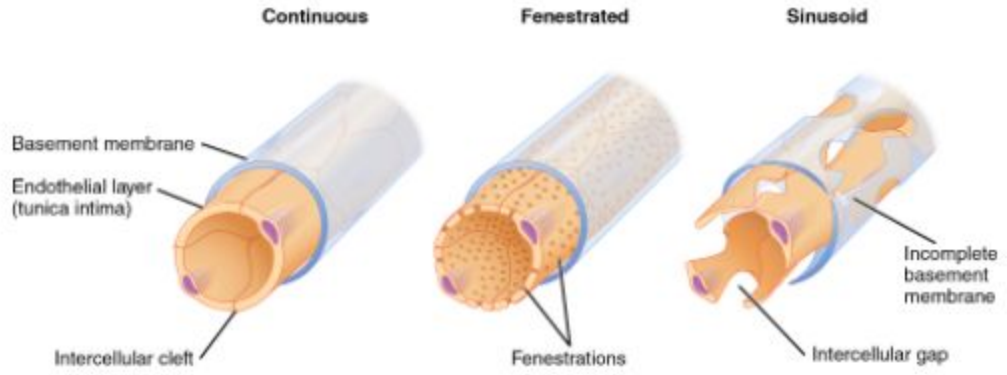


What is the BBB?

- It is a barrier that prevents free movement of certain substances between the circulating blood and the nervous system through various mechanisms

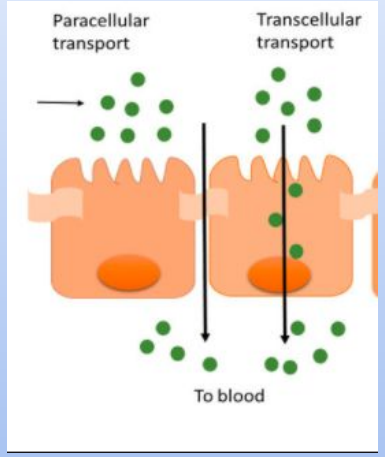


What are the types of capillaries?



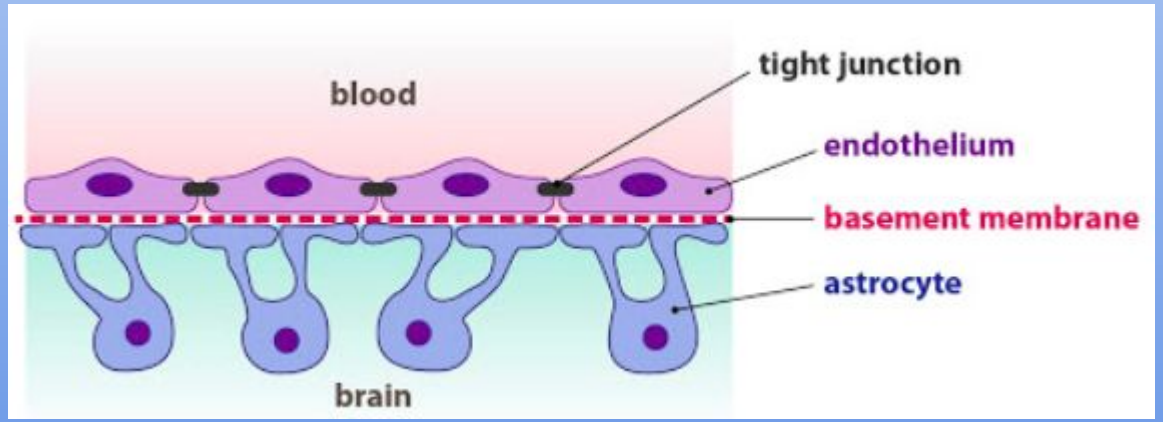
The three major types of capillaries: continuous, fenestrated, and sinusoid.

Layers of the BBB?



Starting intravascularly and moving outwards

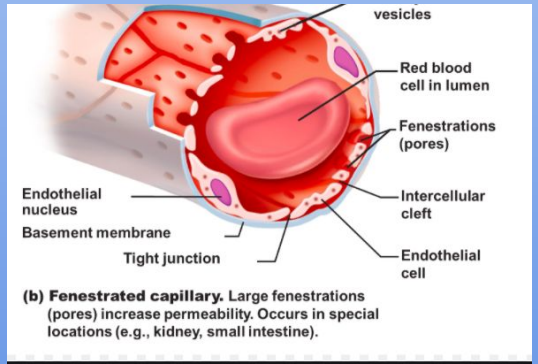
- Continuous capillaries
  - They have lots of tight junctions!!!!!
- Basement membrane
- Projections from astrocytes that surround 80%-90% of the basement membrane



Function of astrocytes in the BBB

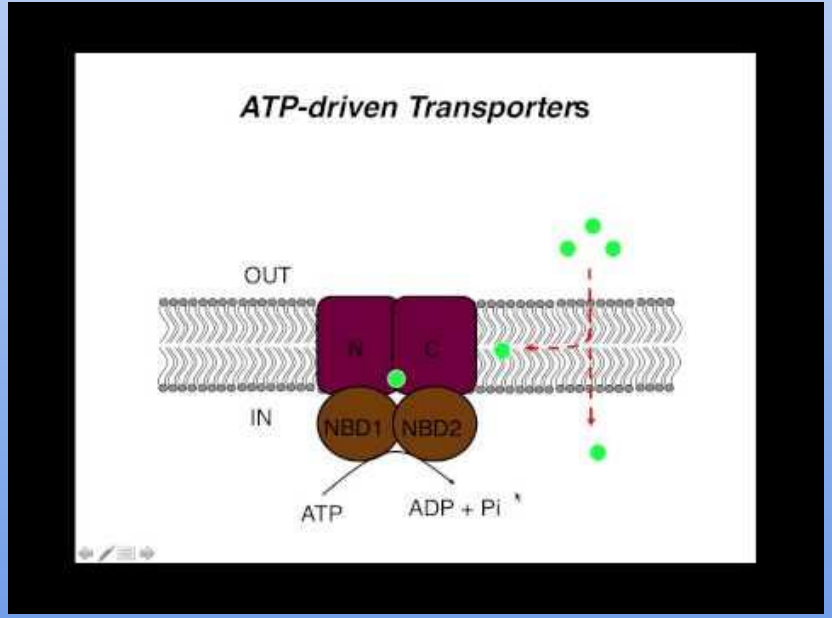
- Their projections cover 80%-90% of the endothelial basement membrane
  - “Covering” isn’t primary function

- Their main purpose is to produce certain substances that induce the formation of the occludin claudin protein that help make the endothelial lining even tighter!
  - Proof… In brain tumours, the vessels that reside within the tumour oftentimes have no tight junctions



Special feature of the endothelial cells

- They contain P-glycoproteins (multidrug resistance protein 1)
  - ATP dependent!



Function of the BBB

- Blood can contain waste products, pathogens, antibodies, hormones, macrophages, neurotransmitters, etc etc etc. which all can be harmful to neurons

- **Stabilizer**
- **Protector**
- **Holder**
  - **S**ana **P**asses **H**appily

Circumventricular Organs

What are CVOs?

- They are essentially “windows” around the ventricles that allow for easier transfer of substances.
    - Highly permeable capillaries --- Fenestrated / no tight junctions
    - Higher rate of paracellular and transcellular transport

Function of CVOs?

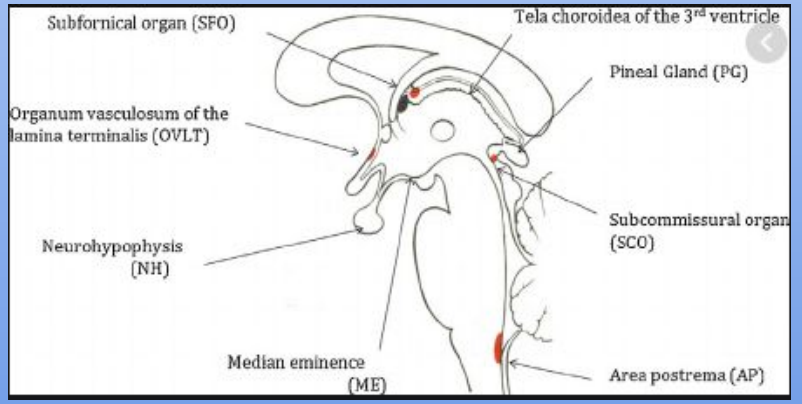
- Sensory

- Secretory

Types of CVOs

- Sensory purpose: Vascular organ of lamina terminalis, Area postrema, Subfornical organ

- Secretory purpose: Pineal gland, Neurohypophysis, Median eminence



More understanding

- Secretory
  - The capillaries in the neurohypophysis (posterior pituitary) don't have the BBB. Why is this important?
  - ADH and Oxytocin is stored in the neurohypophysis and upon stimulation, they are released and need to enter the bloodstream.

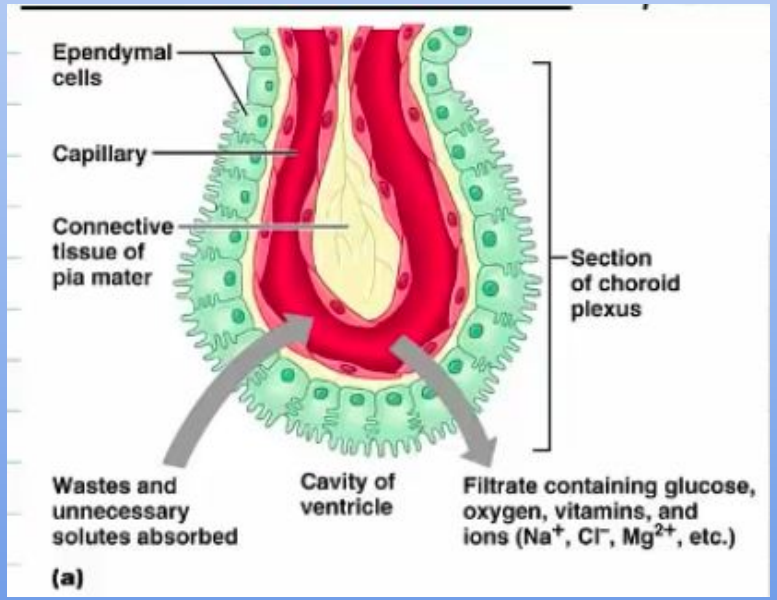
- Sensory
  - The area postrema is a chemoreceptor that is sensitive to certain substances contained in blood and to changes in pH. Can trigger vomiting. Why is it important not to have the BBB present here?

Cerebrospinal Fluid

What is CSF / Composition?

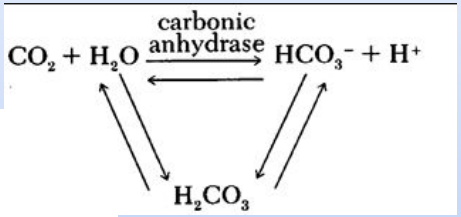
- Produced by the choroid plexus which is present in each ventricle
  - A plexus of capillaries that is surrounded by specialised ependymal cells

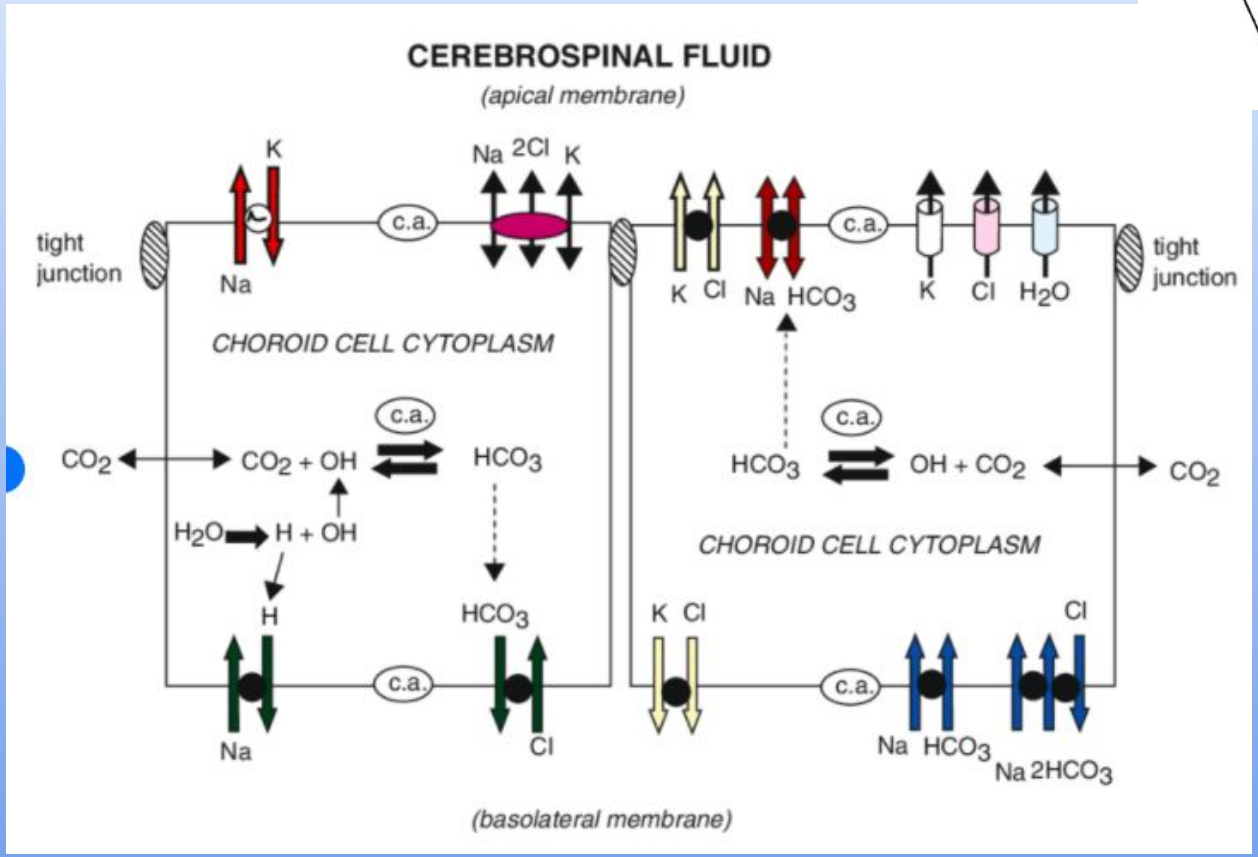
- ~99% water (99.13%)
- ~1% solids (0.87%)
  - Ions (Na+, K+, HCO3-, Cl-, etc..)
  - Glucose
  - Cells (very few lymphocytes)
  - Proteins



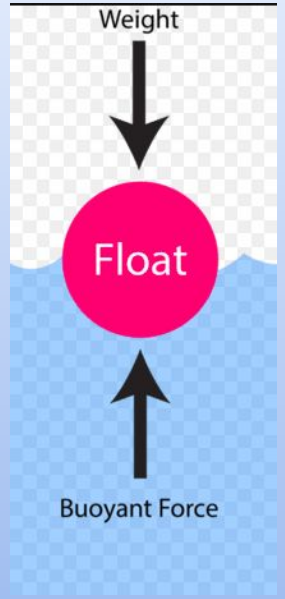
How is CSF synthesized?

- Firstly, since the capillaries are fenestrated, blood plasma is able to move into the interstitial space.
- There is a Na+/K+ ATPase on the apical part of the ependymal cell. 3 Na+ pumped out into ventricle and 2 K+ pumped into the cell ---> K+ can flow down electrochemical gradient
    - Electric gradient
    - This sets up the mechanism for secondary active transport
- Cl- will follow Na+ passively into the ventricles and also through the Na-K-2CL (NKCC) cotransporter
    - Increases osmotic pressure -----> Water will follow
- There are also glucose transporters (not efficient)


carbonic
anhydrase
$CO_2 + H_2O$
$HCO_3^- + H^+$
H_2CO_3


CEREBROSPINAL FLUID
(apical membrane)
tight junction
K
Na
c.a.
Na 2Cl K
CHOROID CELL CYTOPLASM
K Cl
Na HCO3
K Cl H2O
tight junction
CO2
CO2 + OH
HCO3
H2O
H + OH
H
HCO3
Na
Cl
HCO3
OH + CO2
CO2
CHOROID CELL CYTOPLASM
K Cl
Cl
Na HCO3
Na 2HCO3
(basolateral membrane)

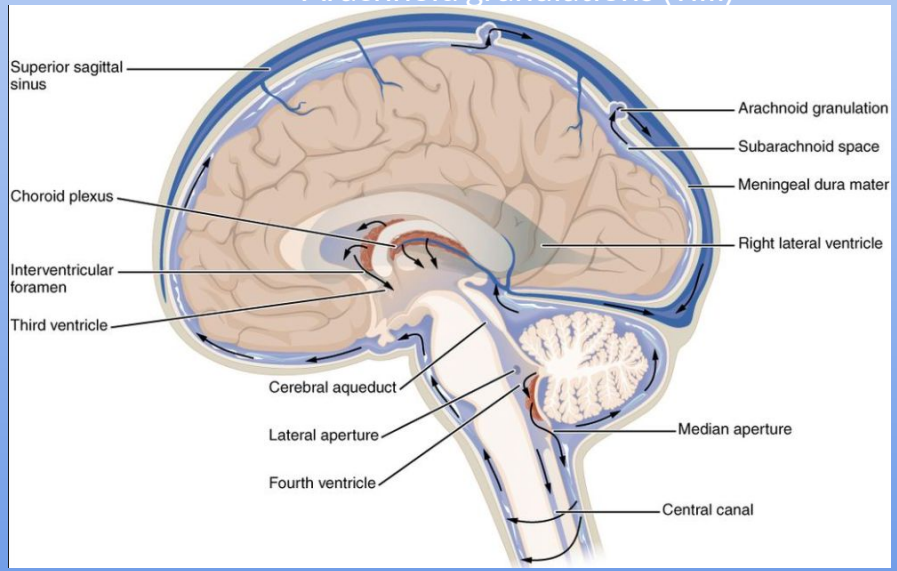
Function of CSF

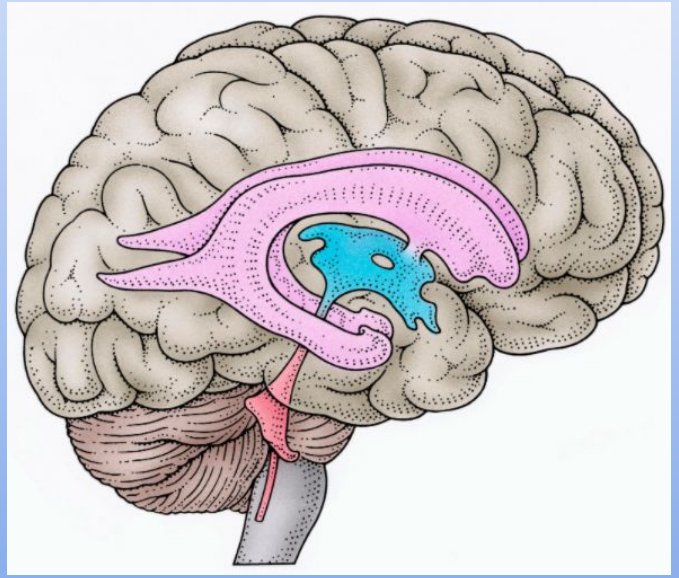


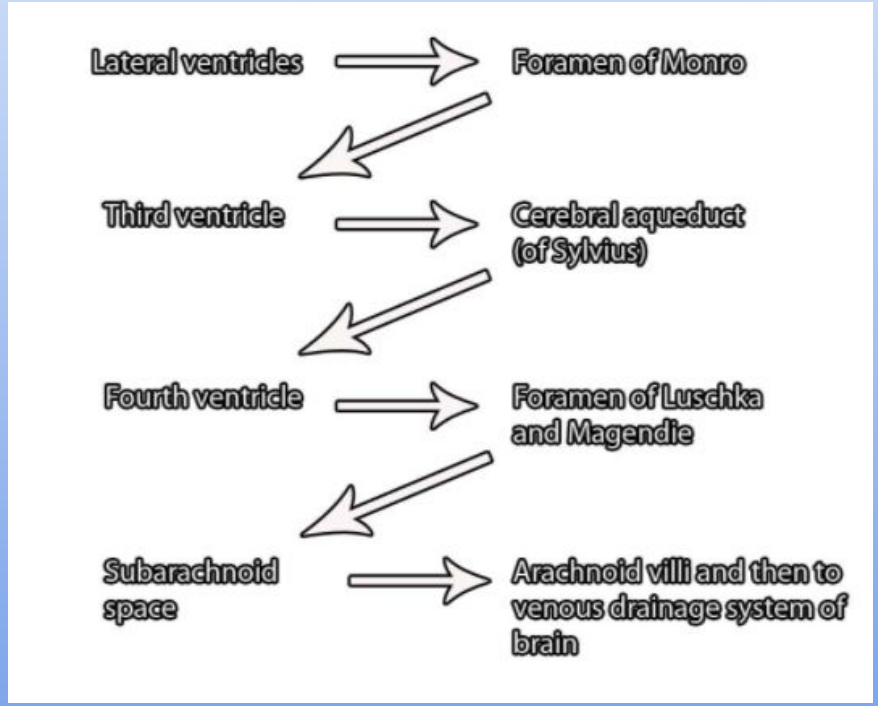
- Buoyancy for the brain (reduces net weight) (1400g → 50g)
- Protection of the brain
- Homeostasis for the brain / Nutrition for the brain / Waste clearance for the brain

Reabsorption of CSF

- Median aperture (foramen of Magendie
- Lateral aperture (foramen of Luschka)
- Arachnoid granulations (villi)



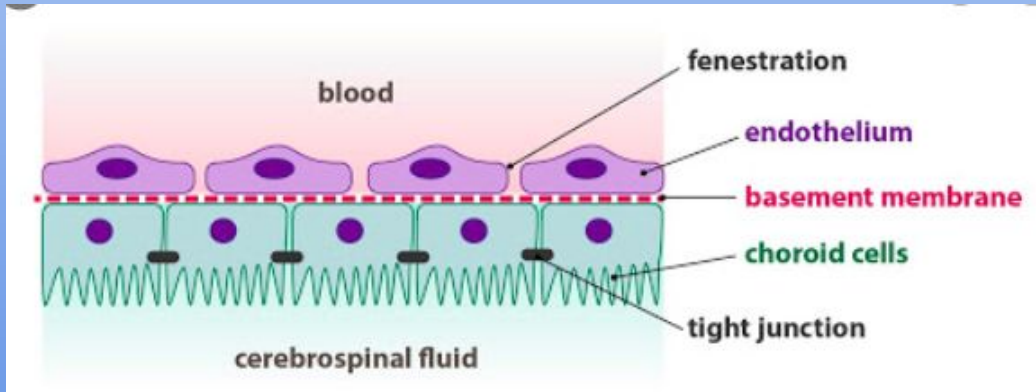



Lateral ventricles
Foramen of Monro
Third ventricle
Cerebral aqueduct (of Sylvius)
Fourth ventricle
Foramen of Luschka and Magendie
Subarachnoid space
Arachnoid villi and then to venous drainage system of brain

Layers of the Blood-CSF Barrier (BCSFB)

Starting intravascularly and moving outwards

- Fenestrated capillaries
  - No tight junctions!!!!!
- Basement membrane
- Ependymal cells
  - They have lots of tight junctions!!!!!
    - Importance? (next slide)

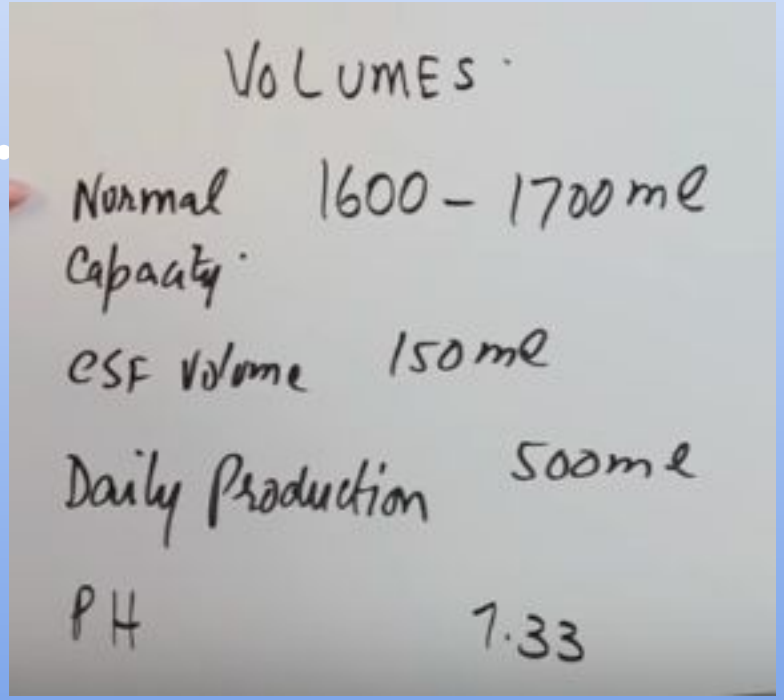


Importance?

- If the endothelial cells had tight junctions and were tightly connected…. It would be difficult for components of blood plasma to move into the interstitial space and eventually into the ventricles and form CSF

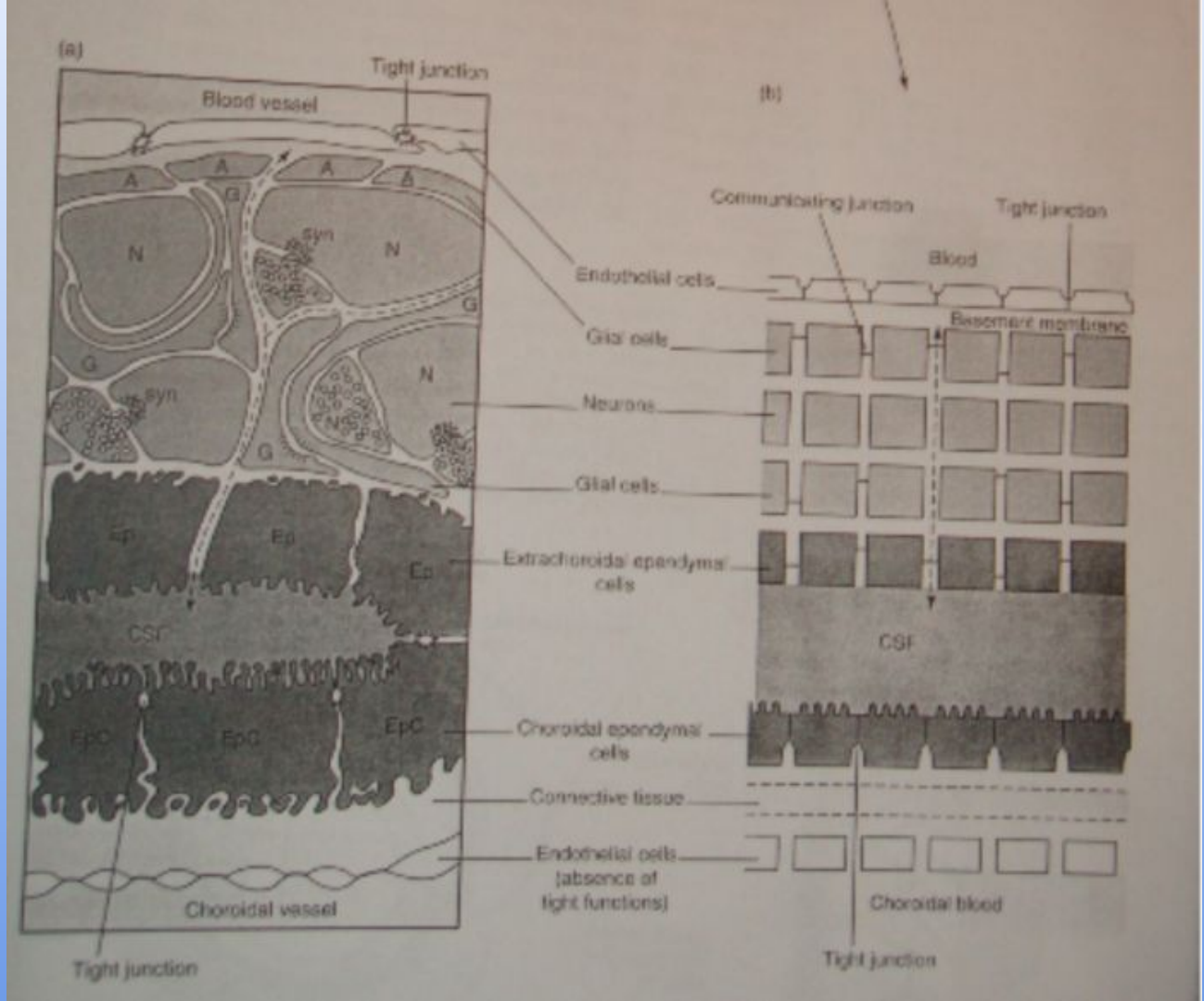
- It’s important for ependymal cells to have tight junctions so that they have some regulation of the composition of CSF

Volumes


VOLUMES
Normal Capacity 1600 – 1700 ml
CSF Volume 150 ml
Daily Production 500 ml
PH 7.33

Difference between BBB and BCSFB

--	BBB	BCSF
Types of capillary	Continuous	Fenestrated
Tight junctions	Yes on the endothelial cells lining the capillaries	Yes on the ependymal cells lining the ventricles
Location of the “barrier”	Endothelial lining	Ependymal lining


(a)
Tight junction
Blood vessel
A
A
A
A
G
N
Syn
N
G
G
Syn
N
G
Ep
Ep
Ep
CSF
EpC
EpC
EpC
Choroidal vessel
Tight junction
(b)
Communicating junction
Tight junction
Blood
Basement membrane
Endothelial cells
Glial cells
Neurons
Glial cells
Extrachoroidal ependymal cells
CSF
Choroidal ependymal cells
Connective tissue
Endothelial cells (absence of tight functions)
Choroidal blood
Tight junction

Thank you!