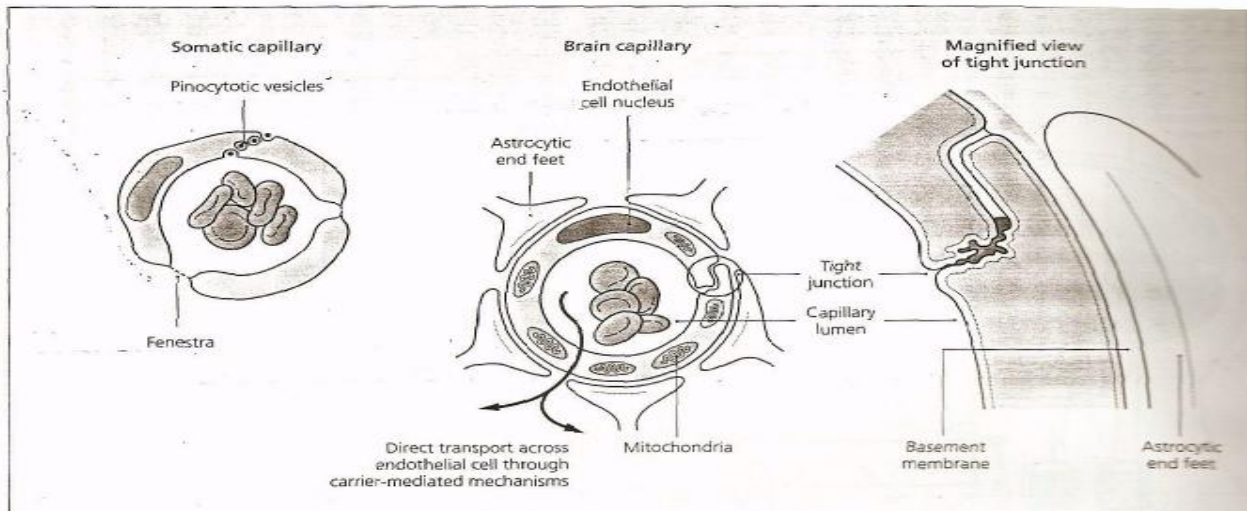
Blood Brain Barrier (BBB)

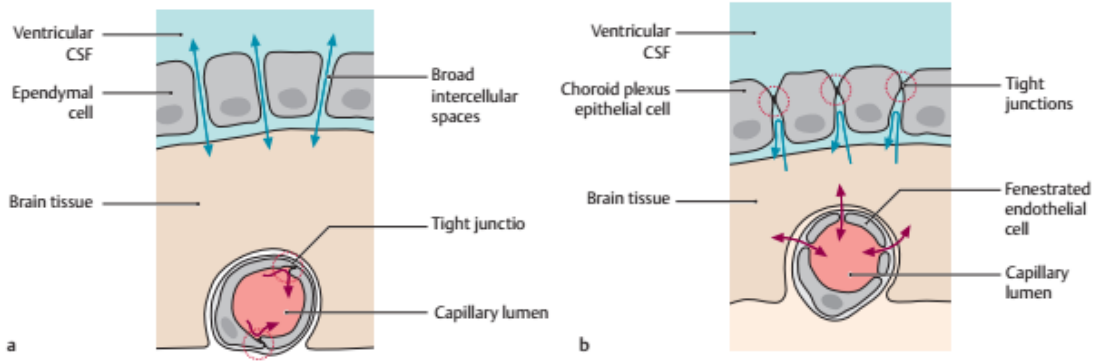
Not all substances that are carried in the blood reach neural tissue-a barrier blocks the entry of many substances in to the brain. This barrier resides in the cerebral capillaries. its function is to regulate the flow of biologically active substances in to the brain and to protect the sensitive neural tissue from toxic materials.



Differences between somatic and brain capillaries

In somatic capillary, fenestration between endothelial cell allow free flow of plasma Component in to the tissue. In addition, there is bulky flow of plasma component across endothelial cell via pinocytotic vesicles. In brain capillary the endothelial cell is attached to each other by tight junctions and there are no intervening fenestrae. these tight junctions act as a barrier to the passive movement of many substances across the endothelium.

So, the BBB consists from capillary endothelial tight junctions, endothelial pinocytic activity and astrocytic foot processes.



There are two mechanisms by which materials may be transported across endothelial cells:

(1) Lipid soluble substances can usually penetrate all capillary endothelial cell membrane in passive manner.

(2) Amino acid and sugar are transported across the capillary endothelium by specific carrier-mediated mechanisms.
There are large number of mitochondria in the brain endothelial cells generate energy for active transport.
When there is disruption of BBB by any cause, plasma components easily cross the barrier in to the neural tissue, causing vasogenic edema.

Causes of BBB breakdown

(1) Anesthesia
(2) Sepsis and CNS infection: When infection involves the CNS and its covering, there seem to be a breakdown in the physical integrity of the BBB. Patients with sepsis often demonstrate an alter state of consciousness because the neural amino acid-carrier protein seems to be modified which lead to an abnormal accumulation of certain amino acids (e.g., phenylalanine, tryptophan) in the brain with subsequent derangement of general and neurotransmitter metabolism.
(3) X-radiation: the damage to the cerebral endothelial cell is dose-related and is greatest in the adventitia
(4) Brain tumors: the growth of both primary and secondary brain tumor requires new capillaries developments. The capillaries may demonstrate cellular fenestrations. wide intercellular junction and pinocytotic vesicles, so the normally excluded large molecules penetrate the BBB. This is the basis of contrast enhancement of lesion in CT and MRI brain scan.
(5) Loss of cerebral auto regulation: Cerebral auto regulation is the compensatory
Change in response to variations in vascular pressure. Usually, regulation of resistance to flow occurs between 60-160 mmhg of systemic arterial blood pressure.
The conditions that produce loss of auto regulation and subsequent vasodilatation often lead to stretching of the capillary endothelium (opening of the tight junction) and pinocytosis (e.g., in hypertension)
(6) Drug: Tight junctions can be transiently opened by mannitol which dehydrate the endothelial cells. During this brief interval, which least for few hours, certain chemotherapeutics or other agents can be administered that would not otherwise cross the barrier.
(7) Cerebral ischemia: The cerebrovascular endothelium is more resistant than other cellular elements of the brain to ischemia and hypoxia. Therefore, damage to BBB occurs in late stages of cerebral ischemia.
(8) Traumatic brain injury: The early opening of BBB is thought to contribute to the development of cerebral edema, although the pathogenesis of the disruption is not clear. In late stage, cell membrane damage occurs which result in breakdown of BBB.
(9) Epilepsy: The change in BBB permeability during epilepsy is blood pressure related, as changes could be ameliorated by preventing an increase in blood pressure.
(10) Aging: Aging of cerebral microcirculation results in a significant alteration of the BBB.