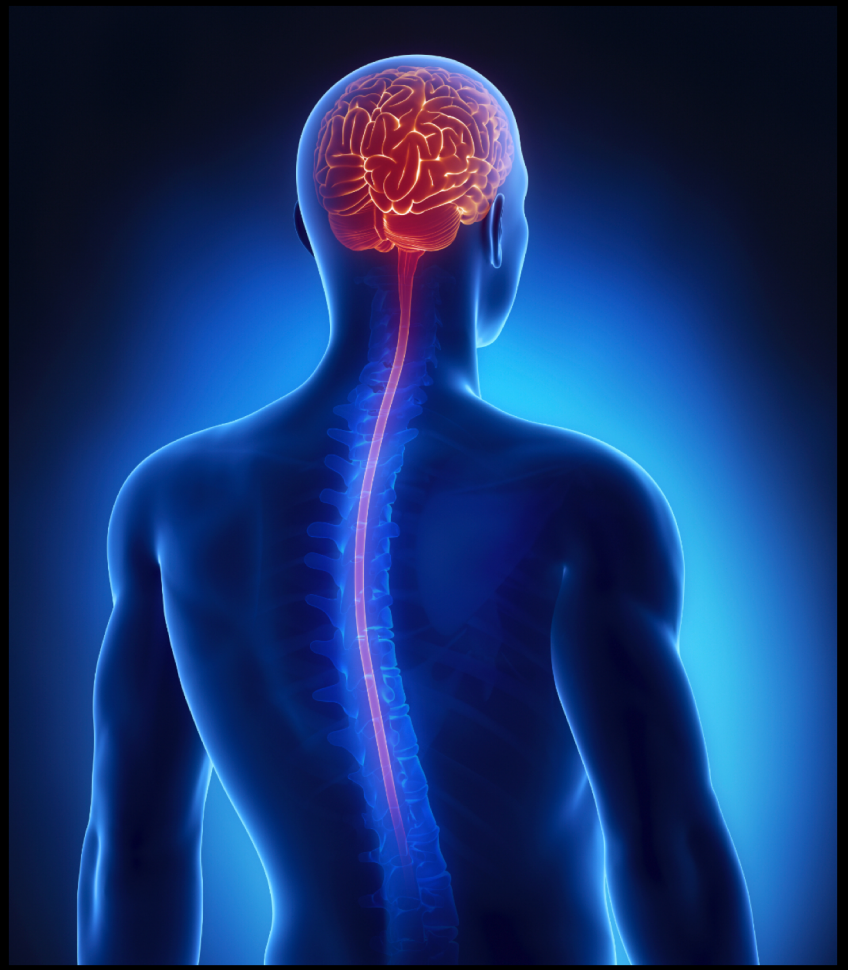
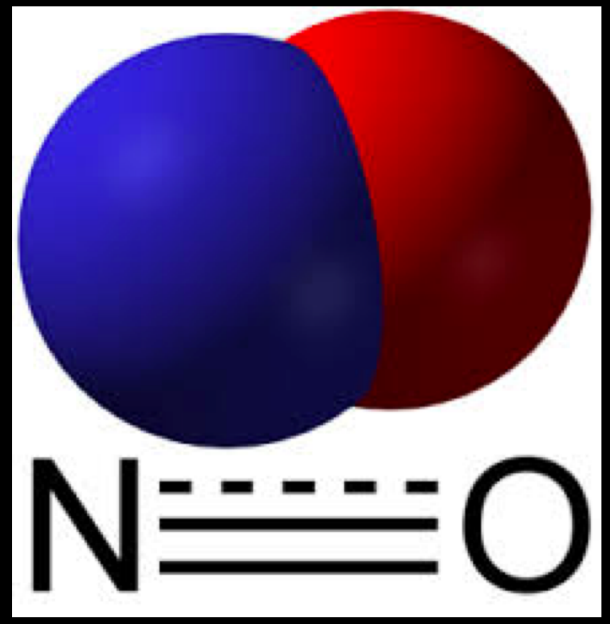
Chapter 2: Cerebral & Spinal Cord Blood Flow



Cellular Mechanisms of Cerebral Vascular Tone

- Nitric oxide
- Vasoactive Peptides
- Potassium Channels
- Prostaglandins
- Endothelin

Nitric Oxide



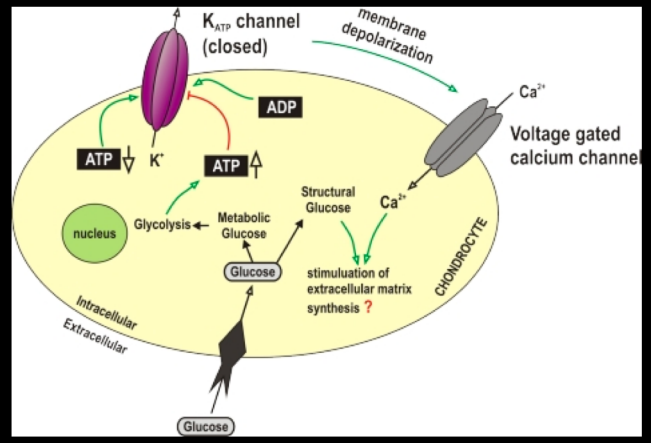
- Signaling molecule, potent vasodilator
- Cerebral blood flow and vascular smooth muscle are regulated by NO, derived from endothelial cells and neurons
- NO regulates cerebrovascular effects of oxygen, carbon dioxide, and cerebral autoregulation
- ***NO increases cerebral blood flow***

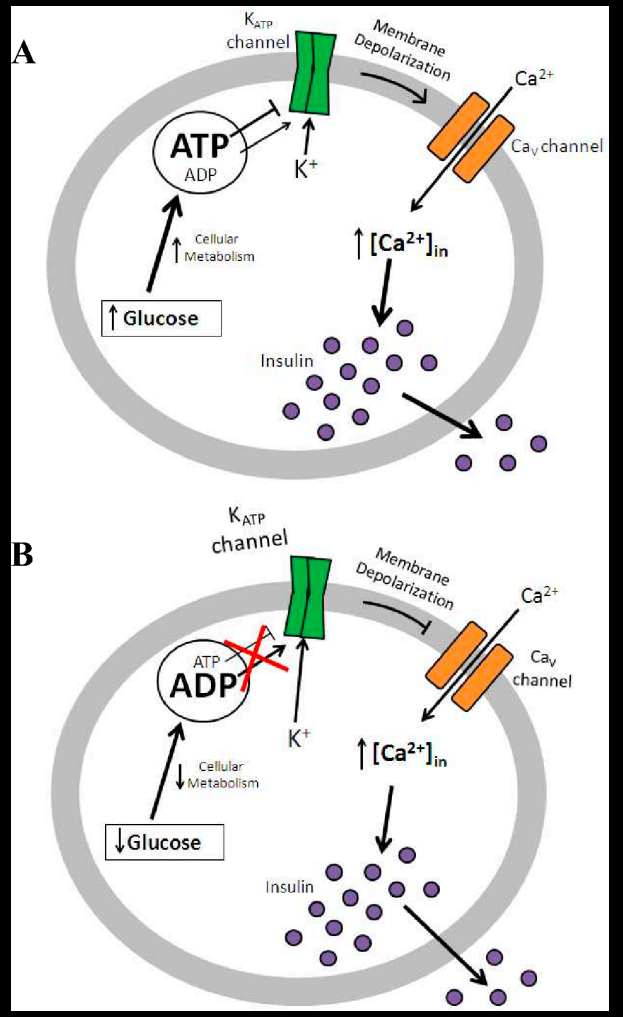
Vasoactive Peptides

- ***Calcitonin Gene-Related Peptide (CGRP)*** – increases intracellular cAMP and mediates cerebral vasodilation
- ***Substance P*** – neuropeptide released from terminals of sensory nerves, potent vasodilator, dependent on NO release
- ***Neurokinin A*** – neuropeptide similar to Substance P, involved in pain transmission and inflammatory processes, also a potent vasodilator

Potassium Channels

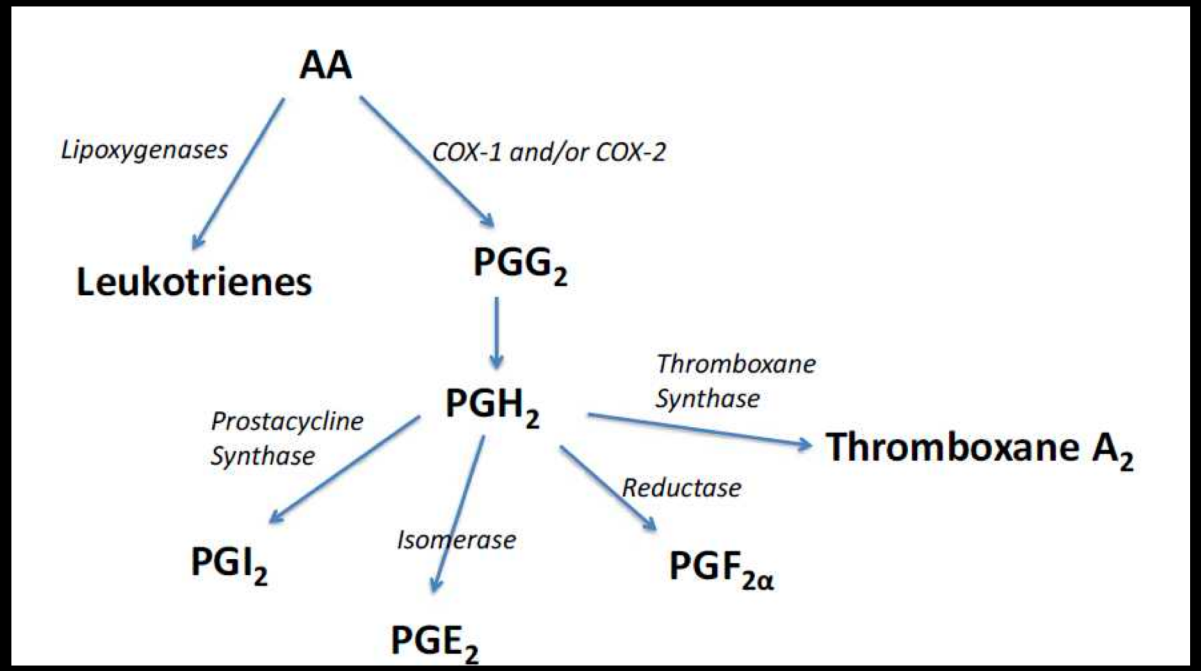
- Mechanism: opening of K^+ channels triggers K^+ efflux from VSM cells, hyperpolarizes membrane, closes the voltage dependent calcium channels, decreases calcium entry into cells and relaxes the muscle
- Types
  - K+-ATP
  - K+-Ca2+
  - Delayed Rectifier K+ Channel



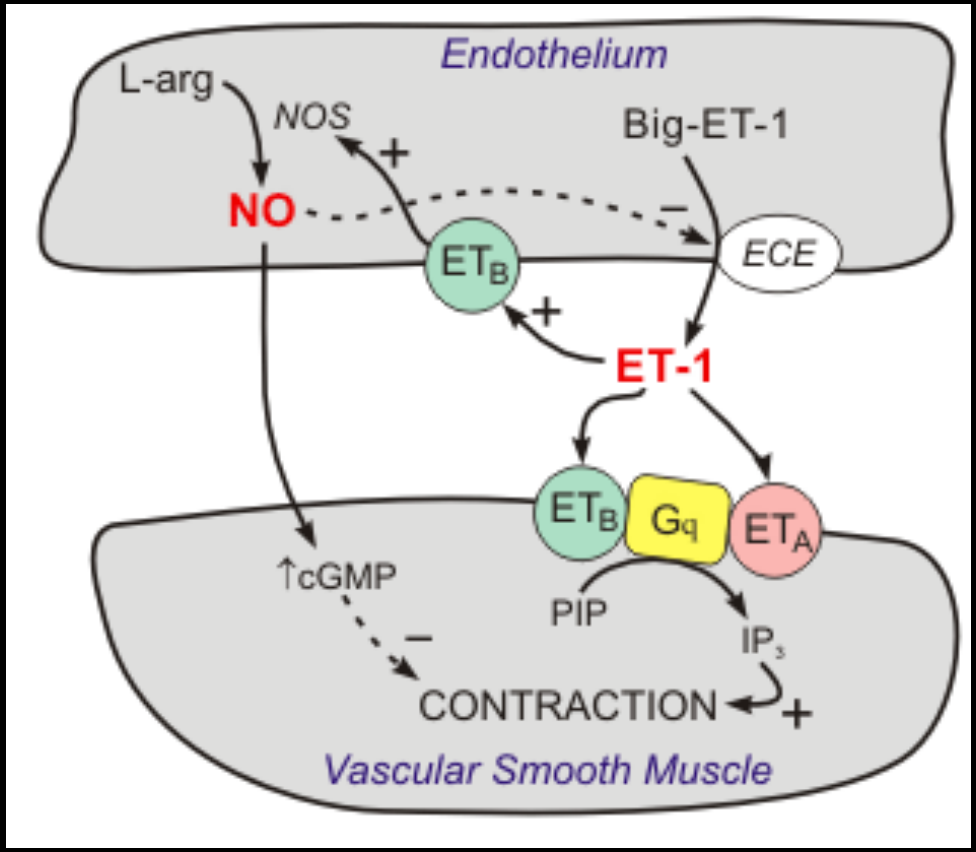


Prostaglandins

- PGE_2 and PGI_2 = vasodilators
- TXA_2 and $PGF_{2\text{-alpha}}$ = vasoconstrictors
- Synthesized by phospholipase and cyclooxygenase (COX)



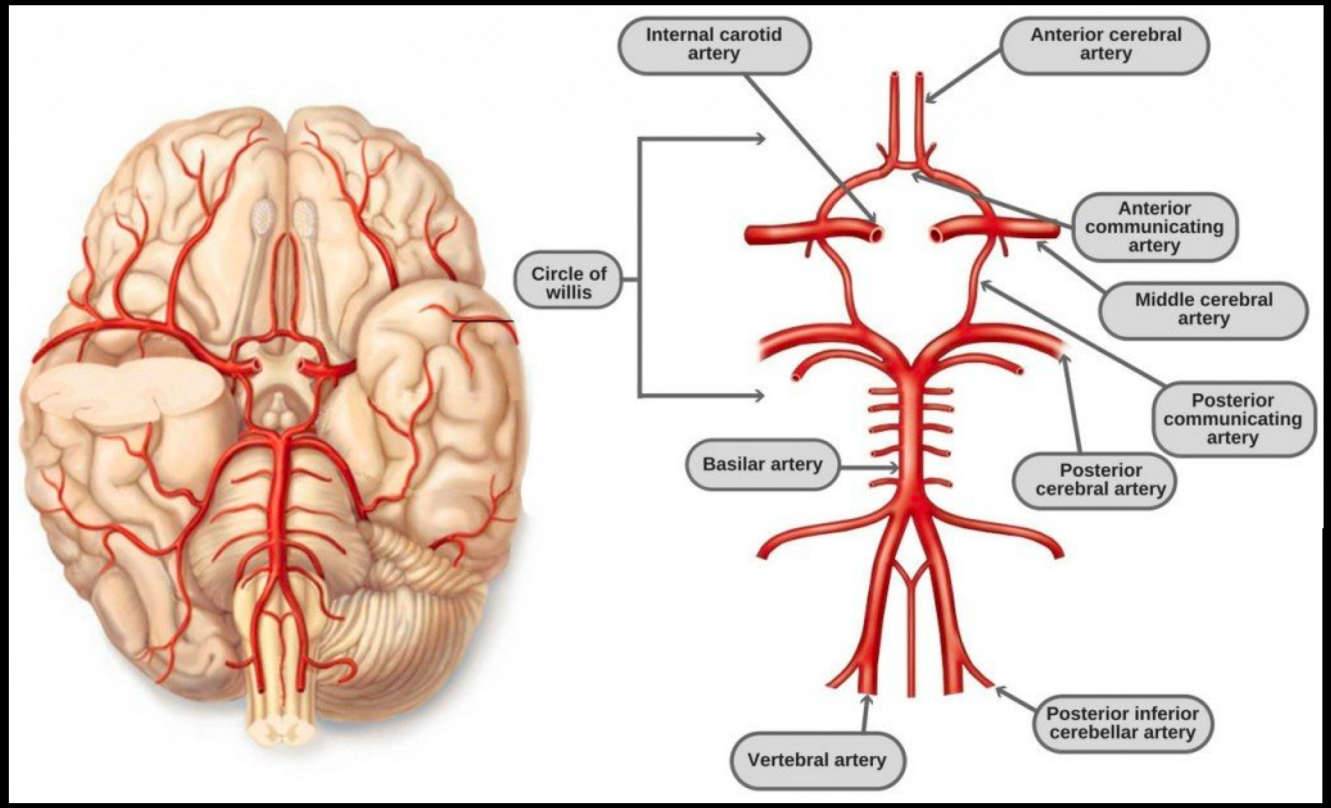
Endothelin

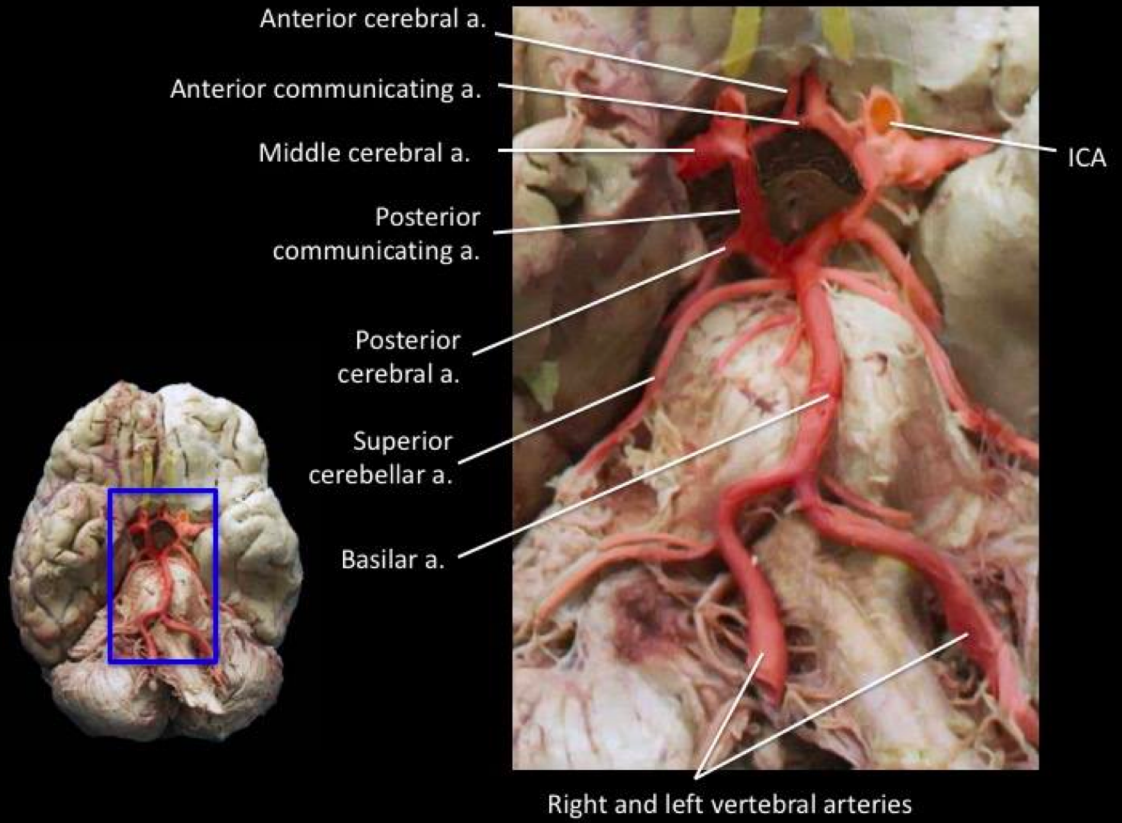


- Vasoactive peptide synthesized by brain and vascular endothelium
- Acts via influx of extracellular calcium mediated by protein kinases
- 2 Receptors for endothelin
  - ETA – activation → vasoconstriction
  - ETB – activation → vasoconstriction or vasodilation

Anatomic Considerations

- Anterior Circulation
  - Two carotid arteries – 80% of supply to the brain
- Posterior Circulation
  - Two vertebral arteries
- Circle of Willis
  - ***Complete COW is only present in 18-20% of patients***
- System of collaterals
- Watershed Infarcts


Internal carotid artery
Anterior cerebral artery
Anterior communicating artery
Middle cerebral artery
Circle of willis
Posterior communicating artery
Basilar artery
Posterior cerebral artery
Posterior inferior cerebellar artery
Vertebral artery


Anterior cerebral a.
Anterior communicating a.
Middle cerebral a.
Posterior communicating a.
Posterior cerebral a.
Superior cerebellar a.
Basilar a.
ICA
Right and left vertebral arteries

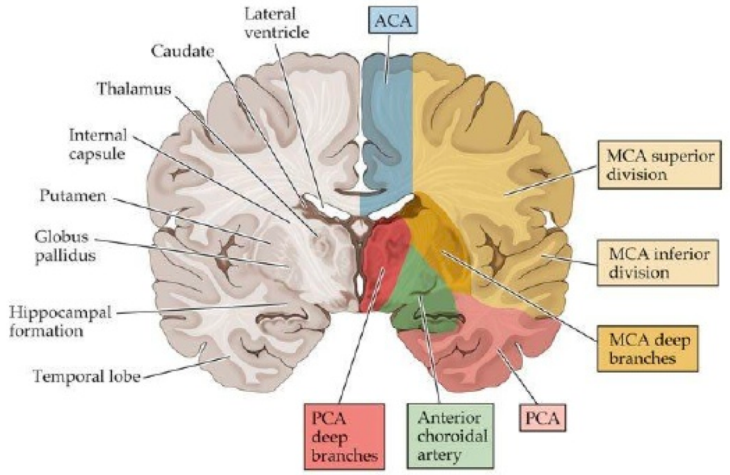


Figure 17. Topography of the cerebral main vascular territories

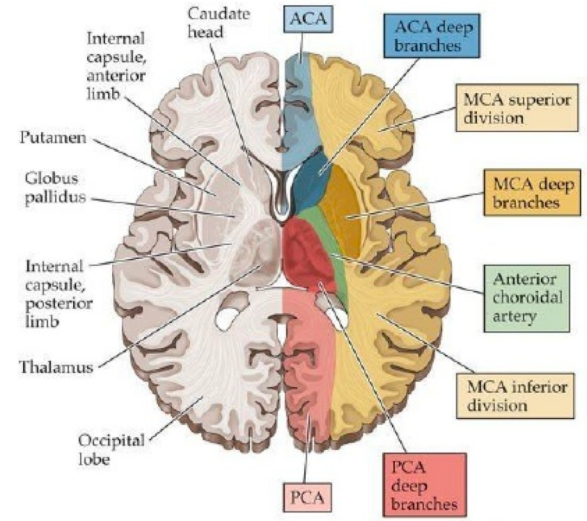
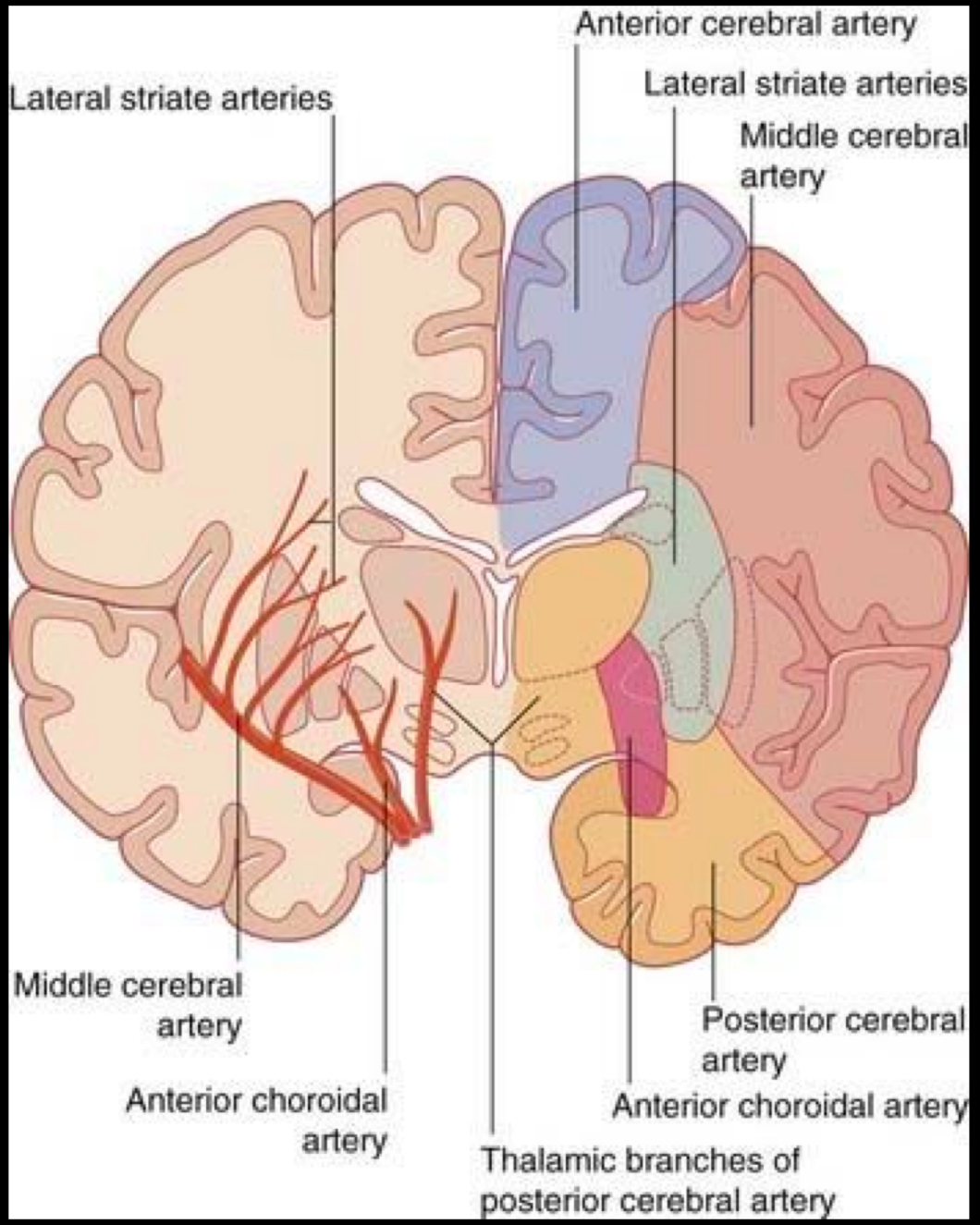
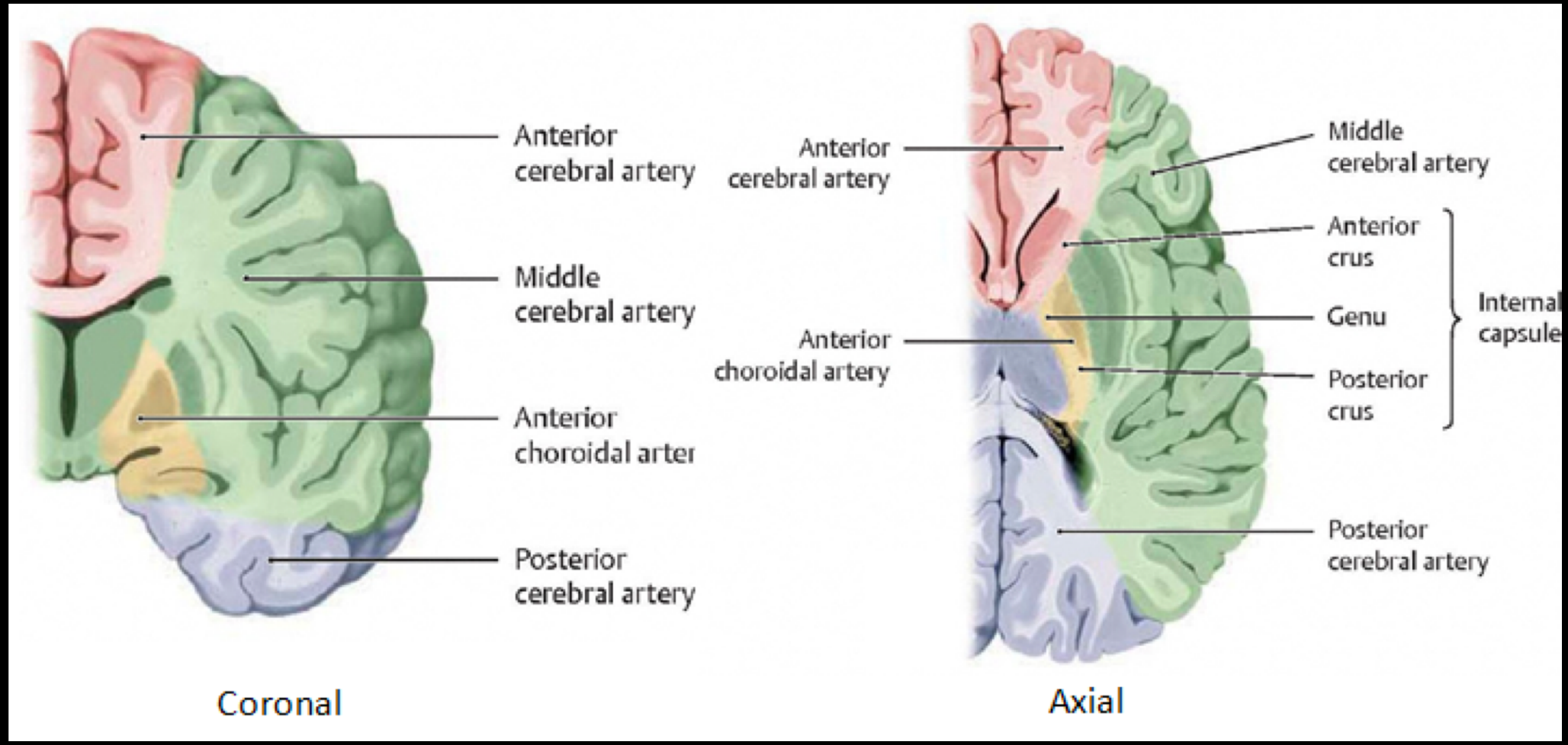


Figure 18. Topography of the cerebral main vascular territories



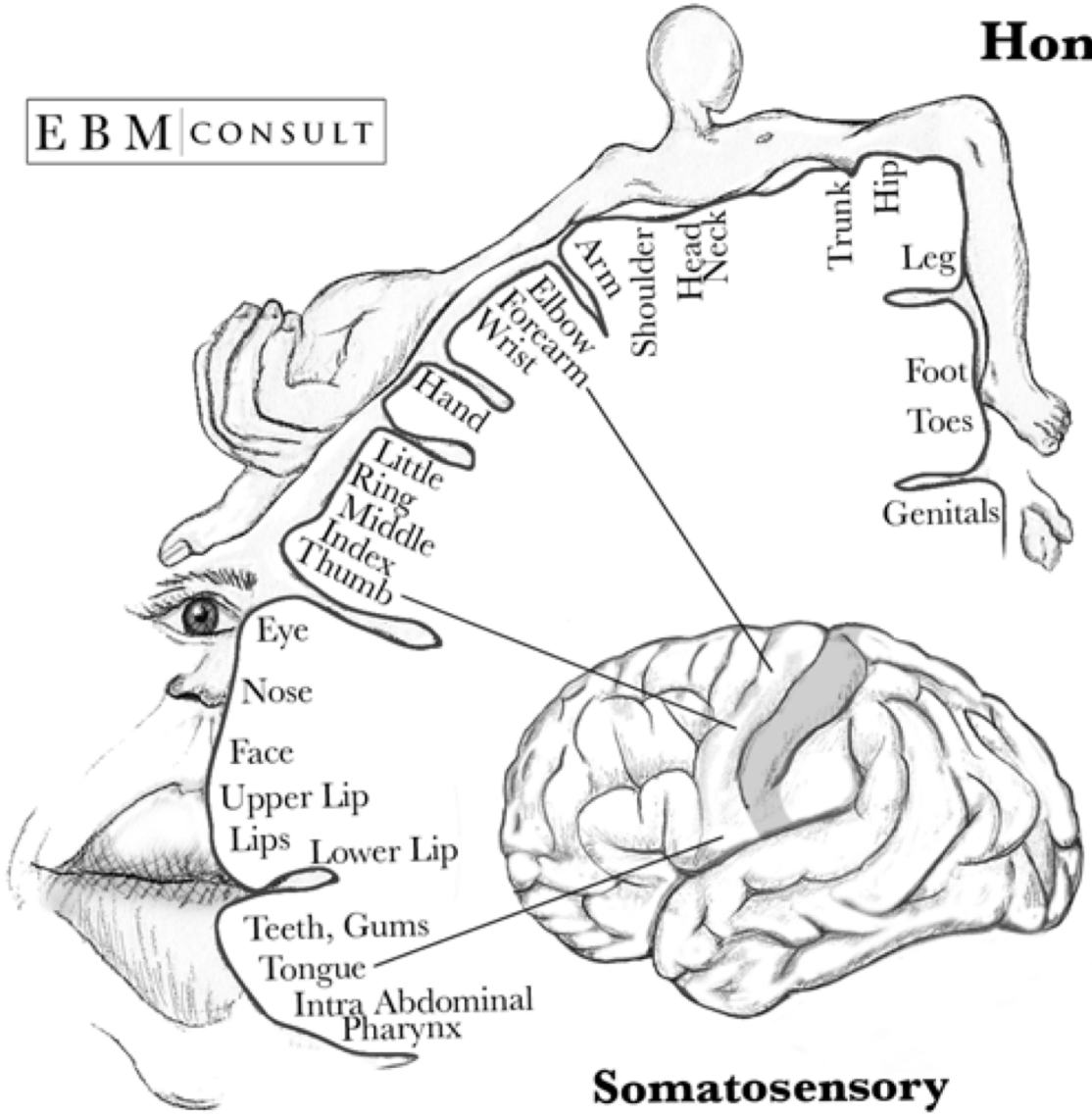

Anterior cerebral artery
Middle cerebral artery
Anterior choroidal arter
Posterior cerebral artery
Coronal
Anterior cerebral artery
Anterior choroidal artery
Middle cerebral artery
Anterior crus
Genu
Posterior crus
Internal capsule
Posterior cerebral artery
Axial

Watershed Infarcts

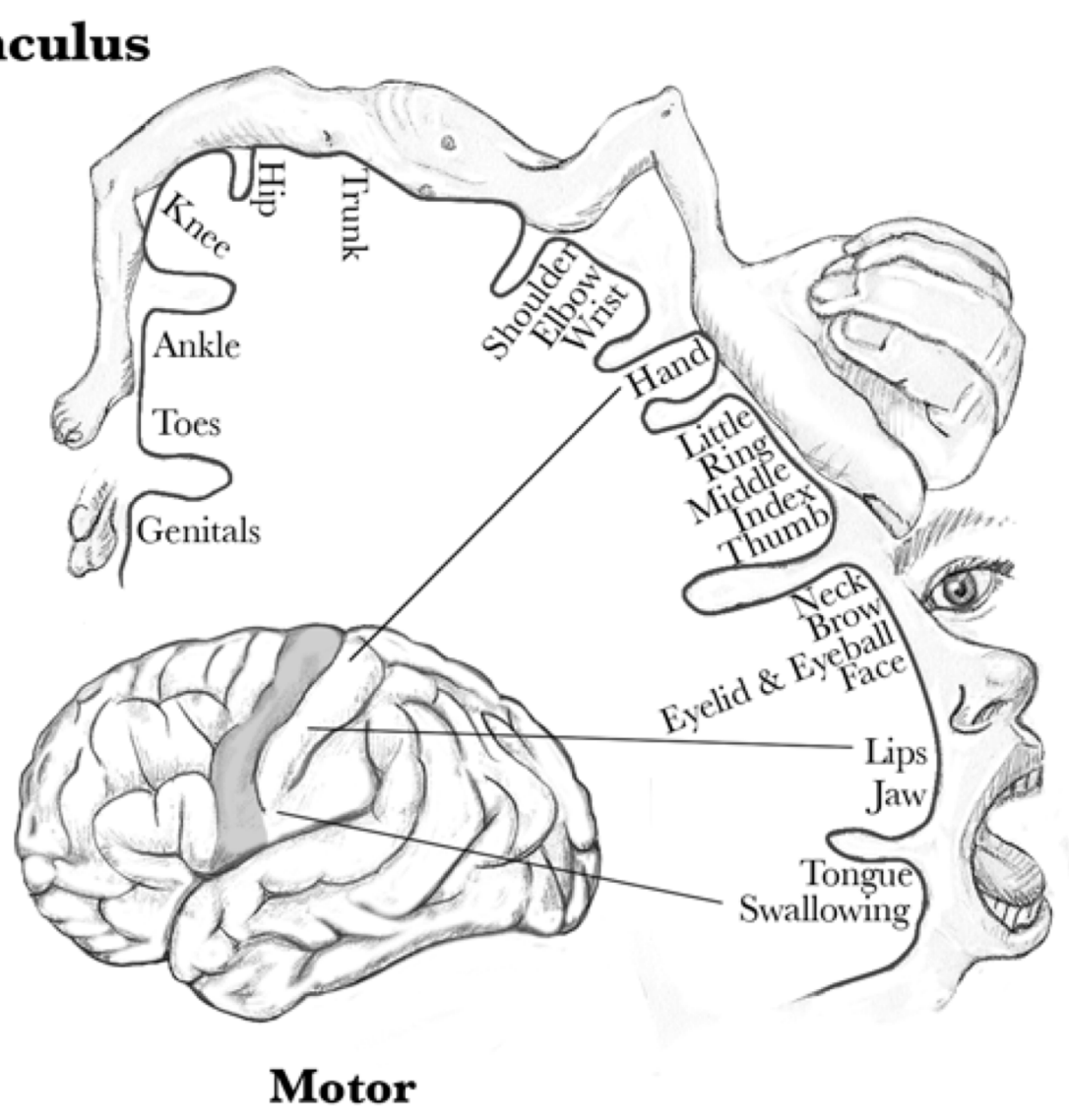
- Hypoperfusion or ischemia that occurs at the border between cerebral vascular territories where the tissue is farthest from arterial supply
- Pathology
  - Episodes of hypoperfusion
  - Embolism
- Classification
  - Cortical – between ACA, MCA, PCA territories
  - Deep – between ACA, MCA, PCA territories and perforating medullary, lenticulostriate, and anterior choroidal arteries

Homunculus

EBM CONSULT



Somatosensory



Motor

Pressure Regulation

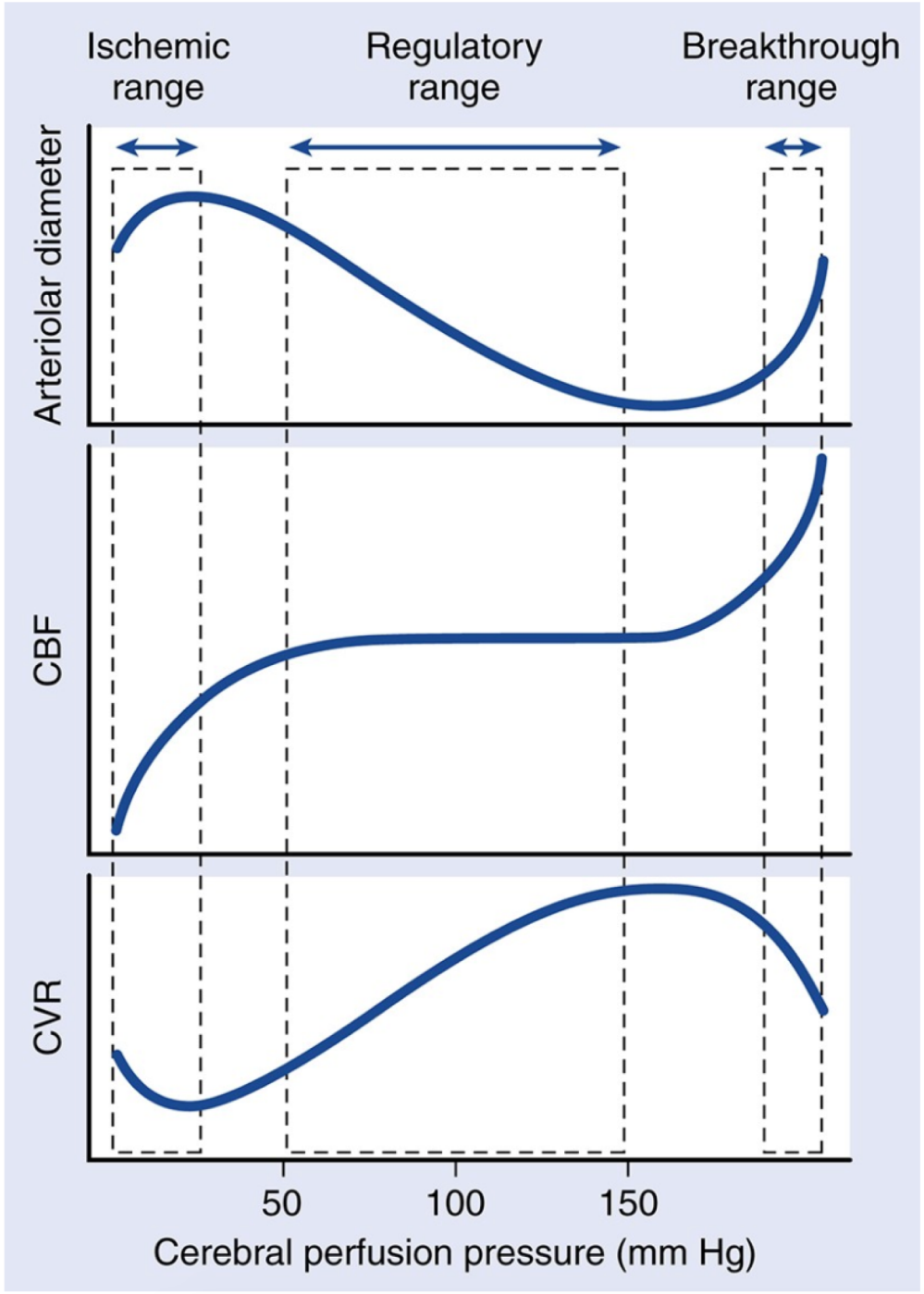
- Cerebral circulation – ***Ohm's Law***

$$Q = (P_i - P_o) / R, \text{ where } P_i - P_o = CPP$$

- Drugs exert effects on CBF by changing CPP and CVR
- Circulatory resistance can be modeled in terms of the Hagen-Poiseuille Law

$$R = 8 l \mu / r^4$$

  - Vessel diameter is preeminent mode of vascular regulation
  - Flow is proportional to the fourth power of the conduit's radius
  - CBF Is constant at a CPP of 50—150 mmHg

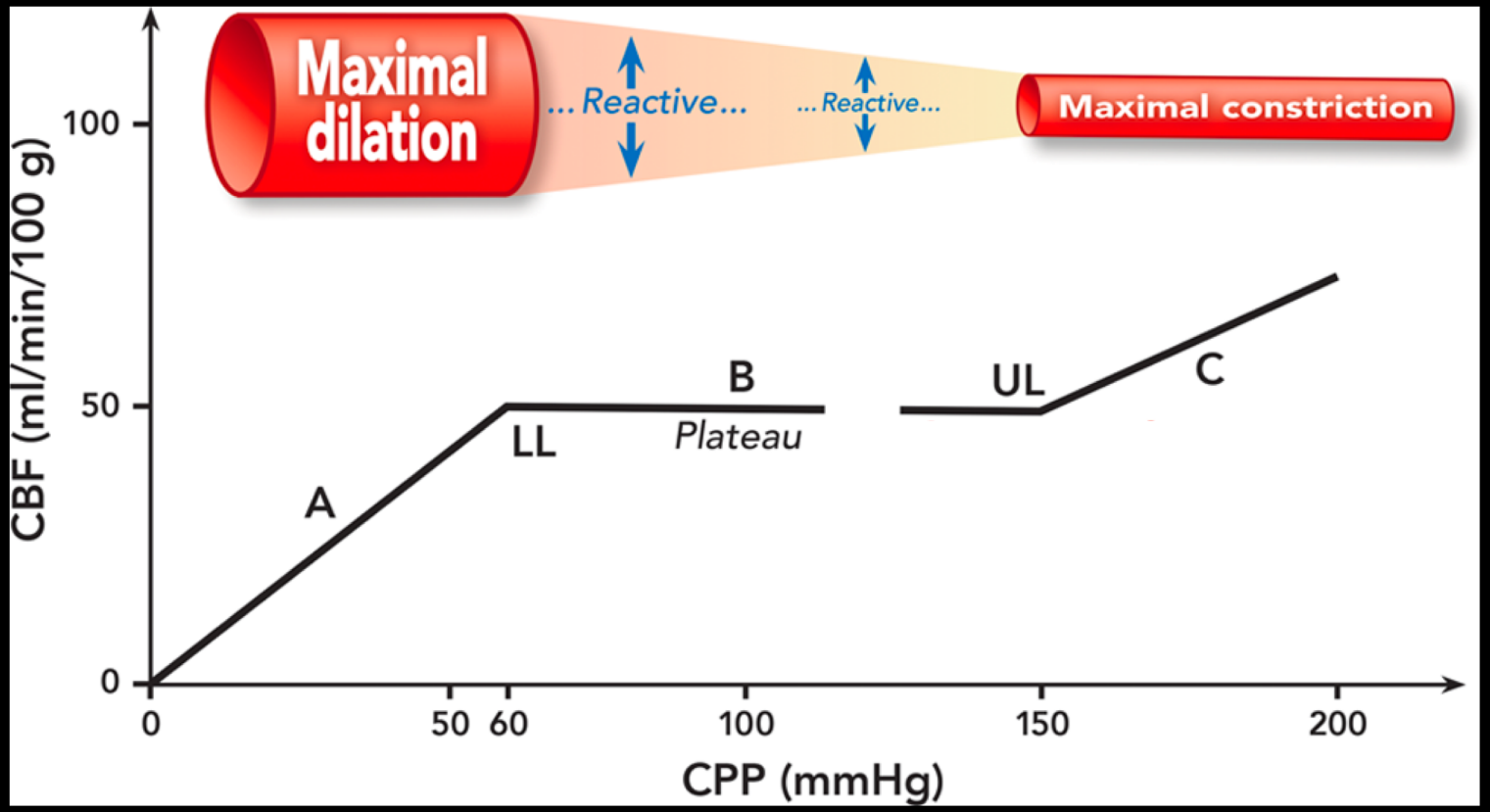


Pressure autoregulation in terms of CBF, CVR and arteriolar diameter

****Statistical depiction of how the general population responds****

Individual response varies greatly!

- **Autoregulation:** intrinsic ability of an organ to maintain a constant blood flow despite changes in perfusion pressure



Autoregulation

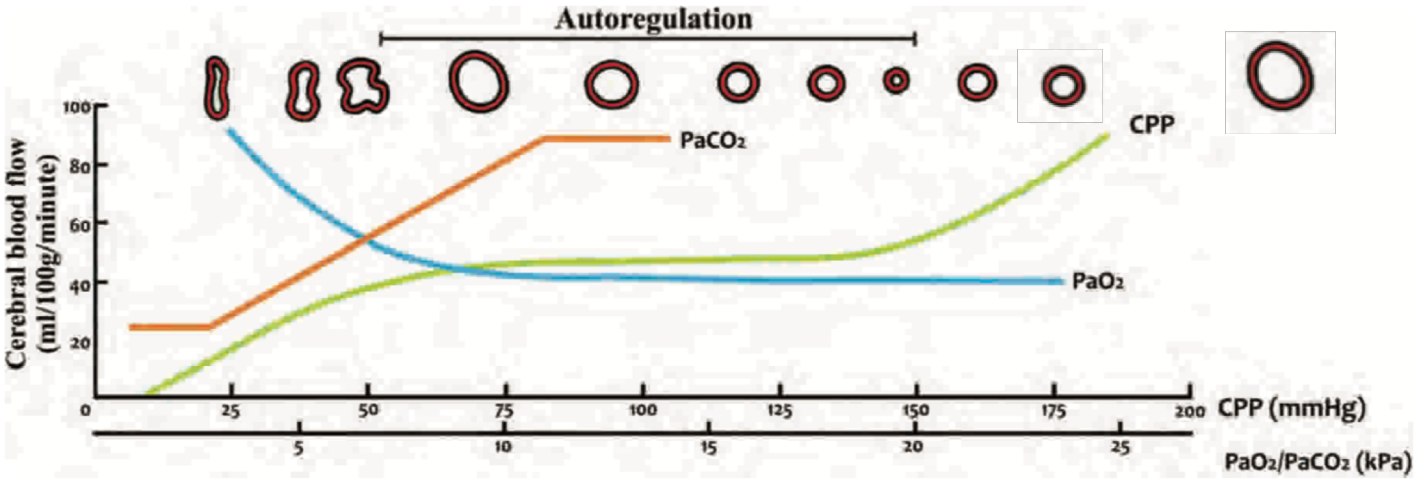


Fig 3 Effect of changes in MAP, arterial oxygen and carbon dioxide tensions, and cerebral vascular resistance on cerebral blood flow. Reproduced with permission from Shardlow and Jackson.[10] Elsevier Limited.

- Increased MAP = increased transmural vessel tension → depolarization of vascular smooth muscle → vasoconstriction
  - ***Occurs between MAP 60-160 mm Hg/ CPP 50-150 mmHg***
- Above the plateau CBF becomes pressure dependent

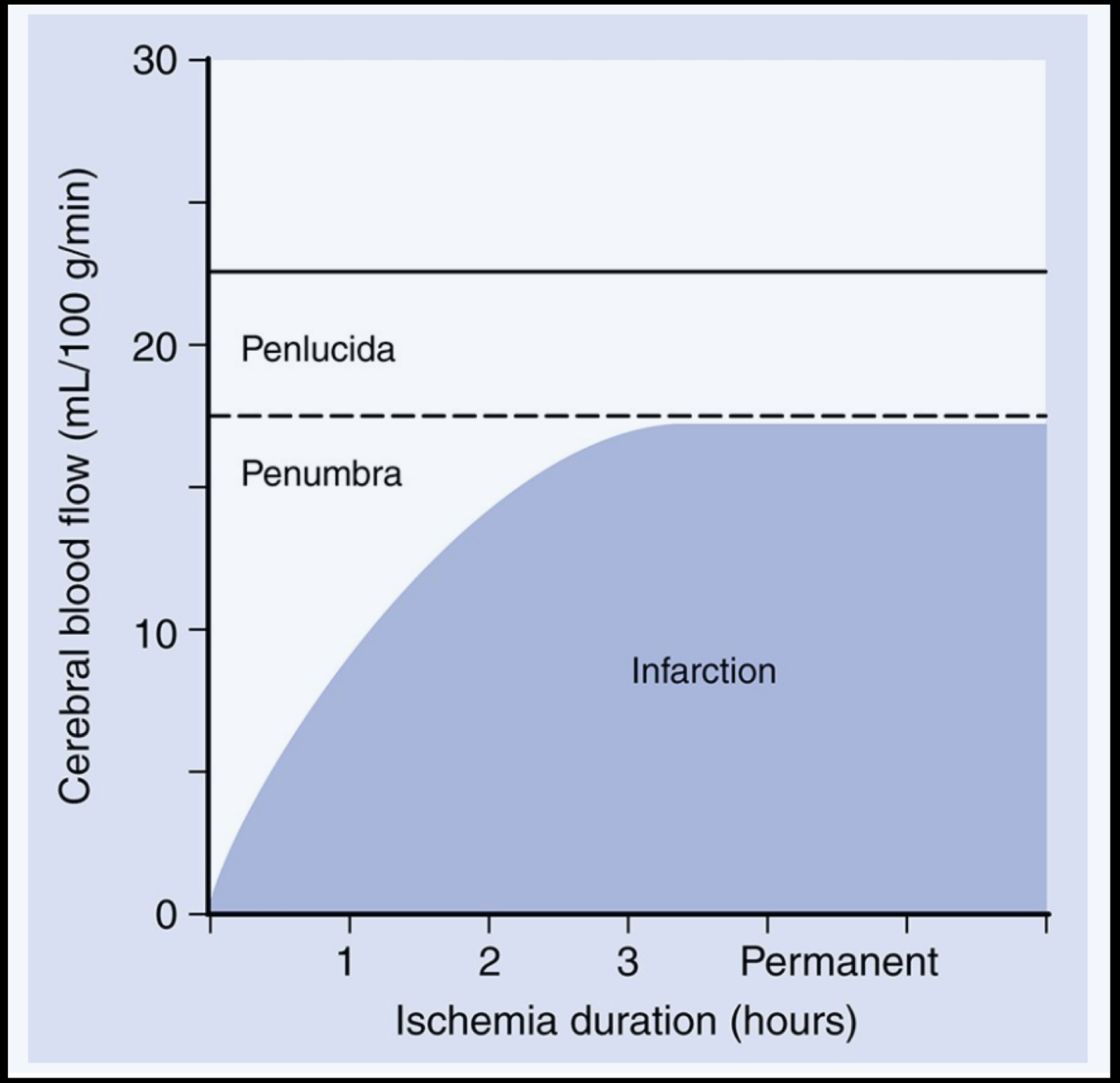
Autoregulatory Failure

- Hypoperfusion and Ischemia
- Hyperperfusion and Circulatory Breakthrough
- Reperfusion Injury
- Hemodynamic Considerations during Autoregulatory Failure

- Cerebral autoregulation is disturbed in several disease states
  - Acute ischemia, mass lesions, trauma, inflammation
- What causes autoregulation to fail???
  - Tissue acidosis, noxious metabolites
  - Loss of CO_2 reactivity
  - Loss of pressure regulation
- Hyperperfusion
- Hypoperfusion

Hypoperfusion & Ischemia

- Hypoperfusion → ischemia
- As CPP decreases, arterioles dilate and CBV increases
  - Capacity for vasodilation is exhausted
  - Circulation cannot decrease resistance further to maintain flow
  - CBF declines passively as CPP decreases further
  - At first an increase in oxygen extraction compensates for the passive decline in CBF
  - When oxygen extraction is maximal, $CMRO_2$ begins to diminish
- Synaptic transmission becomes impaired and fails completely (isoelectric EEG)
- At even lower flow levels, membrane failure occurs producing cytotoxic edema

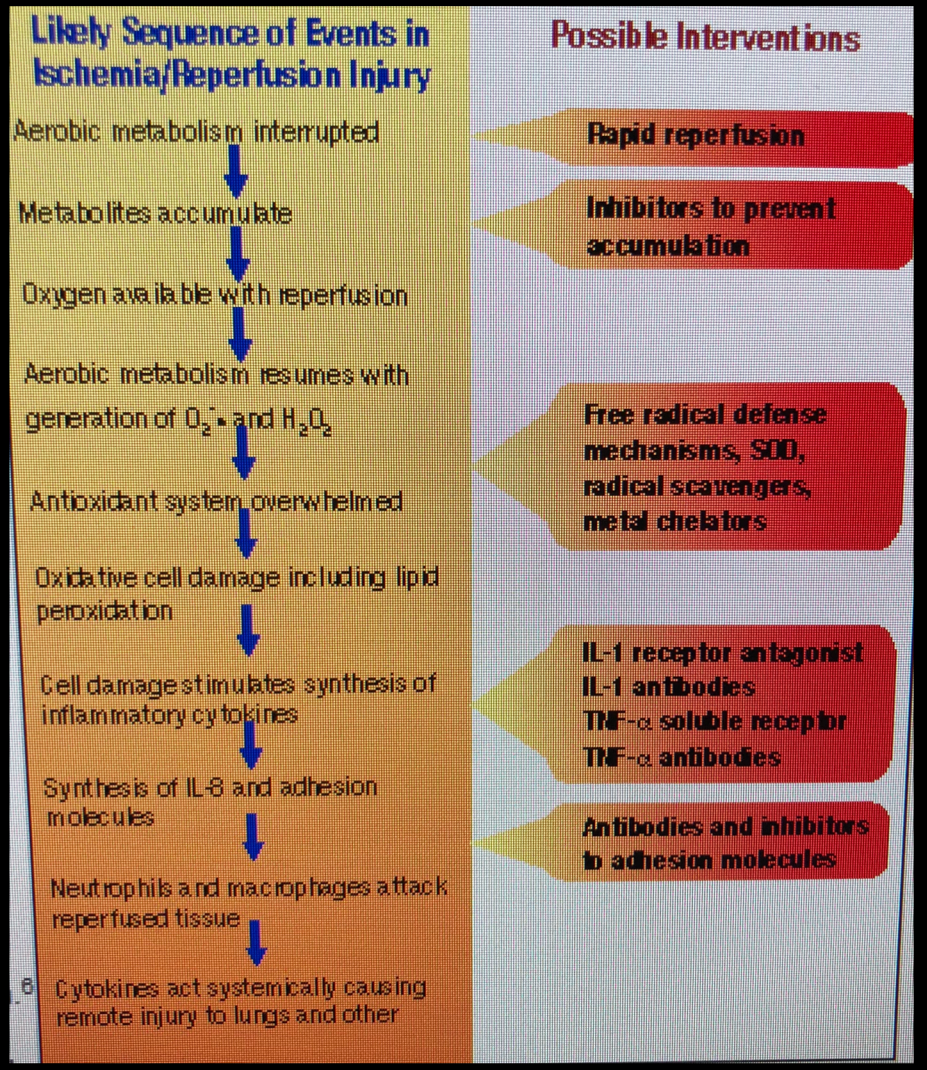

30
20
10
0
Cerebral blood flow (mL/100 g/min)
Penlucida
Penumbra
Infarction
1
2
3
Permanent
Ischemia duration (hours)

Hyperperfusion & Circulatory Breakthrough

- If CPP exceeds upper limit of autoregulation, flow initially increases with a fixed maximal arteriolar resistance
- At some point the arteriolar bed dilates under the increasing pressure and resistance falls
  - Brain edema from vascular engorgement
  - Vasogenic edema from opening of BBB
  - Intracerebral hemorrhage from vessel rupture
- Long state of maximal dilation may → vasomotor paralysis

Reperfusion Injury

- Tissue damage caused when blood supply returns to tissue after a period of ischemia
  - Absence of oxygen and nutrients creates an environment where restoration of circulation results in inflammation and oxidative damage/stress
  - Activated endothelial cells produce reactive oxygen species, less production of nitric oxide -- produces an inflammatory response
  - WBCs release inflammatory factors as well
  - Triggers apoptosis



Hemodynamic Considerations During Autoregulatory Failure

- Cerebrovascular Reserve
- Cerebral Steal
- Vessel Length and Viscosity
- Collateral Failure

Cerebrovascular Reserve

- Stenotic vessels → regions of brain with reduced blood flow
  - Normal resting flow
  - Limited potential for further vasodilation
  - Decrease in CPP → no ability to vasodilate to increase blood flow (no Cerebrovascular Reserve)
- Vasodilators can assess cerebrovascular reserve
- Acetazolamide Challenge!!!
  - Blood vessels in affected areas of brain are unable to dilate in respond to acetazolamide, compromised perfusion

Cerebral Steal

- Decreased blood flow to ischemic areas caused by blood vessel dilation in non-ischemic areas
  - Diverts blood away from areas that need it

Vessel Length & Viscosity

- After exhaustion of vasodilatory capacity, flow is dependent on:
  - Passive pressure
  - Vessel length
  - Blood viscosity (Hct!)
- With maximal distal vasodilation, the areas with lowest pressure are those farthest from arterial input = highest resistance, lowest flow
- Viscosity reduction is also important for prevention and treatment of vasospasm
  - Excessive hemoglobin can produce a hyperviscous state

Spinal Cord Blood Flow

Spinal Cord Blood Flow

- Comparison of CBF and Spinal Cord Blood Flow
- Blood Pressure
- CO_2 and O_2 Tension
- Temperature
- Neurogenic Control
- Anesthetics

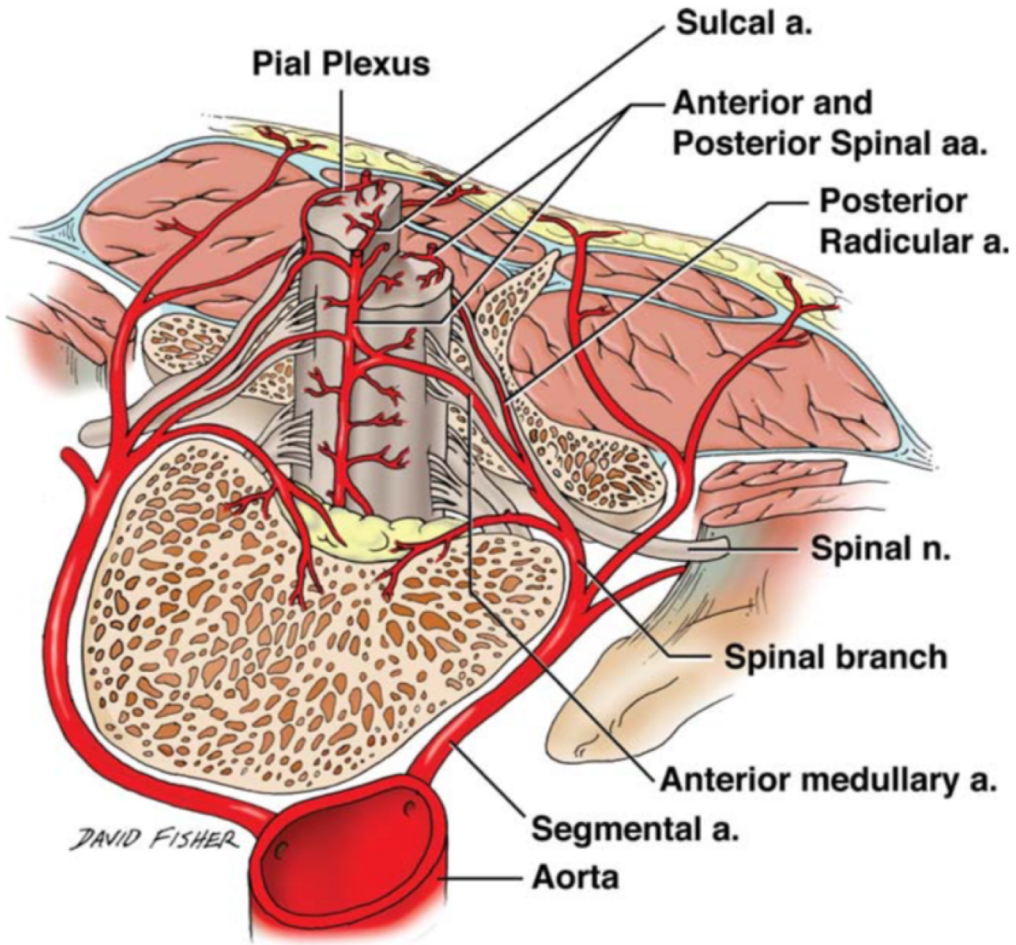


Fig. 1. Schematic view of the blood supply of the spinal cord stemming from the aorta. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

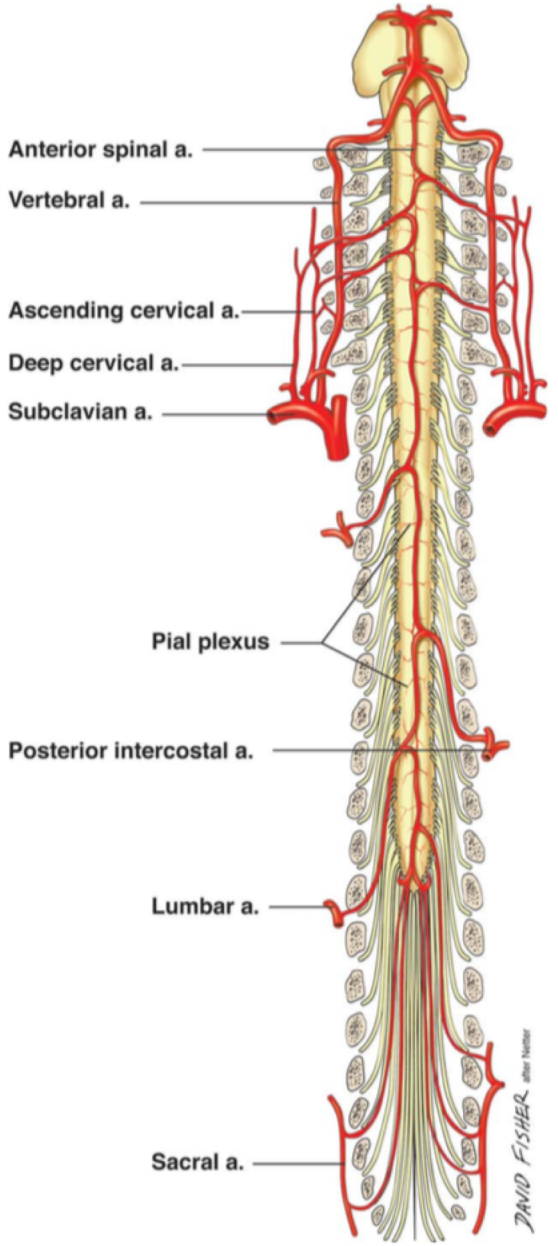


Fig. 3. Longitudinal schematic of the blood supply to the spinal cord from regional sources. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Comparison of CBF and SCBF

- Regional differences in blood flow exist for spinal cord in the same way they do as the brain
- Mean blood flow is approx. 40% higher in the cervical and lumbar segments vs the thoracic segments
  - Less gray matter in thoracic cord
- SCBF is metabolically linked to the local level of electrical activity
  - Unilateral stimulation of the sciatic and femoral nerves is reflected by a 50% increase in flow in the ipsilateral lumbosacral gray matter

Blood Pressure

- Autoregulation exists for SCBF (~50-140 mmHg)

CO_2 and O_2 Tension

- SCBF increases with hypercapnia
- SCBF decreases with hypocapnia
- Absolute change in CBF per unit changes in CO_2 tension is greater than corresponding change in SCBF
- NO plays major role in CO_2 responsiveness in spc

Temperature

- SCBF decreases with hypothermia
- Local spc hypothermia within 4 hrs of injury may limit progression of spc injury
  - However, hypothermia also reduces SCBF

Anesthetics

Anesth Analg. 1993 May;76(5):971-5.

The effects of propofol on cerebral and spinal cord blood flow in rats.

Werner C[1], Hoffman WE, Kochs E, Schulte am Esch J, Albrecht RF.

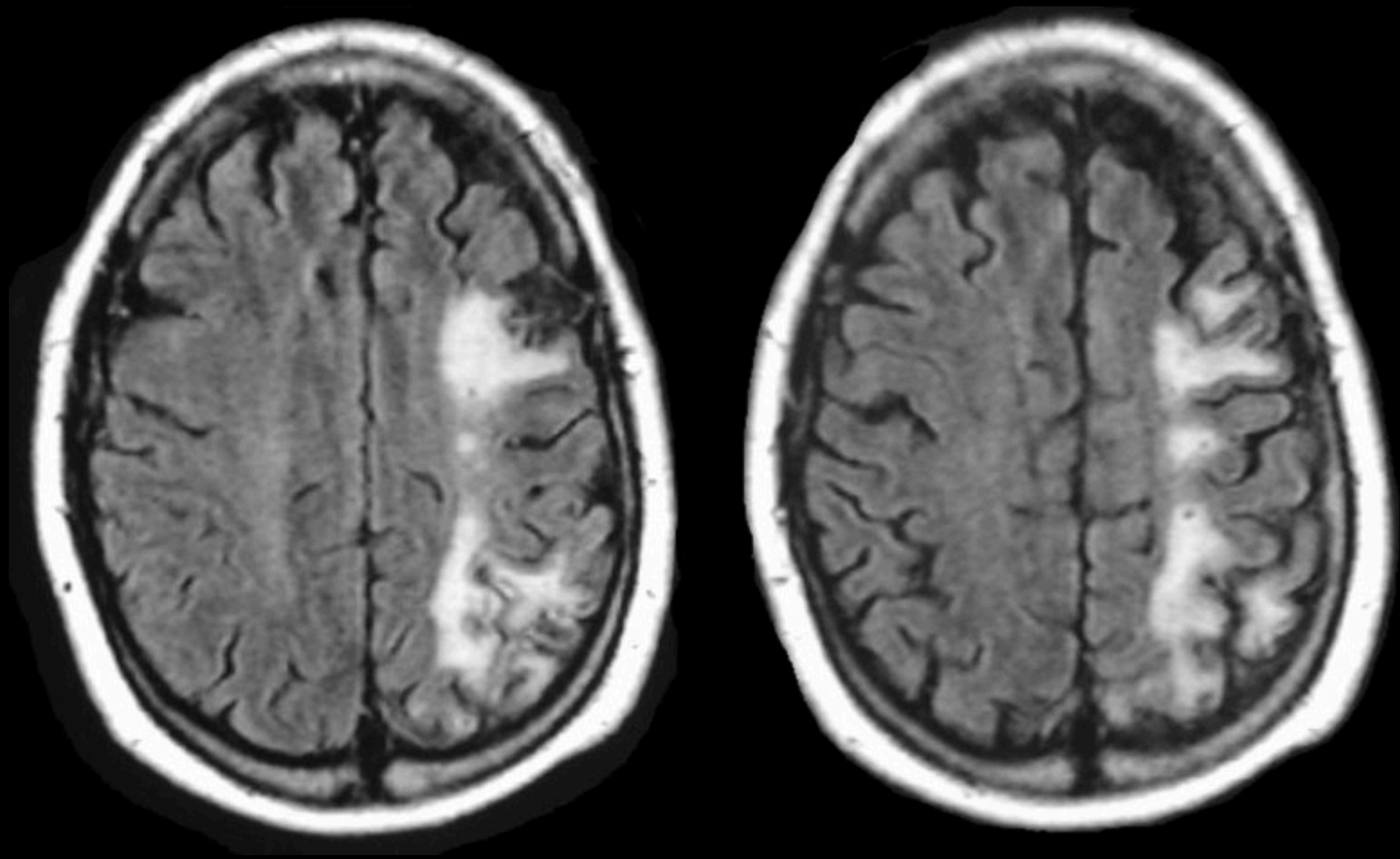
- *Propofol decreased cortical CBF 60%, decreased SCBF 20% with MAP between 50-140 mmHg*
- Autoregulation keeps CBF and SCBF constant
- Regional differences in CBF and SCBF can be elicited as responses to variations in local metabolic activity
- ***CO_2 tension is single most significant physiologic variable affecting both CBF and SCBF***

Clinical Cases

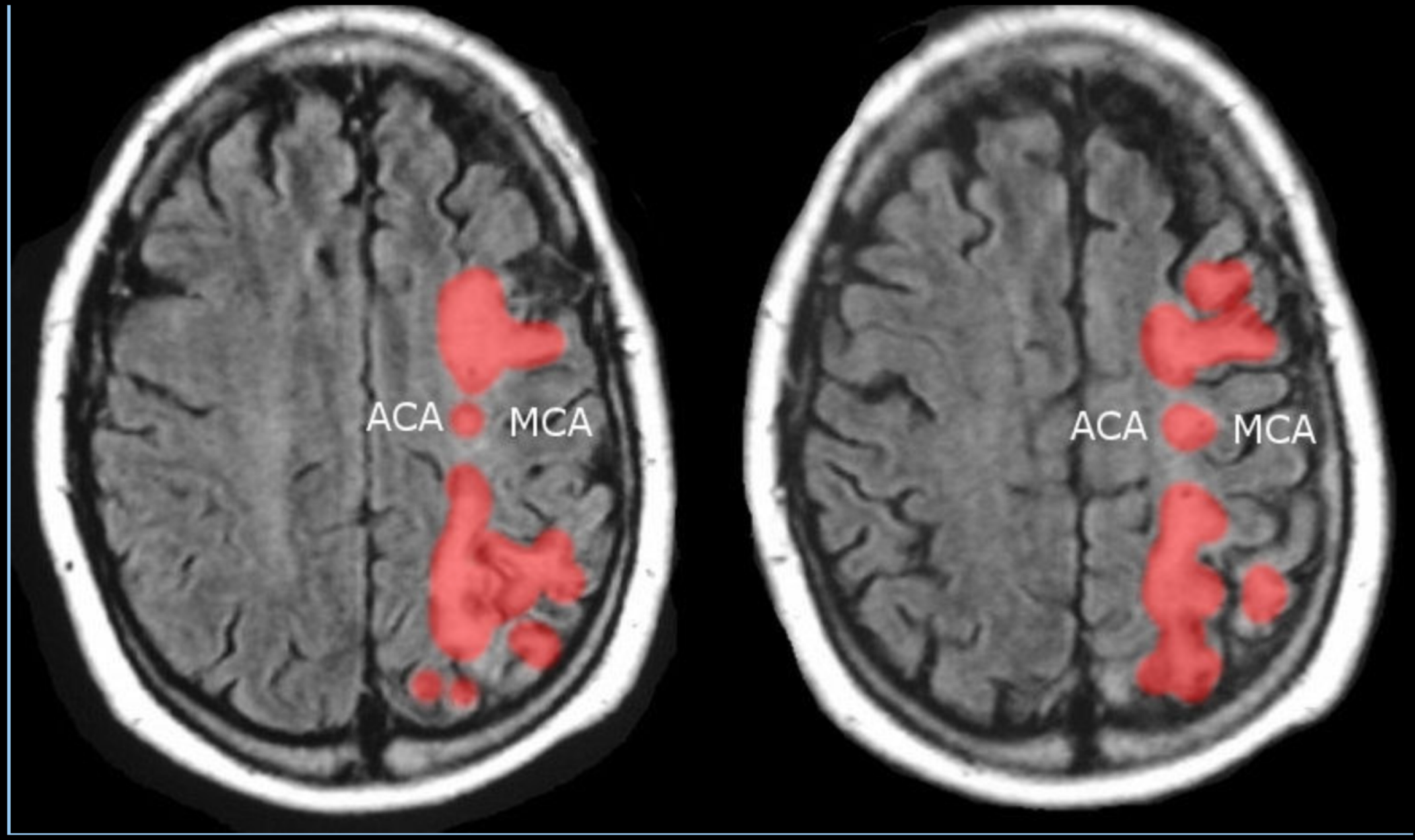
CASE 1

- 62 yo M with upper GI bleed complicated by severe hypotension, several days after surgical repair of bleeding gastric ulcer he was noted to have significant weakness of R shoulder and hip girdle muscles

- Where is the stroke?



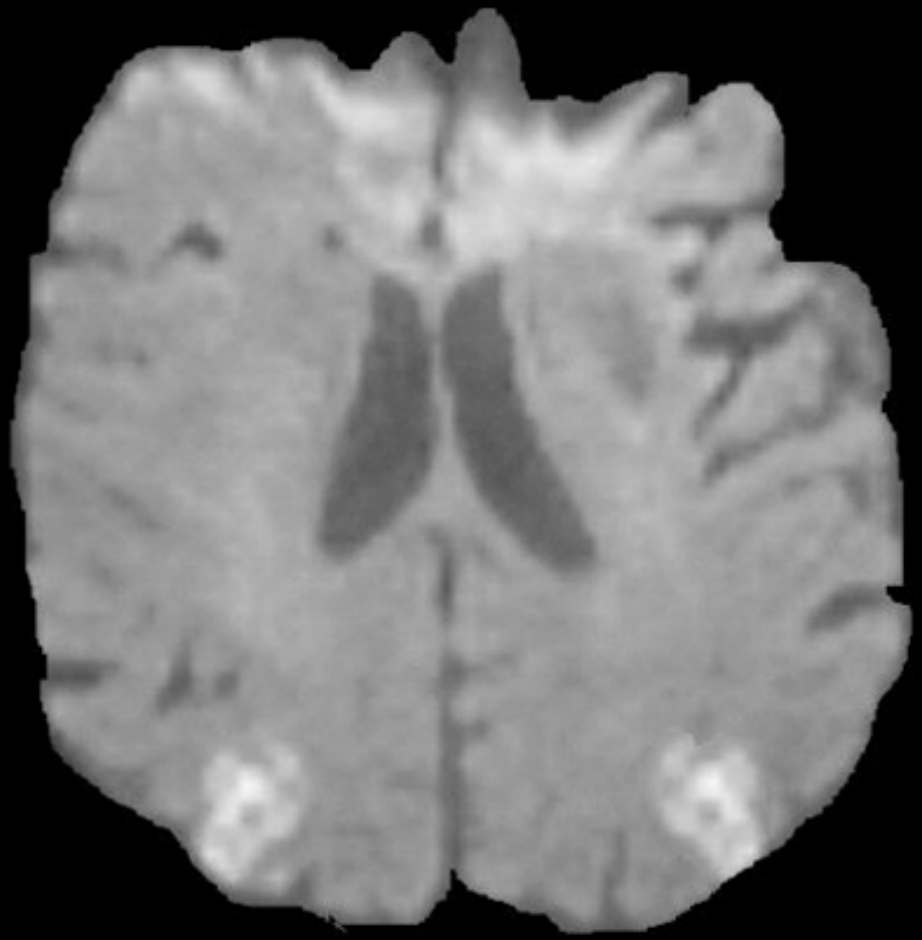
middle cerebral artery (MCA) and anterior cerebral artery (ACA) on the left side of the brain.



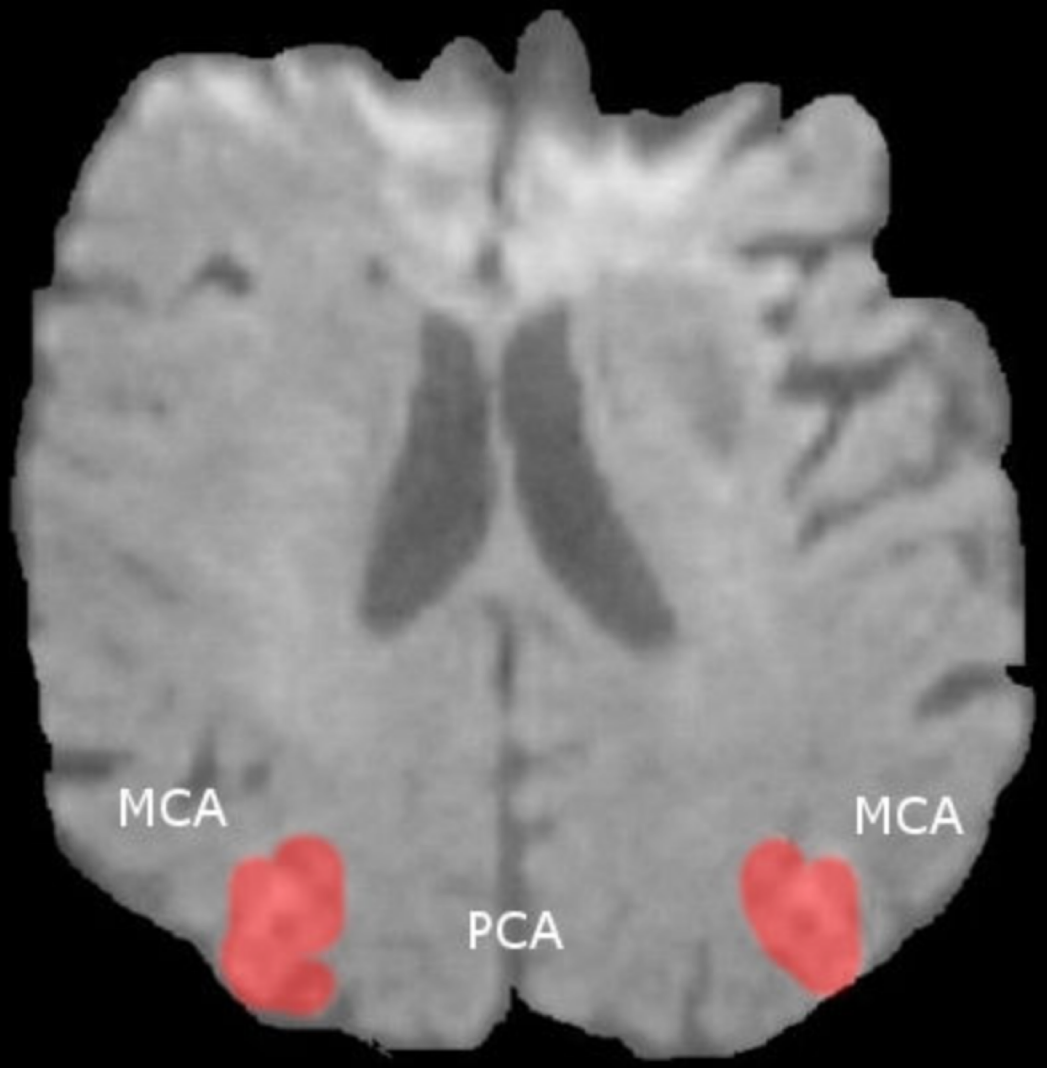
Case 2

- 67 yo M found unable to see following cardiac arrest and sustained hypotension.

- Where is the lesion?

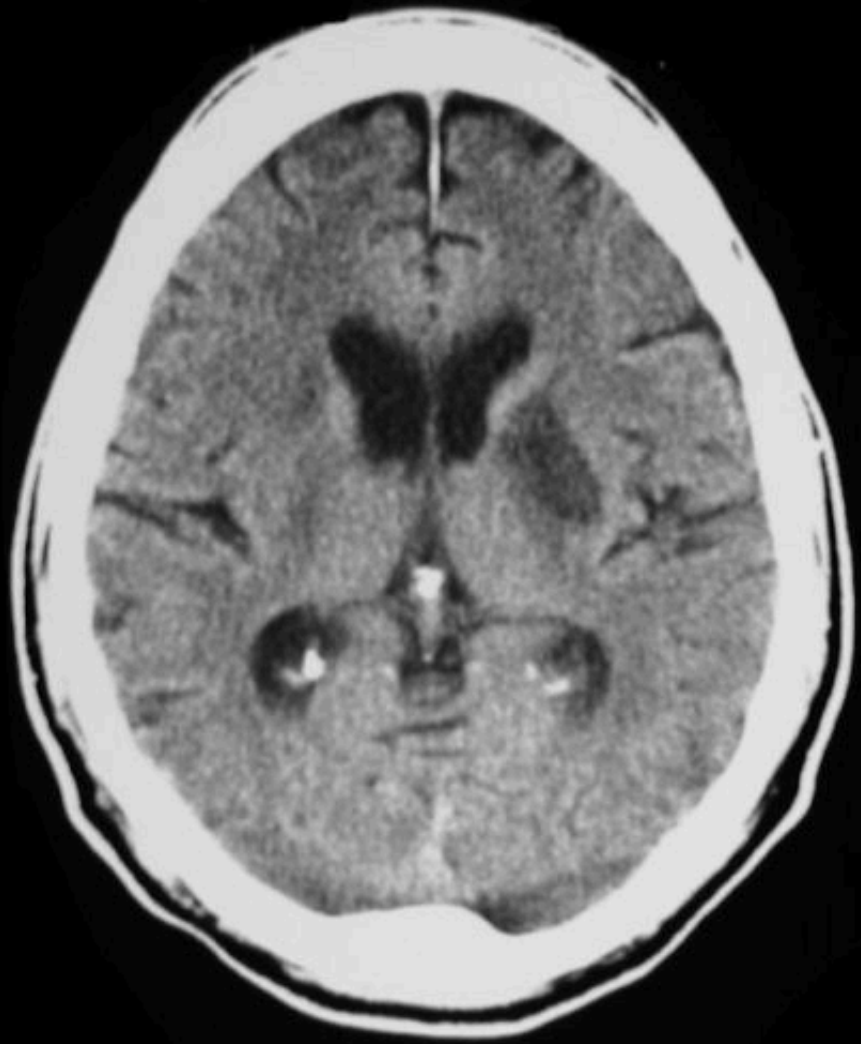


Posterior watershed infarctions usually follow hypoperfusion and are usually bilateral, especially following cardiac arrest

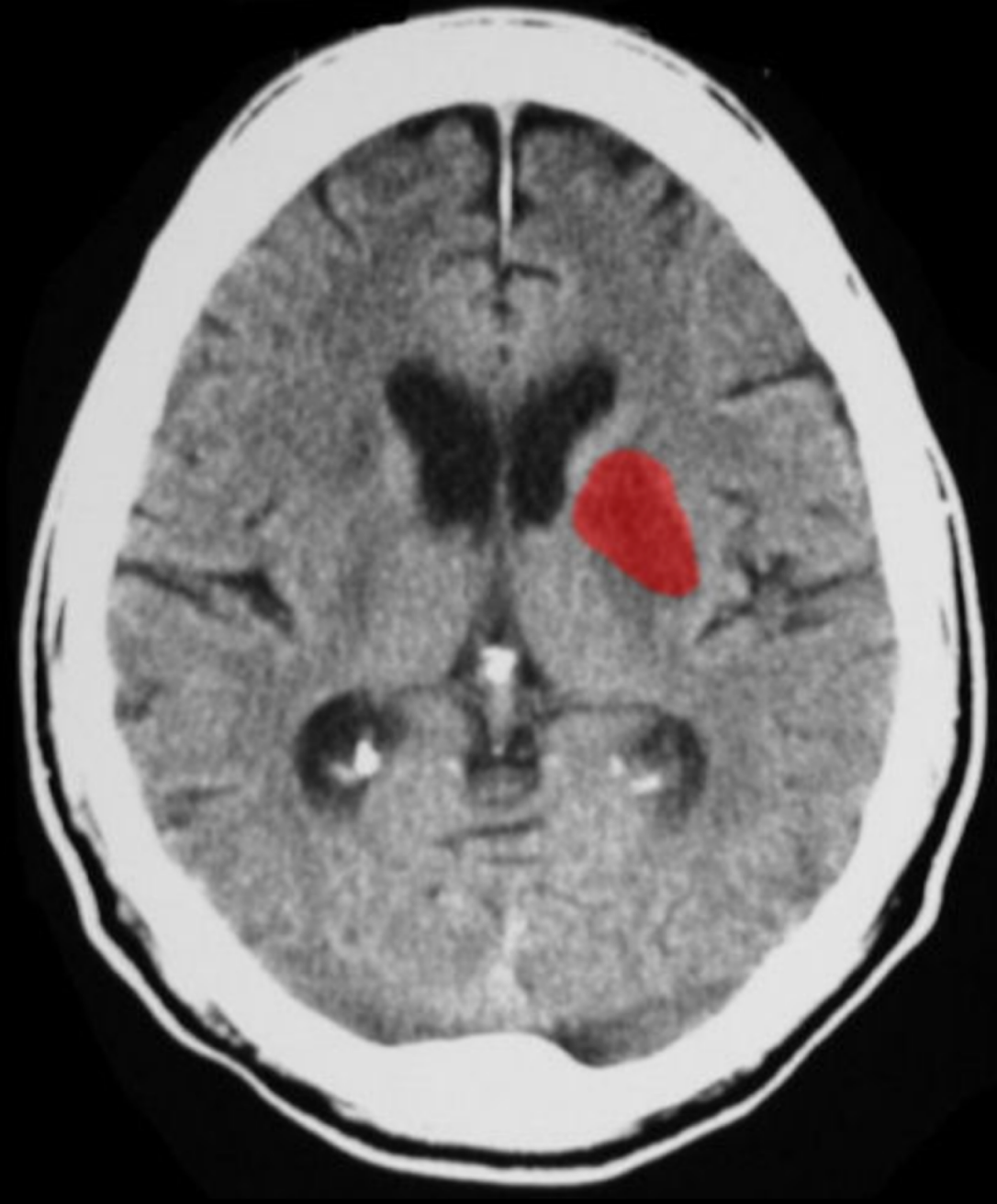


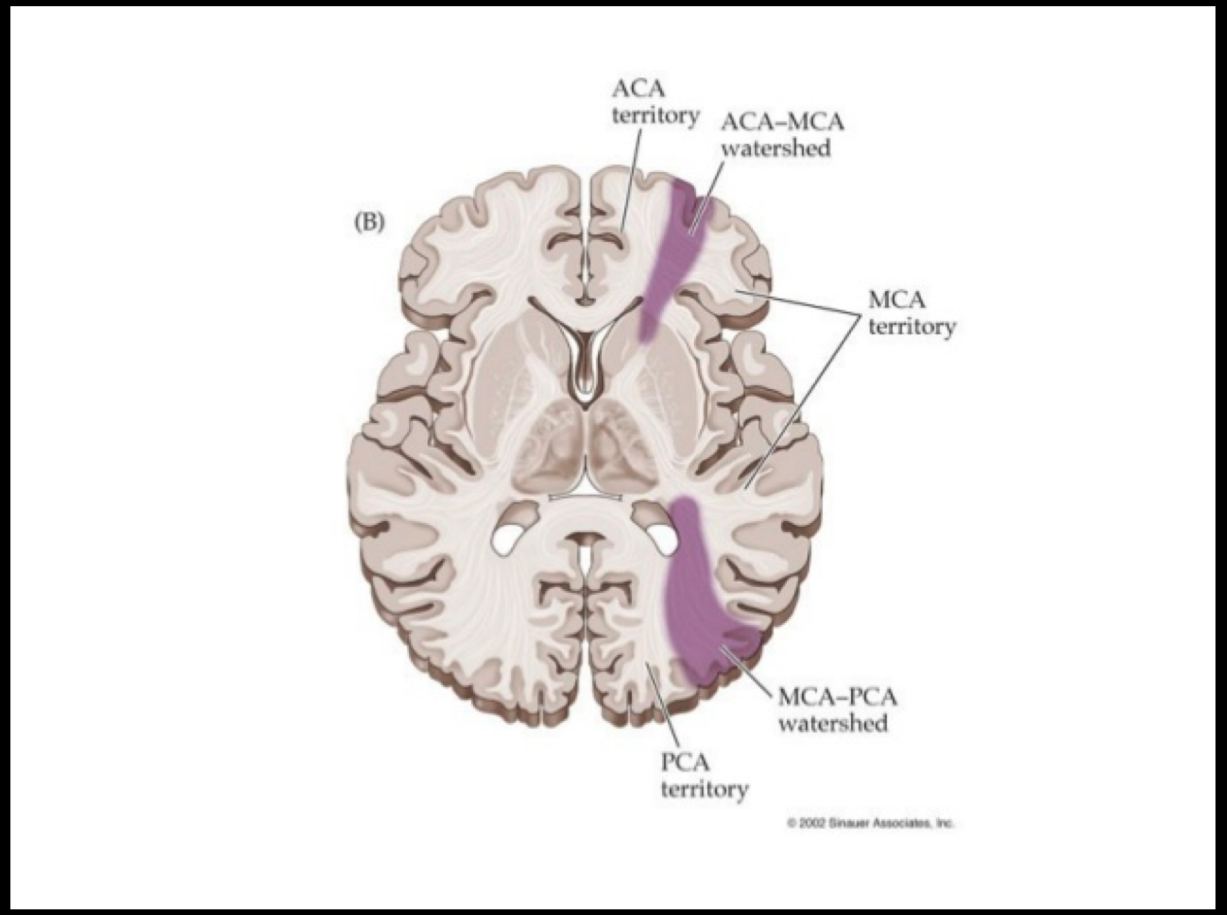
Case 3

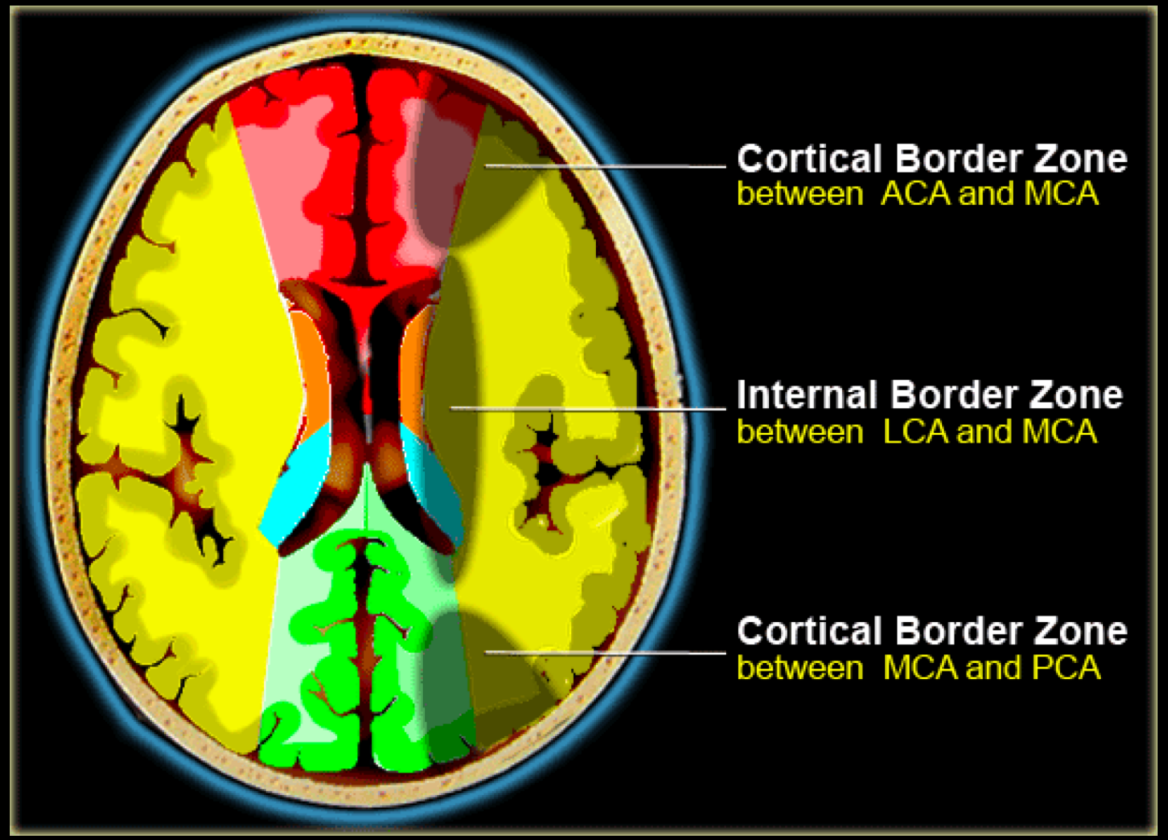
- A 64 year-old man with hypertension and atrial fibrillation abruptly developed a right hemiparesis affecting the face, arm and leg, accompanied by an expressive aphasia. Within 2 days, his language improved, but the hemiparesis remained.



Note the large hypodensity in the left basal ganglia and internal capsule. Although watershed infarcts are most often thought of as areas between two major blood vessels, there is a deep watershed area between the superficial cortical arteries and the deep penetrating arteries that are both terminal branches of the middle cerebral artery. Thus, a large, deep infarct of this size can be caused by large vessel disease of the middle cerebral artery (i.e., thrombosis or embolus) and not by disease of small penetrating arteries that result in lacunar strokes, which are much smaller




ACA
territory
ACA–MCA
watershed
(B)
MCA
territory
MCA–PCA
watershed
PCA
territory
© 2002 Sinauer Associates, Inc.


Cortical Border Zone
between ACA and MCA
Internal Border Zone
between LCA and MCA
Cortical Border Zone
between MCA and PCA

the end.