MUNI
MED

Pathophysiology of Central Nervous System

Brain pathophysiology

Stroke

Craniotrauma

Spinal cord pathophysiology

Intracranial Compatments, Intracranial Pressure and Cerebral Perfusion Pressure

Brain is enclosed in the skull…

… an advantage before trouble occurs…

… big problem after trouble occurs.

Intracranial compartments

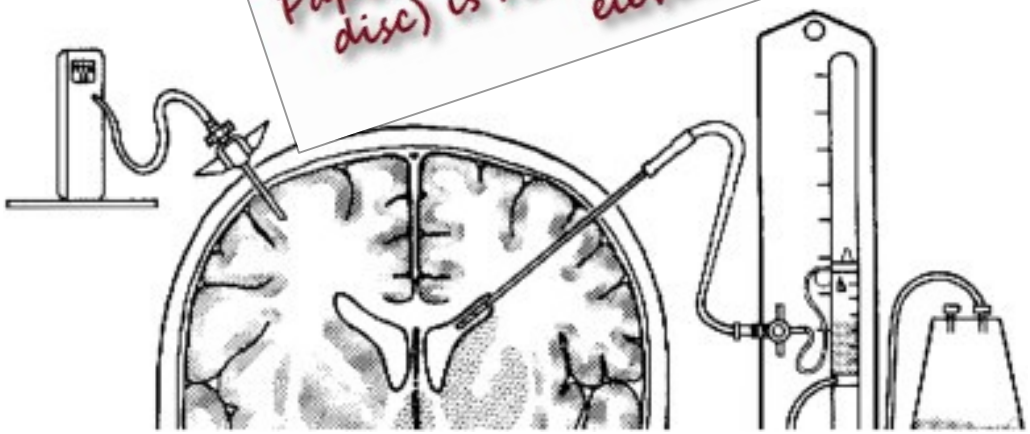
- Brain
- Cerebrospinal fluid (CSF)
- Blood

Intracranial pressure (ICP)

- **Pressure inside the skull**

Physiological values
ICP: 7 - 15 mmHg
CPP: 70 - 90 mmHg

Papilledema (swelling of the optic disc) is reliable sign that ICP is elevated



http://ars.els-cdn.com

Cerebral perfusion pressure

- The pressure gradient through which blood flows to the brain

$$\text{CPP} = \text{MAP} - \text{ICP}$$

Cerebral perfusion pressure

Mean arterial pressure

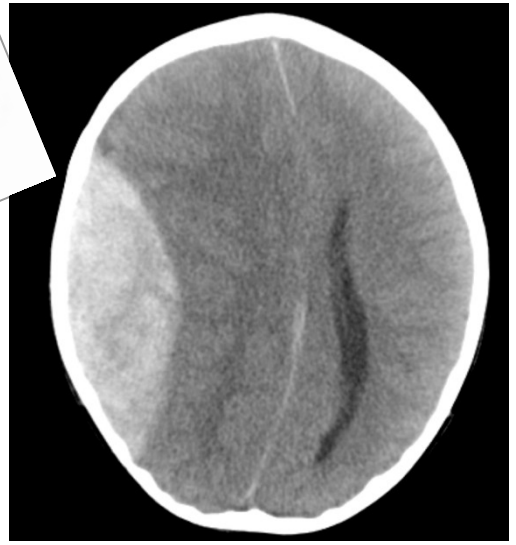
Intracranial pressure

Causes of Intracranial Hypertension

Brain compartment

- Edema
- Tumor
- Hemorrhage
- Infection

Dynamic of development is an important factor.

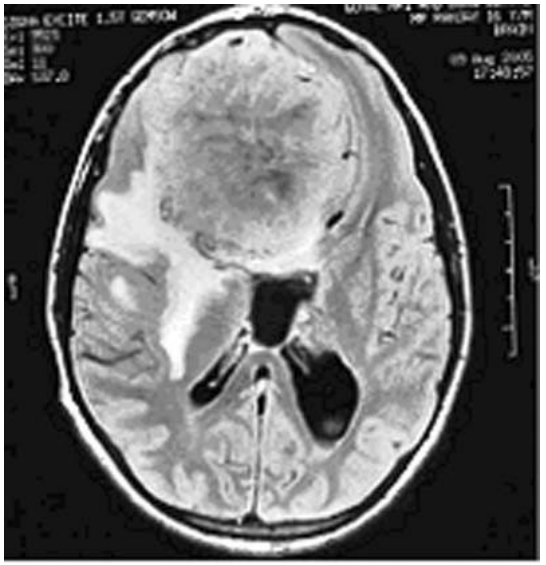


CSF compartment

- Hydrocephalus

Compartment of blood

- Venous sinus thrombosis
- Acidosis - ischemia



Lumbar puncture should not be performed if there is intracranial hypertension. Cerebral herniation may occur in such a case.

Causes of Intracranial Hypertension
Brain Edema

Cytotoxic (intracellular)

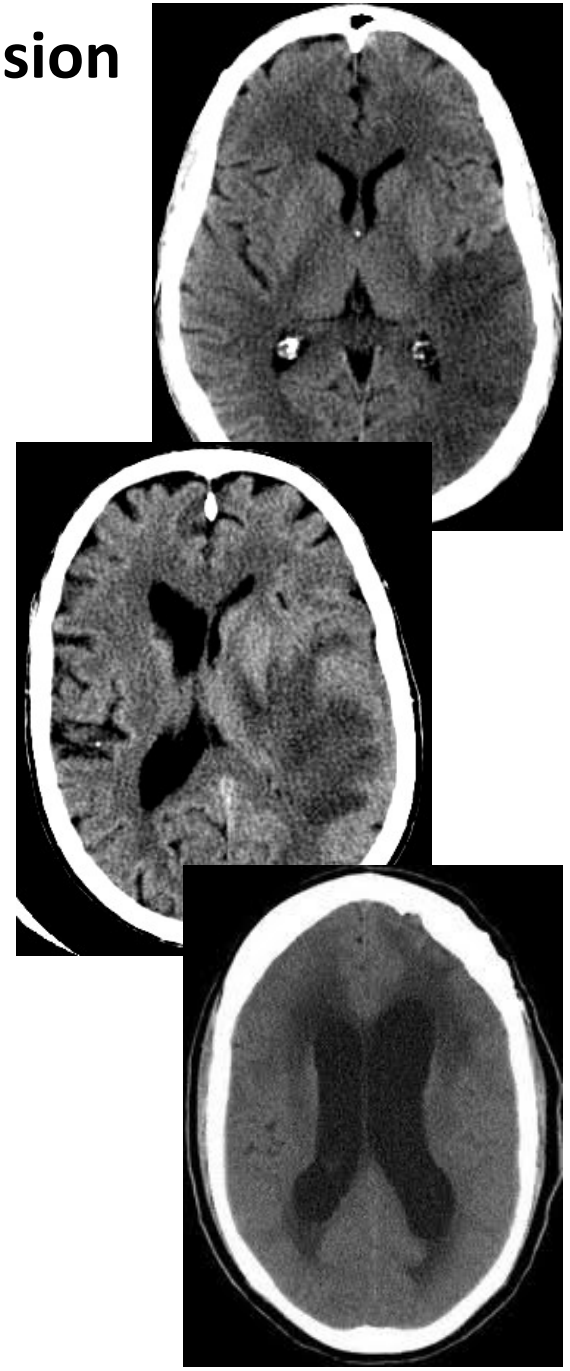
- Na/K ATPase failure
- Na or Ca influx
- H_2O
- Mainly occurs in first 24 h. following insult

Vazogenic (extracellular)

- Damage of endothelial cells and Blood – Brain barrier
- Extravasation of proteins and electrolytes into Interstitial space
- Mainly occurs at 24 h. after insult and later
- Neovascularization of tumor – imperfect vessels

Interstitial

- Obstruction of CSF circulation
- Mechanical damage of CSF- brain barrier
- Infiltration of CSF into intersticial space



Causes of Intracranial Hypertension
Hydrocephalus

Abnormal accumulation of CSF in liquor space

CSF production

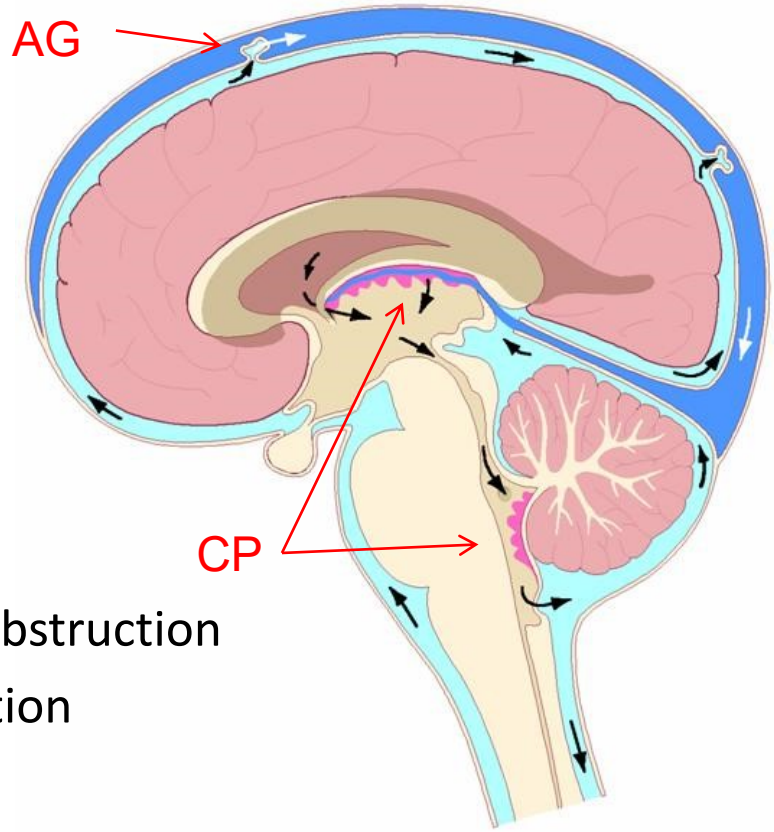
- Choroid plexus (CP)
- 450-750 ml/day

CSF resorption

- Archnoid granulations (AG)

Hydrocephalus

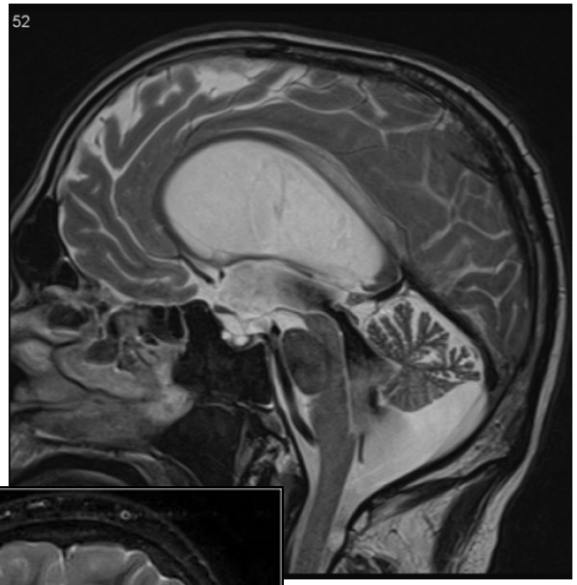
- Obstructive (Non- communicating)
  - ✓ Impaired CSF circulation due to obstruction
  - ✓ For example: ventricular obstruction
- Non – obstructive (Communicating)
  - ✓ Impaired CSF resorption

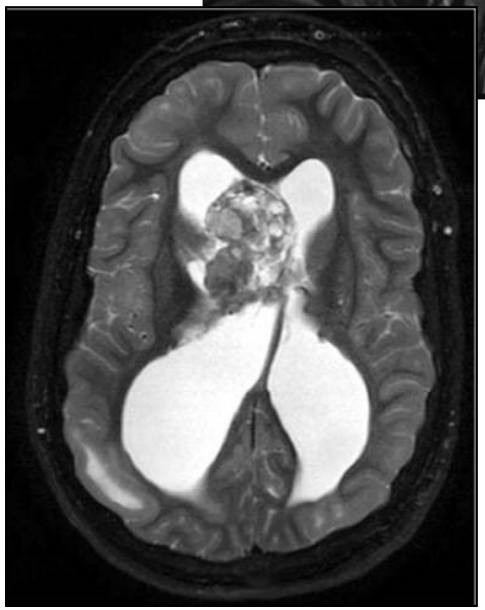


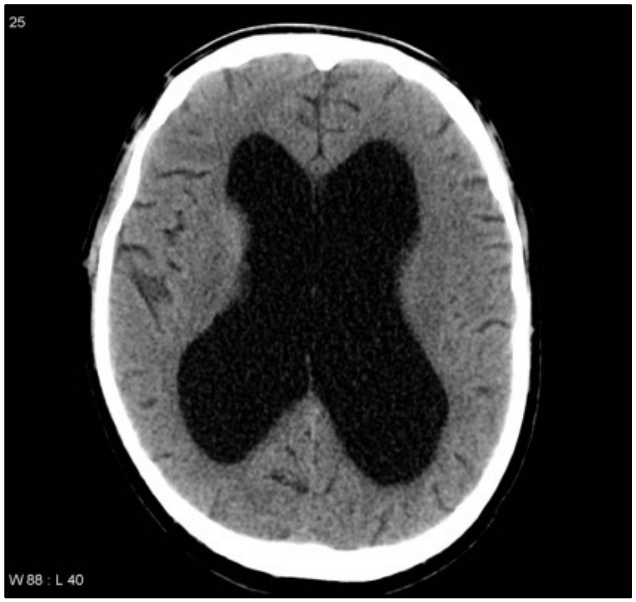
http://www.control.tfe.umu.se

Acute X Chronic

Causes of Intracranial Hypertension
Hydrocephalus







Consequences of Intracranial Hypertension

Compression

of adjacent tissue

- **Ischemization**

Infratentorial lesions

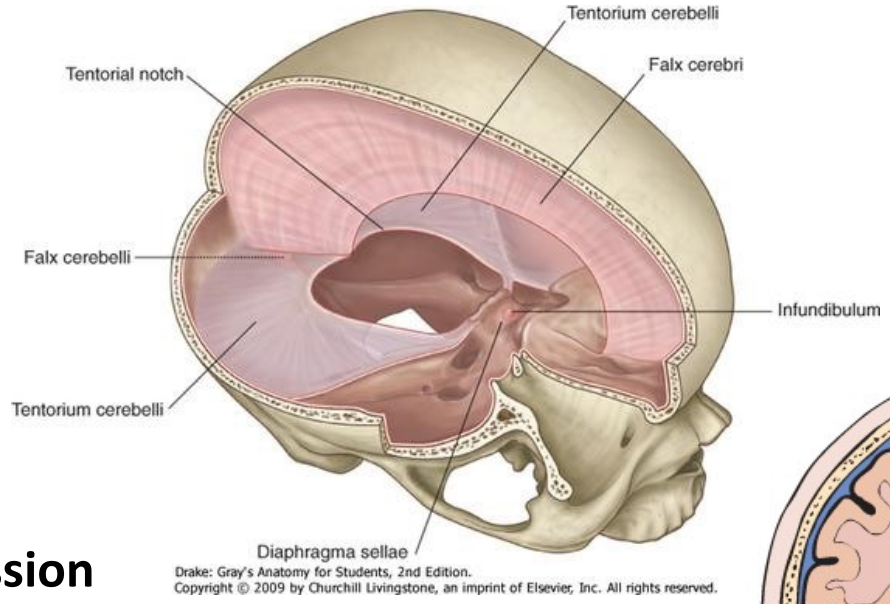
- Allvays acute
- **Risk of brain**
- **stem compression**

Cerebral herniation

- Subfalcine
- Transtentorial
- Tonsillar
- Central

✓ Permanent damage of brain

✓ Risk of brain stem compression



http://edutoolanatomy.wikispaces.com

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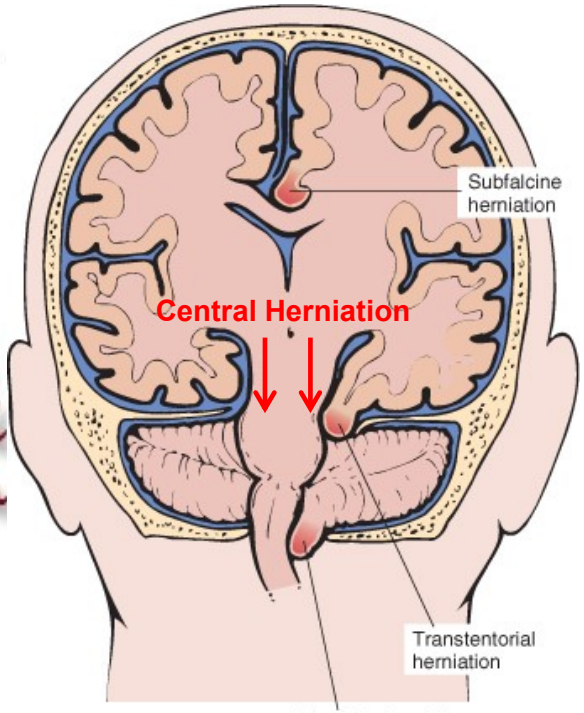
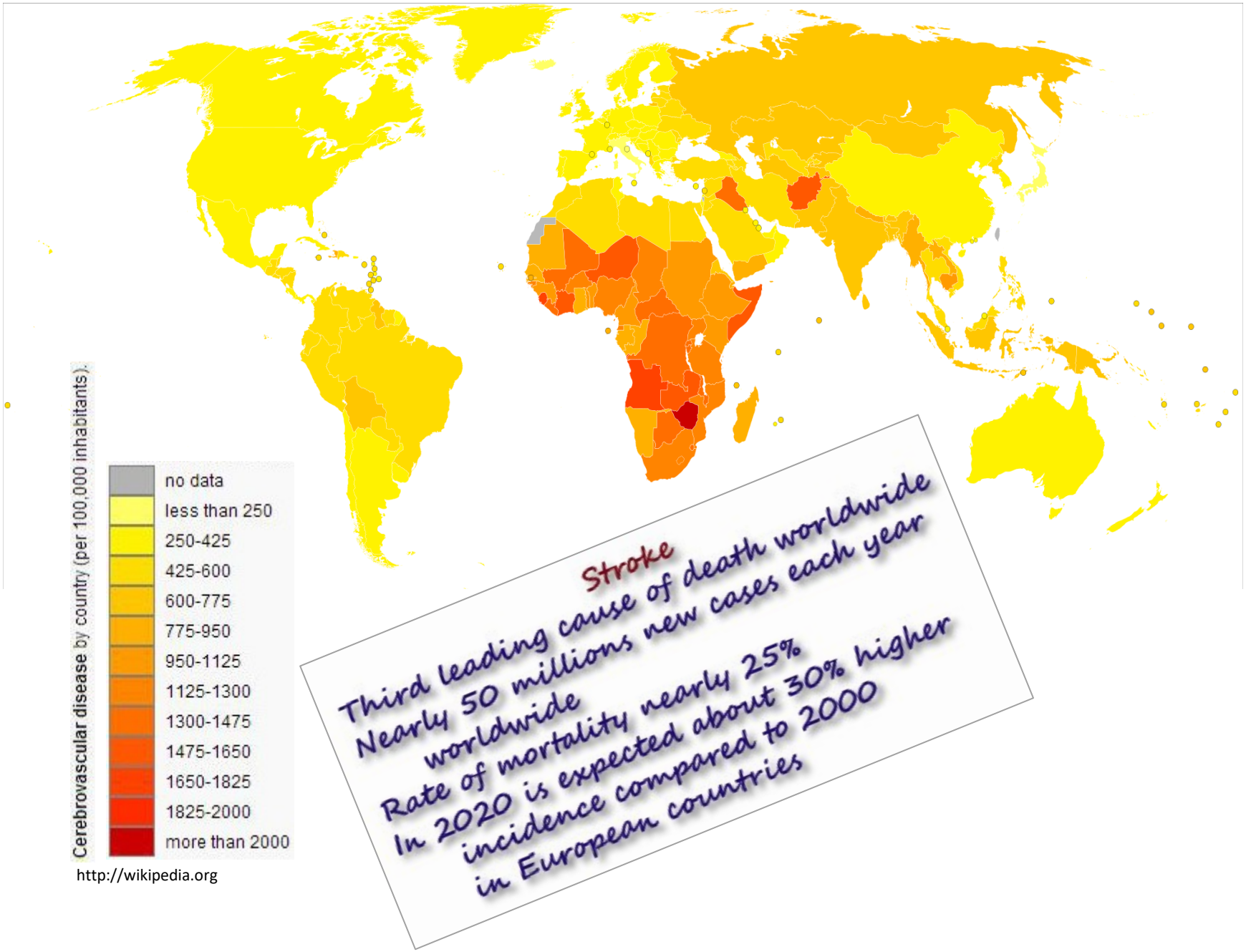


http://slideshare.net

Stroke



http://wikipedia.org

Stroke

Stroke is an acute neurological dysfunction due to vascular disturbance resulting in rapid loss of brain functions

Vascular pathologies

- Disturbance of vessel wall permeability
- Disturbance of vessel contractility
- Vessel occlusion
  - ✓ Thrombosis
  - ✓ Embolism
- Vessel rupture

Atherosclerosis

Types o f stroke

- Ischemic (70%)
- Hemorrhagic (30%)
  - ✓ Intracerebral hematoma
  - ✓ Subarachnoid hemorrhage

Ischemic Stroke

Critical parameters

- Extent of ischemia
- Duration of ischemia

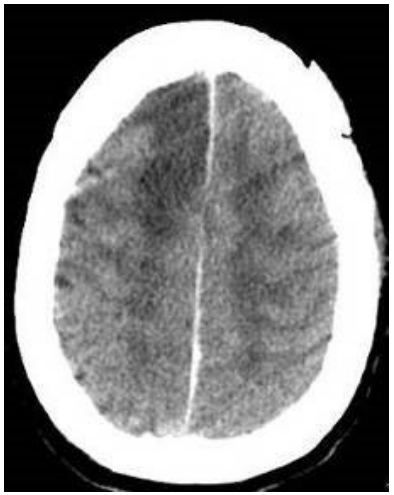
Atherosclerosis

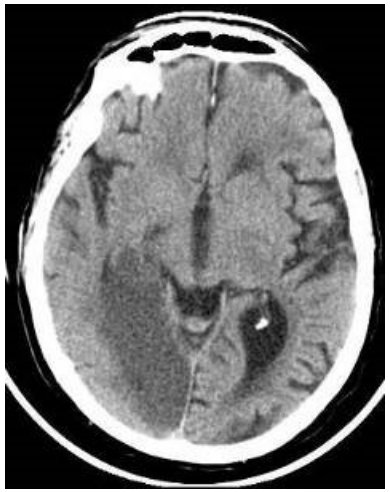
Focal ischemic stroke

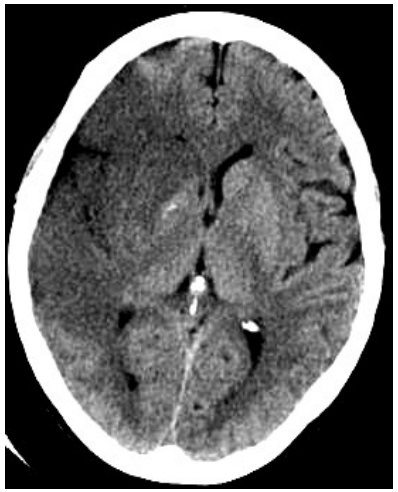
- ***Transient***
  - ✓ Transient ischemic attack (TIA)
  - ✓ Prolonged reversible neurological deficit
- ***Permanent***
  - ✓ Cerebral infarction
    - ❖ Embolism
    - ❖ Thrombosis

Global ischemic stroke

- ***Transient***
  - ✓ Syncope
- ***Permanent***
  - ✓ Hypoxic ischemic encephalopathy







Why is brain sensitive to ischemia?

http://assassinscreed.ubi.com

Tissue resistance to ischcemia
Brain: less than 5 min.
Liver and kidney: 15 - 20 min.
Sceletal muscle: 60 - 90 min.
Visceral muscle: 24 - 72 hours
Hair: several days

High metabolic activity

- Membrane potential maintaining – repolaristion (Na/K pumps)
- Almost exclusivelly oxidative phosphorylation
- Consumption
  - ✓ Oxygen- 20% of body consumption
  - ✓ Glucose – 25% of body consumption

Small amount of energy reserves

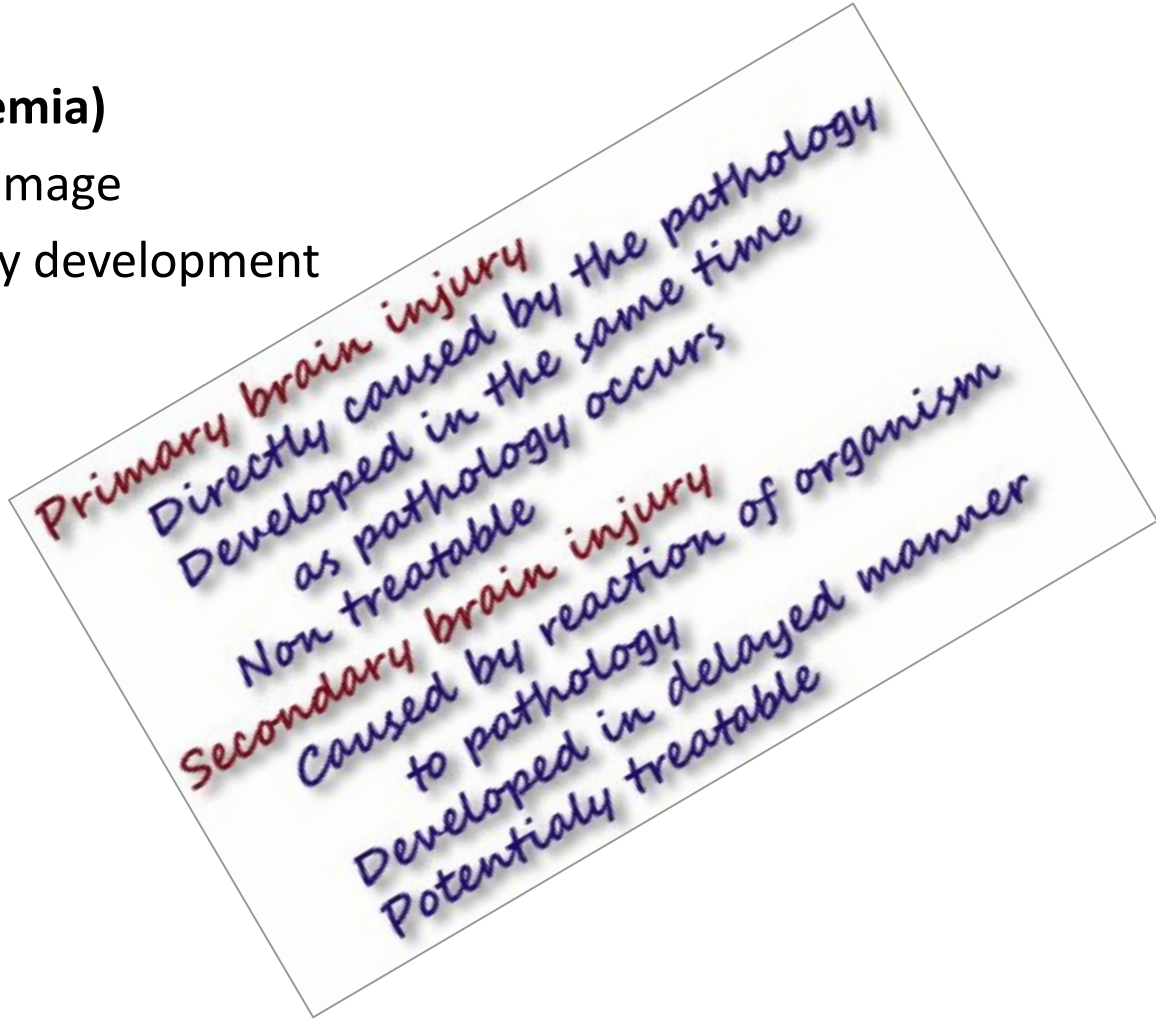
Ischemic Stroke

Core of infarction (centre of ischemia)

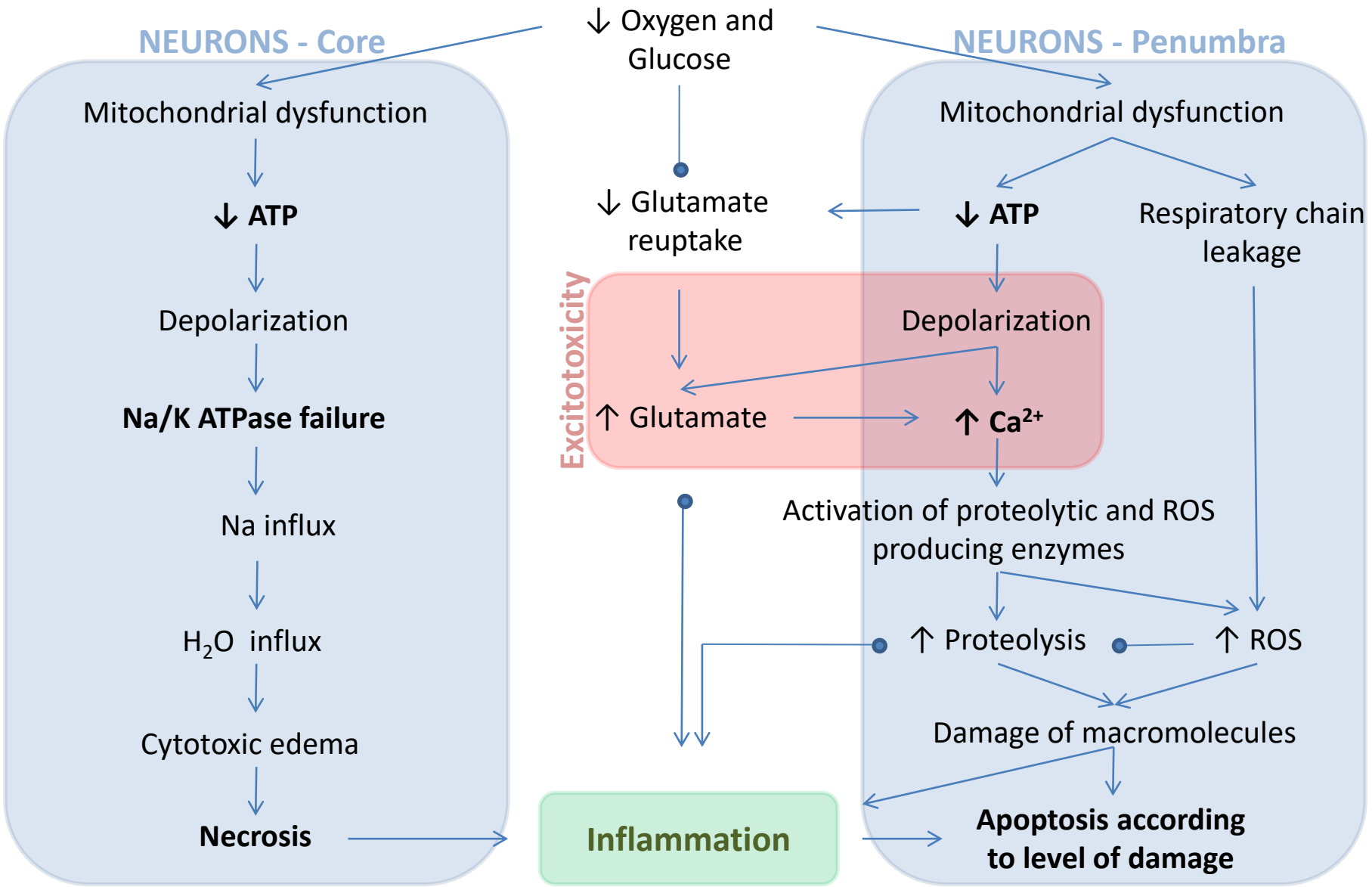
- Ireversible neuronal damage
- Primary injury

Penumbra (periphery of ischemia)

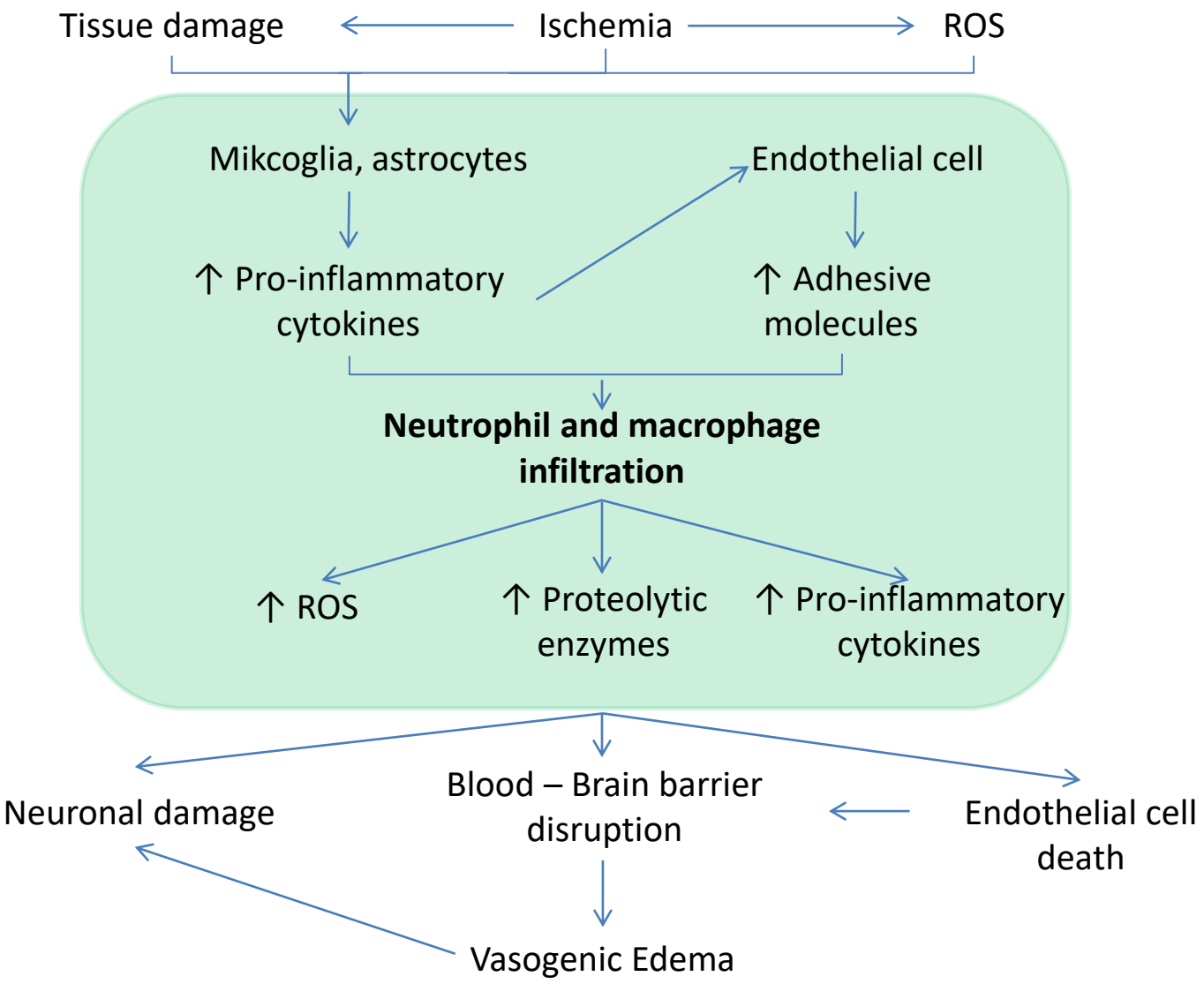
- Reversible neuronal damage
- Risk of secondary injury development



Ischemic Cascade



Role of Inflammation in Ischemic Cascade



Mechanisms of Ischemic Damage
Excitotoxicity

Accumulation of excitatory neurotransmiters in extracellular space

- Glutamate
- Aspartate

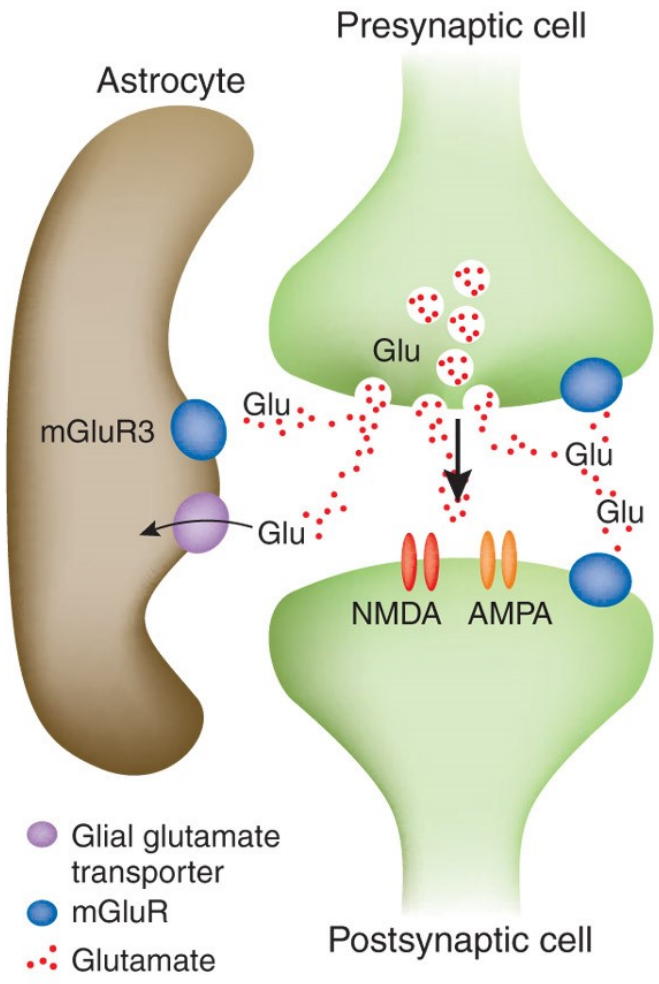
Neuronal dmage due to excessive stimulation

Cause

- Depolarization
- Decreased reupteke

Consequence

- Stimulation of adjacent neurons
- Ca overload
  - Proteolysis
  - Excessive ROS production
  - Cytotoxic edema



www.nature.com

Mechanisms of Ischemic Damage
Reactive oxygen species (ROS)

ROS are highly reactive particles

ROS are mainlu produced during reperfusion

Reactive oxygen species
Superoxide: $O_2^{\bullet -}$
Hydroxyl radlcal: $OH^{\bullet}$
Hydrogen peroxide: H_2O_2

Cause

- Intracellular
  - ✓ Respiratory chain leakage
    - ❖ Disruption of electron transport chains in mitochindria
  - ✓ Ca – overload – activation of ROS producing enzymes
- Extracellular
  - ✓ Inflammation

Consequence

- Lipid peroxidation – damage of membranes
- Protein oxidation – damage of enzymes and structural proteins
- Oxidation of purin a pyrimidine bases – damage of DNA
- Stimulation of inflammatory response

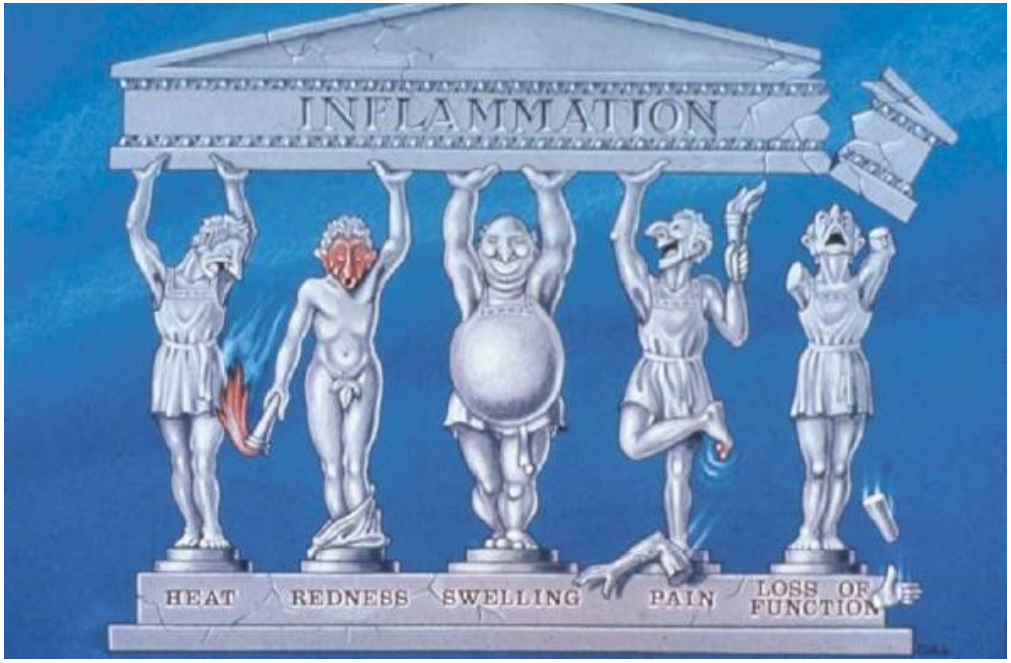
Mechanisms of Ischemic Damage
Inflammation

Cause

- Ischemia and tissue damage trigger production of
  - ✓ Pro – inflammatory cytokines – activation of leukocytes in periphery
  - ✓ Adhessive molecules – attraction of leukocytes to dmaaged area
- Infiltrating leukocytes produce
  - ✓ Proteolytic enzymes –
  - ✓ Pro – infl. Cytokines
  - ✓ ROS

Consequence

- Damage of
  - ✓ Endothelial cells
  - ✓ Blood – Brain barrier
  - ✓ Neuronal cells



http://3.bp.blogspot.com

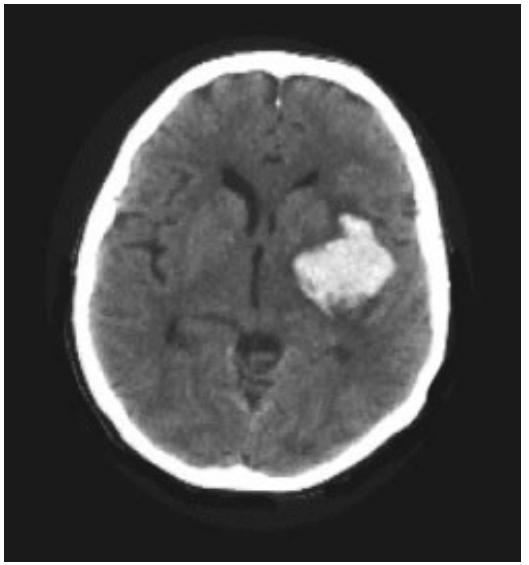
Hemorrhagic Stroke
Intracerebral hematoma (ICH)

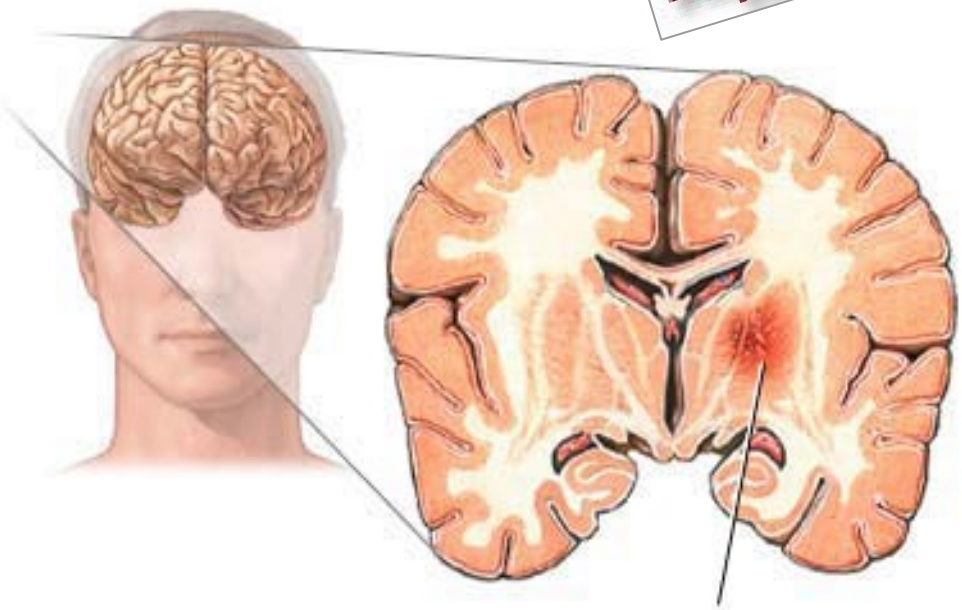
Bleeding into the brain parenchyma (intraaxial)

The most often localization

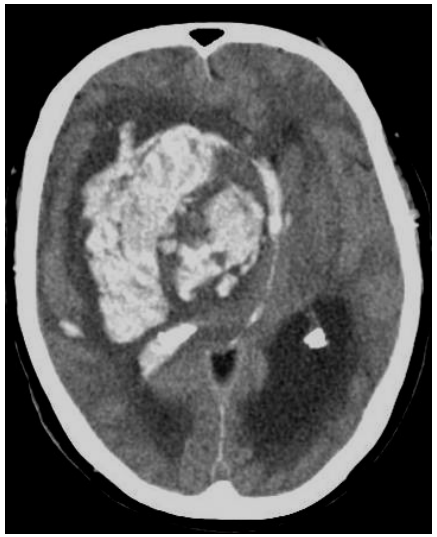
- Basal ganglia
- Thalamus

Arterial hypertension

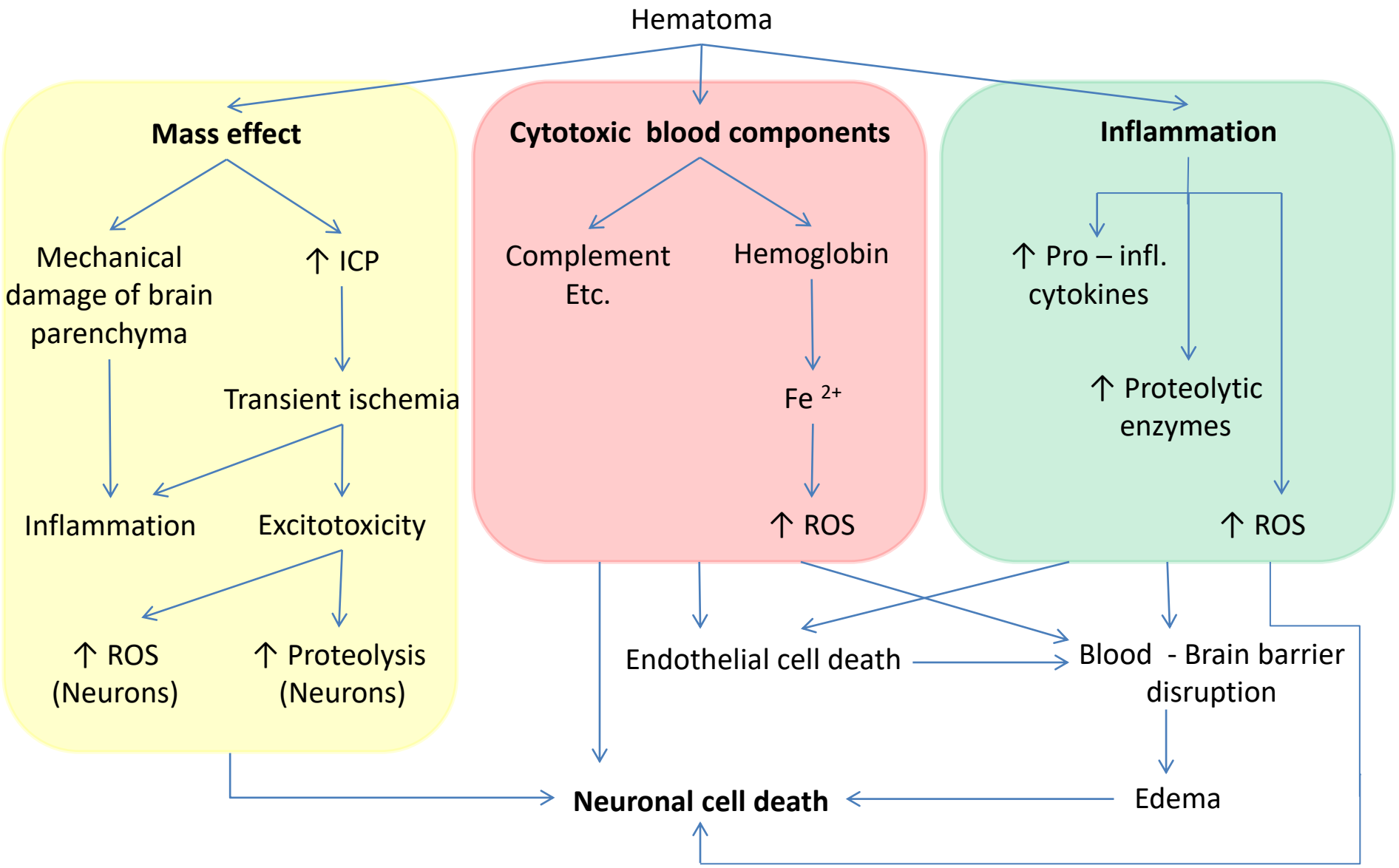




http://umm.edu



Pathophysiology of ICH

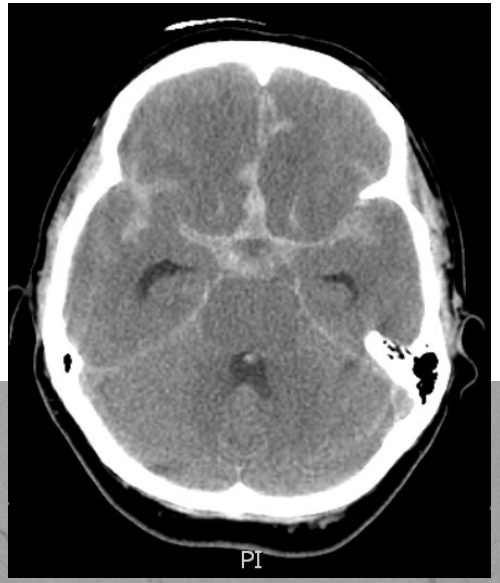


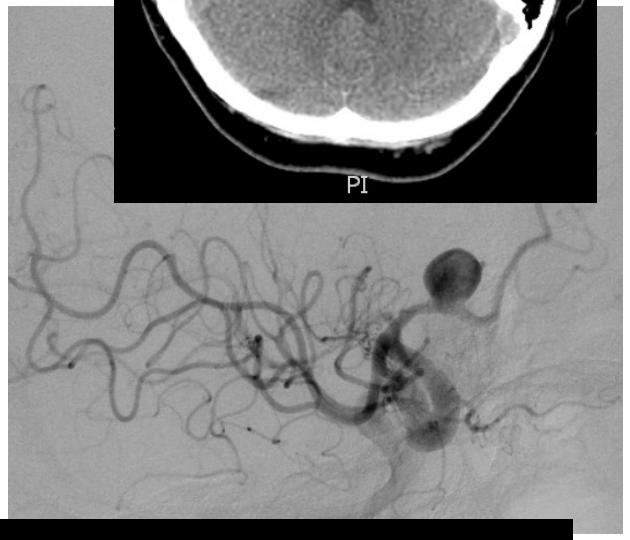
Hemorrhagic Stroke
Subarachnoid Hemorrhage (SAH)

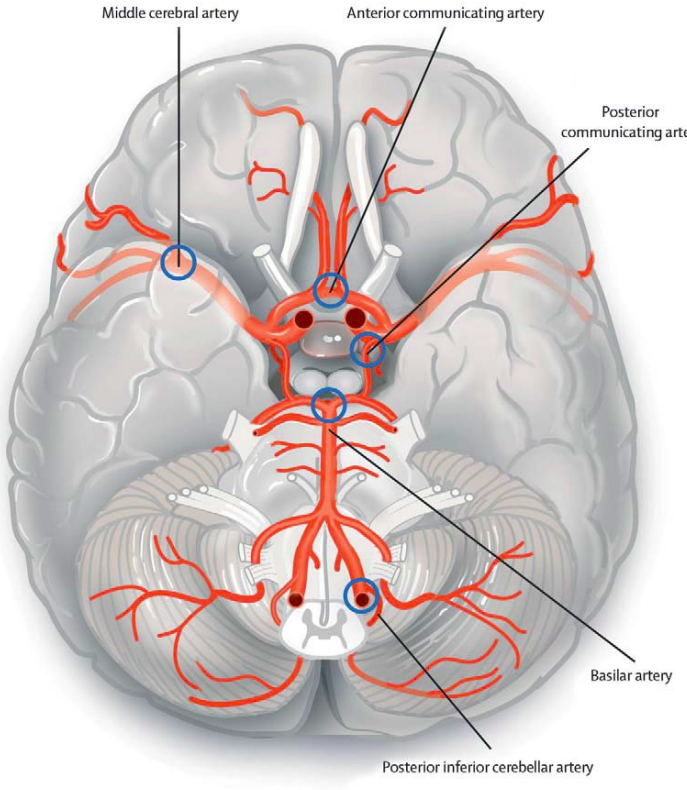
Bleeding into the subarachnoid space (extraaxial)

The most often cause – cerebral aneurysm rupture

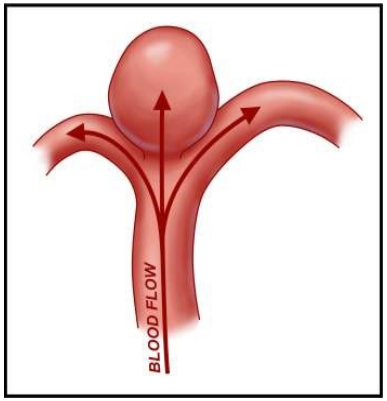
The most often localiztion of aneurysm - Willis circle







van Gijn J, Rinkel GJ. Subarachnoid haemorrhage: diagnosis, causes and management. *Brain.*2001;124:249–278.



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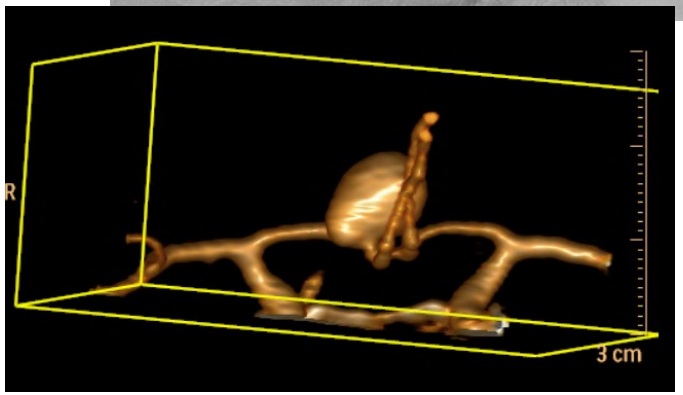
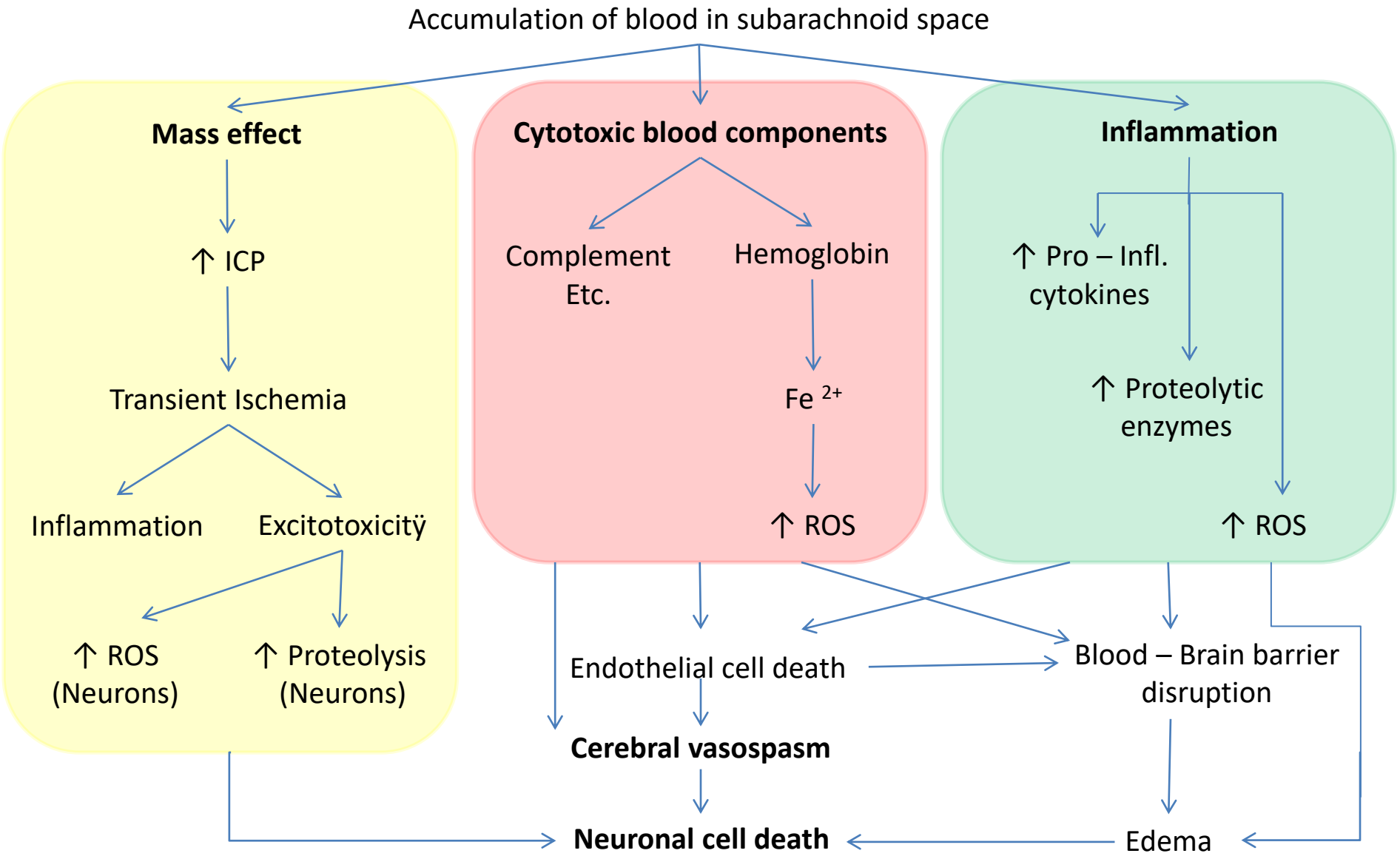


Pathophysiology of SAH



Traumatic Brain Injury

Traumatic Brain Injury
Introduction

Traumatic brain injury
150 cases/ 100 000 persons
The most often cause of death among
people up to 45 years

The most often causes

- Traffic accidents
- Falls
- Sport injuries

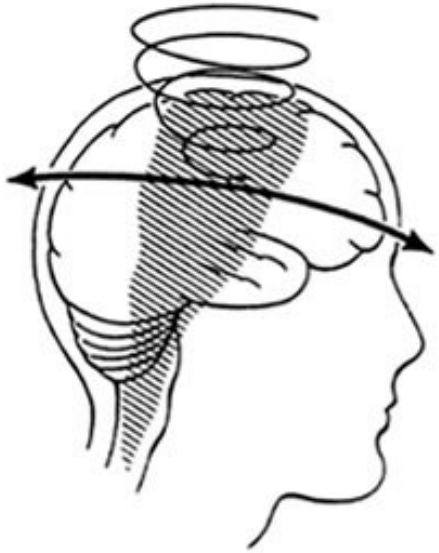
Classificarion

- Primary
  - ✓ Results from trauma…
- Sekundární
  - ✓ Results from reactions initiated by trauma

- Focal
- Difuse

http://www.seattlecaraccidentlawyerblog.com

Diffuse Brain Injury



Diffuse axonal injury

- Structural damage of axons (white matter)
- Acceleration – deceleration, rotational forces
- No macroscopically detectable pathology
- Microscopicly detectable axonal swelling
- Wallerian degeneration develops later
  - ✓ Degeneration of axon distally to injury
  - ✓ No axonal regeneration inCNS

Concussion

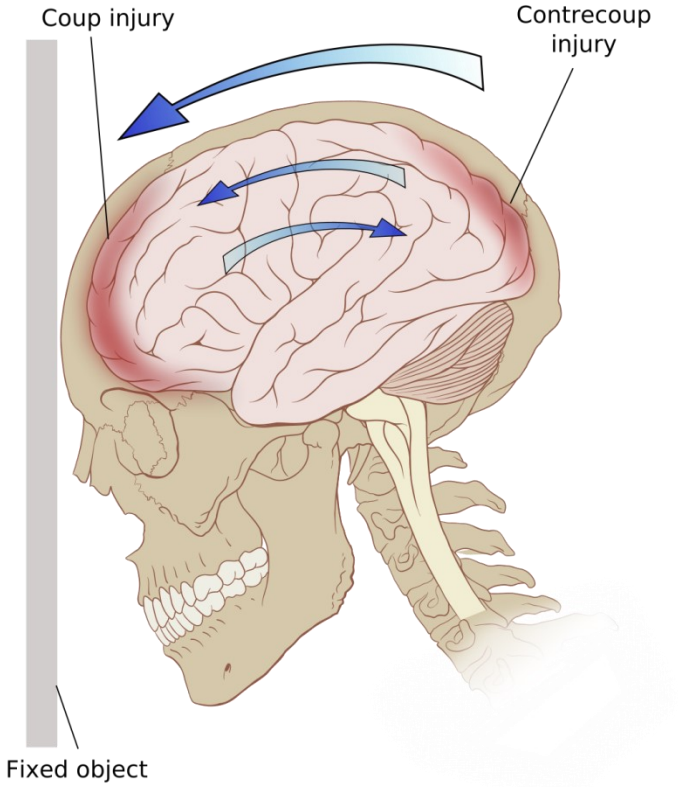
- The mildest grade of diffuse axonal injury
- No structural tissue damage
- Transient functional damage (loss of consciousness not longer than 10 minutes)

http://www.givengain.com

Primary Brain Injury

Mechanism of production

- ***Contact injury***
  - ✓ Head hits the object or head is hited by the object
  - ✓ Risk skull fracture
    - ❖ Impressive – small objects
    - ❖ Linear – big objects
  - ✓ Gunshot injury
- ➢ Par coup injury
  - ✓ Contusion close to impact site
- ➢ Par contre coup
  - Contusion opposite to impact site
- ***Noncontact injury***
  - Acceleration – deceleration injury



http://www.yalescientific.org

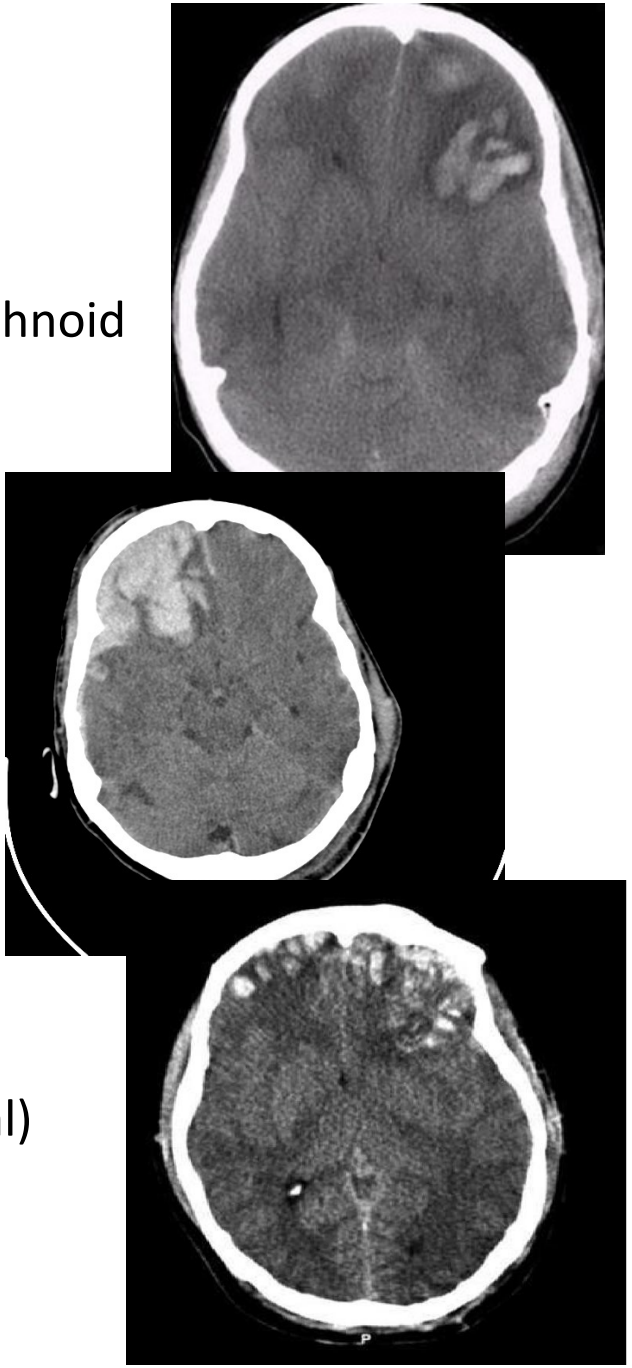
Focal injury

Contusion

- Mechanical damage of brain tissue, pia – arachnoid membranes not damaged
- Smoot transition between contusion and ICH
- The most often localizations
  - ✓ Frontal lobe
  - ✓ Temporal lobe

Laceration

- The most severe grade of contusion
- Mechanical damage of both brain tissue and pia-arachnoid membranes
- Contusion + traumatic subarachnoid (subdural) hemorrhage



Secondary Brain Injury

Edema

- Cytotoxic
- Vasogenic

Ischemia

Brain swelling

- Causes
  - ✓ Acidosis - vasodilatation
  - ✓ Diffuse microvascular injury
    - ➢ Vascular autoregulation failure
  - ✓ Damage brain areas responsible for vasoregulation
    - ➢ Thalamus, brain stem
    - ➢ Vasoparalysis

Secondary injury results in ICP increase

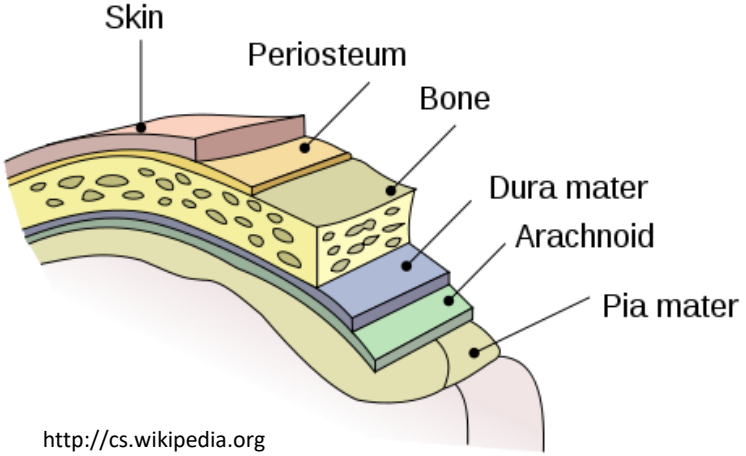
Traumatic Hematomas

Intraaxial

- Intracerebral

Extraaxial

- Epidural
- Subdural
- Subarachnoid



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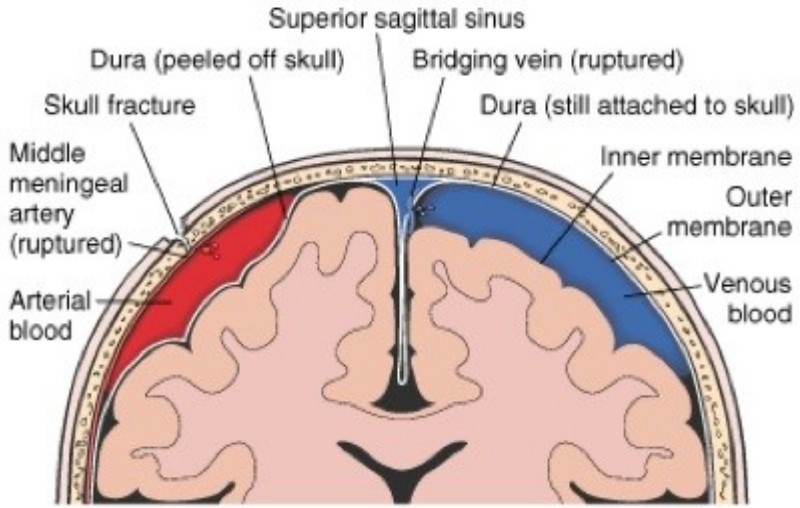
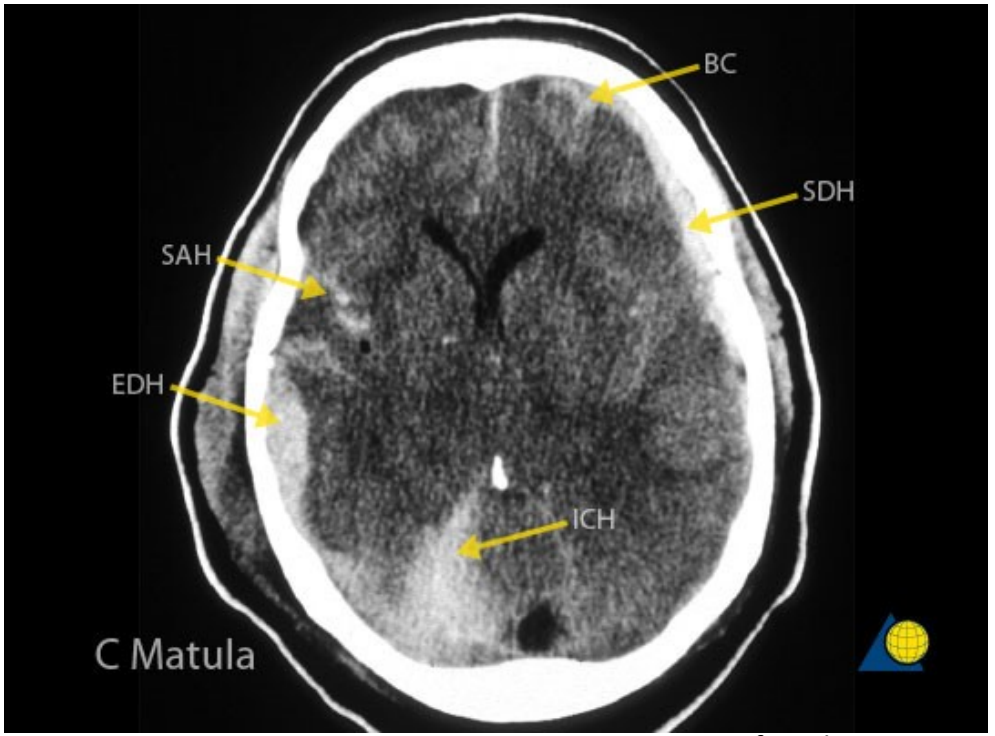


A. Epidural hematoma B. Subdural hematoma



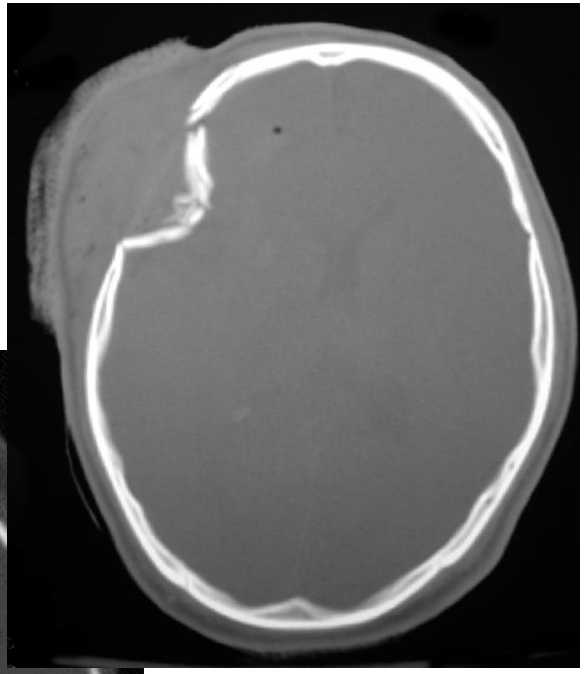
www2.aofoundation.org

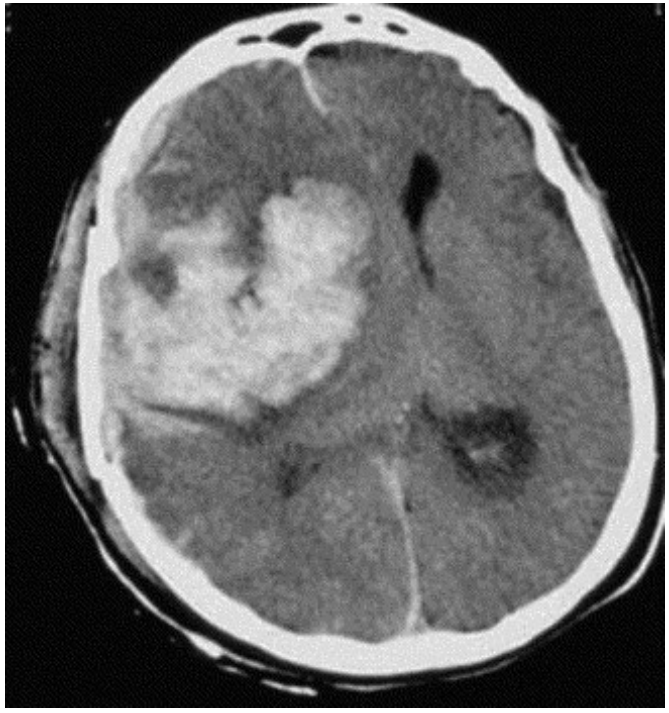
Intracerebral Hemorrhage

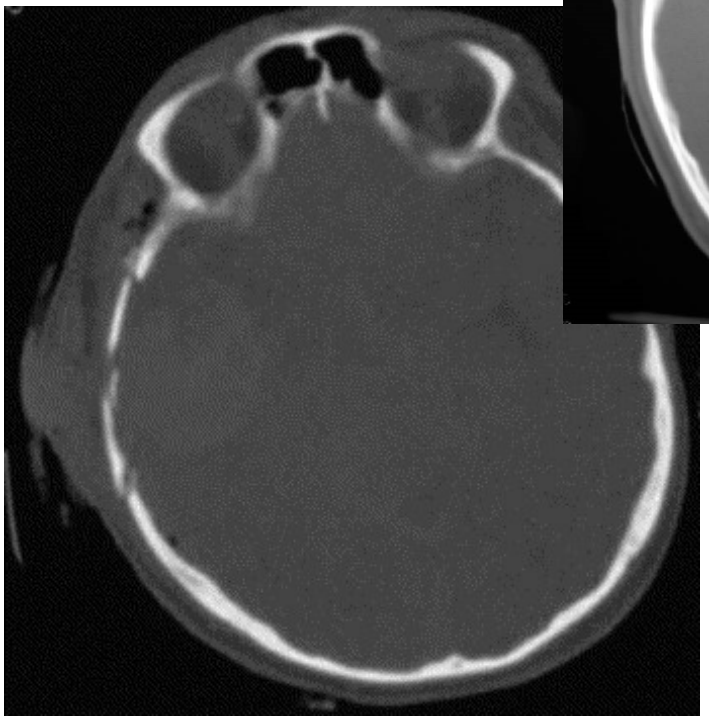
- Smoot transition between contusion and ICH according to sverity of injury

The most often localization

- Temporal lobe
- Frontal lobe





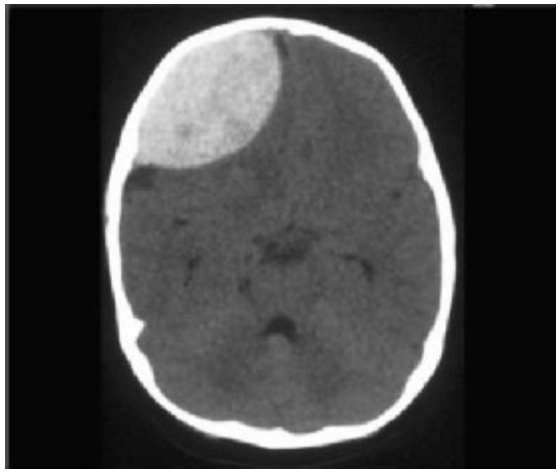


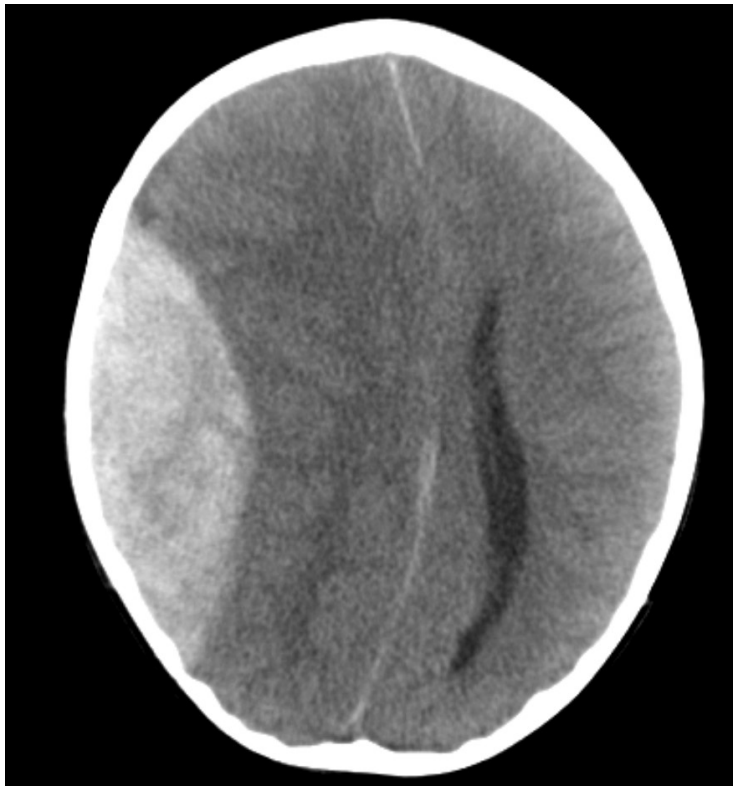
Epidural Hematoma

- Blood collection between the skull and dura mater
- The most often cause is skull fracture, which leads to damage of meningeal artery (contact injury)
- Separation of dura from the skull – convex shape

The most often localization

- Temporo - basal
- Temporo - parietal



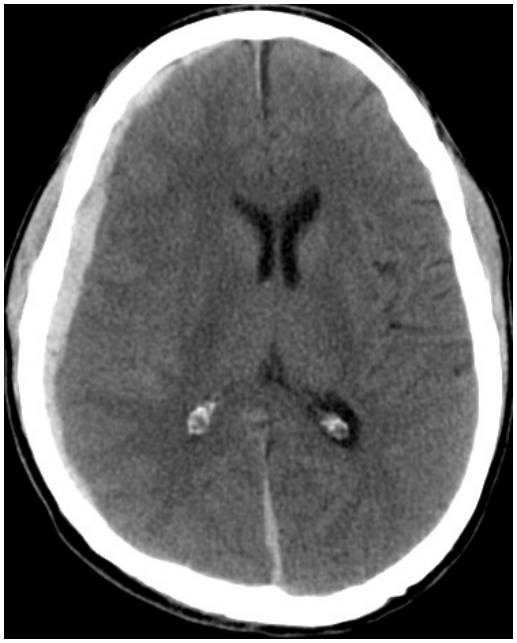


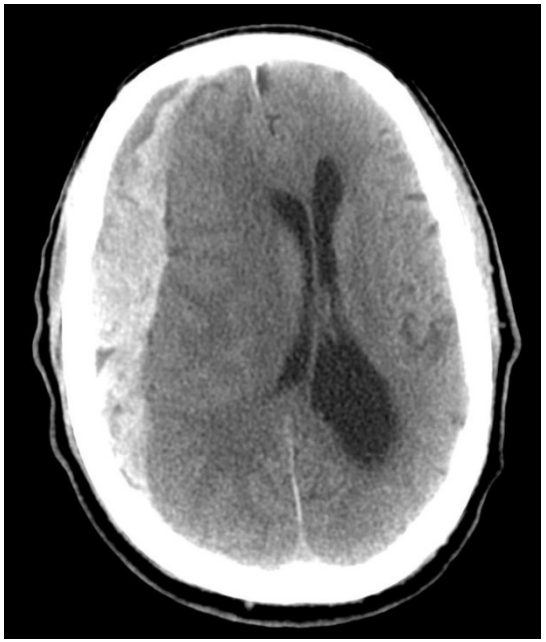
Subdural Hematoma

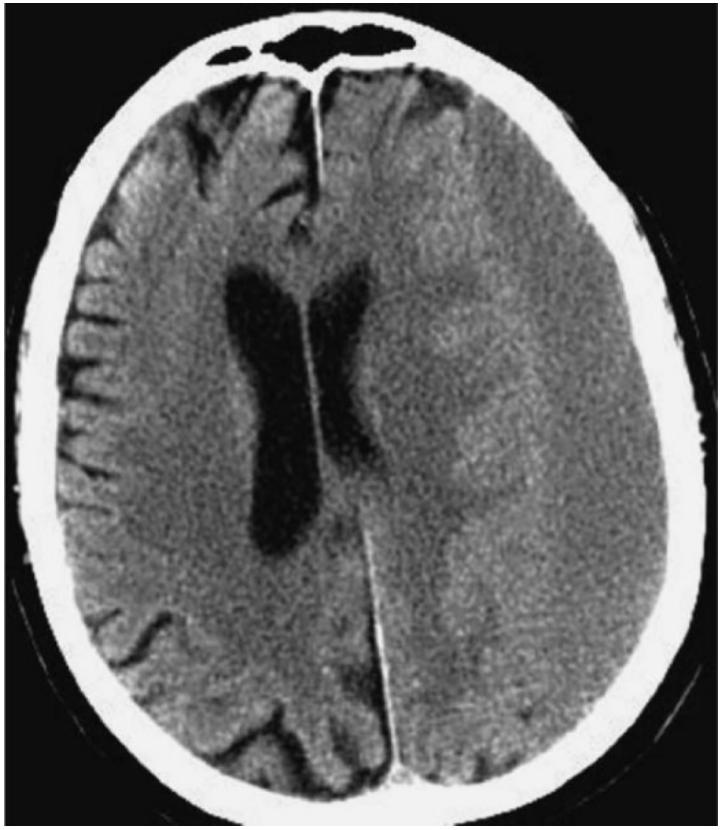
- Blood collection between dura mater and arachnoidea
- The most often results from tears in briding veins which cross subdural space (acceleration – deceleration injury)

Acute – fresh blood

Chronic – colliquated blood

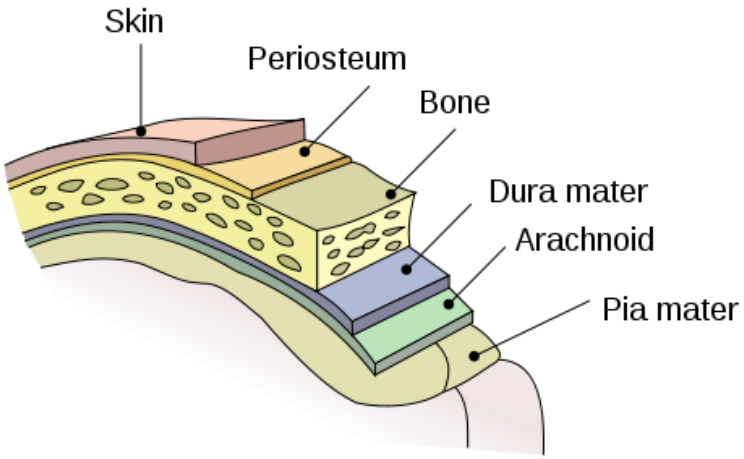




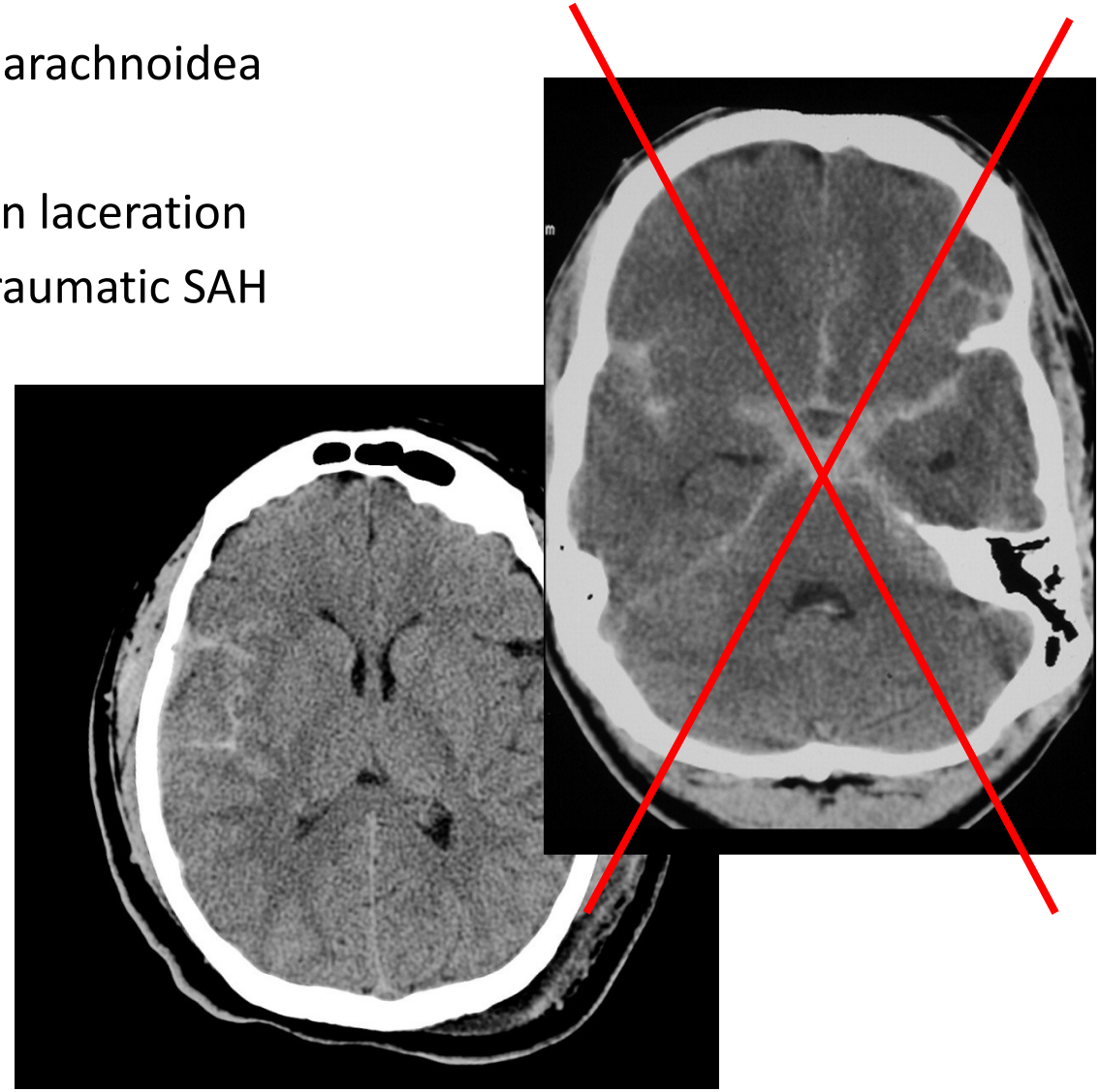


Traumatic Subarachnoid Hemorrhage

- Blood collection between arachnoidea and pia mater
- Often associates with brain laceration
- No vasospasm occurs in traumatic SAH



http://cs.wikipedia.org



Consequences of Brain Injury

- **Impairment of consciousness**
- **Cognitive impairment (including executive functions)**
- **Focal neurological deficit**

Impairment of Consciousness

Qualitative

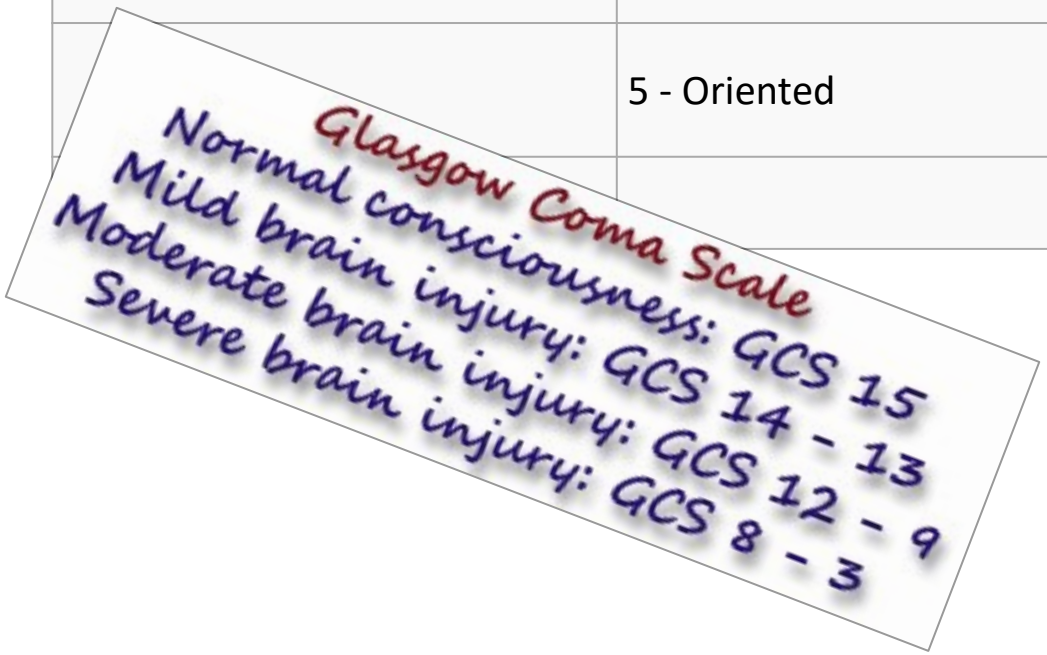
- Normal vigility, impairment of content
- Disorientation

Quantitative

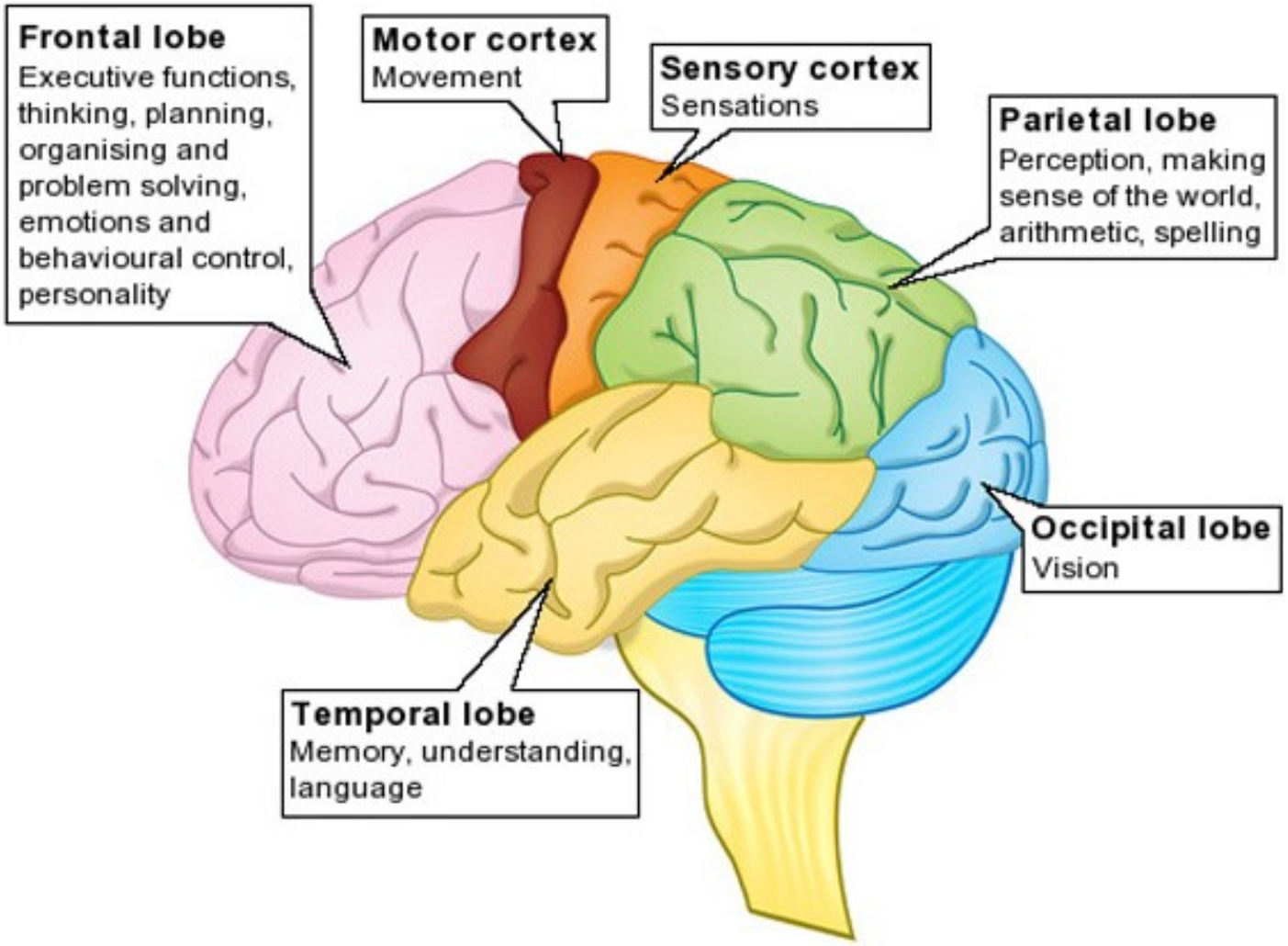
- Impairment od vigility
- ***Somnolence*** – state of near-sleep, responsivnes
- ***Stupor*** – responsivness only to base stimuli (pain)
- ***Coma*** - unresponsivness

Glasgow Coma Scale

Best eye opening	Best verbal	Best motor
1 - None	1 - None	1 - None
2 – To pain	2 - Incomprehensible	2 – Extensor (decerebrate)
3 – To speech	3 - Inappropriate	3 – Flexion (decorticate)
4 - Spontaneous	4 - Confused	4 – Withdraws to pain
	5 - Oriented	5 – Localizes pain
		6 - Obeys

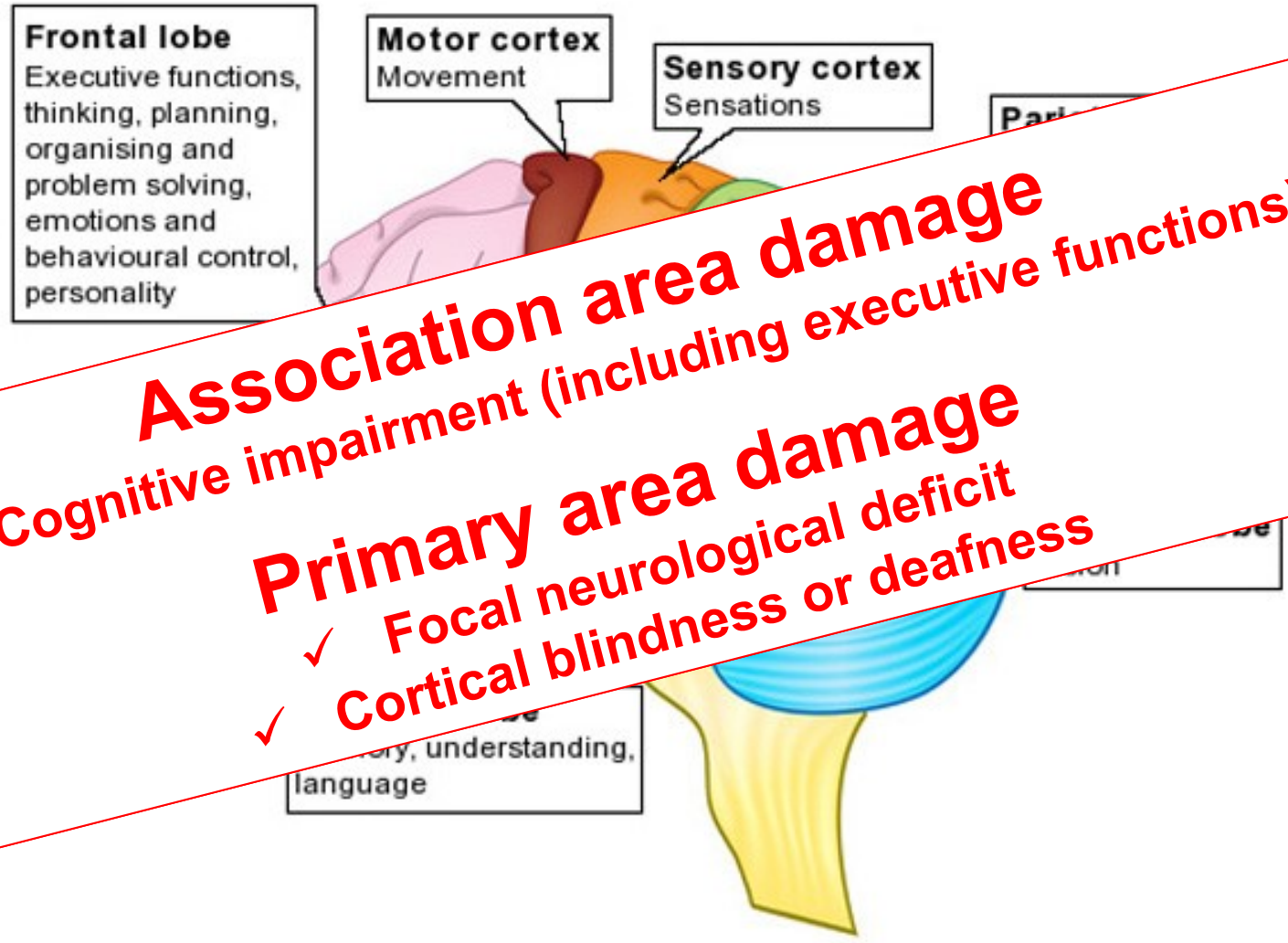


Cognitive Impairment and Focal Neurological Deficit



http://www.modernfamilyideas.com

Cognitive impairment and Focal Neurological Deficit



Association area damage

✓ **Cognitive impairment (including executive functions)**

Primary area damage

✓ **Focal neurological deficit**

✓ **Cortical blindness or deafness**

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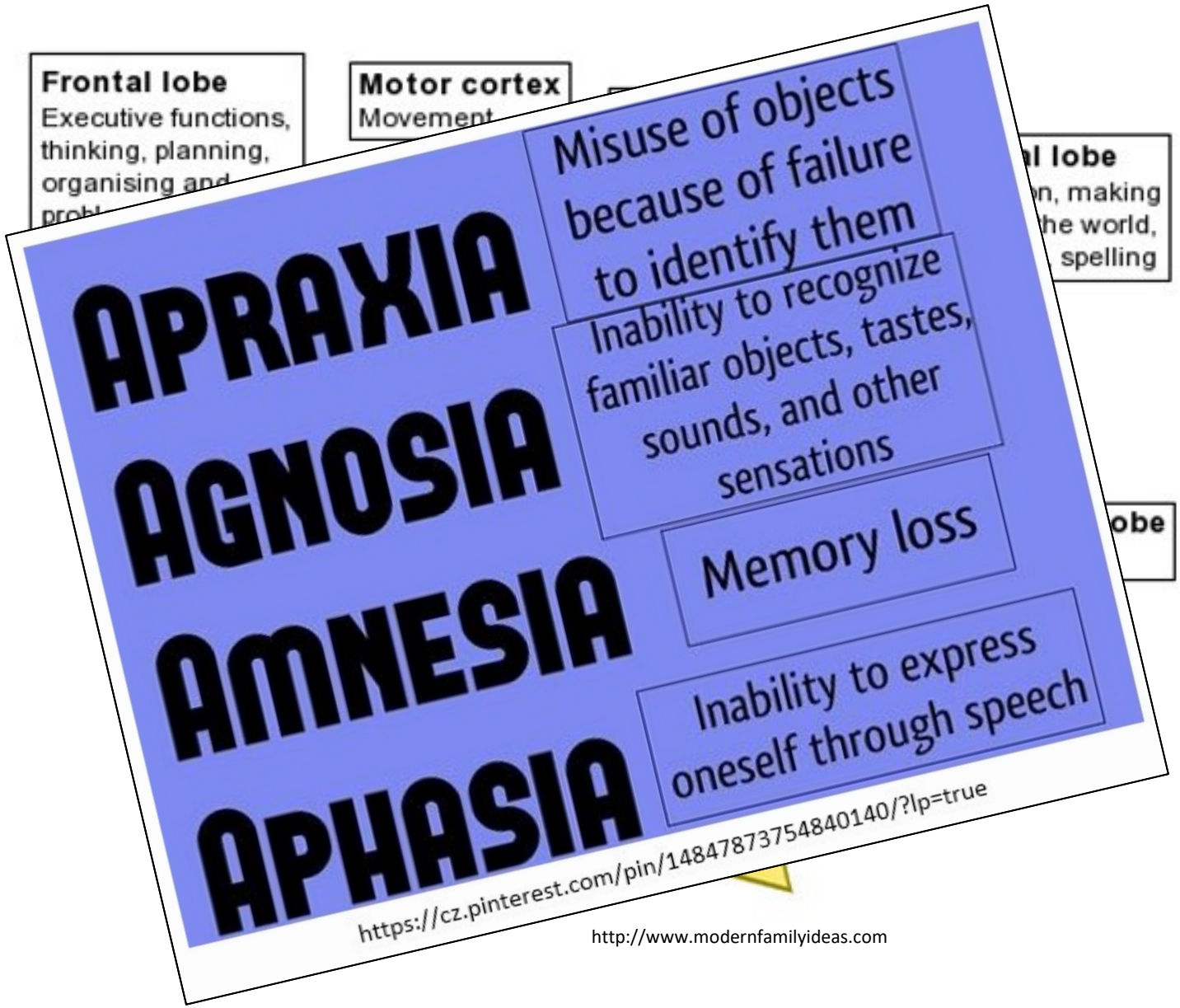
„Dementia“ and Focal Neurological Deficit



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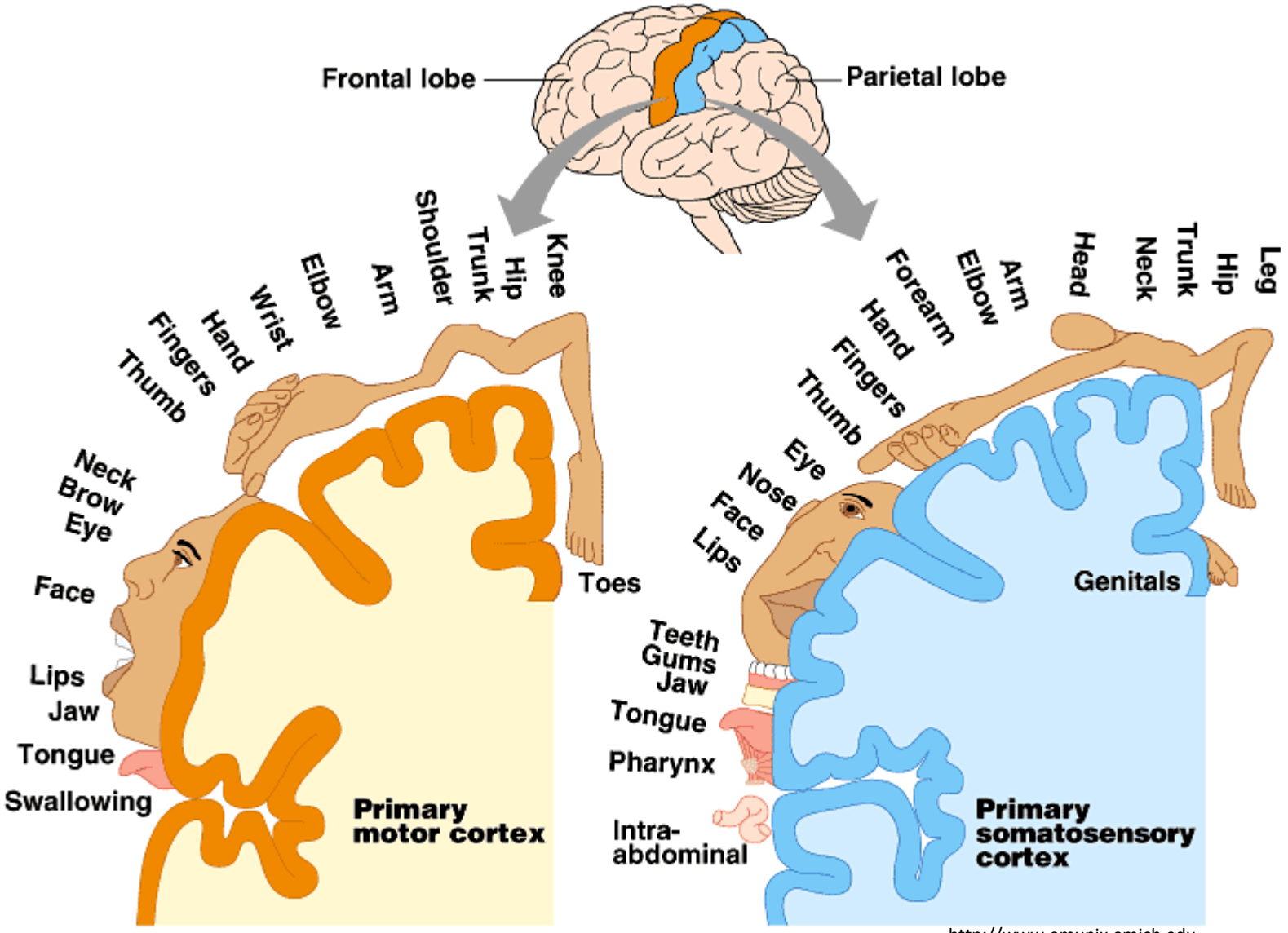
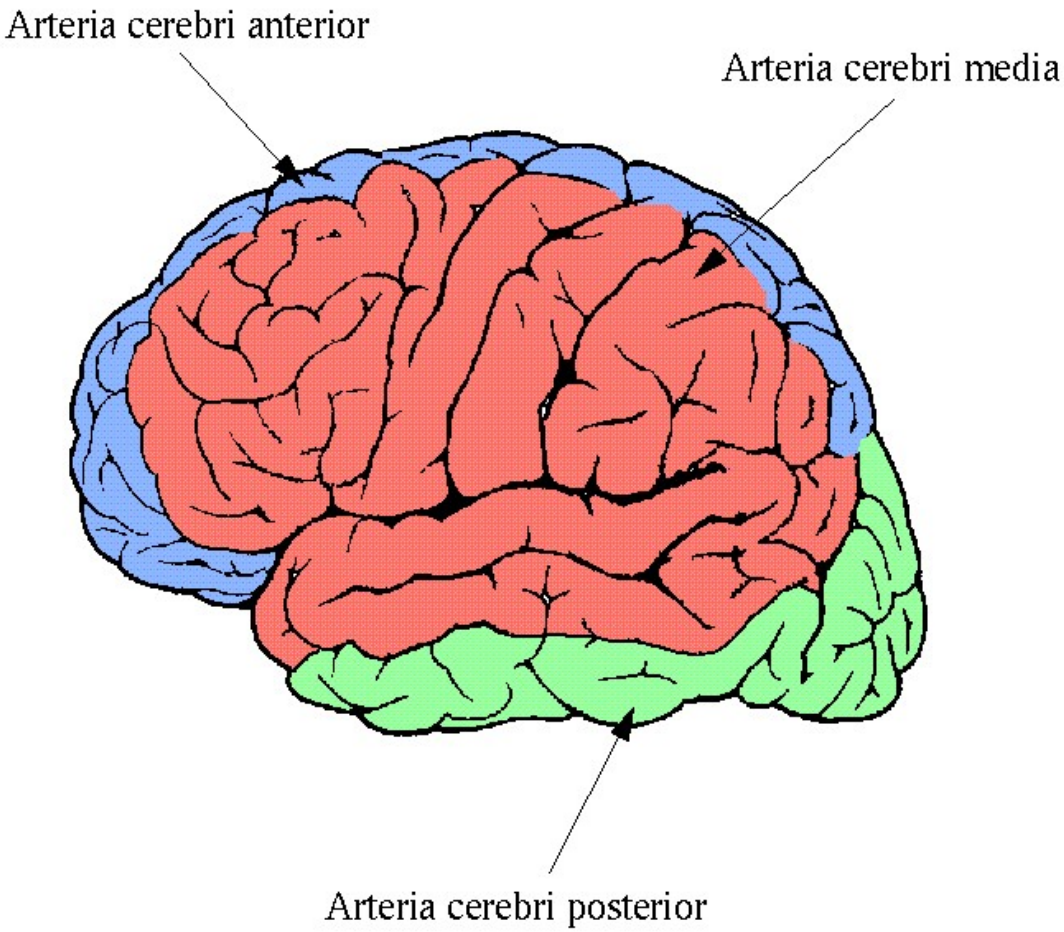
Focal Neurological Deficit



http://www.emunix.emich.edu

Focal Neurological Deficit



http://www.ims.uni-stuttgart.de

Focal Neurological Deficit
Examples of Ishcemia

Arteria cerebri anterior

- ✓ Contralateral hemiparesis accentes on lower limb (FL)
- ✓ Behavioral impairment- billateral oclusion (FL)

Arteria cerebri media

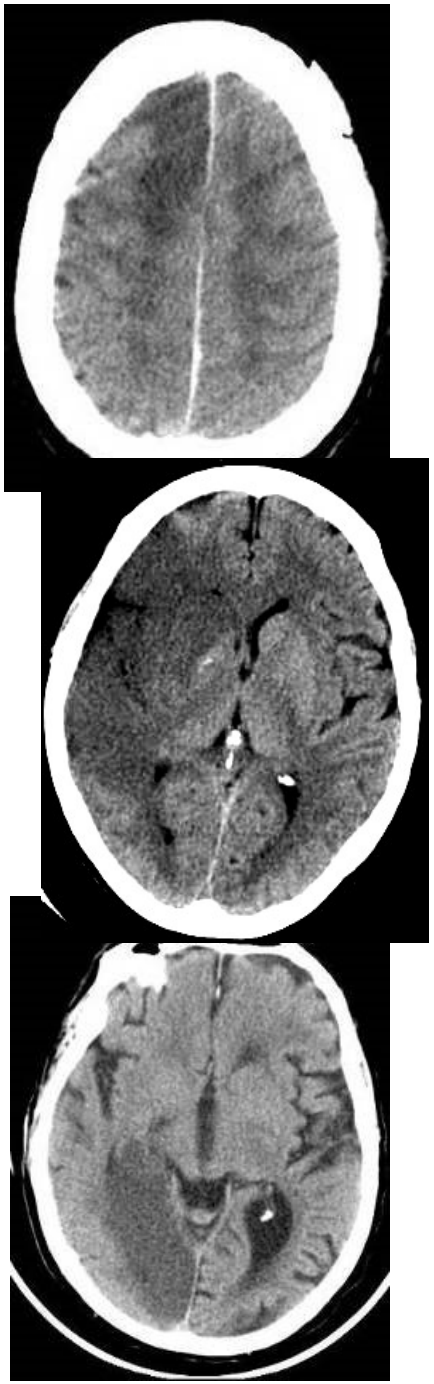
- ✓ Contralateral hemiparesis accentes on upper limb (FL)
- ✓ Impairment of speech functions – left side occlusion (FL, TL)
- ✓ Impairment of writing, counting, right – left orientation (TL)
- ✓ Impairment of spatial orientation when non-dominant parietal lobe affected

Arteria cerebri posterior

- ✓ Impairment of vision (OL)
- ✓ Reading disorders (Corpus callosum, PL)

Vertebrobasilar arteries

- ✓ Cerebellar symptomatology
- ✓ Brain stem symptomatology
  - ✓ Vertigo, nystagmus, diplopia, bilateral hemiaresis, paresis of cranial nerves respiratory disorders



Spinal Cord Injury

Spinal Cord Injury

Spinal Cord Injury
3-4 / 100 000 persons per year
Almost 50% of patients are younger than 25 years

The most often causes

- Traffic accidents
- Work and sports injuries

Mechanisms of injury

- Extensive Flection, extension or rotation
- Direct impact

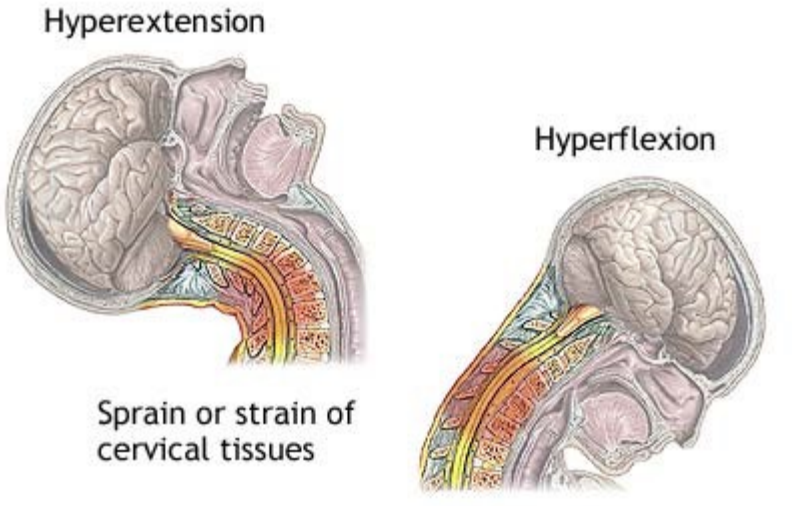
Back injury

- Vertebrae
  - ✓ Fracture
  - ✓ Dislocation
- Ligaments
- Intervertebral disc

Spinal cord injury

- Streetch
- Pressure

The most often localization of injury C4-C6 a Th11-L2



Spinal Cord Injury

Commotion

- Transient functional disability
- Reversible

Contusion

- Incomplete spinal cord injury
- Complete spinal cord injury
  - ✓ Phase 1 – spinal shock
    - ❖ Areflexia and loss of descending facilitation distally from injury
    - ❖ Atony of urinary bladder detrusor with retention of urine and ishuria paradoxa
  - ✓ Phase 2 – spinal automatism
    - ❖ Hyperreflexia/spasticity distally from injury, loss voluntary motoric activity and loss of descending facilitation
    - ❖ Spasticity of urine bladder

Consequences of Spinal Cord Injury
Paralysis

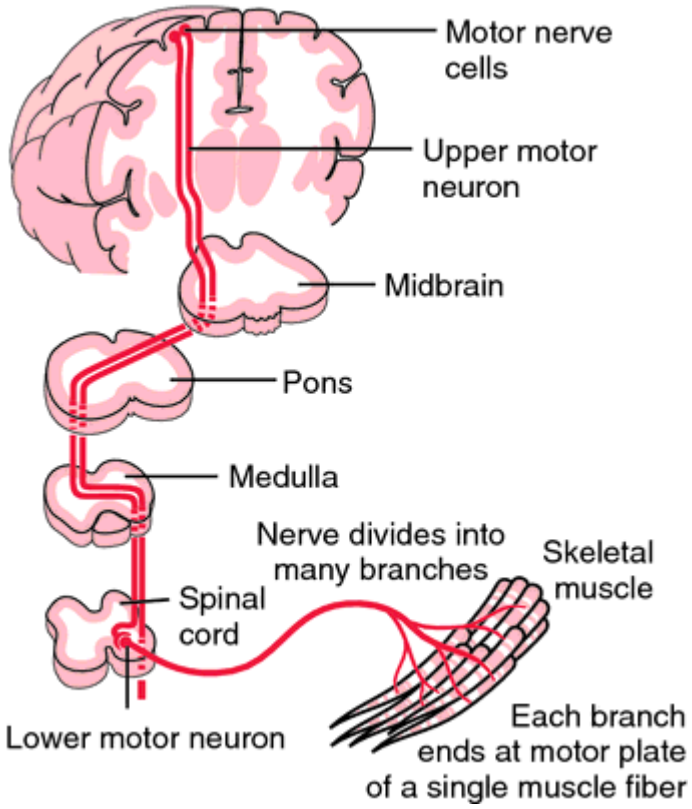
- Loss of muscle function most often caused by damage of nervous system

Plegia

- Total paralysis

Paresis

- Partial paralysis
- Mono-, di-, quadru-, para-, hemi-
- ***Central***
  - ✓ Loss of upper motor neuron
  - ✓ First flaccid
    - ❖ Spinal shock
  - ✓ Then spastic
    - ❖ Activity of lower motor neuron
- ***Peripheral***
  - ✓ Loss of lower motor neuron
  - ✓ Flaccid



http://medical-dictionary.thefreedictionary.com

Consequences of Spinal Cord Injury
Paralysis

Spinal cord (SC) and spine (S) segments

- ***Upper cervical:*** SC=S
- ***Lower cervical and upper thoracic:*** SC=S+1
- ***Middle thoracic hrudní:*** SC=S+2
- ***Lower thoracic:*** SC=S+3
- **Medulary cone: L1 –L2**

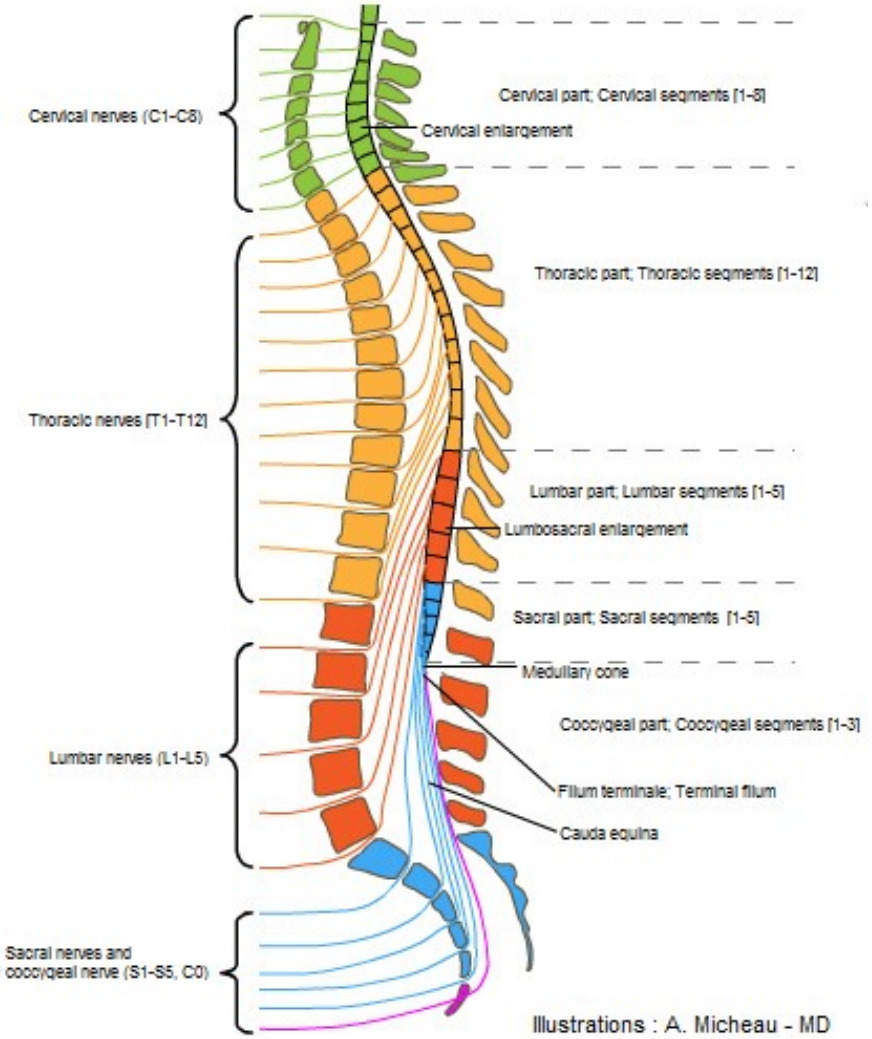
Plexus cervicalis: C1-C4

C4 – nervus phrenicus

Plexus brachialis: C5 – Th1

Plexus lumbalis: L1-L4

Plexus sacralis: S1-S5



http://www.jhu.edu

Consequences of Spinal Cord Injury
Paralysis

C1 – C4

- ✓ Spastic quadruplegia
- ✓ Sphincter function disorders

C5 – Th2

- ✓ Upper limbs: flaccid paresis/plegia
- ✓ Lower limbs: spastic paresis/plegia
- ✓ Sphincter function disorders

Th3 – Th10

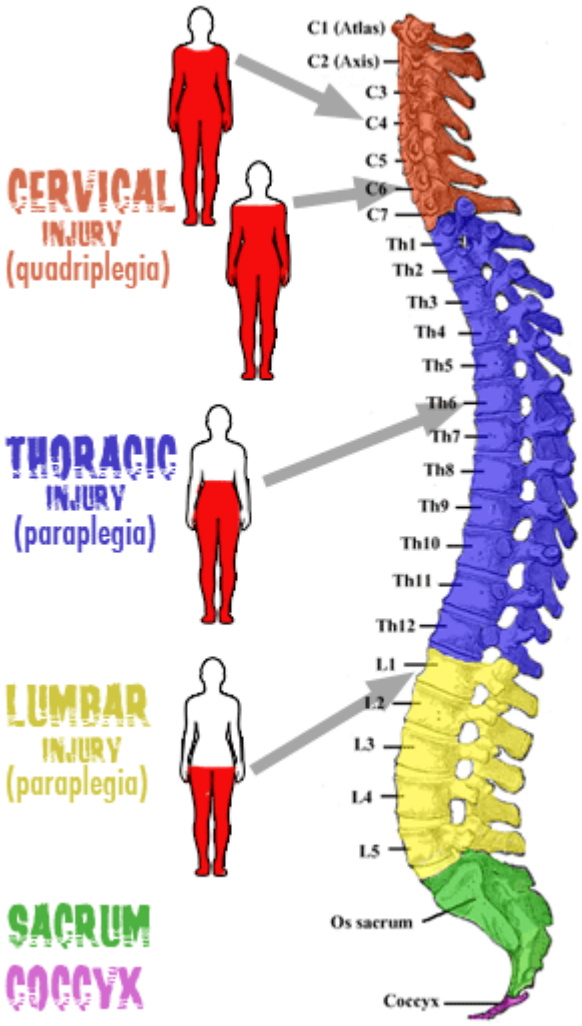
- ✓ Lower limbs: spastic paresis/plegia
- ✓ Sphincter function disorders

Th9 – L2

- ✓ Lower limbs: flaccid paresis/plegia
- ✓ Sphincter function disorders

L3 – S5

- ✓ Sphincter function disorders



http://whyfiles.org

Consequences of Spinal Cord Injury
Paralysis

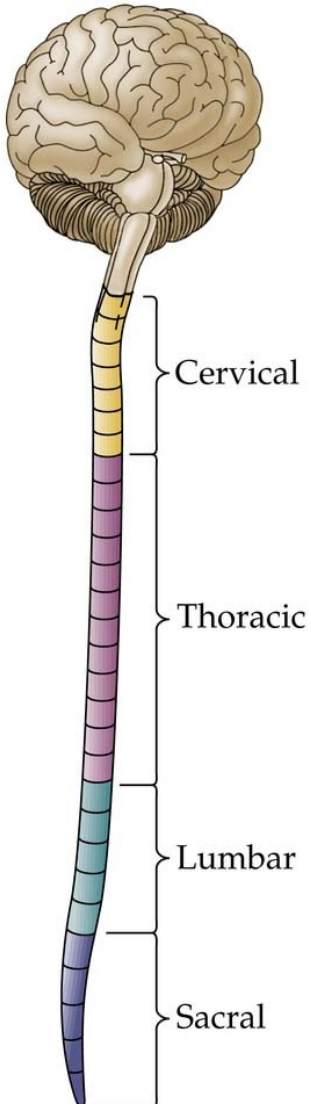
Hypesthesia

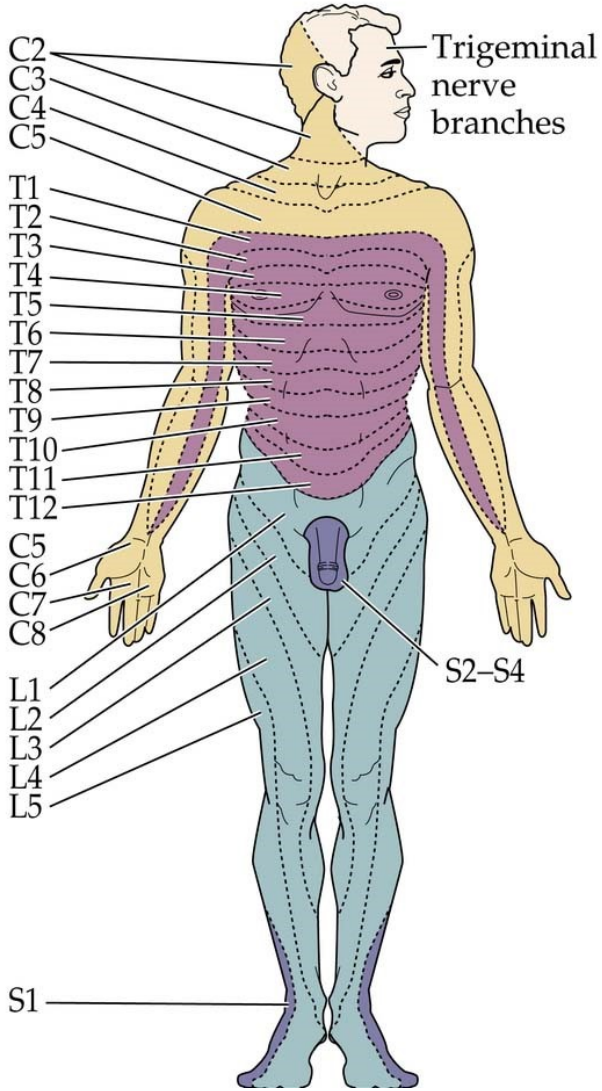
- Incomplete loss of sensation

For example: Thermal hypestesia, tactile hypestesia

Anesthesia

- Complete loss of sensation





http://www.rci.rutgers.edu

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