

MUNI I

MED

Pathophysiology of Central Nervous System

Brain pathophysiology

Stroke

Craniotrauma

Spinal cord pathophysiology

Intracranial Compartments, 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

Cerebral perfusion pressure

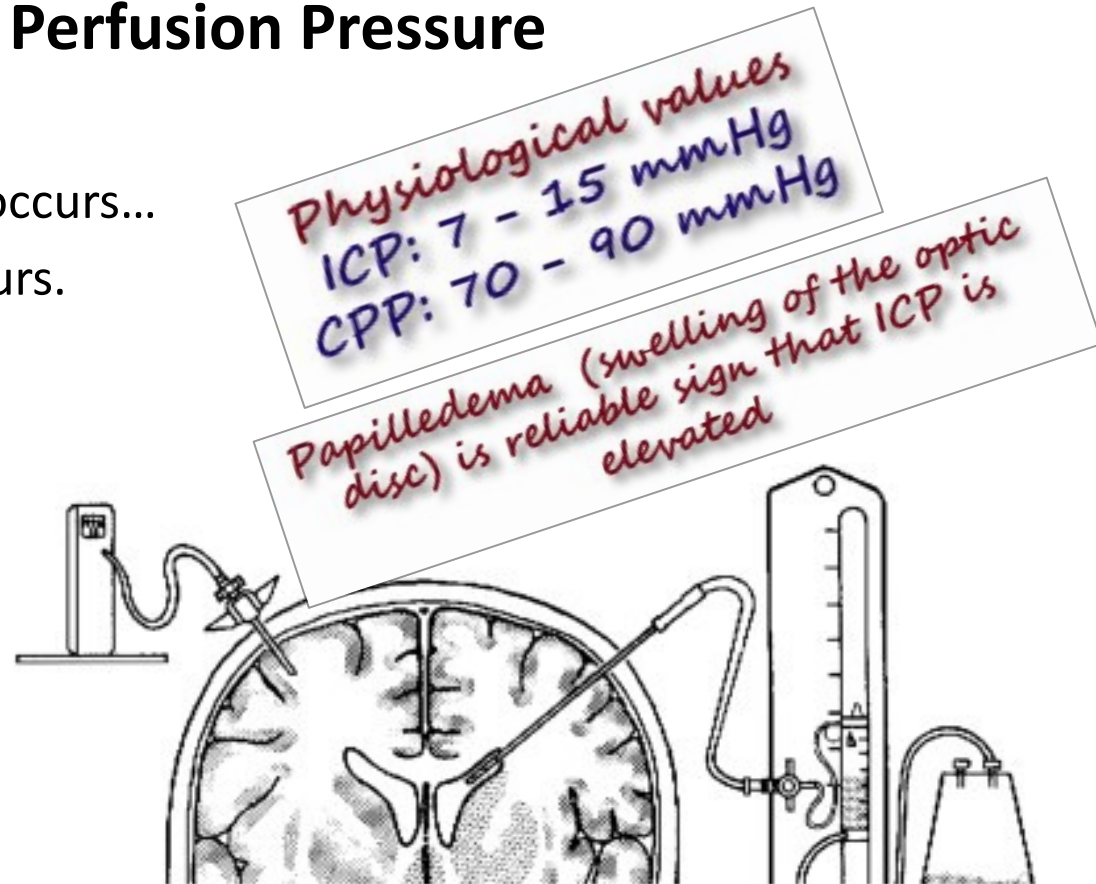
- The pressure gradient through which blood flows to the brain

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

Cerebral perfusion pressure

Intracranial pressure

Mean arterial pressure



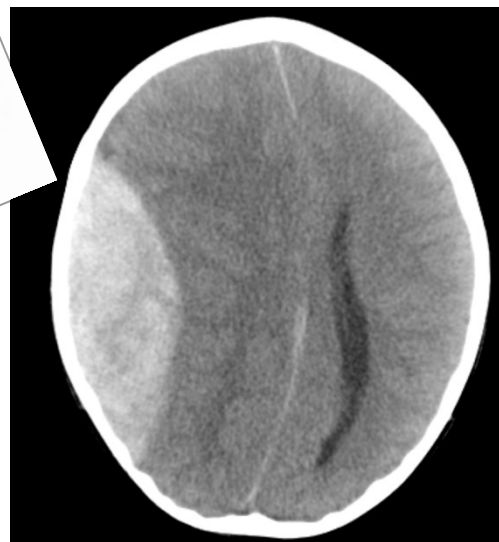
<http://ars.els-cdn.com>

Causes of Intracranial Hypertension

Brain compartment

- Edema
- Tumor
- Hemorrhage
- Infection

Dynamic of development is an important factor.

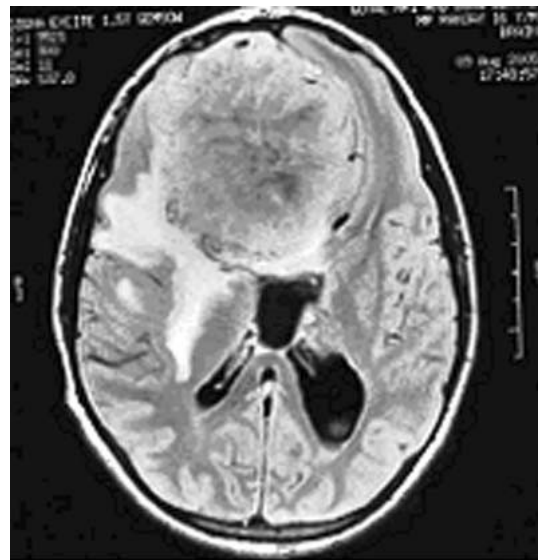


CSF compartment

- 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
- H₂O
- 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 interstitial space



Causes of Intracranial Hypertension

Hydrocephalus

Abnormal accumulation of CSF in liquor space

CSF production

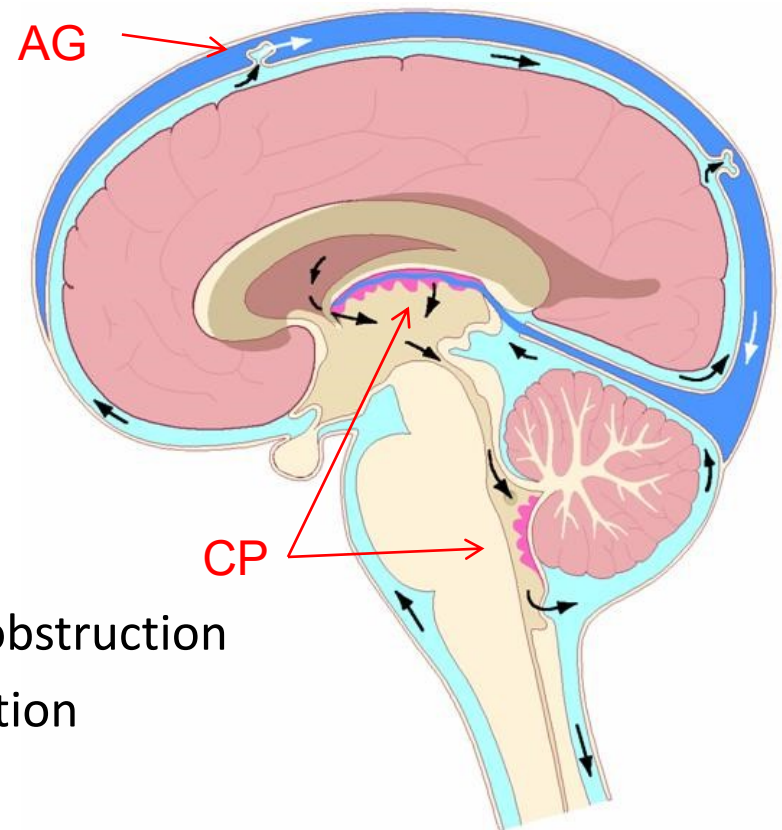
- Choroid plexus (CP)
- 450-750 ml/day

CSF resorption

- Archnoid granulations (AG)

Hydrocephalus

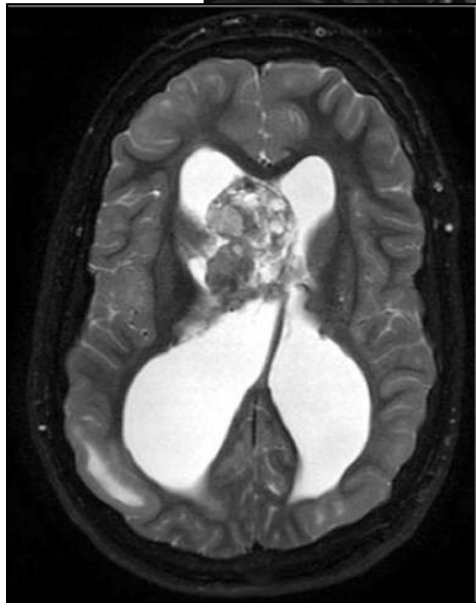
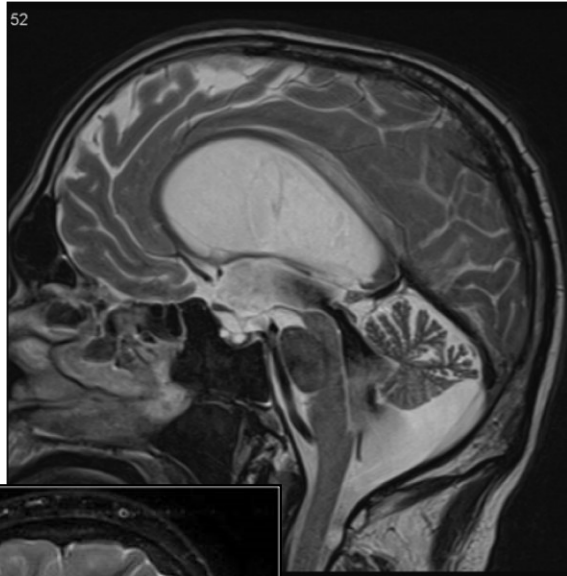
- Obstructive (Non- communicating)
 - ✓ Impaired CSF circulation due to obstruction
 - ✓ For example: ventricular obstruction
- Non – obstructive (Communicating)
 - ✓ Impaired CSF resorption



Acute X Chronic

Causes of Intracranial Hypertension

Hydrocephalus



Consequences of Intracranial Hypertension

Compression of adjacent tissue

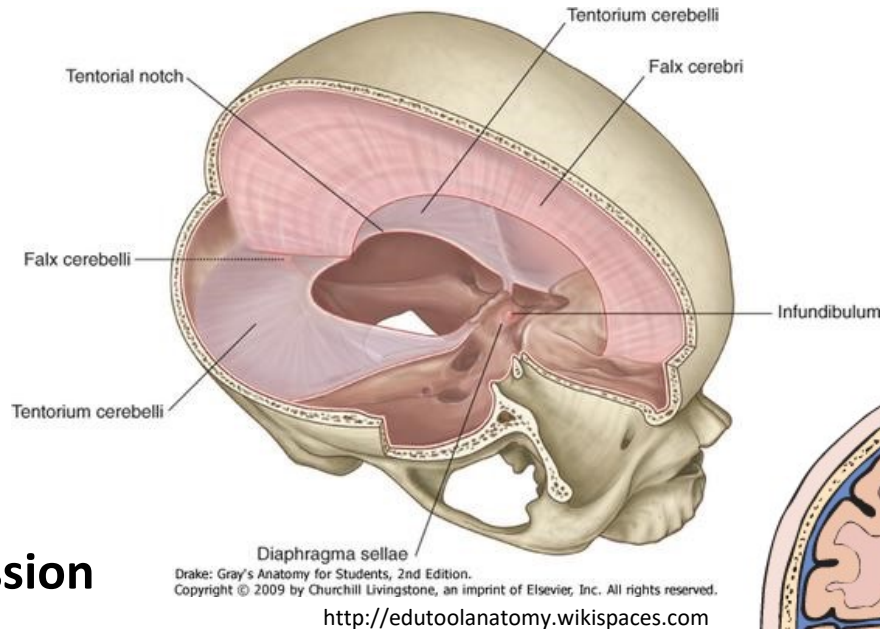
- Ischemization

Infratentorial lesions

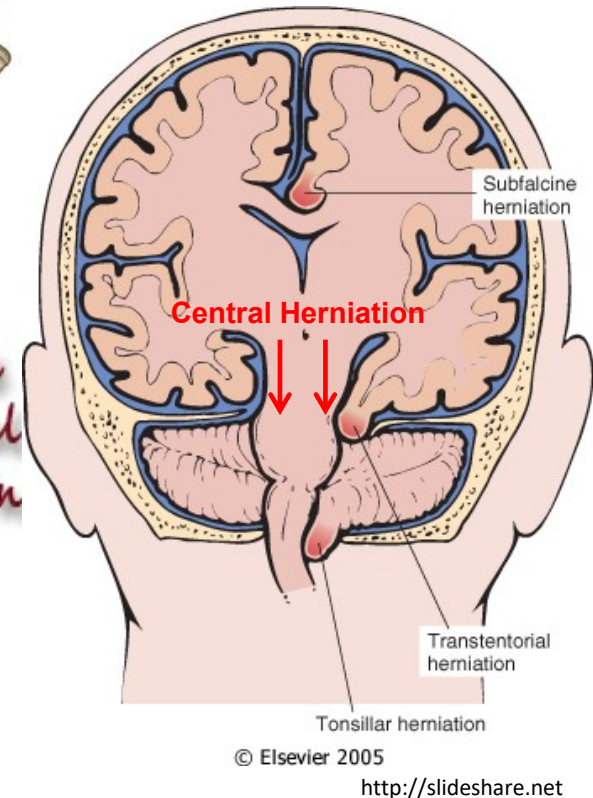
- Always acute
- Risk of brain stem compression
- stem compression

Cerebral herniation

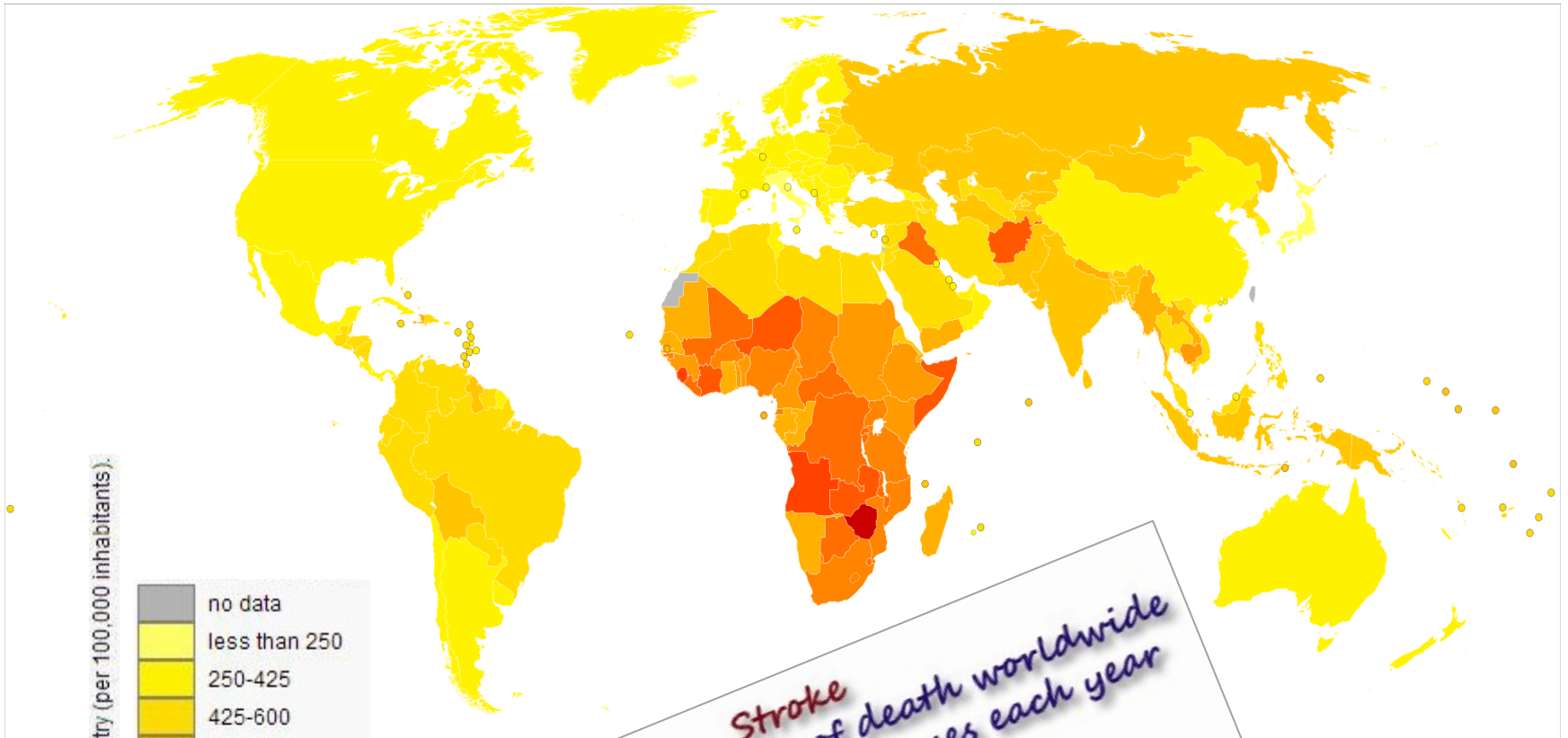
- Subfalcine
- Transtentorial
- Tonsillar
- Central
- ✓ Permanent damage of brain
- ✓ Risk of brain stem compression



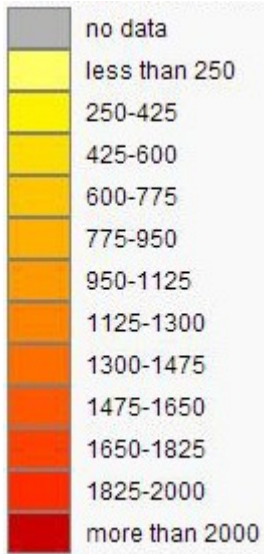
Lumbar puncture should not be performed if there is intracranial hypertension. Cerebral herniation may occur in such a case.



Stroke



Cerebrovascular disease by country (per 100,000 inhabitants).



Stroke
Third leading cause of death worldwide
Nearly 50 millions new cases each year
Rate of mortality nearly 25%
In 2020 is expected about 30% higher
incidence compared to 2000
in European countries

Stroke

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

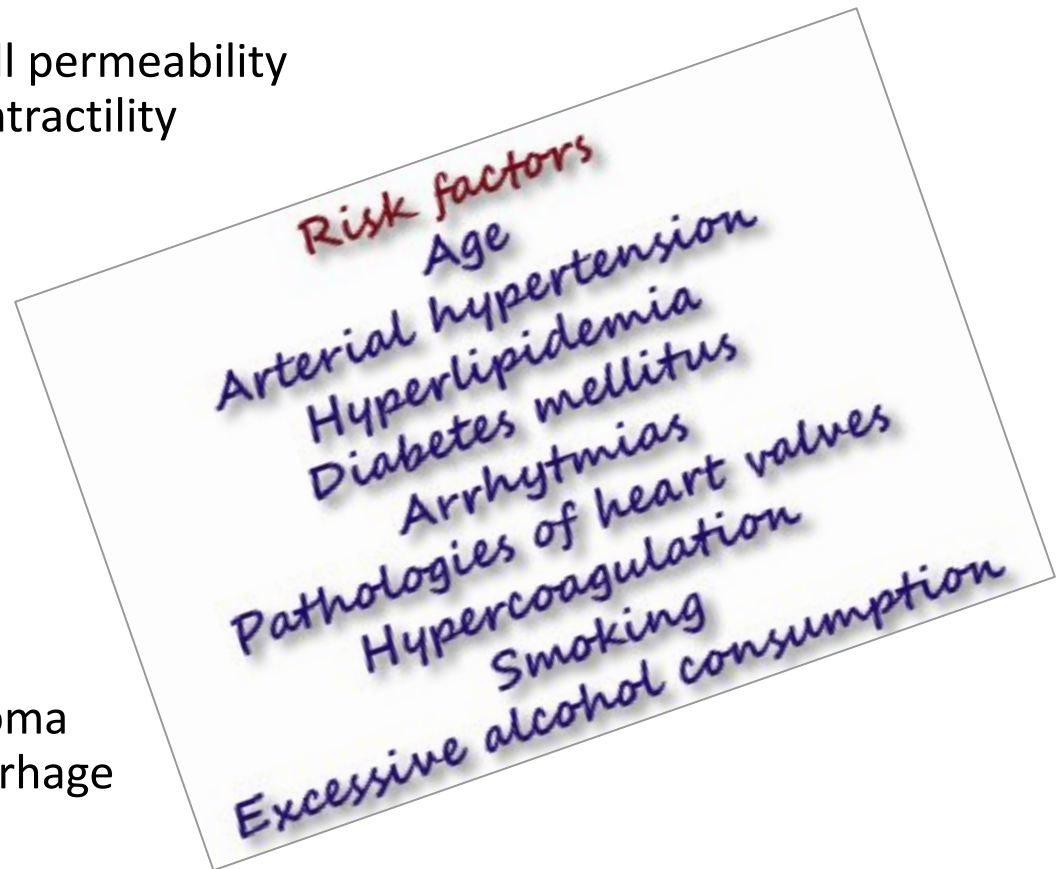
Vascular pathologies

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

Atherosclerosis

Types of stroke

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



Ischemic Stroke

Critical parameters

- Extent of ischemia
- Duration of ischemia

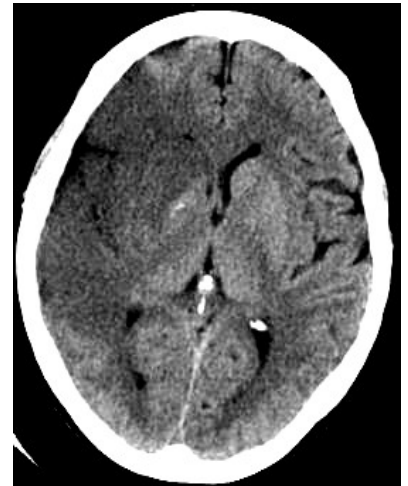
Atherosclerosis

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 ischemia

Brain:	less than 5 min.
Liver and kidney:	15 - 20 min.
Skeletal muscle:	60 - 90 min.
Visceral muscle:	24 - 72 hours
Hair:	several days

High metabolic activity

- Membrane potential maintaining – repolarisation (Na/K pumps)
- Almost exclusively 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)

- Irreversible neuronal damage
- Primary injury

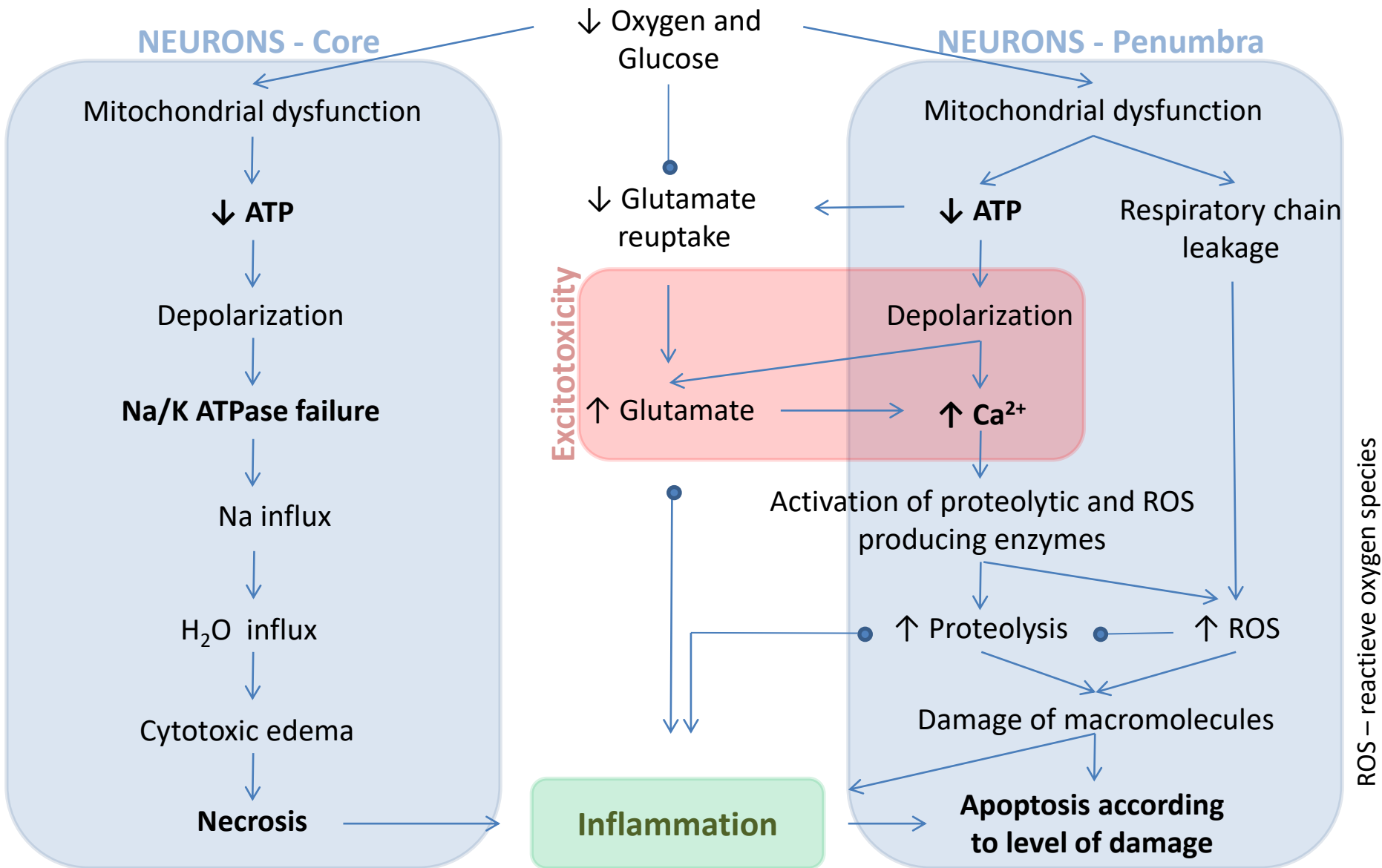
Penumbra (periphery of ischemia)

- Reversible neuronal damage
- Risk of secondary injury development

Primary brain injury
Directly caused by the pathology
Developed in the same time
as pathology occurs
Non treatable

Secondary brain injury
Caused by reaction of organism
to pathology
Developed in delayed manner
Potentially treatable

Ischemic Cascade



Mechanisms of Ischemic Damage

Excitotoxicity

Accumulation of excitatory neurotransmitters in extracellular space

- Glutamate
- Aspartate

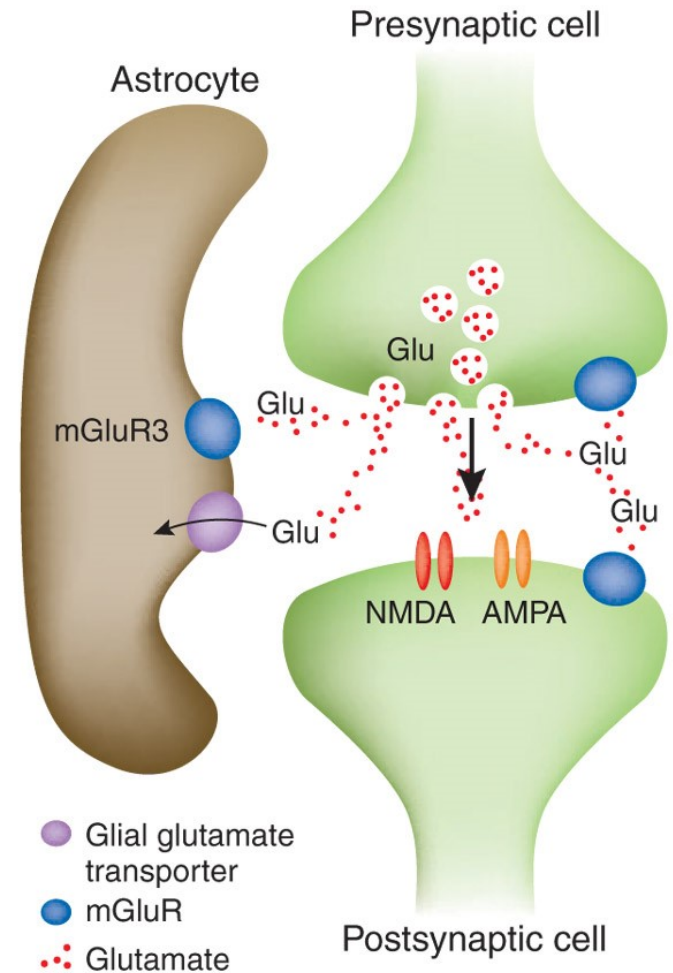
Neuronal damage due to excessive stimulation

Cause

- Depolarization
- Decreased reuptake

Consequence

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



Mechanisms of Ischemic Damage

Reactive oxygen species (ROS)

ROS are highly reactive particles

ROS are mainly produced during reperfusion

Cause

- Intracellular
 - ✓ Respiratory chain leakage
 - ❖ Disruption of electron transport chains in mitochondria
 - ✓ 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

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

Mechanisms of Ischemic Damage

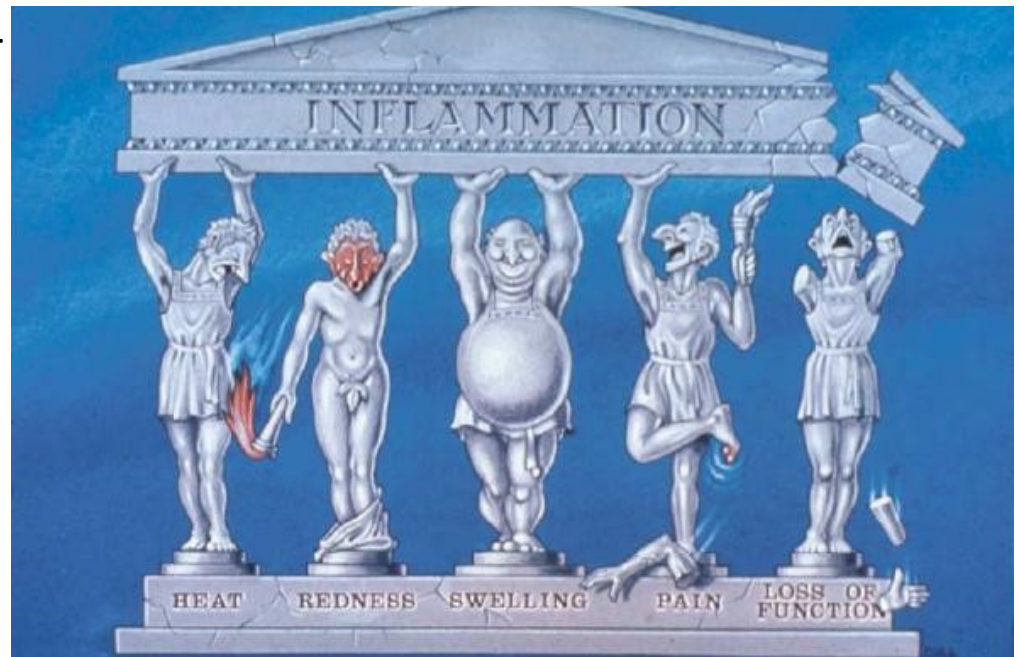
Inflammation

Cause

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

Consequence

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



Hemorrhagic Stroke

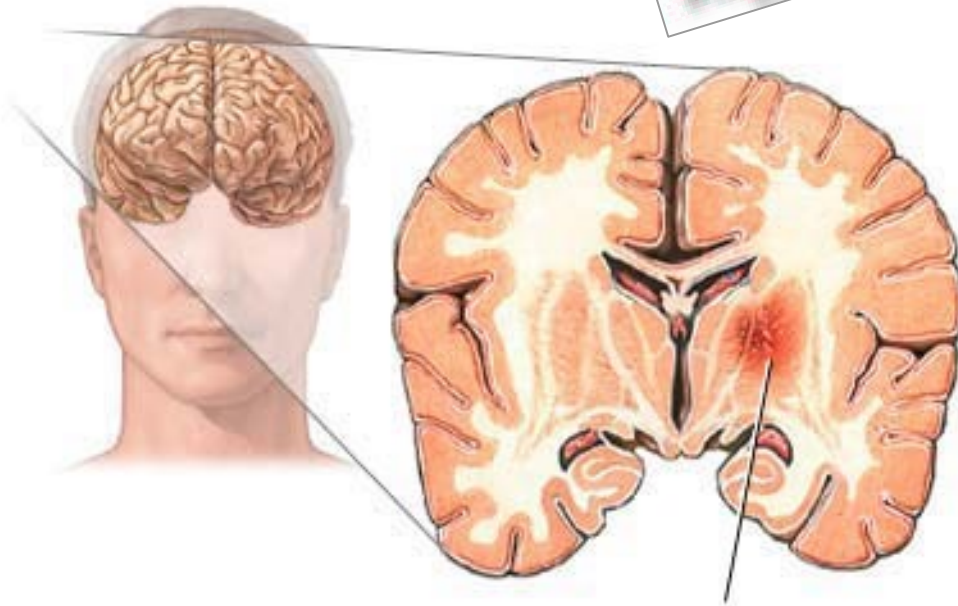
Intracerebral hematoma (ICH)

Bleeding into the brain parenchyma (intraaxial)

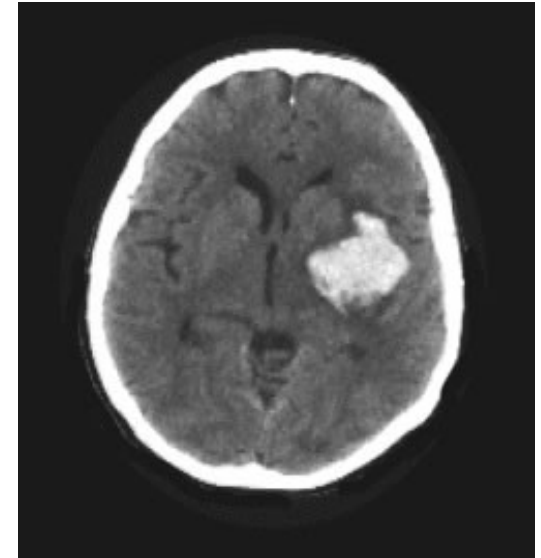
The most often localization

- Basal ganglia
- Thalamus

Arterial hypertension



Intracerebral hemorrhage



Pathophysiology of ICH

Hematoma

Mass effect

Mechanical damage of brain parenchyma

↑ ICP

Transient ischemia

Inflammation

Excitotoxicity

↑ ROS (Neurons)

↑ Proteolysis (Neurons)

Cytotoxic blood components

Complement Etc.

Hemoglobin

Fe²⁺

↑ ROS

Endothelial cell death

Neuronal cell death

Inflammation

↑ Pro - infl. cytokines

↑ Proteolytic enzymes

↑ ROS

Blood - Brain barrier disruption

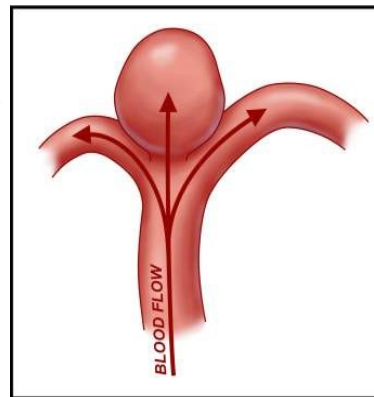
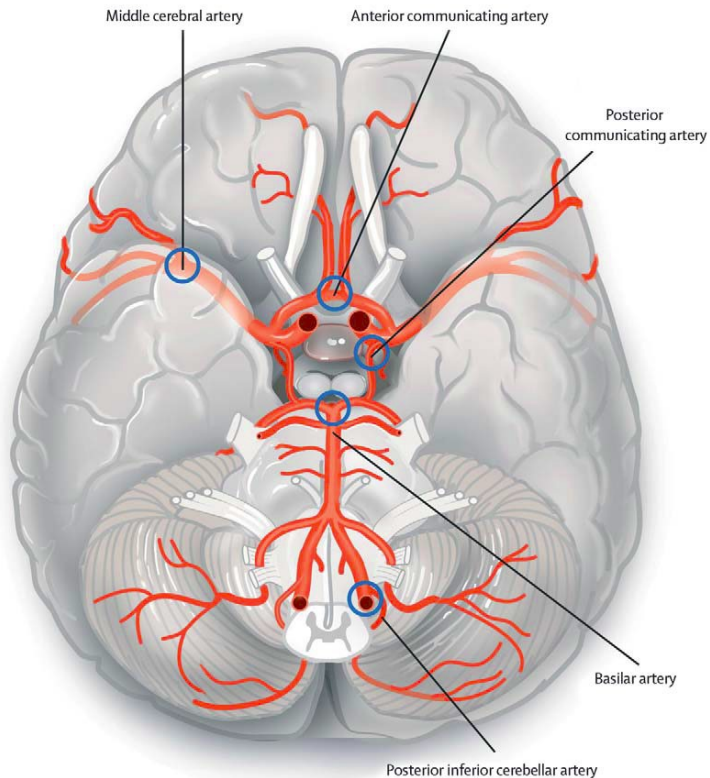
Edema

Hemorrhagic Stroke Subarachnoid Hemorrhage (SAH)

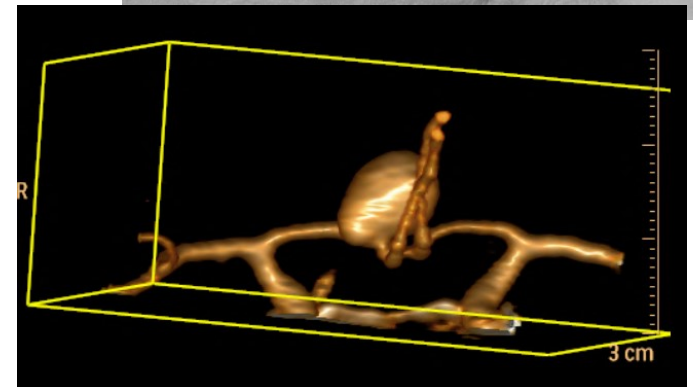
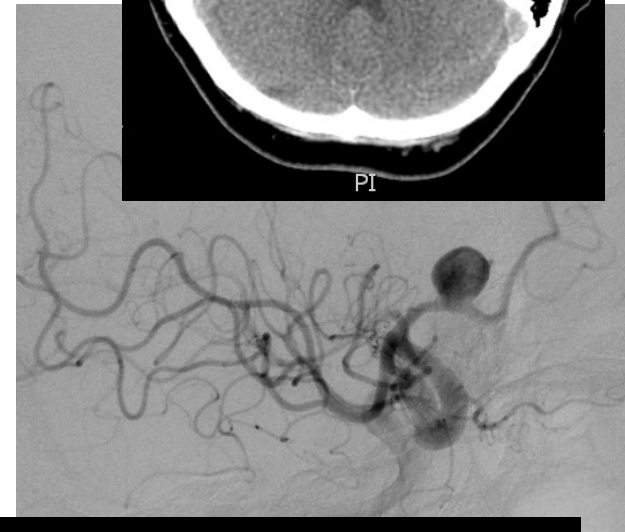
Bleeding into the subarachnoid space (extraaxial)

The most often cause – cerebral aneurysm rupture

The most often localization of aneurysm - Willis circle



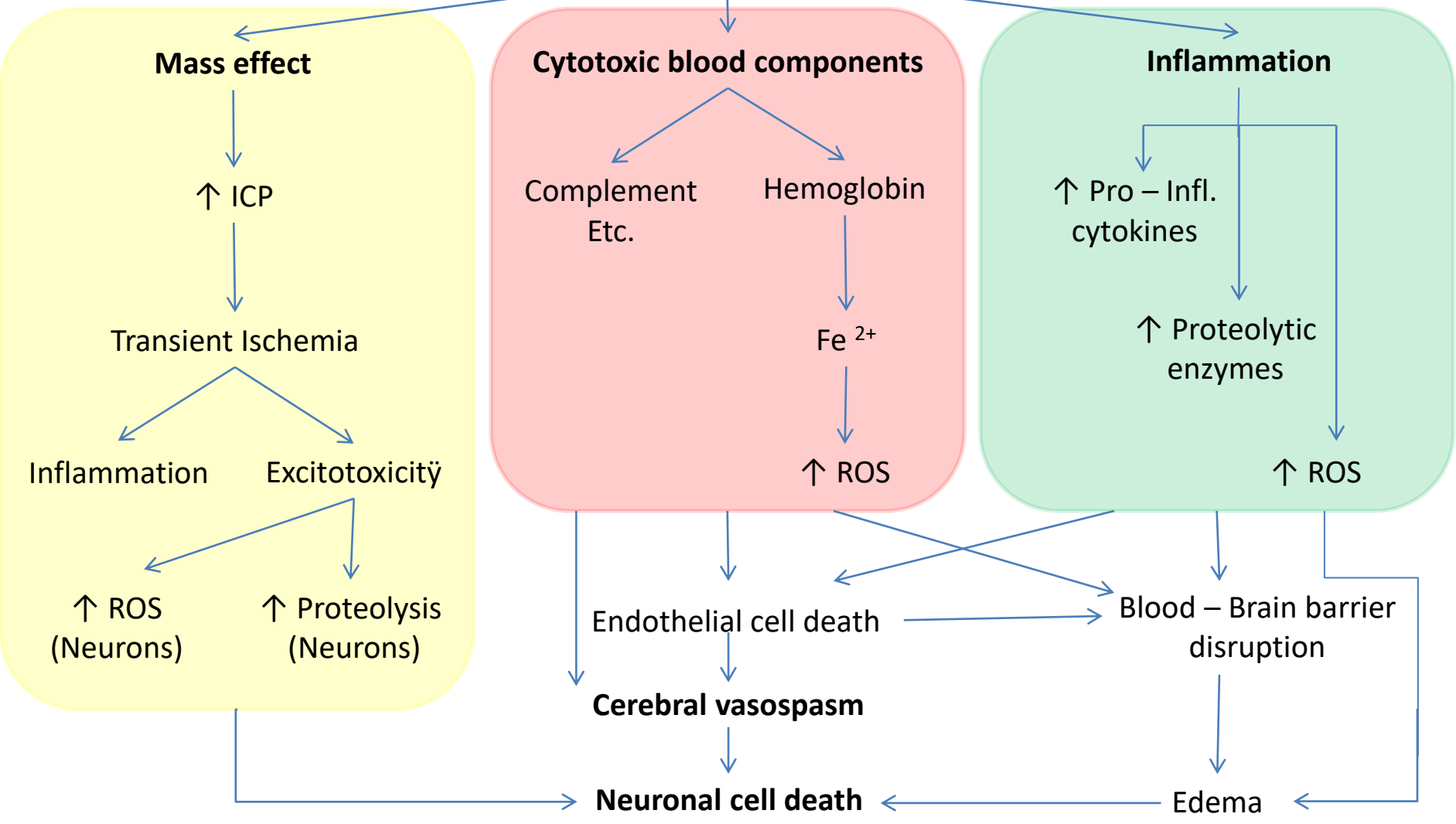
<http://chicago.medicine.uic.edu>



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

Pathophysiology of SAH

Accumulation of blood in subarachnoid space



Traumatic Brain Injury

Traumatic Brain Injury

Introduction

The most often causes

- Traffic accidents
- Falls
- Sport injuries

Classification

- Primary
 - ✓ Results from trauma...
- Sekundární
 - ✓ Results from reactions initiated by trauma
- Focal
- Difuse

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



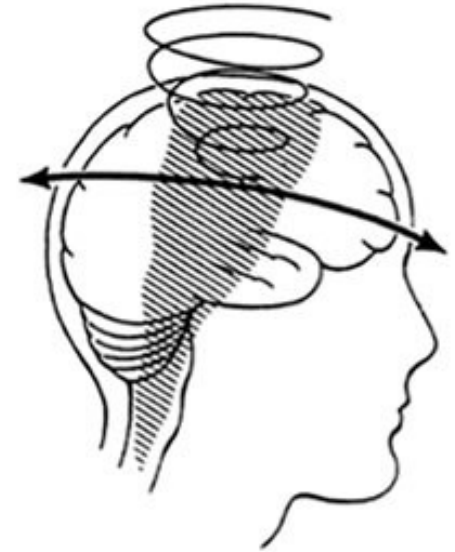
Diffuse Brain Injury

Diffuse axonal injury

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

Concussion

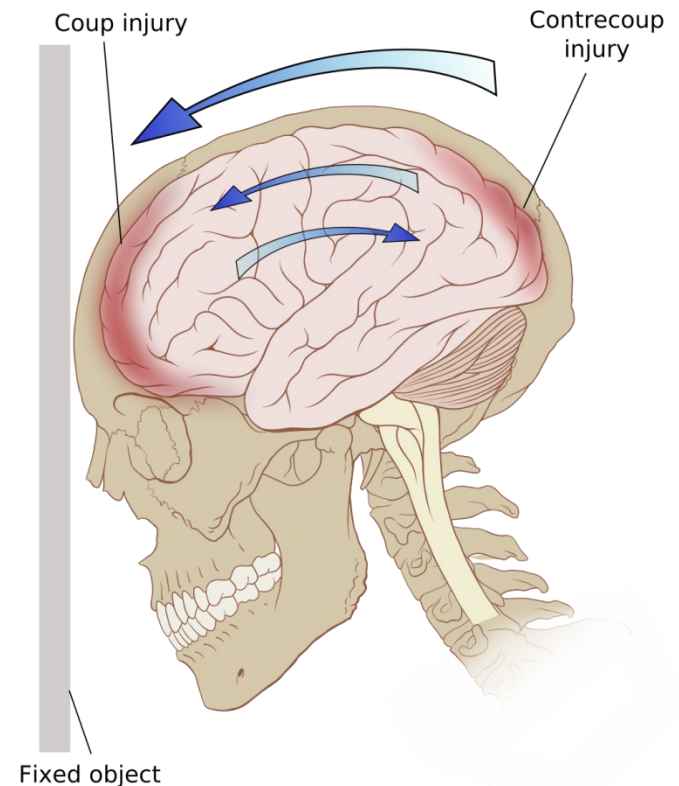
- The mildest grade of diffuse axonal injury
- No structural tissue damage
- Transient functional damage (loss of consciousness not longer than 10 minutes)



Primary Brain Injury

Mechanism of production

- **Contact injury**
 - ✓ Head hits the object or head is hit 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



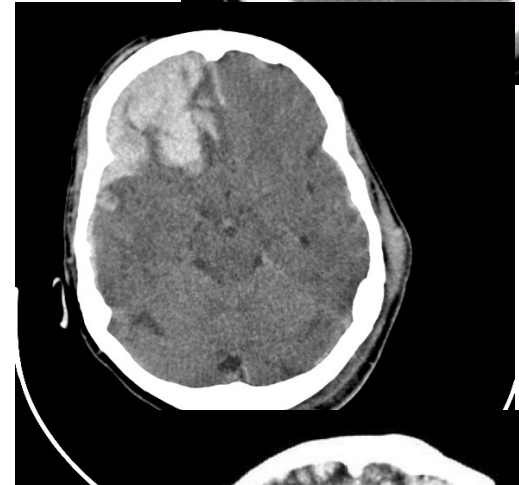
Focal injury

Contusion

- Mechanical damage of brain tissue, pia – arachnoid membranes not damaged
- Smooth 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

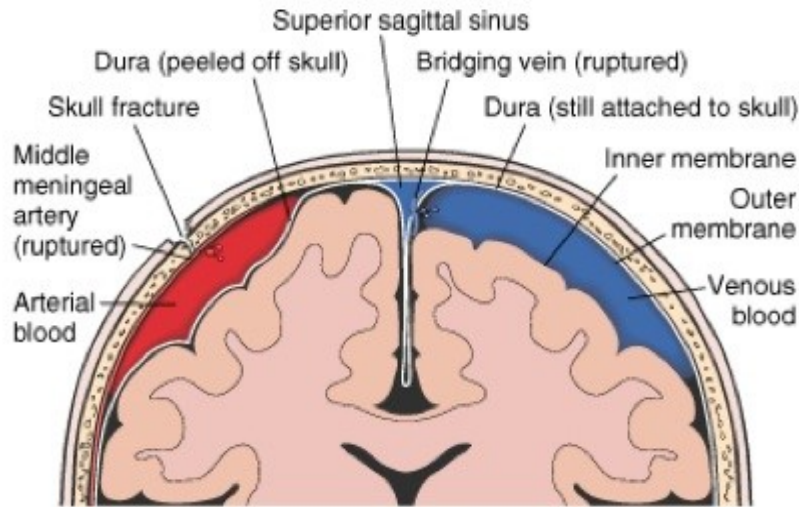
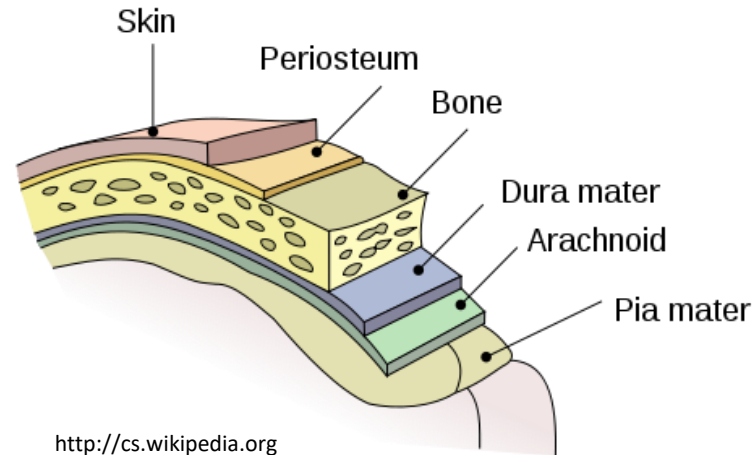
Traumatic Hematomas

Intraaxial

- Intracerebral

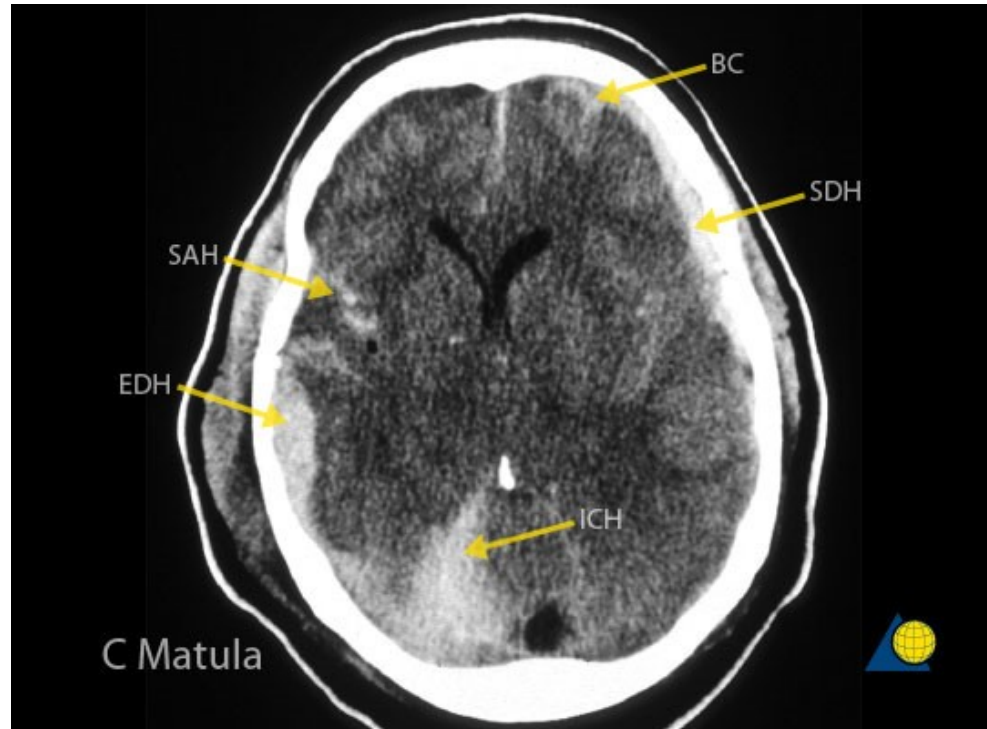
Extraaxial

- Epidural
- Subdural
- Subarachnoid



A. Epidural hematoma

B. Subdural hematoma

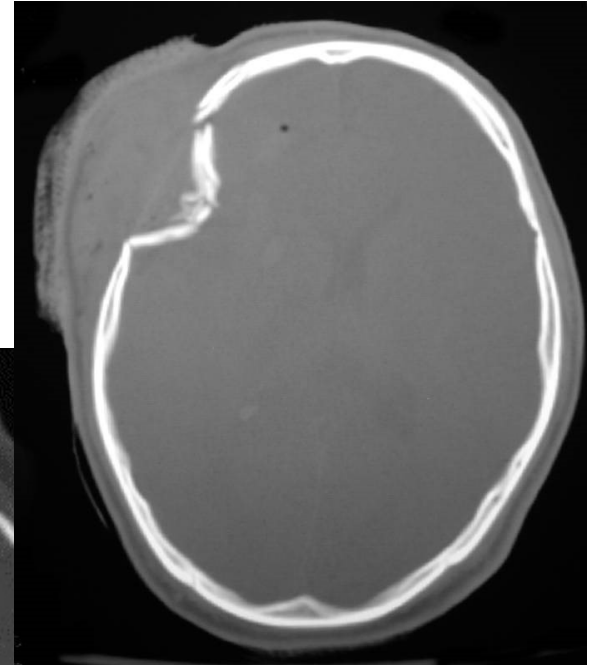
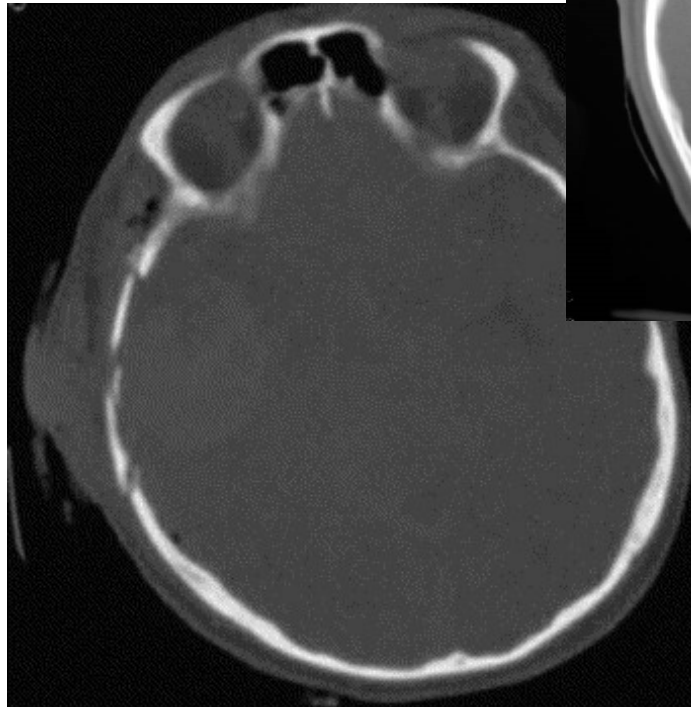
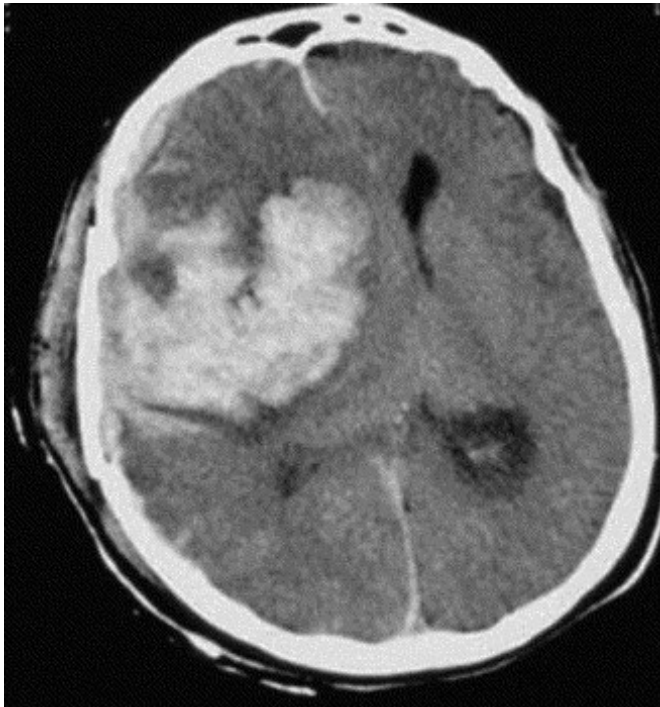


Intracerebral Hemorrhage

- Smooth transition between contusion and ICH according to severity of injury

The most often localization

- Temporal lobe
- Frontal lobe

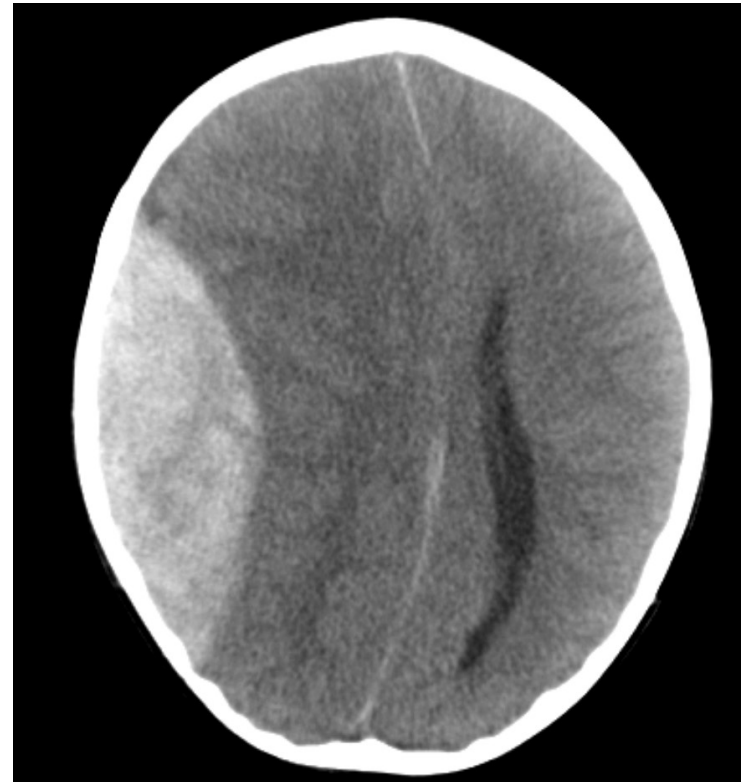
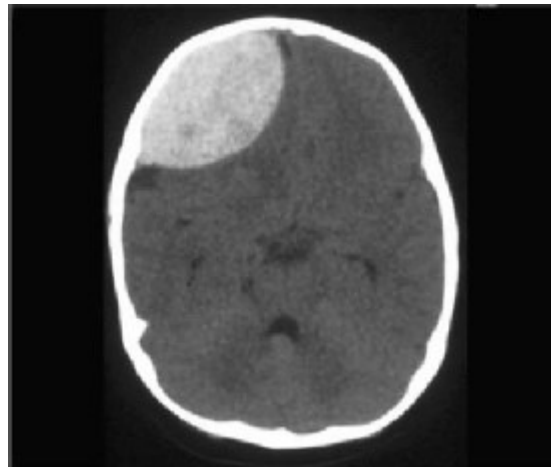


Epidural Hematoma

- 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 bridging veins which cross subdural space (acceleration – deceleration injury)

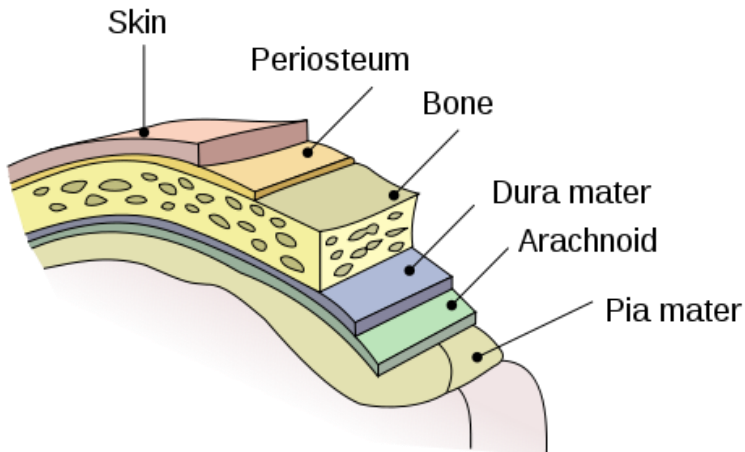
Acute – fresh blood

Chronic – colliquated blood

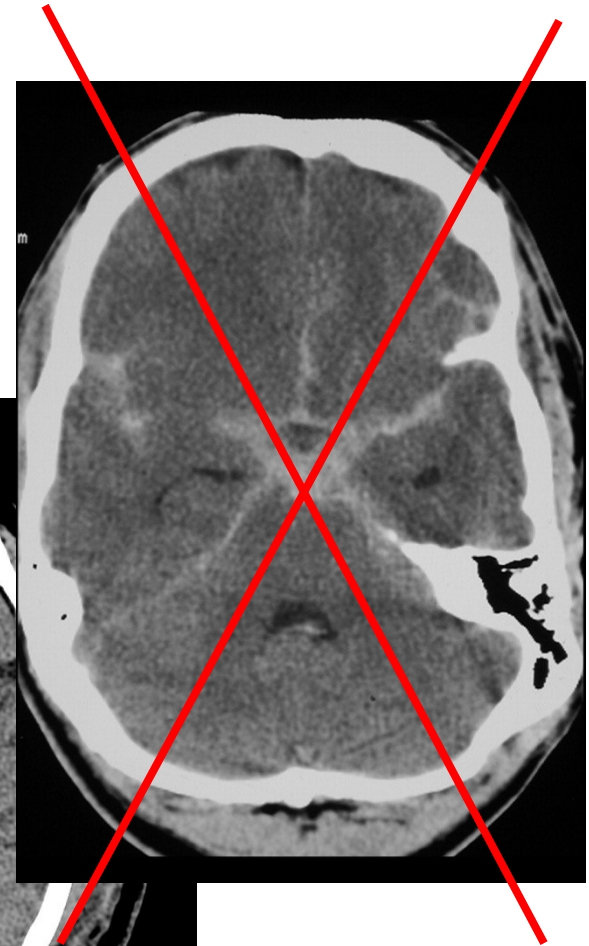
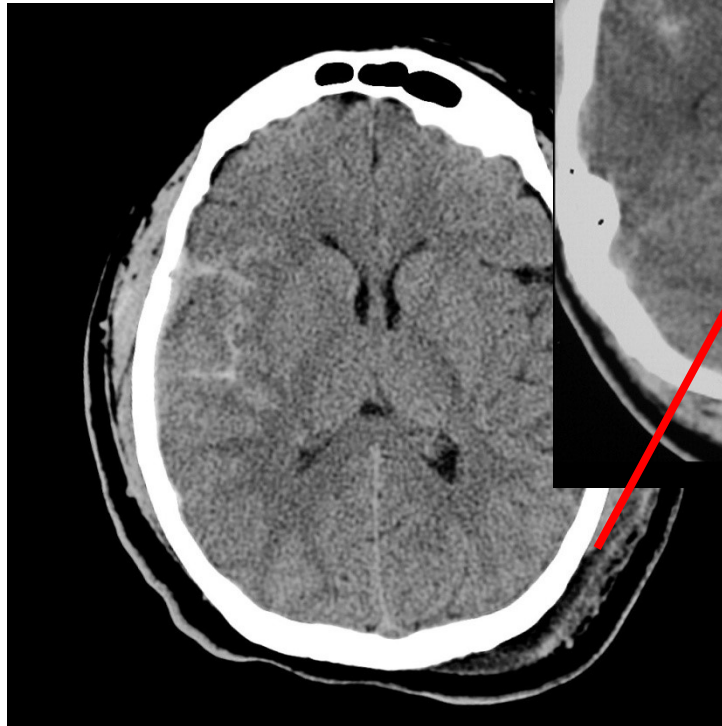


Traumatic Subarachnoid Hemorrhage

- 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 of vigility
 - **Somnolence** – state of near-sleep, responsiveness
 - **Stupor** – responsiveness only to base stimuli (pain)
 - **Coma** - unresponsiveness

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

Glasgow Coma Scale

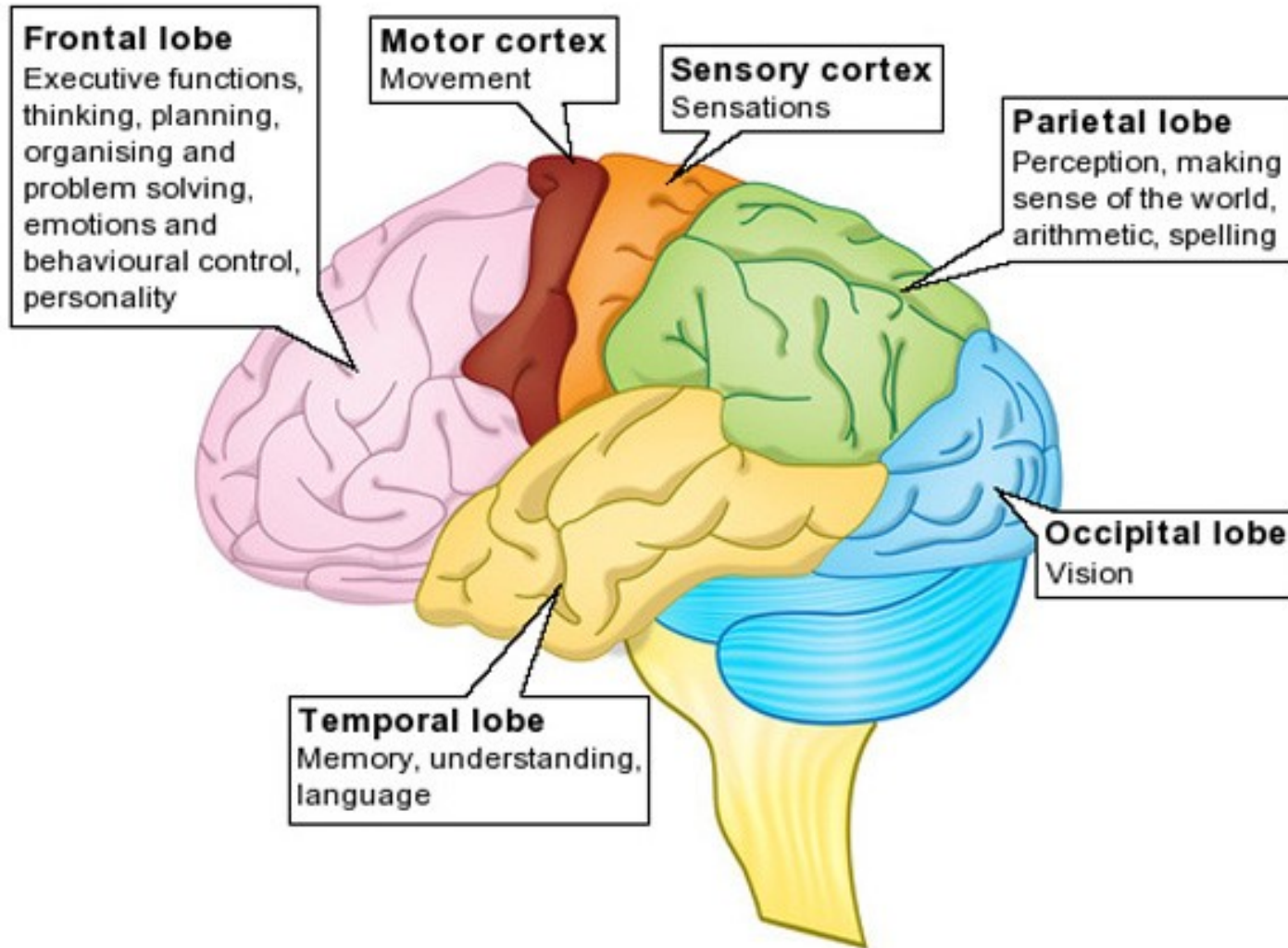
Normal consciousness: GCS 15

Mild brain injury: GCS 14 - 13

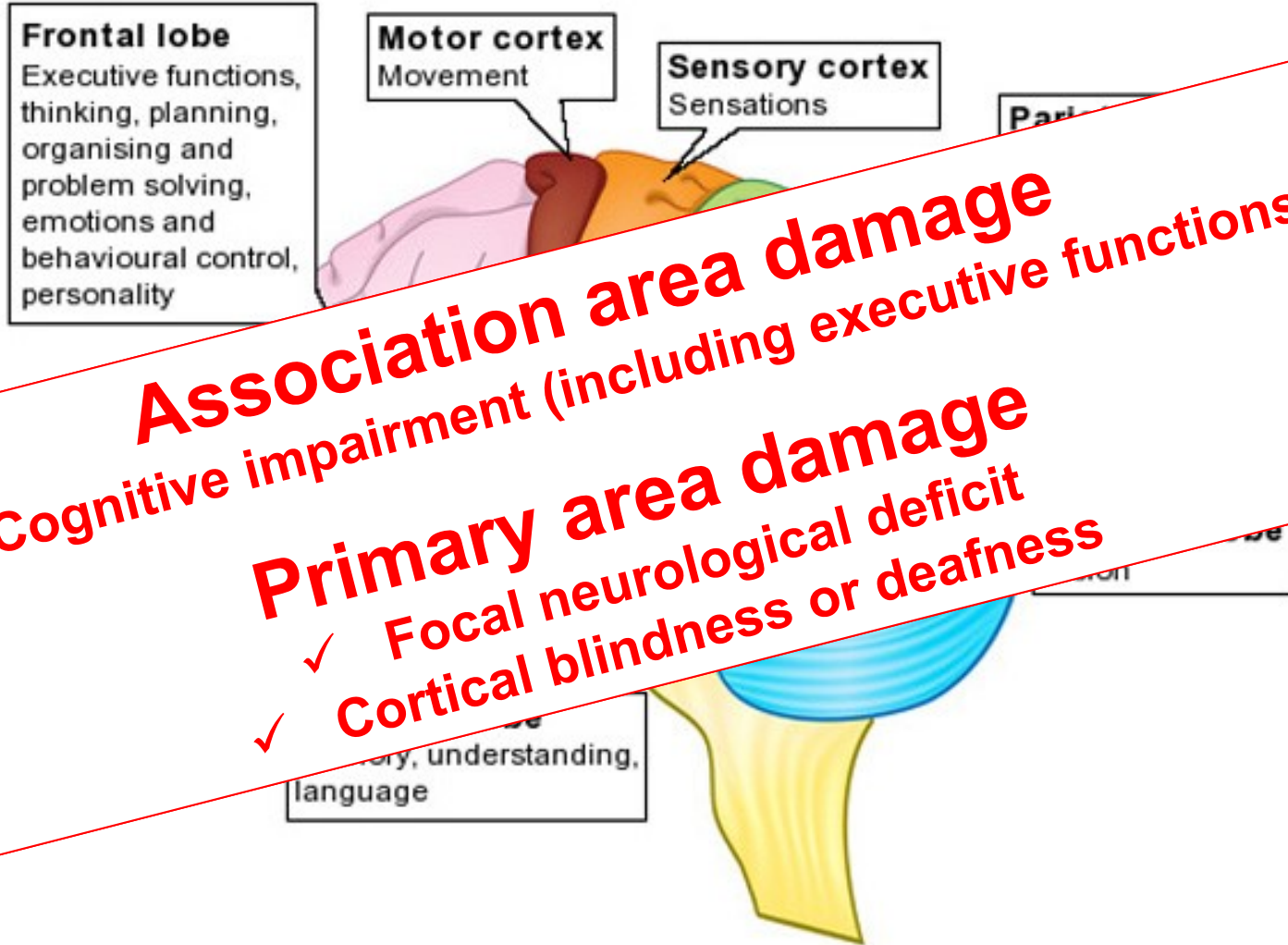
Moderate brain injury: GCS 12 - 9

Severe brain injury: GCS 8 - 3

Cognitive Impairment and Focal Neurological Deficit



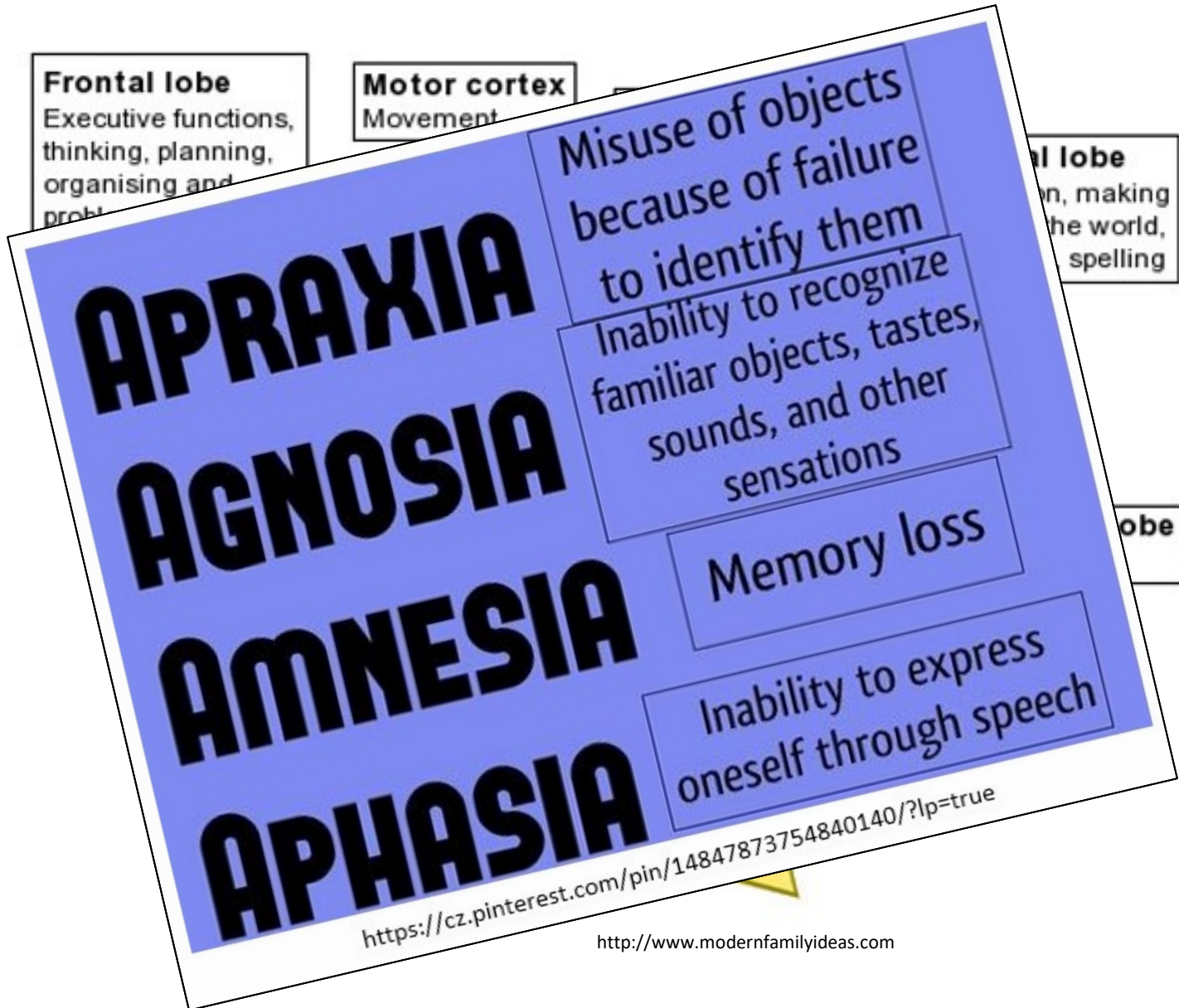
Cognitive impairment and Focal Neurological Deficit



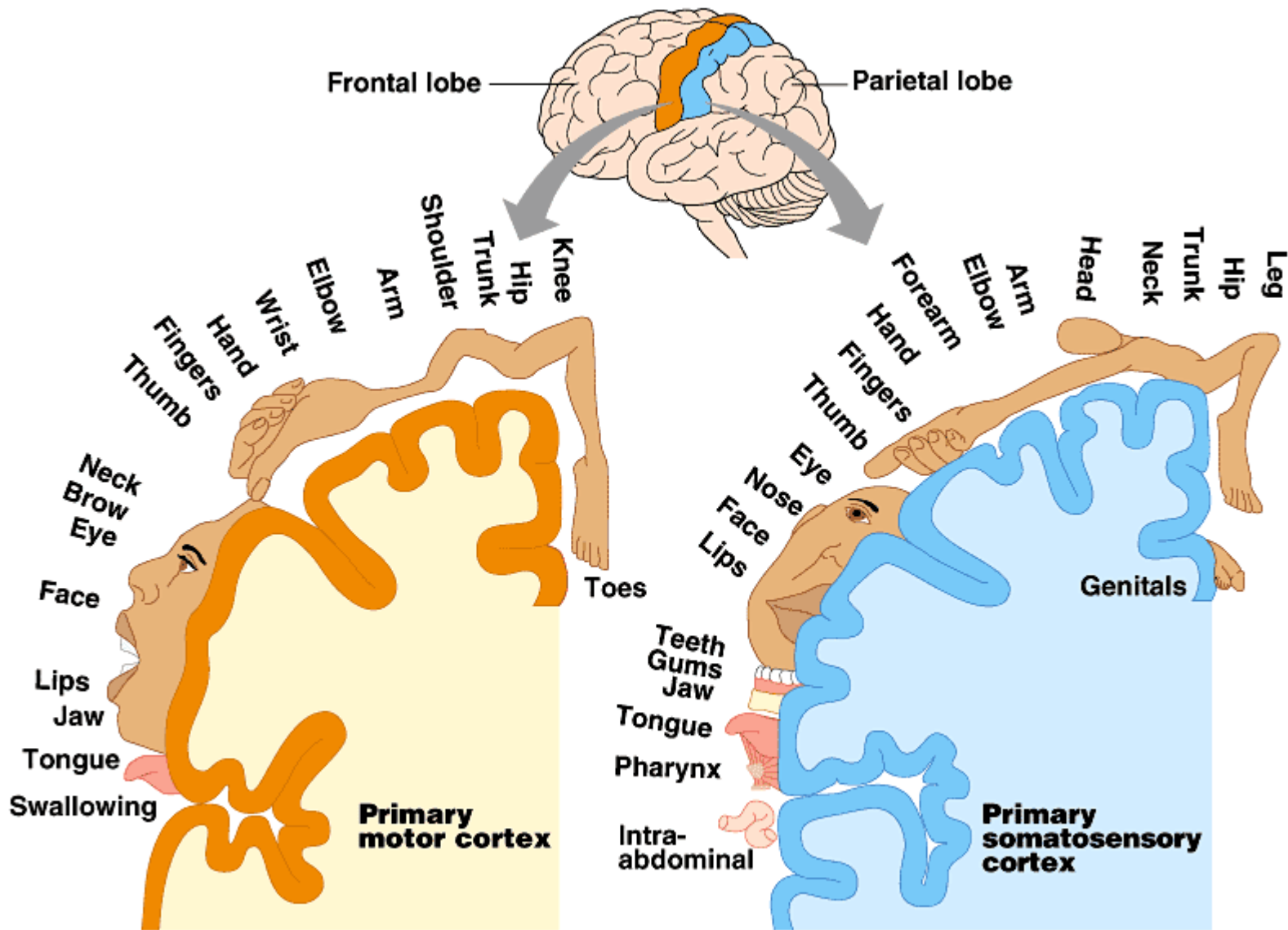
Association area damage
✓ Cognitive impairment (including executive functions)

Primary area damage
✓ Focal neurological deficit
✓ Cortical blindness or deafness

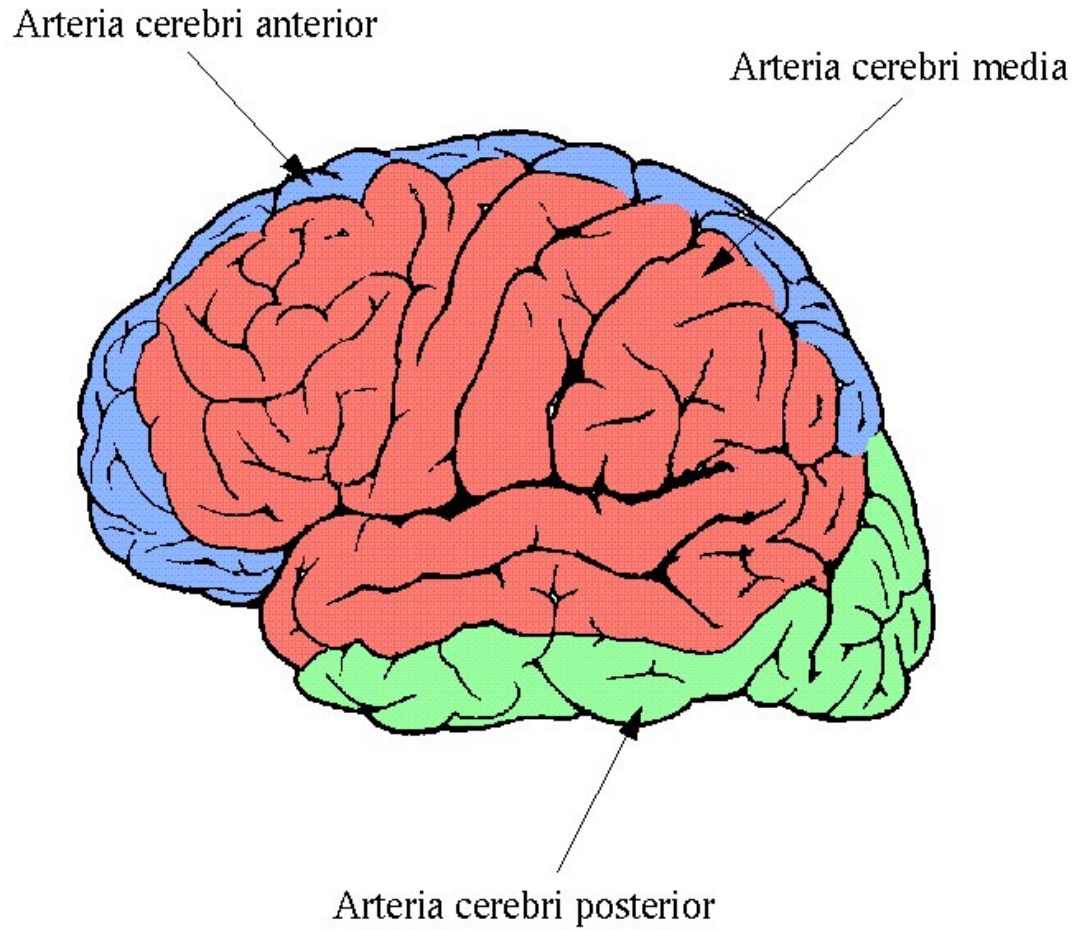
„Dementia“ and Focal Neurological Deficit



Focal Neurological Deficit



Focal Neurological Deficit



Focal Neurological Deficit

Examples of Ischemia

Arteria cerebri anterior

- ✓ Contralateral hemiparesis accentuated on lower limb (FL)
- ✓ Behavioral impairment- bilateral occlusion (FL)

Arteria cerebri media

- ✓ Contralateral hemiparesis accentuated 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 hemiparesis, paresis of cranial nerves respiratory disorders



Spinal Cord Injury

Spinal Cord Injury

The most often causes

- Traffic accidents
- Work and sports injuries

Mechanisms of injury

- Extensive Flexion, extension or rotation
- Direct impact

Back injury

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

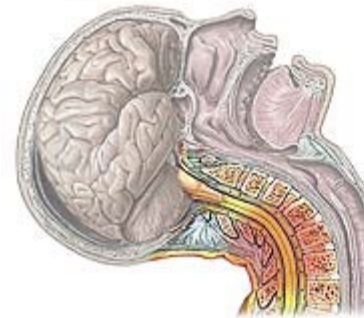
Spinal cord injury

- Stretch
- Pressure

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

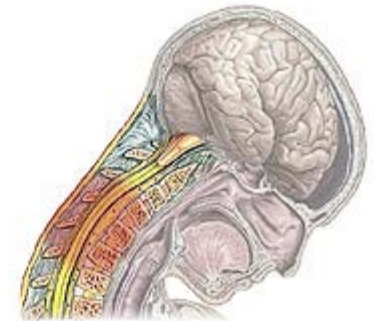
Spinal Cord Injury
3-4 / 100 000 persons per year
Almost 50% of patients are younger than 25 years

Hyperextension



Sprain or strain of cervical tissues

Hyperflexion



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 isshuria 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

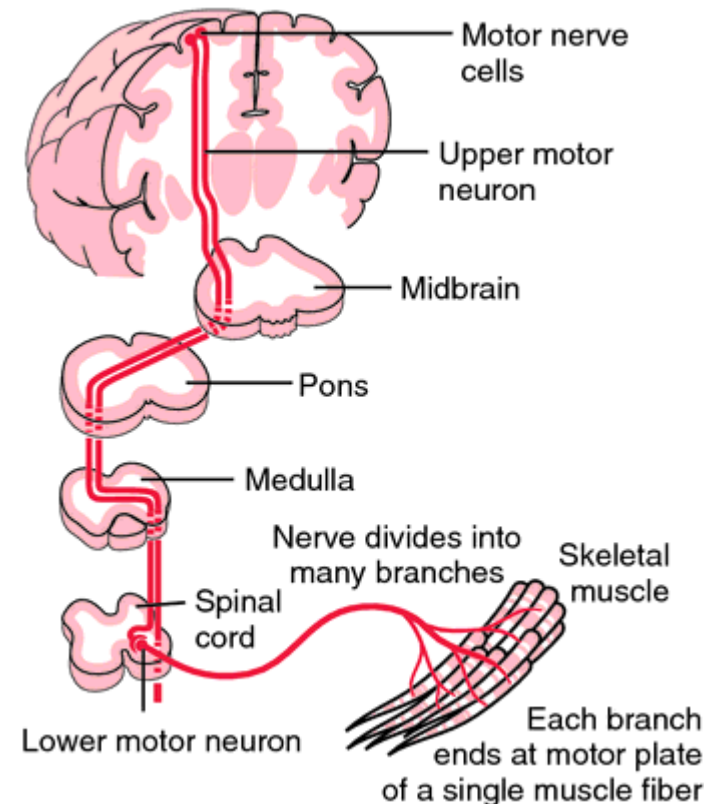
- Loss of muscle function most often caused by damage of nervous system

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



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

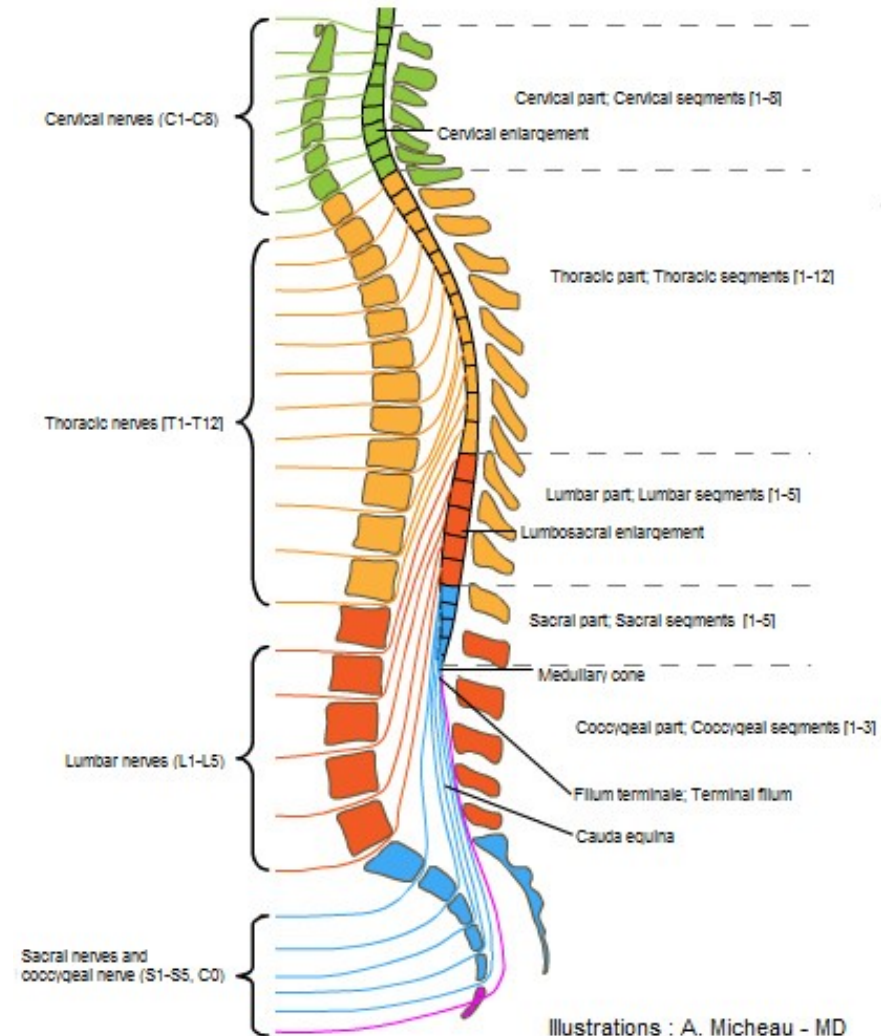
Plexus cervicalis: C1-C4

C4 – nervus phrenicus

Plexus brachialis: C5 – Th1

Plexus lumbalis: L1-L4

Plexus sacralis: S1-S5



Illustrations : A. Micheau - MD

<http://www.jhu.edu>

Consequences of Spinal Cord Injury Paralysis

C1 – C4

- ✓ Spastic quadriplegia
- ✓ Sphincter function disorders

C5 – Th2

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

Th3 – Th10

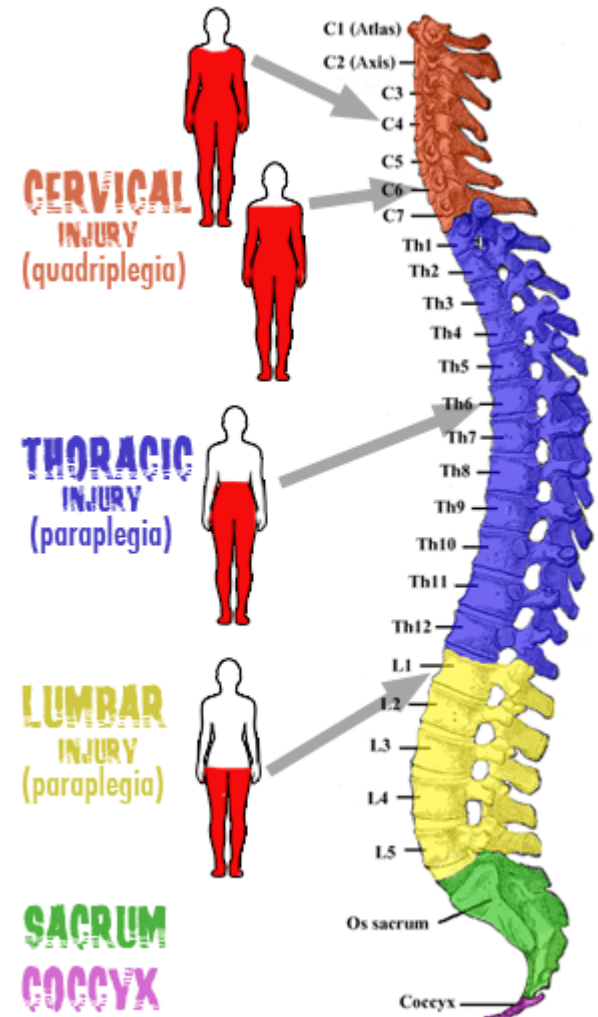
- ✓ Lower limbs: spastic paresis/plegia
- ✓ Sphincter function disorders

Th9 – L2

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

L3 – S5

- ✓ Sphincter function disorders



Consequences of Spinal Cord Injury

Paralysis

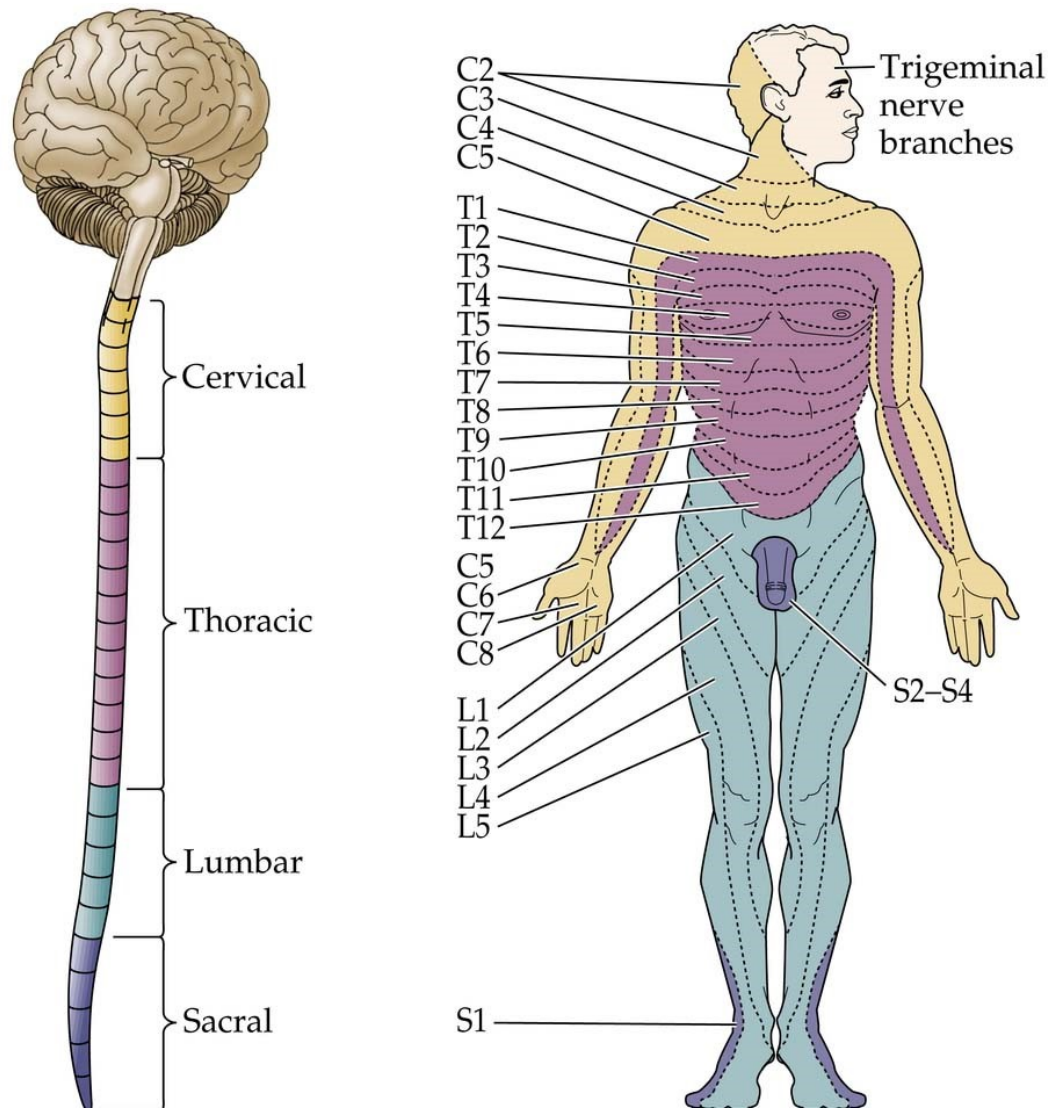
Hypesthesia

- Incomplete loss of sensation

For example: Thermal hypesthesia, tactile hypesthesia

Anesthesia

- Complete loss of sensation



THANK YOU

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