

# **Cerebrovascular diseases**

## **Part I**

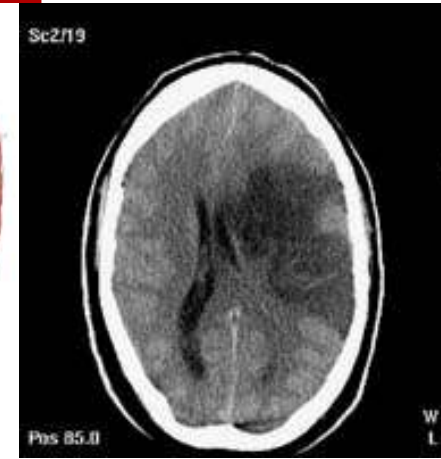
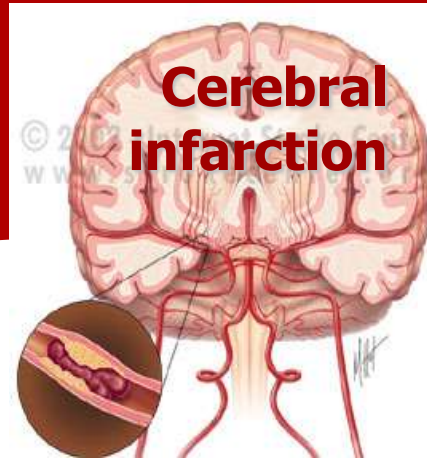
Prof. dr Dejana Jovanović

# Definition

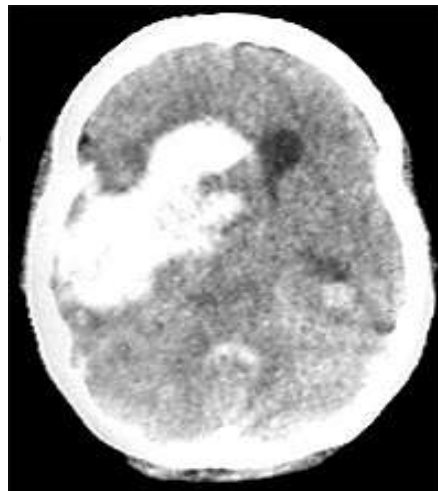
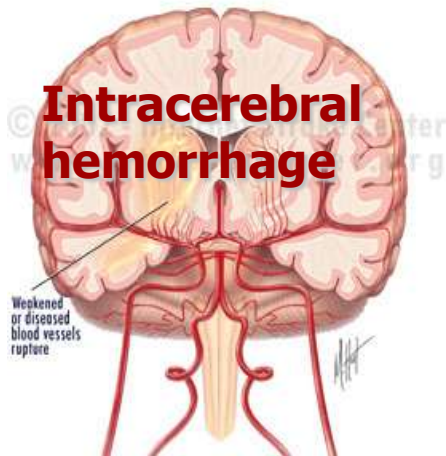
## Stroke

Sudden onset of focal, nonconvulsive, neurological deficit attributed to an acute vascular injury of the central nervous system (CNS)

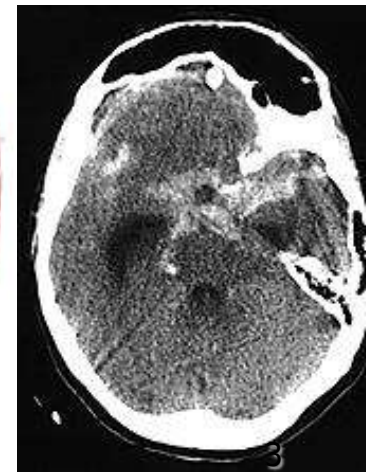
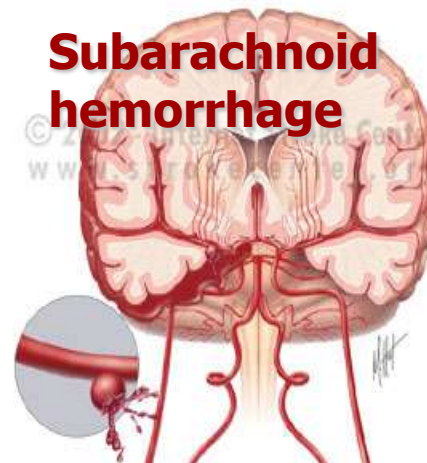
# Classification



75 - 85%



10-15%



1-5%

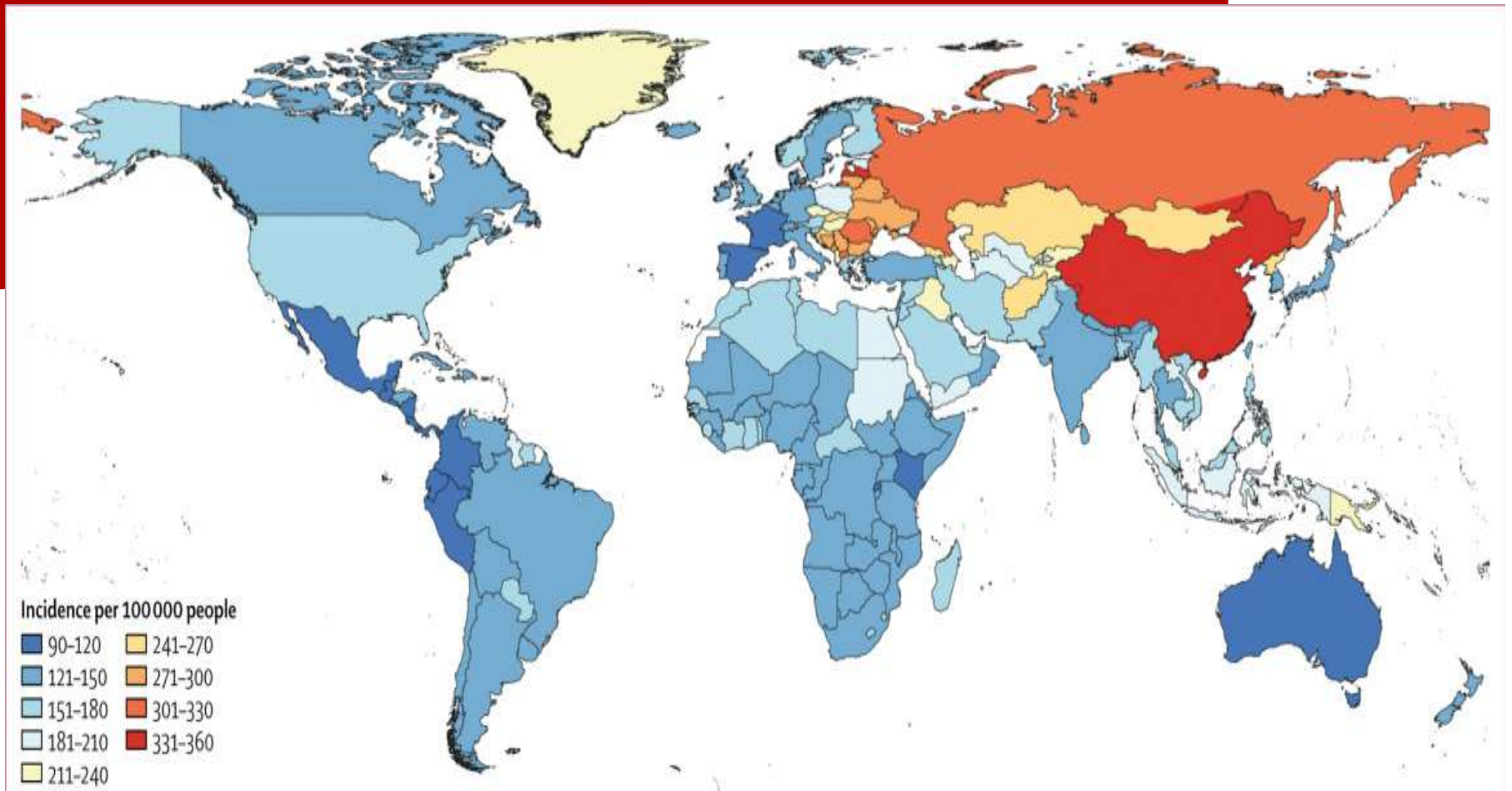


# Epidemiology

- Third leading cause of death in the world (9,6%), after heart diseases (12,7%) and malignancies (12,6%)
- Leading cause of permanent disability

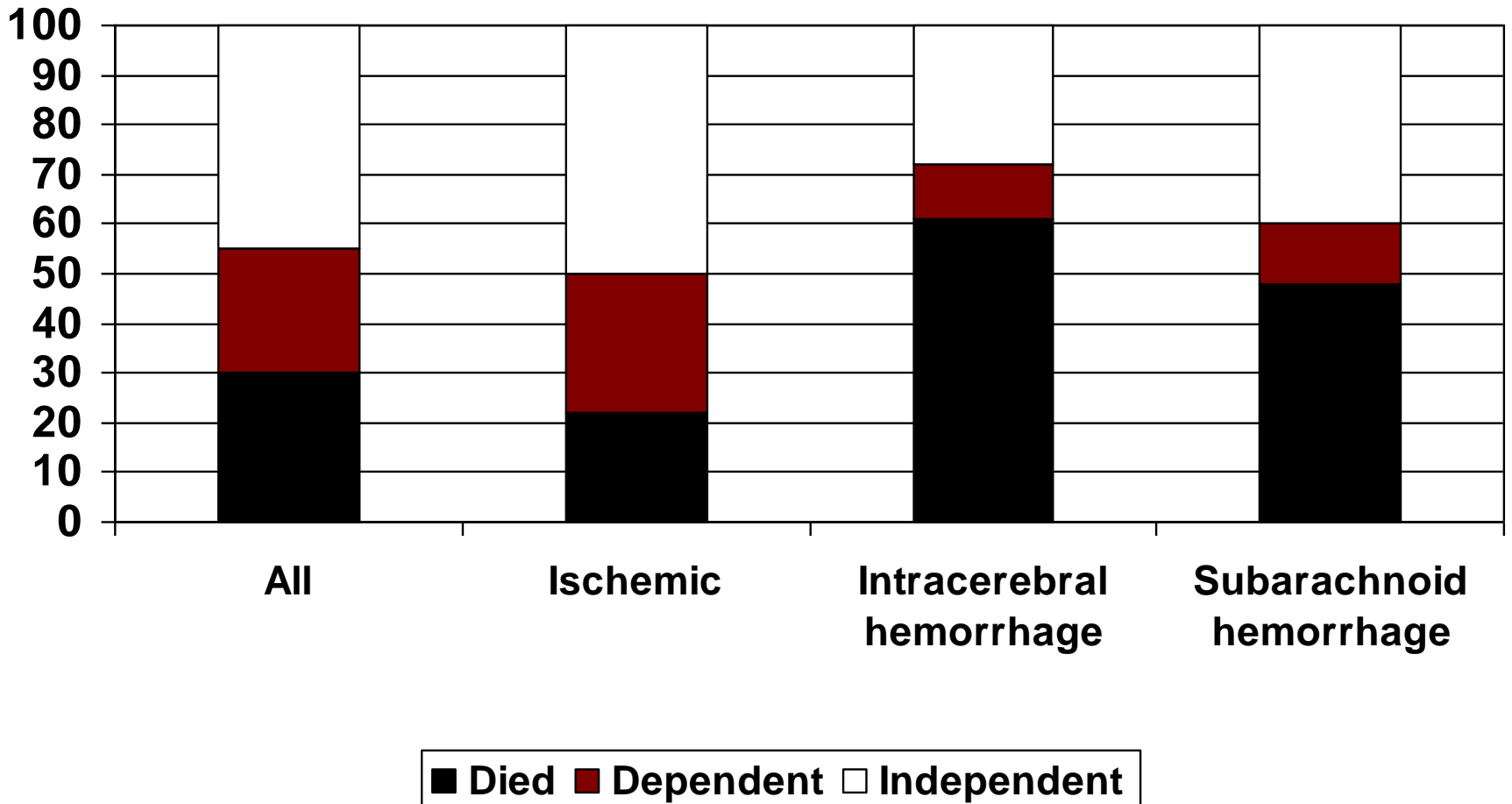


Significant emotional, social and economic consequences for the patient, family and the entire society!



- **1 out of 4 persons is going to get a stroke during lifetime**
- Incidence: 150-200/100000 inhabitants per year
- Prevalence: 600-700/100000 inhabitants per year

# Stroke outcome



# Stroke recurrence

**10 - 14% of patients with stroke or TIA will experience a new stroke within the first year and as many as 20% of them within 2 years**



# Risk factors

## **Risk factors that can not be corrected**

- Age
- Sex
- Race/ethnicity
- Heredity

## **Risk factors that can be corrected**

- Hypertension
- Heart diseases and/oratrial fibrillation
- Diabetes mellitus
- Hyperlipidemia
- Smoking
- Alcohol





The risk for stroke doubles with every decade of life



Men have a higher risk of stroke, but the stroke prevalence is higher among women because they live longer.



African-Americans in the USA have twice the risk for stroke than Caucasians; also Japanese and Indoasians.



Paternal presence of stroke increases the risk for stroke by 2.4 times, and maternal 1.4.

# Hypertension

**Hypertensive patients have at least 3 times greater risk for stroke**

- the stroke risk increases linearly with the increase in blood pressure
- **there is no safe threshold**



The risk of stroke is increased in younger people with hypertension, especially for hemorrhagic stroke

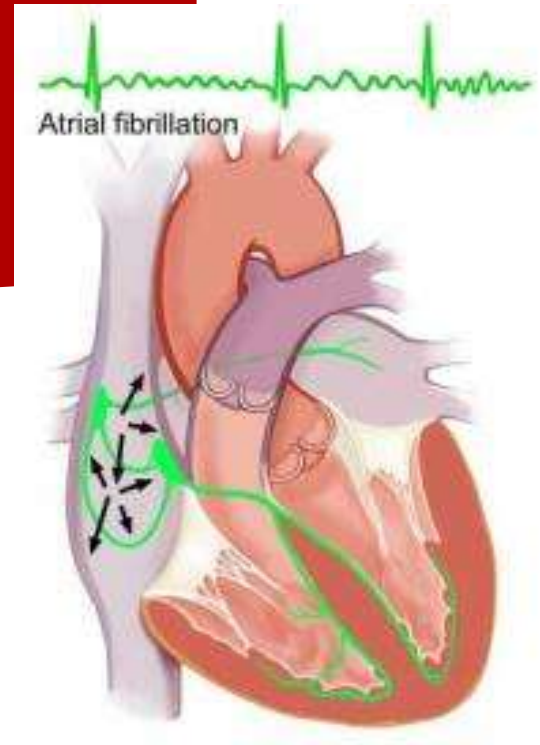
# Hypertension

## Risk Factors for Stroke



- **The treatment of hypertension reduces the risk of stroke by 50%**

# Atrial fibrillation



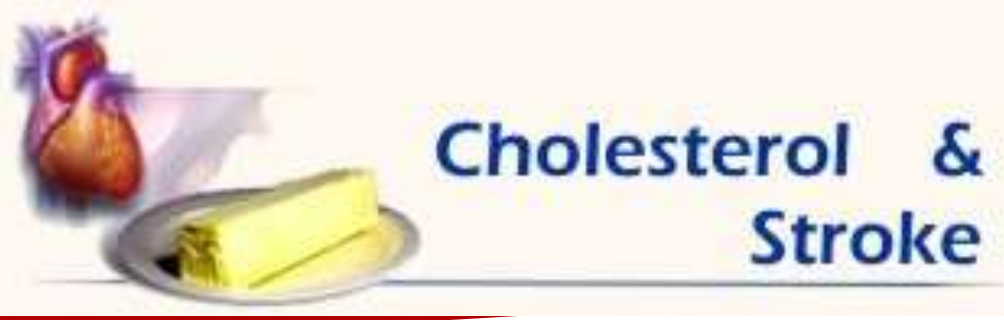
- 15-25% of all strokes are associated with atrial fibrillation
- **Atrial fibrillation increases the risk of stroke by 4-5 times**
- Anticoagulant therapy reduces the risk of stroke by 70%

# Diabetes mellitus



**2 times greater risk for stroke in diabetes**

# Hyperlipidemia



**The risk for stroke in hyperlipidemia is 2-3 times**

- High total and LDL cholesterol, triglycerides and lipoprotein (a), as well as low HDL cholesterol increase the risk of ischemic stroke, but not hemorrhagic

# Smoking

**The risk for stroke in active smokers is 3 times higher than for non-smokers**



Smoking cessation reduces the risk of stroke by 50% after 1 year, but the stroke risk of a non-smoker is reached only after 5-9 years.

**Passive smokers are at increased risk of developing stroke!**

# Alcohol

- Protective effect of up to 2 drinks/day and increased risk for more than 5 drinks/day
- Acute alcohol intoxication carries a stroke risk among young adults





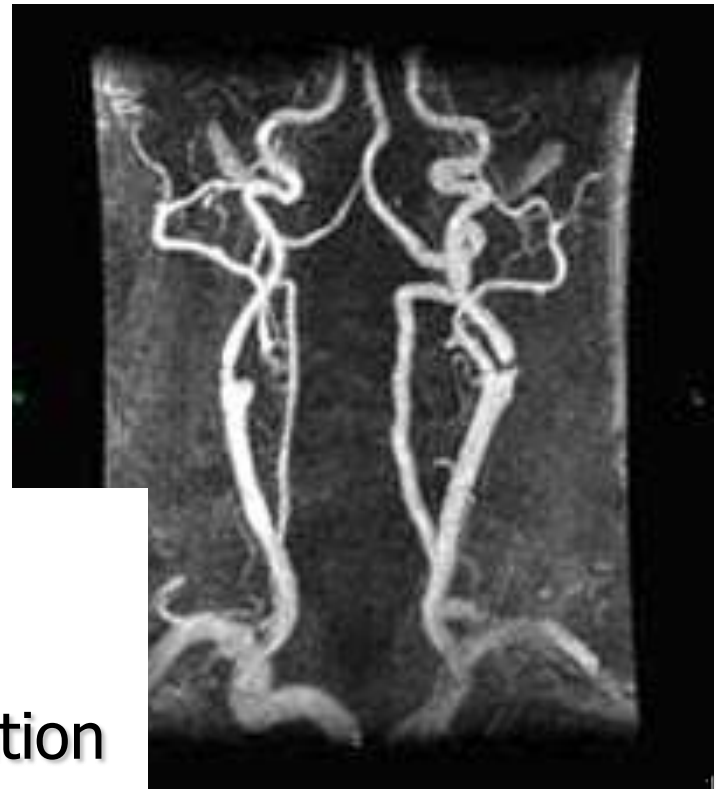
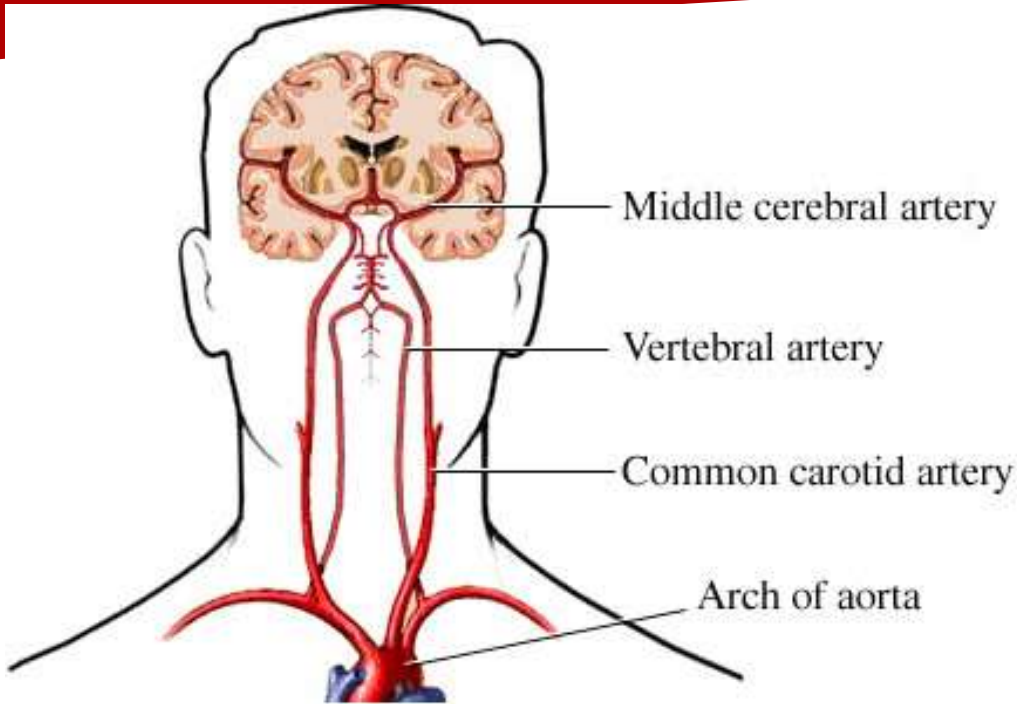
# Unconfirmed risk factors



- Obesity
- Physical inactivity
- Nutrition
- Hormone replacement therapy
- Oral contraceptives
- Hyperhomocysteinemia

# **Ischemic stroke**

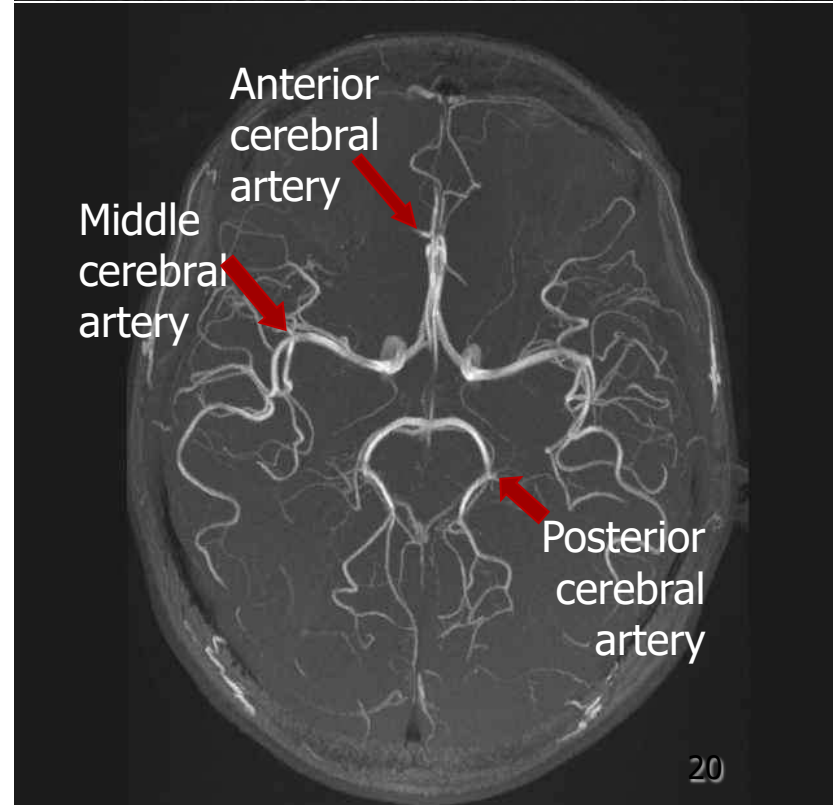
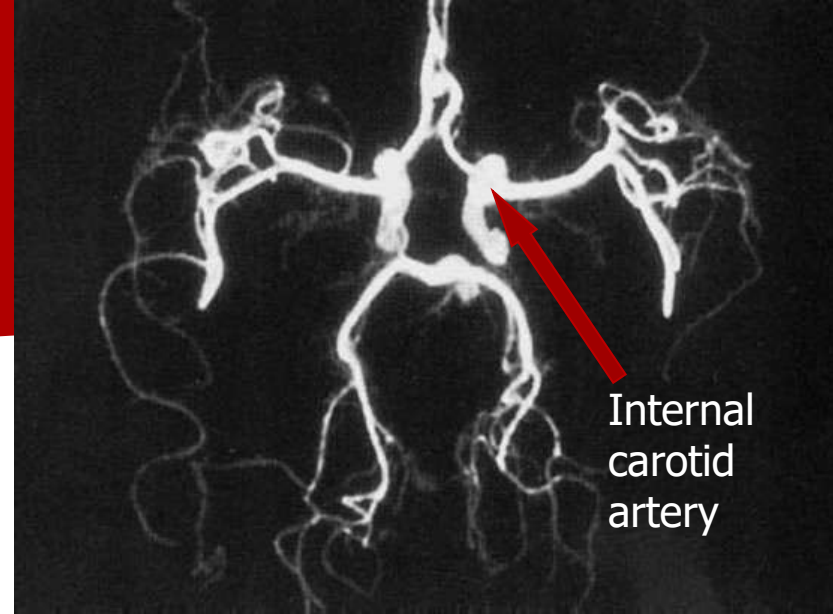
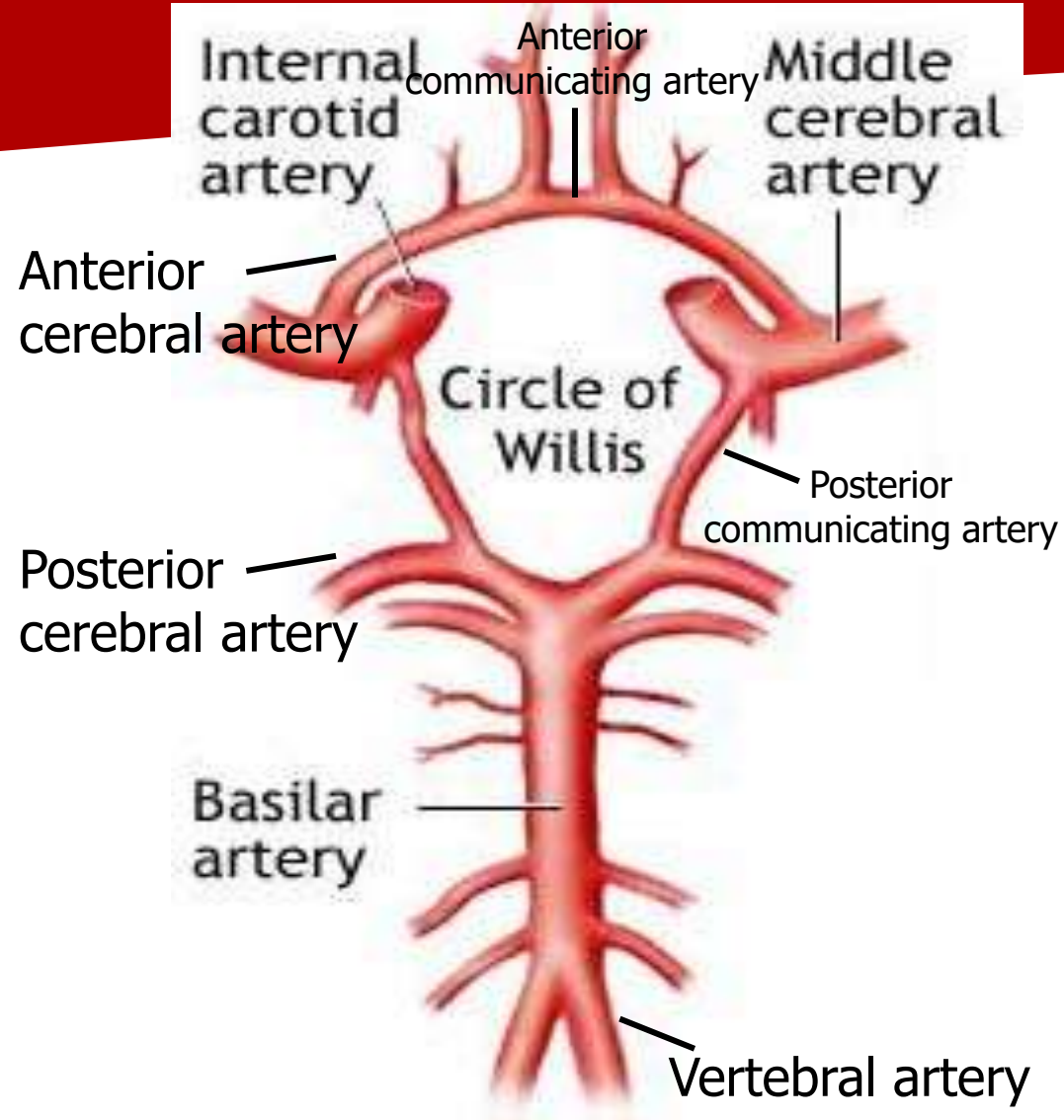
# Brain vascular anatomy



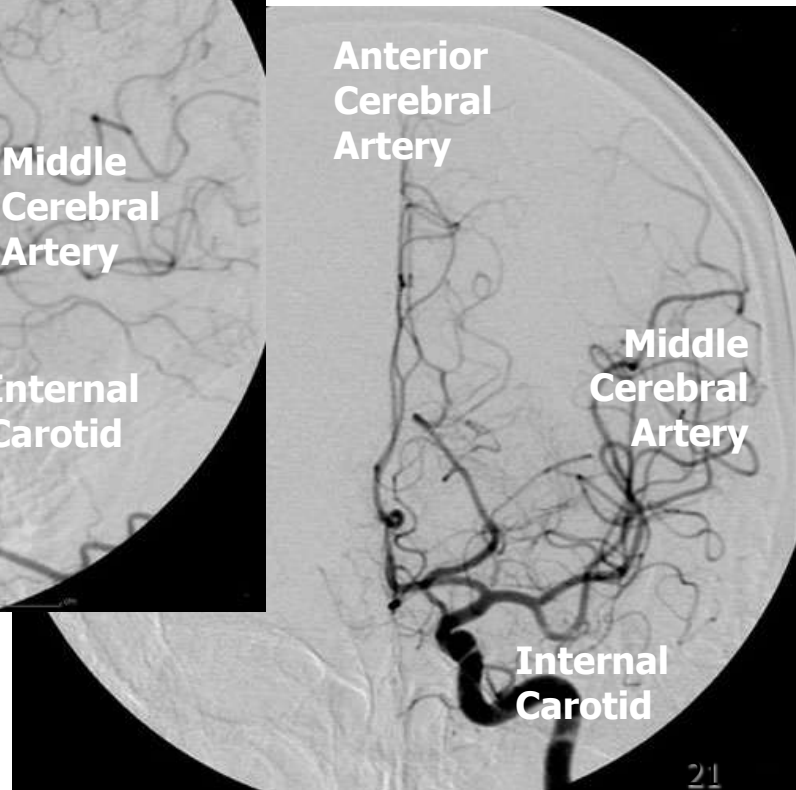
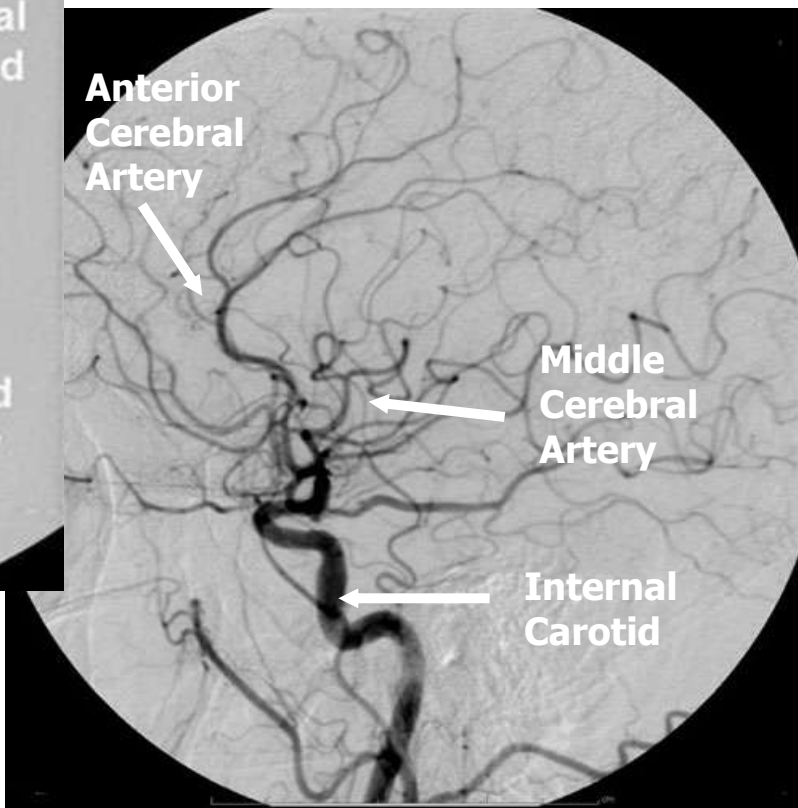
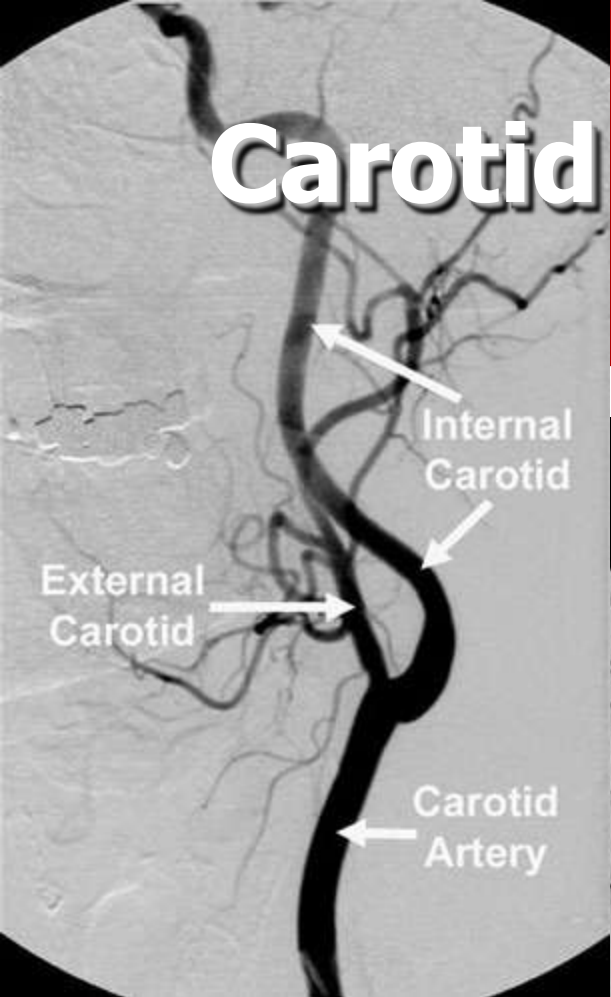
## Cerebral blood supply:

- anterior (carotid) circulation
- posterior (vertebrobasilar) circulation

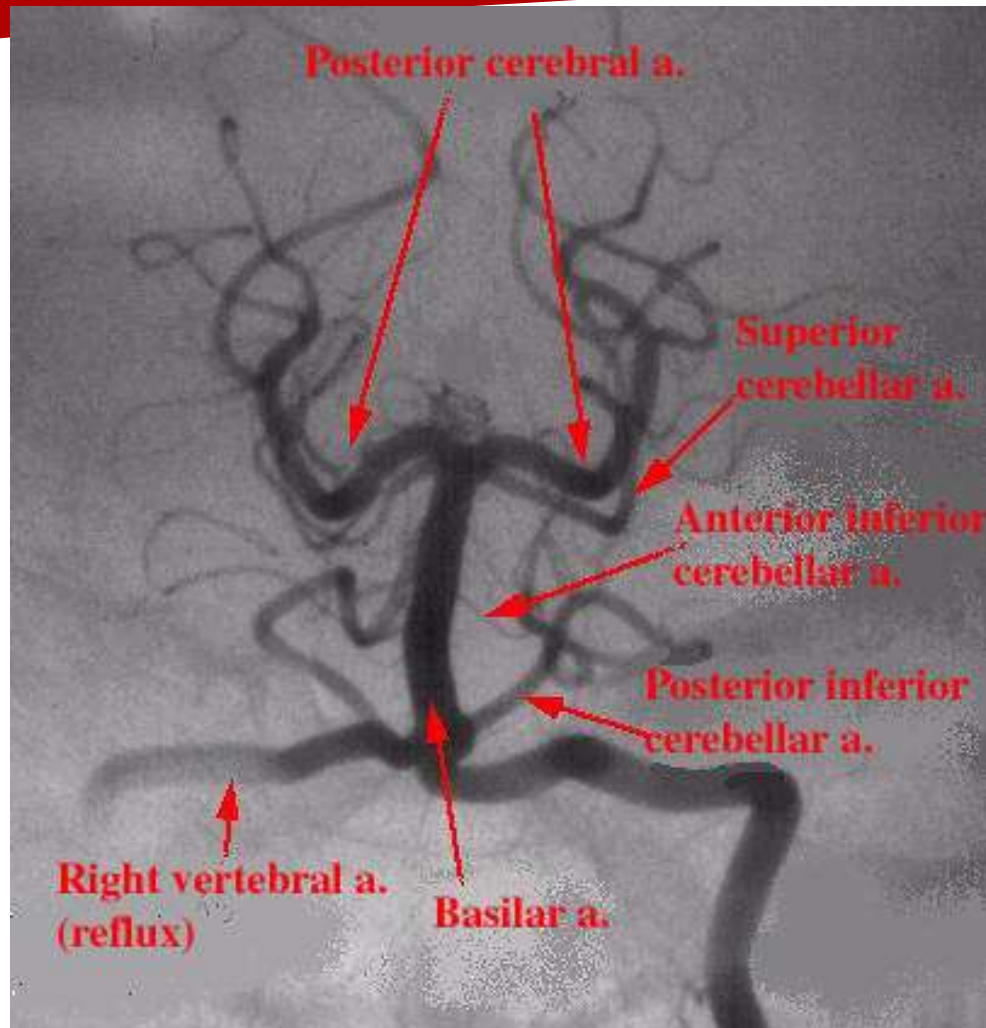
# Circle of Willis



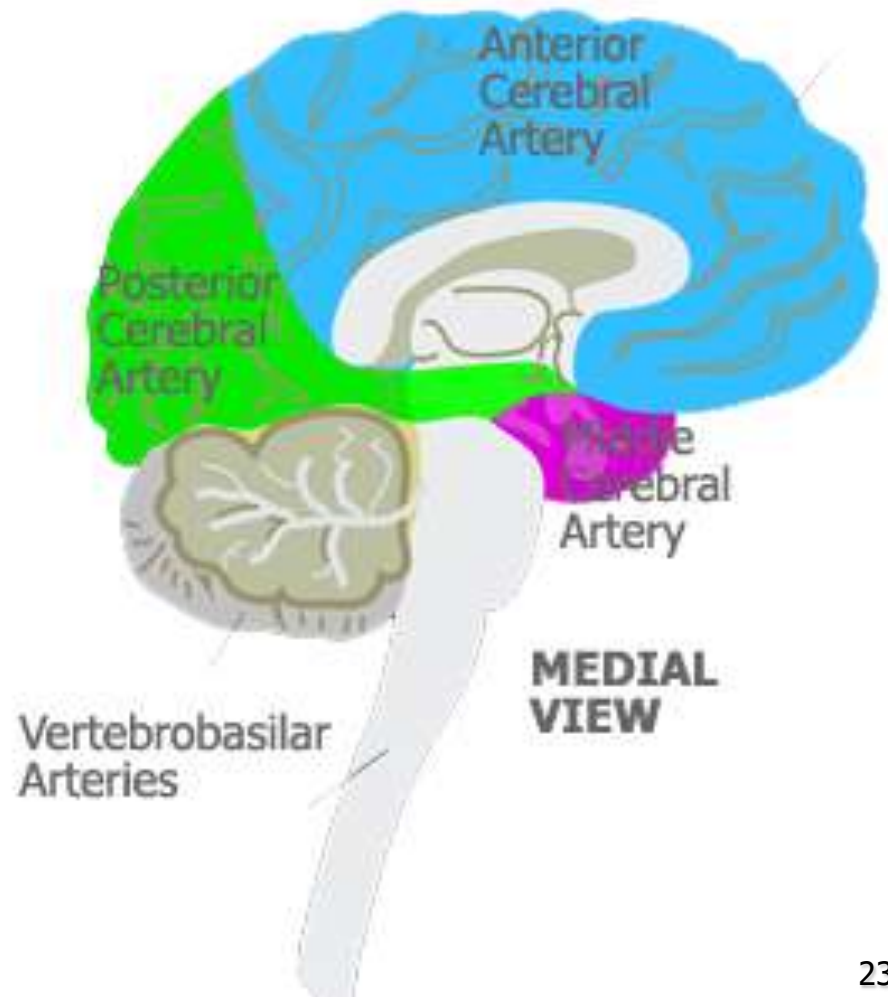
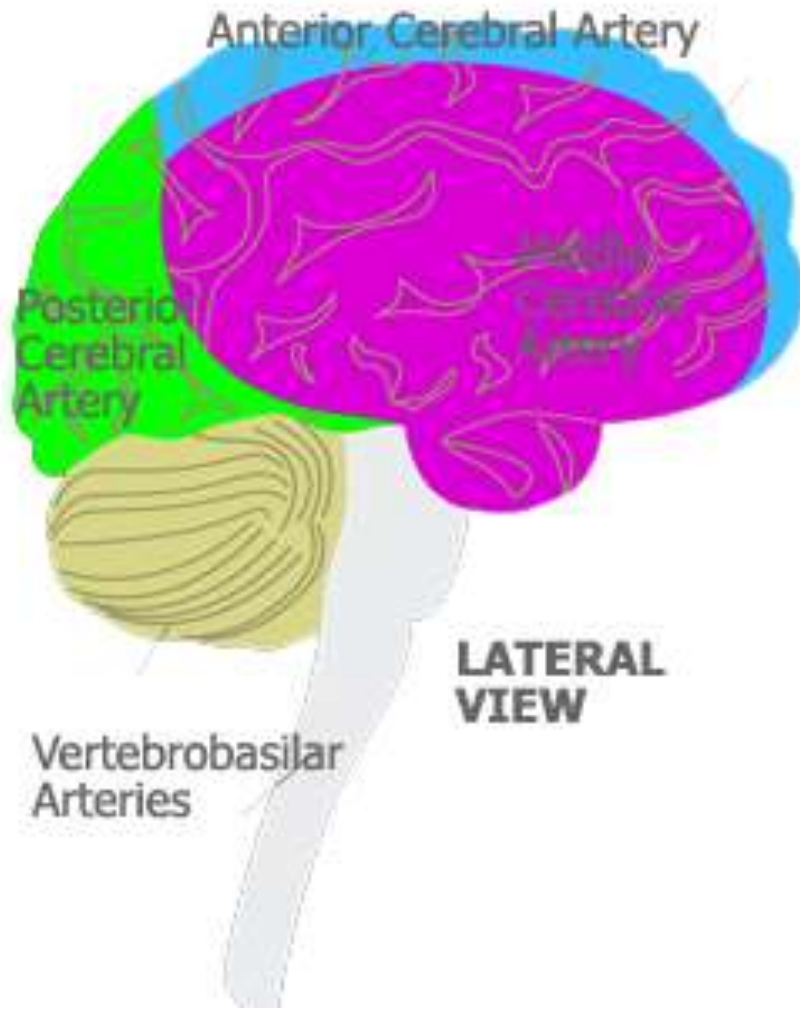
# Carotid angiograms



# Vertebrobasilar angiogram



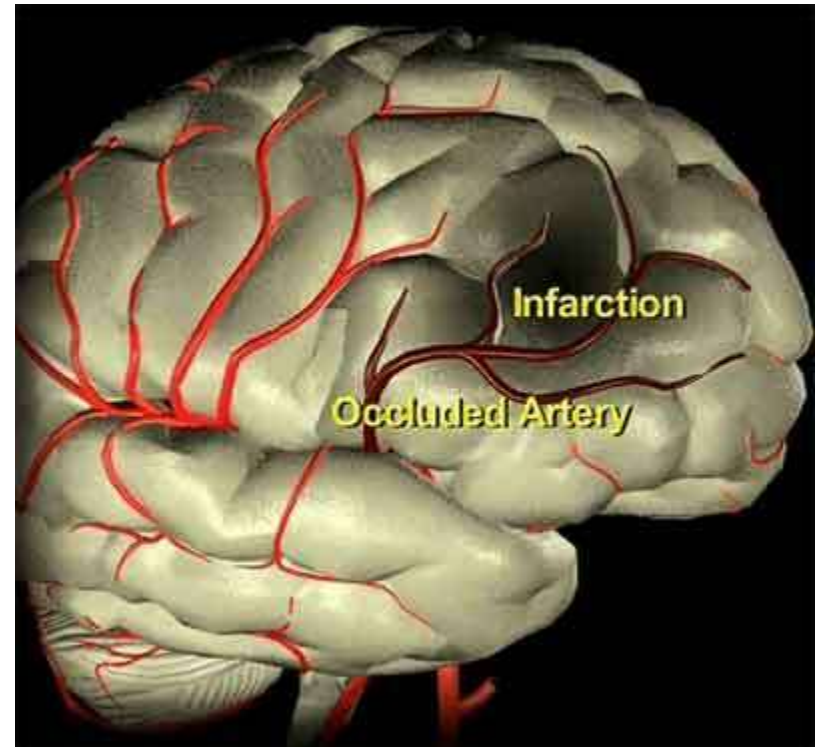
# Areas of brain artery supply



**Decreased or absent cerebral blood flow initiates reduced oxygen and glucose brain supply.**

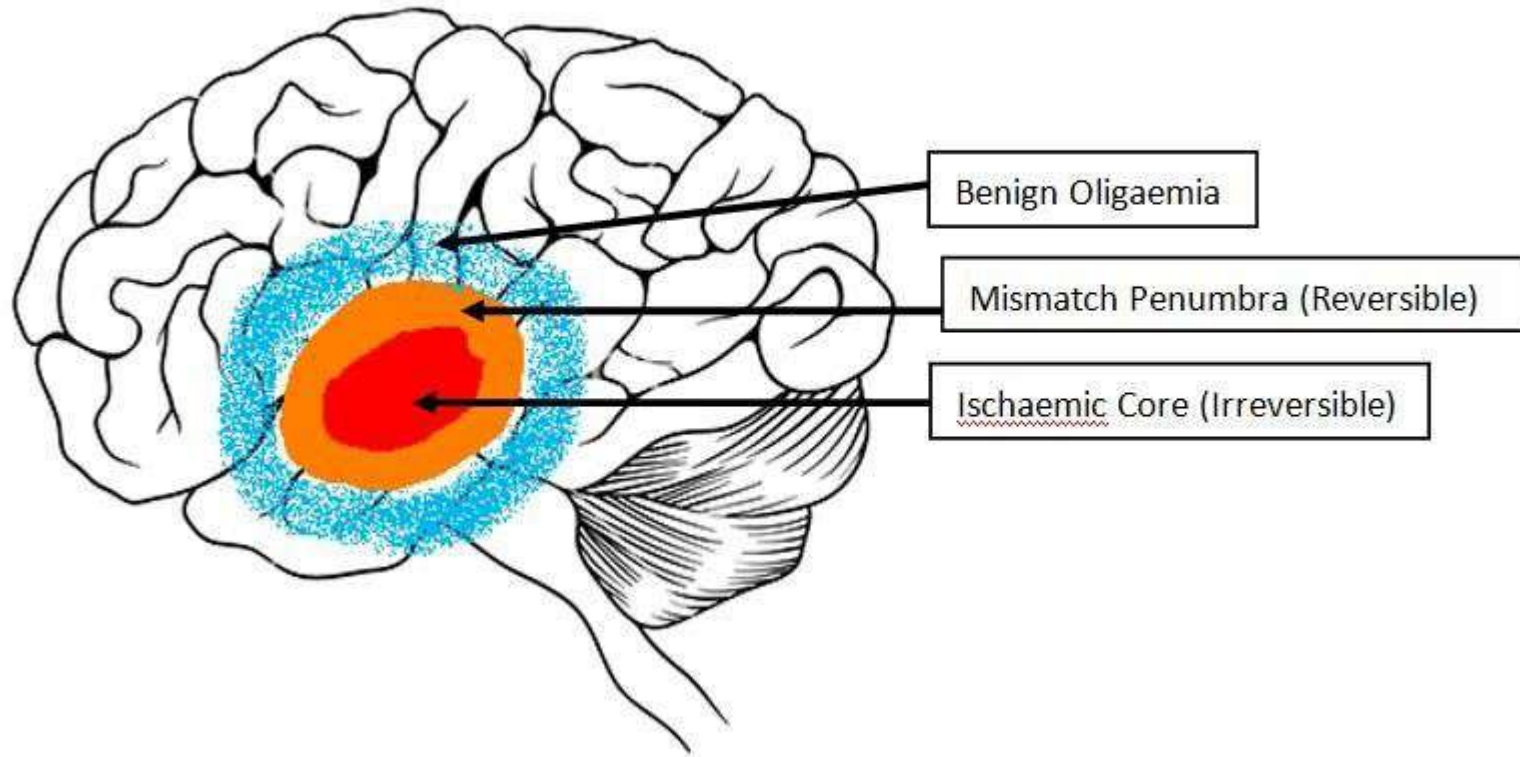
### **After:**

- 30 sec – impaired brain metabolism
- 1 min – impaired neuronal functions
- 5 min – metabolic cascade leading to brain infarction



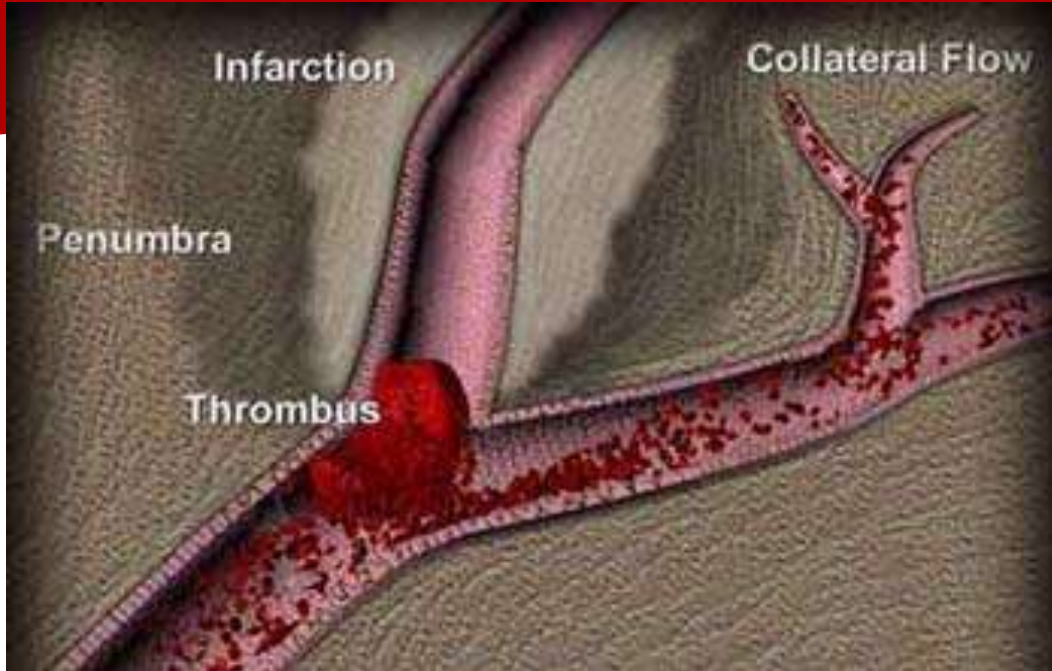


# Brain ischemia



The margins between ischemic core and normal CBF surroundings are not sharp

# Ischemic penumbra

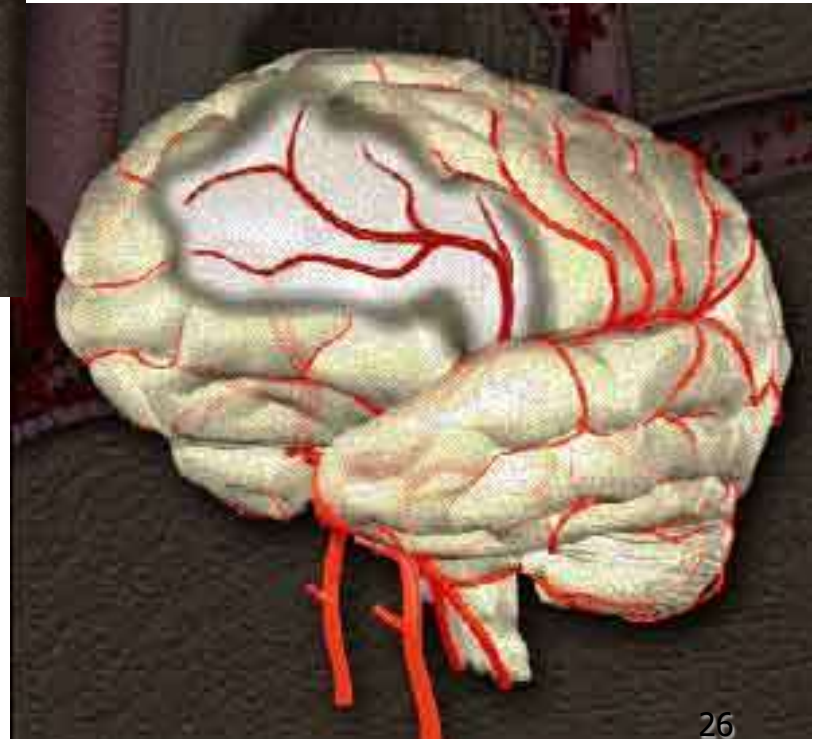


## Infarction core

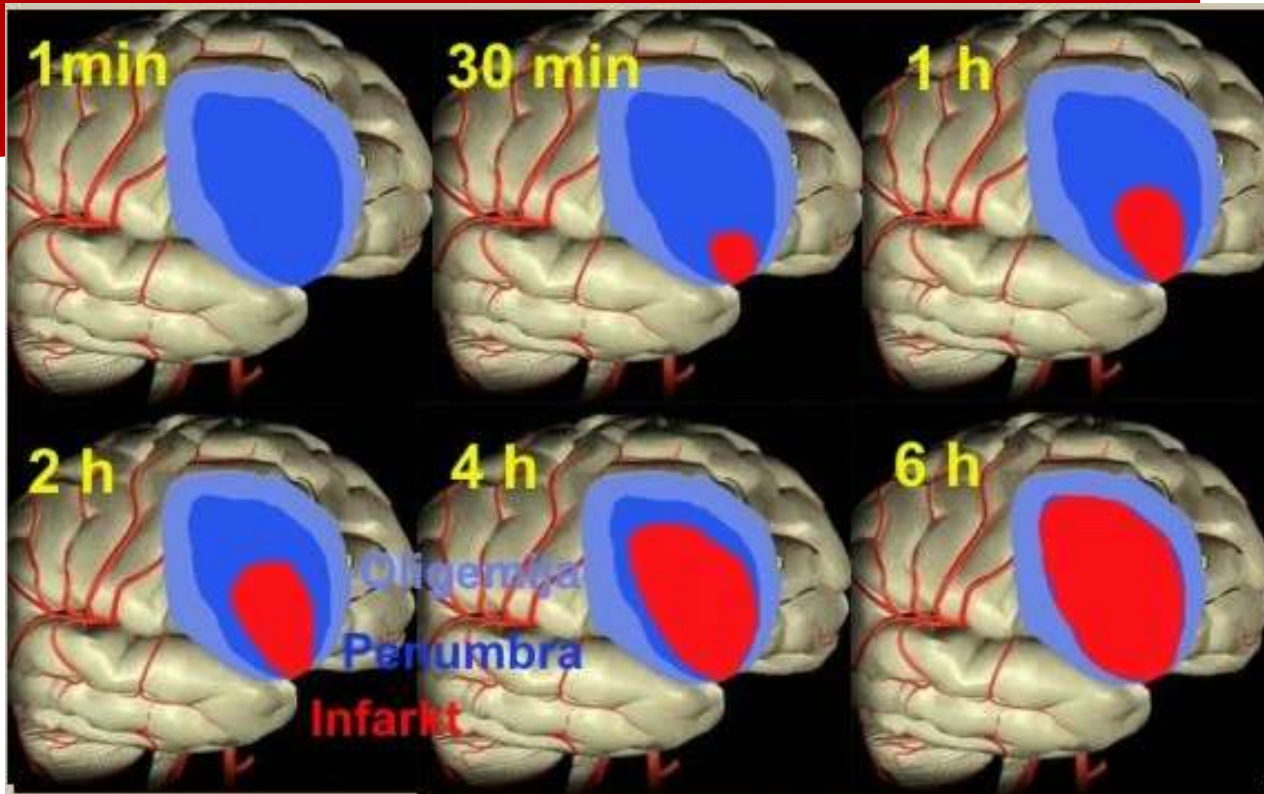
- irreversible neuronal damage

## Ischemic penumbra

- functionally silent neurons, without structural damage
- potentially reversible neuronal changes



# Penumbra changes

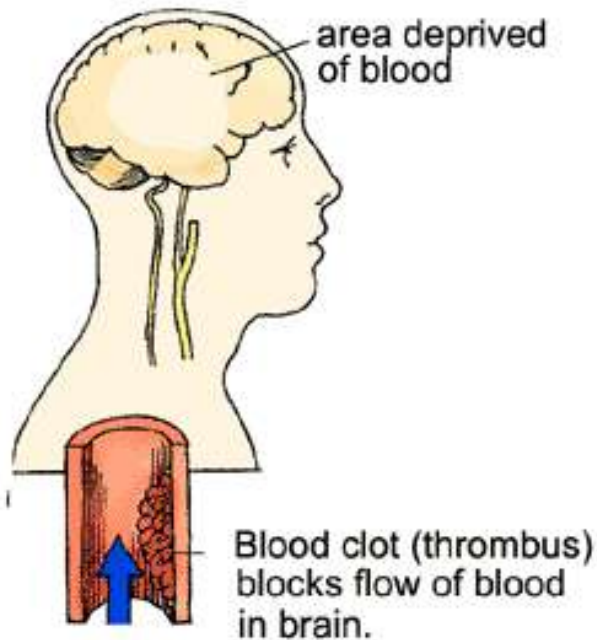


- Central infarction core progressively spread over the ischemic penumbra
- Early recanalisation and restoration of the blood flow can prevent spreading of infarction

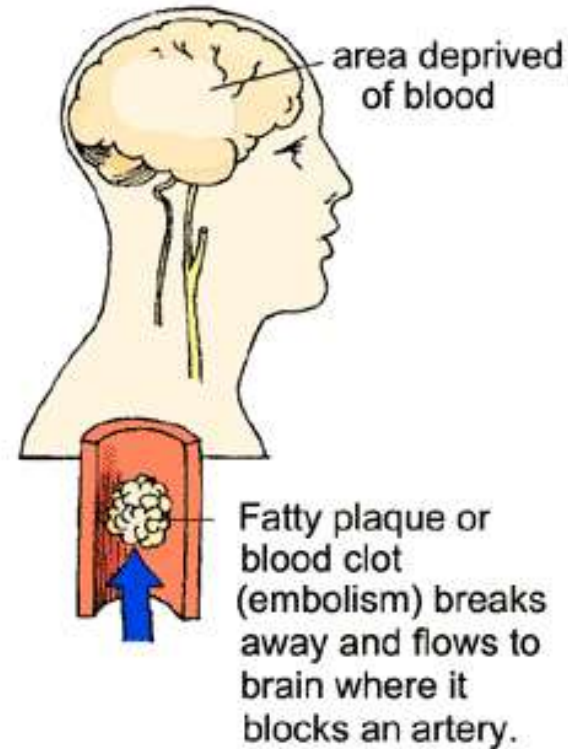
# Ischemic stroke

## Patophysiologic mechanisms

Thrombotic Stroke



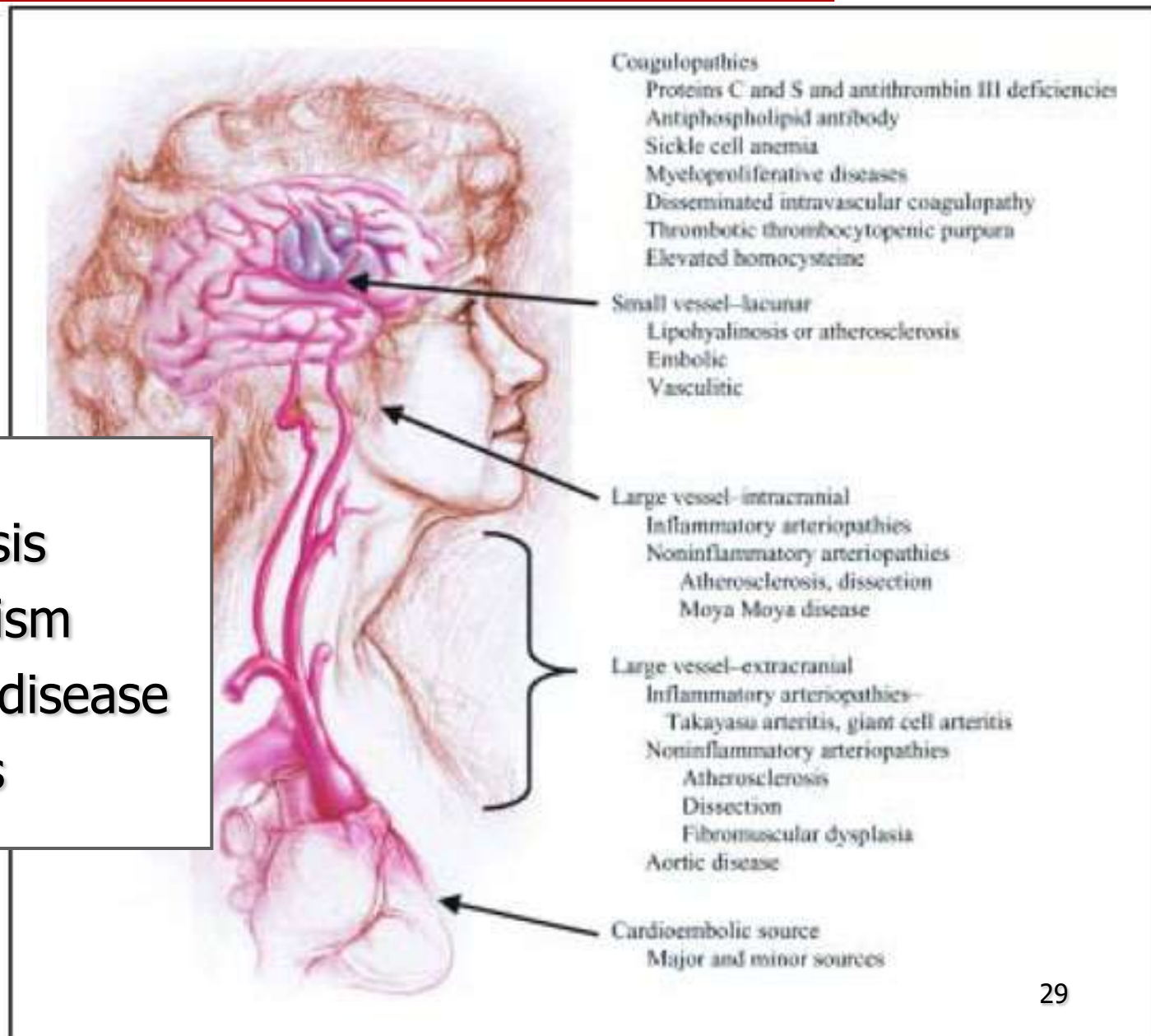
Embolic Stroke



- Arterial wall (on site) thrombosis
- Embolism (distal, cardiogenic, paradoxical)
- Lacunar stroke
- Hypoperfusion

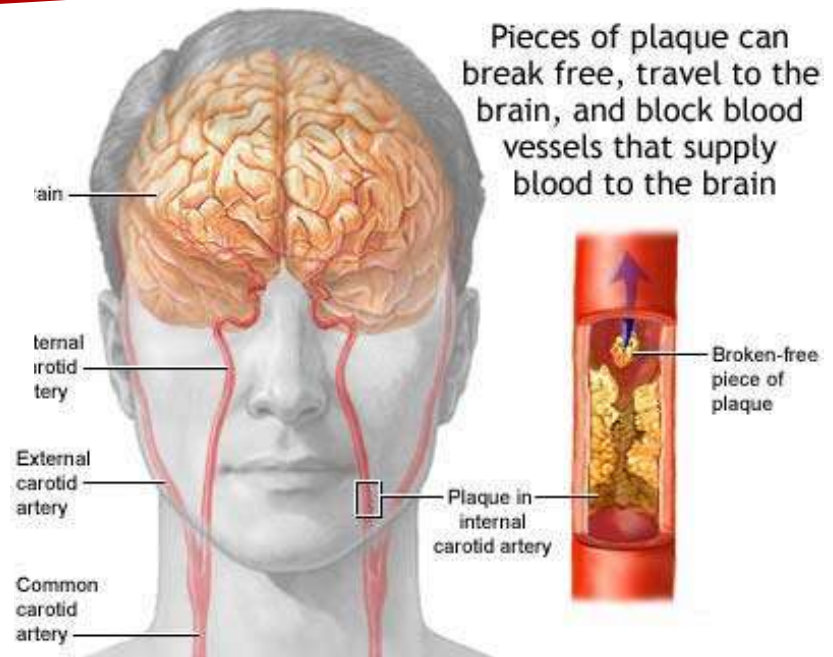
# Etiology of ischemic stroke

- Large-artery atherosclerosis
- Cardioembolism
- Small artery disease
- Other causes

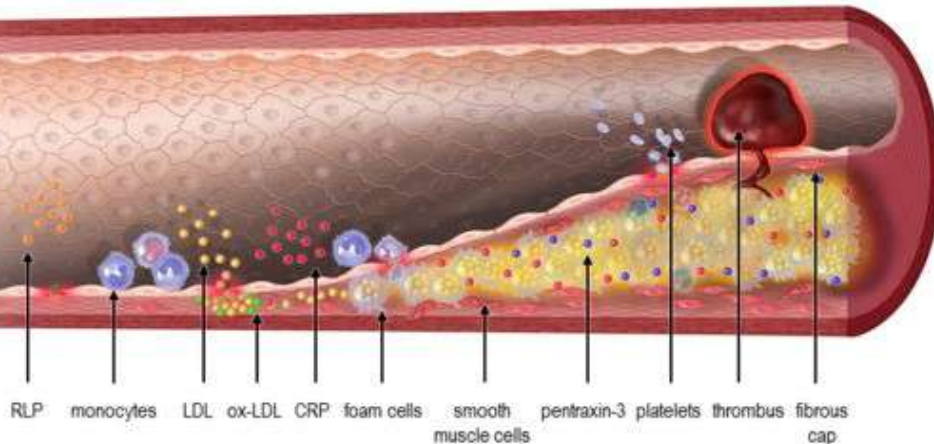


# Large-artery atherosclerosis

- Significant artery stenosis  $\geq 70\%$
- Numerous risk factors
- Patients  $\geq 65$  years



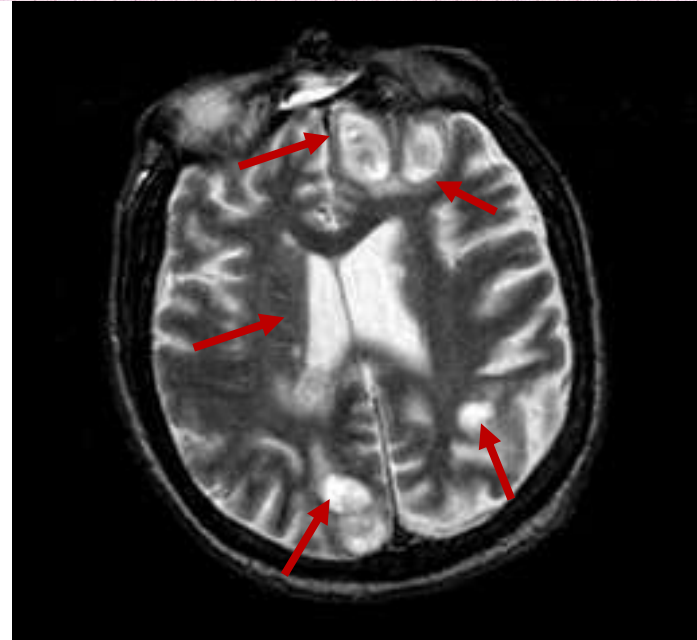
Monocyte adhesion    LDL oxidation    Macrophage infiltration    Foam cell formation    Smooth muscle cell proliferation and migration    Fibrous cap formation    Plaque rupture and thrombus formation



- Thrombosis in situ
- Distal embolism

# Cardioembolism

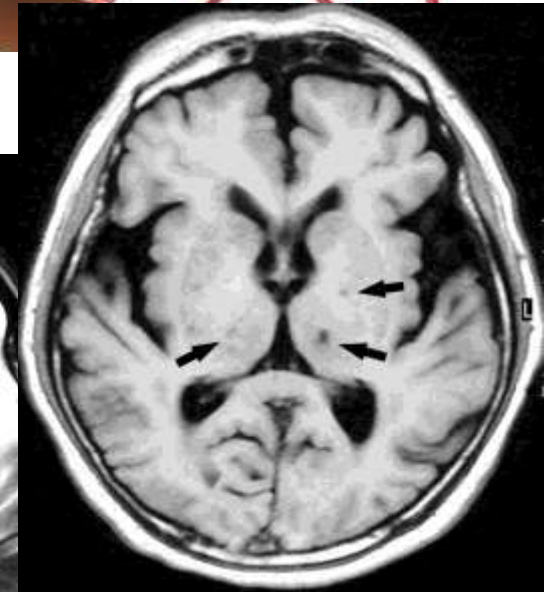
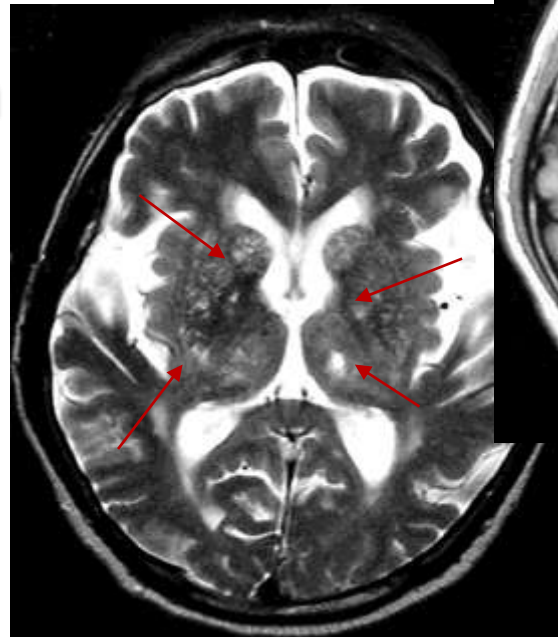
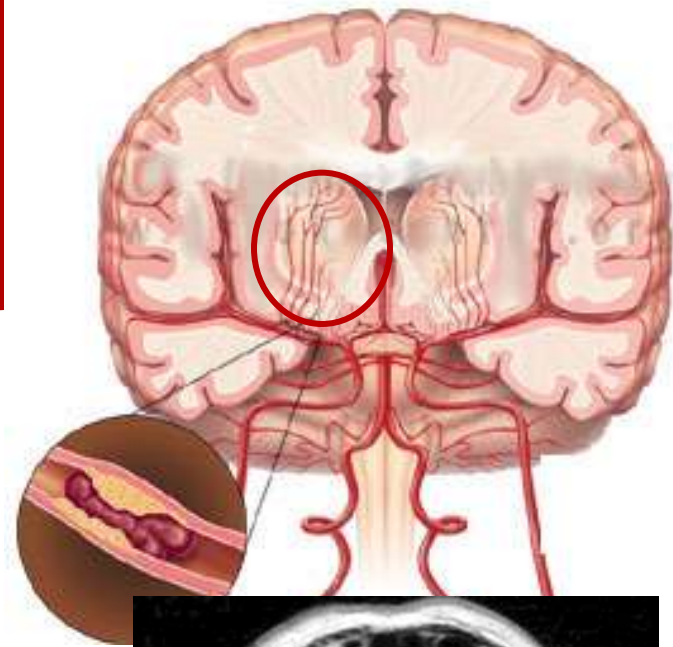
- Heart disease
  - atrial fibrillation
  - mitral stenosis
  - arteficial valves
  - dilated cardiomyopathy
  - endocarditis, ...
- Younger age patients



Multiple infarctions in different vascular territories

# Small-artery disease

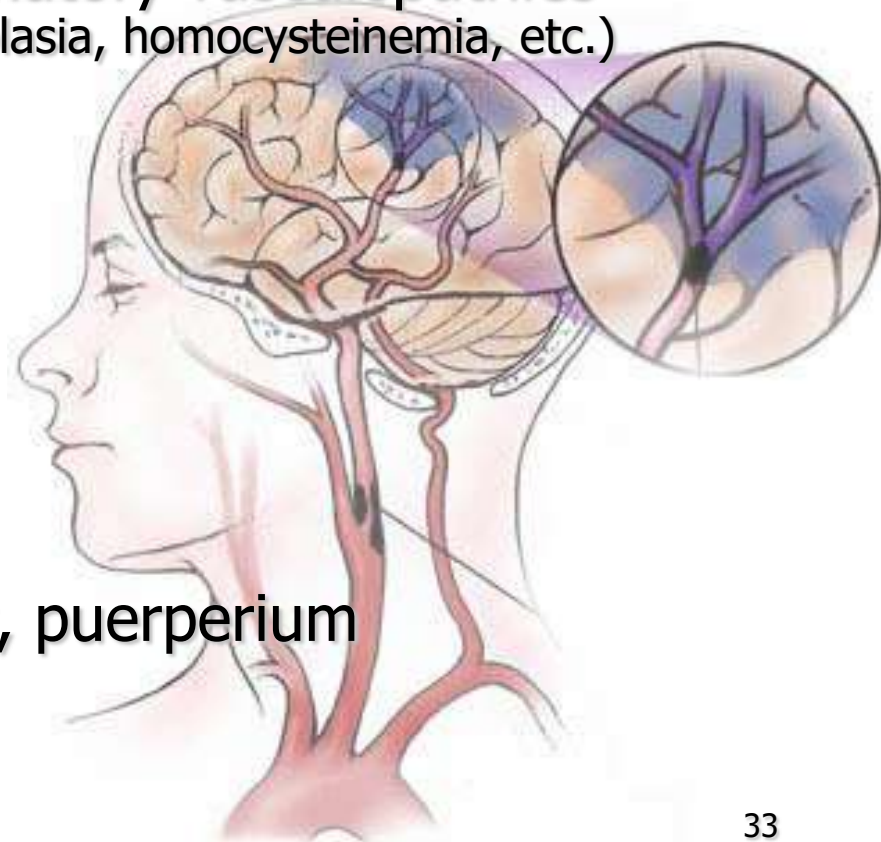
- Small perforating arteries affected
- Deep subcortical areas
- Small lacunar infarctions ( $\leq 15$  mm)
- Long-lasting hypertension





# Other causes

- Nonatherosclerotic inflammatory vasculopathies (vasculitis)
- Nonatherosclerotic non-inflammatory vasculopathies (**arterial dissection**, fibromuscular dysplasia, homocysteinemia, etc.)
- Coagulopathies
- Vasospasm
- Systemic hypotension
- Drug or alcohol abuse
- Oral contraceptives, pregnancy, puerperium
- Local vessel-wall compression



# Clinical presentation

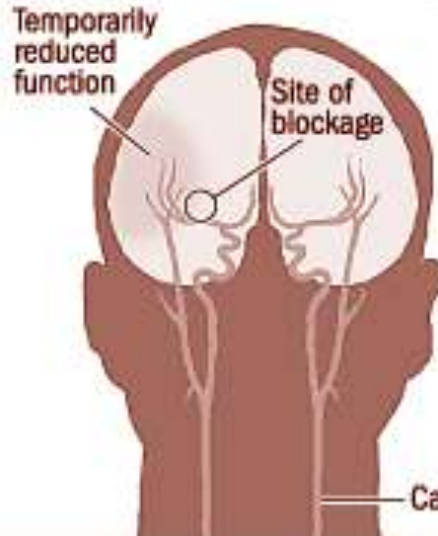
# Time profile

## Stroke and mini-stroke

Transient ischemic attacks – TIAs, or mini-strokes – result when a cerebral artery is temporarily blocked, decreasing blood flow to the brain. Many strokes result from a complete blockage of a cerebral artery, leading to death of brain cells and permanent loss of certain functions.

### TIA

Artery temporarily blocked

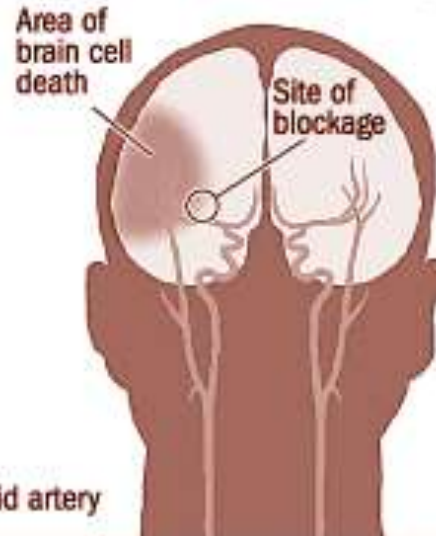


### TIA (transient ischemic attack)

functional brain impairment,  
without structural changes

### Stroke

Artery completely blocked



### Complete ischemic stroke

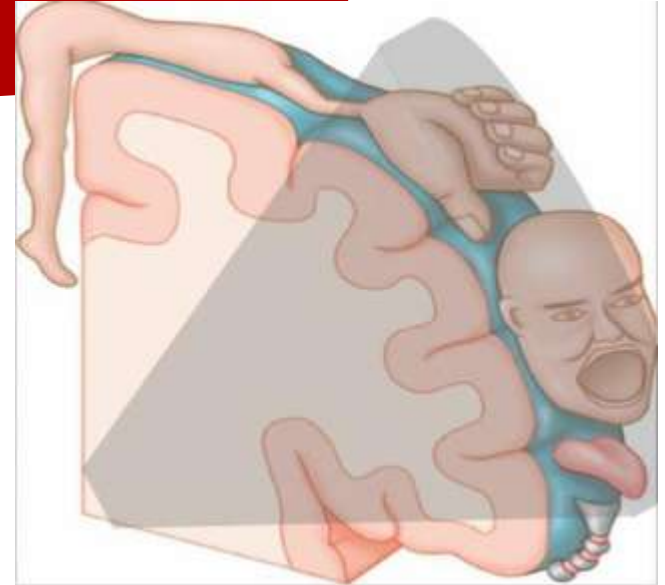
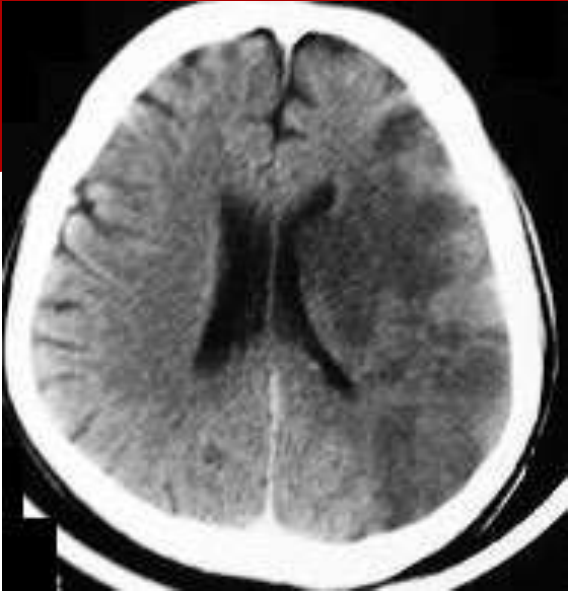
stroke symptoms completed immediately after onset

# Clinical presentation

## TIA

- short-lasting episode of neurological dysfunction caused by focal brain or retinal ischemia
- lasts < 60min, usually 5-20 min
- complete recovery
- no signs of acute infarction on neuroimaging (CT or MRI)
- precedes stroke in 20% of patients, usually in 2 days before stroke onset

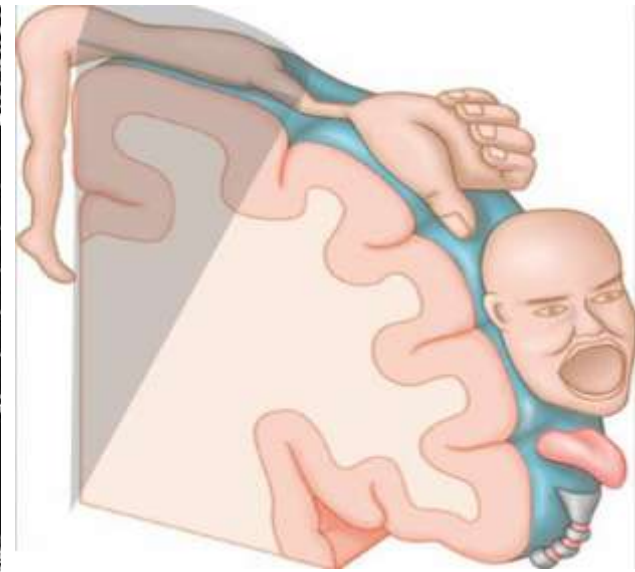
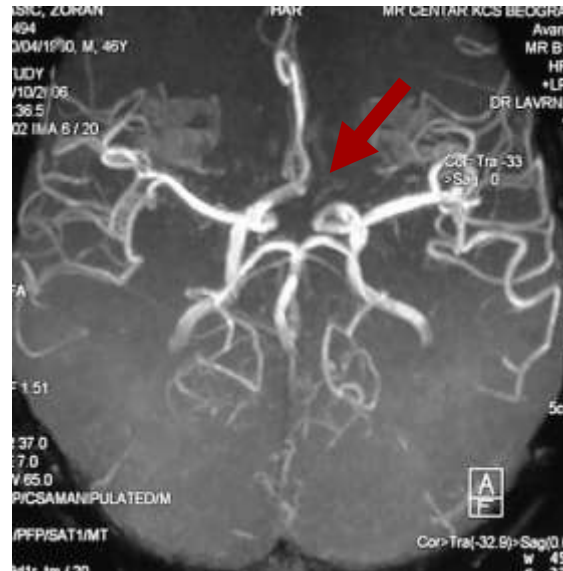
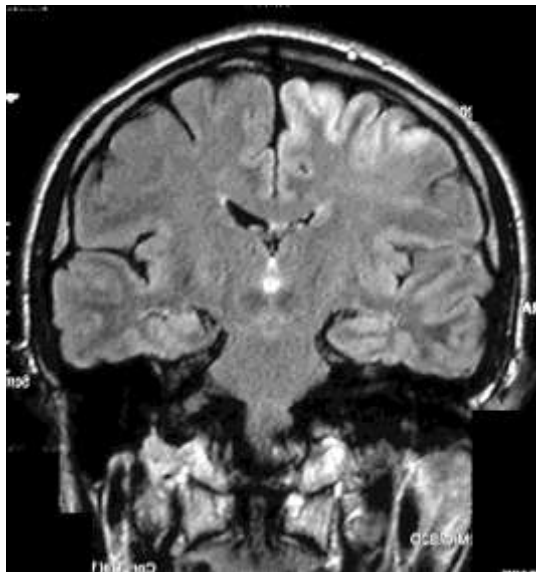
# Clinical presentation



## Middle cerebral artery occlusion

- Contralateral hemiplegia (faciobrachial type)
- Contralateral sensitive loss
- Speech arrest - aphasia (dominant hemisphere)
- Space and body neglect (subdominant hemisphere)
- Contralateral hemianopsia
- Possible consciousness disturbance (usually after 48 hours)

# Clinical presentation



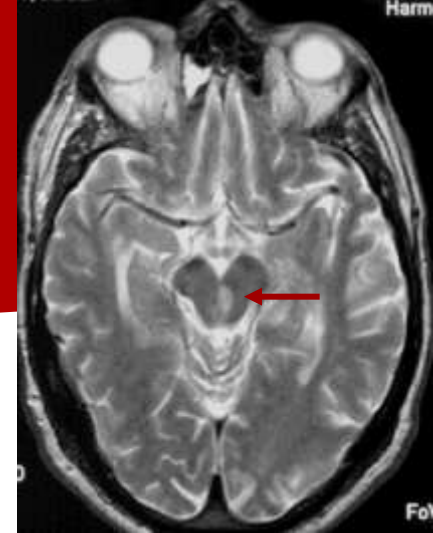
## Anterior cerebral artery occlusion

- Contralateral hemiplegia (crural type)
- Contralateral sensitive loss in leg
- Urine incontinence

# Clinical presentation

## Posterior cerebral artery occlusion

- Proximal occlusion – Ipsilateral ophthalmoplegia (III nerve palsy), contralateral hemiplegia, thalamic syndrome, involuntary movements (ballistic, choreatic), hemisensory loss
- Cortical branch occlusion - homonym hemianopsia with preserved macular vision
- Bilateral occlusion – cortical blindness



# Clinical presentation

## Basilar artery thrombosis

- headache, ataxia, dizziness
- quadriplegia, coma
- “locked-in” syndrome

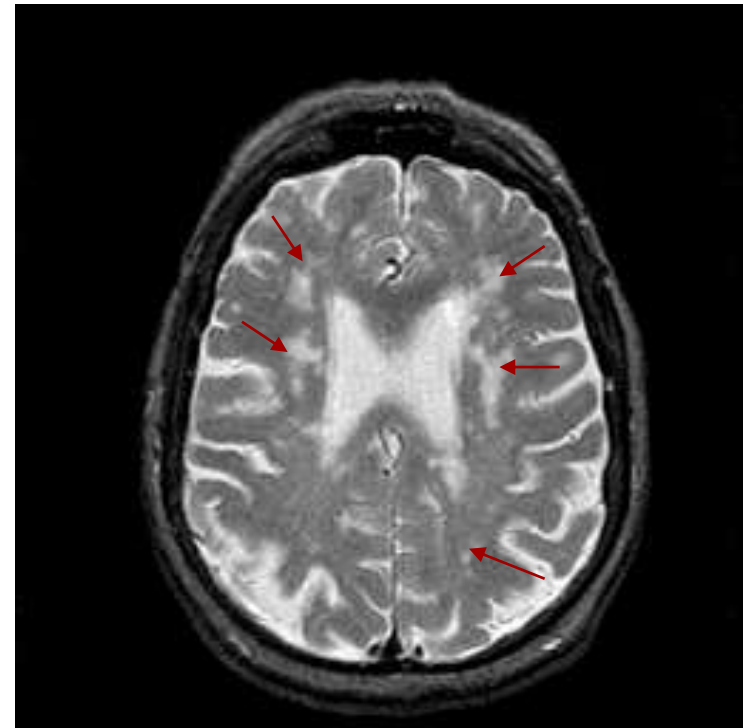


# Clinical presentation



## Typical lacunar syndromes

- Pure motor hemiparesis
- Pure sensitive syndrome
- Ataxic hemiparesis
- Dysarthria – clumsy hand syndrome





# Clinical presentation

## General symptoms

- Seizures – not so often; with emboligenic infarctions
- Headache – rare in ischemic stroke
- Nausea/vomiting – vertebrobasilar infarctions
- Coma – initial symptom in BA infarctions  
after 3-5 days in large MCA infarctions

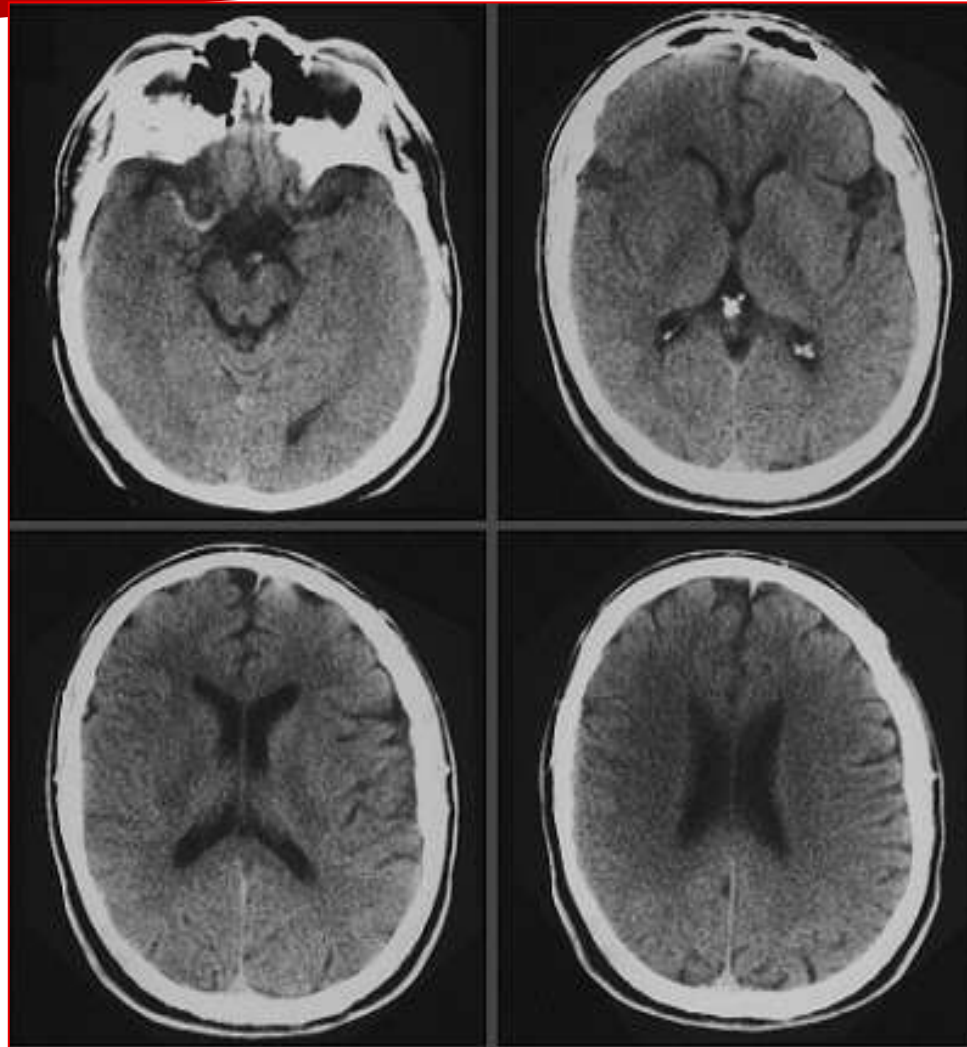
# Stroke complications

- Deep vein thrombosis and pulmonary embolism
- Hypostatic or aspiration pneumonia
- Heart arrhythmias
- Electrolyte disturbances
- Infections
- Decubital ulcers
- Sepsis

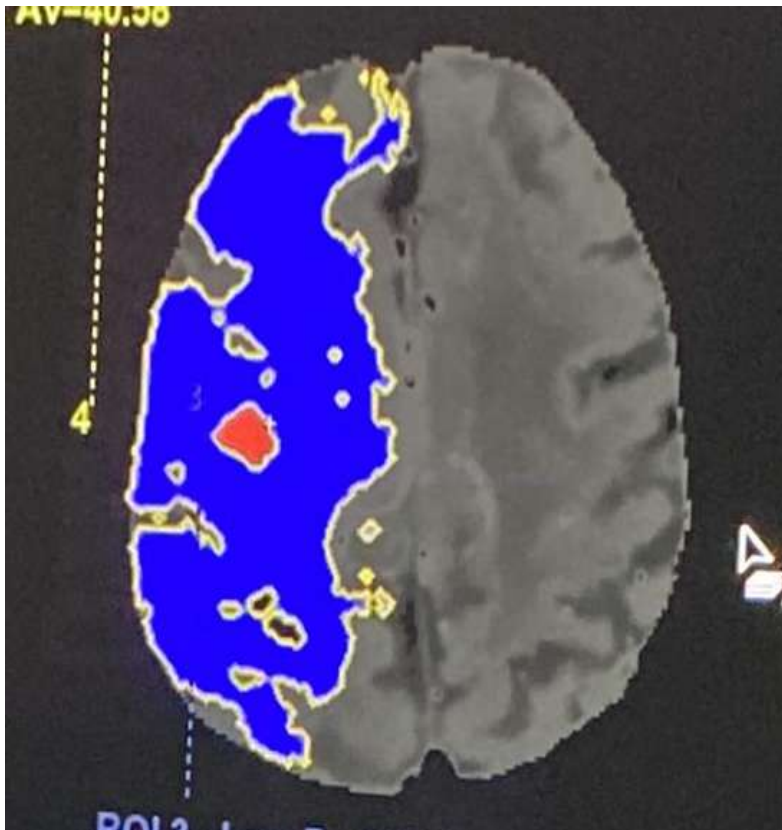
# Diagnostic procedures

Immediately	Delayed
Routine blood and urine analyses (CBC, SR, PT, PTT, Gly, urea, creatinine, electrolytes, lipids, ...)	Additional laboratory test (immunoserological, VDRL, blood coagulation tests, ...)
Electrocardiogram	Head MRI
<b>Head CT/CT perfusion</b>	Angiography (MRA, CTA, DSA)
<b>CT angiography</b>	Vascular ultrasound (cervical arteries, TCD)
	Echocardiography
	Lumber puncture

# Head CT after 2.5h of stroke onset



# CT perfusion – penumbra detection

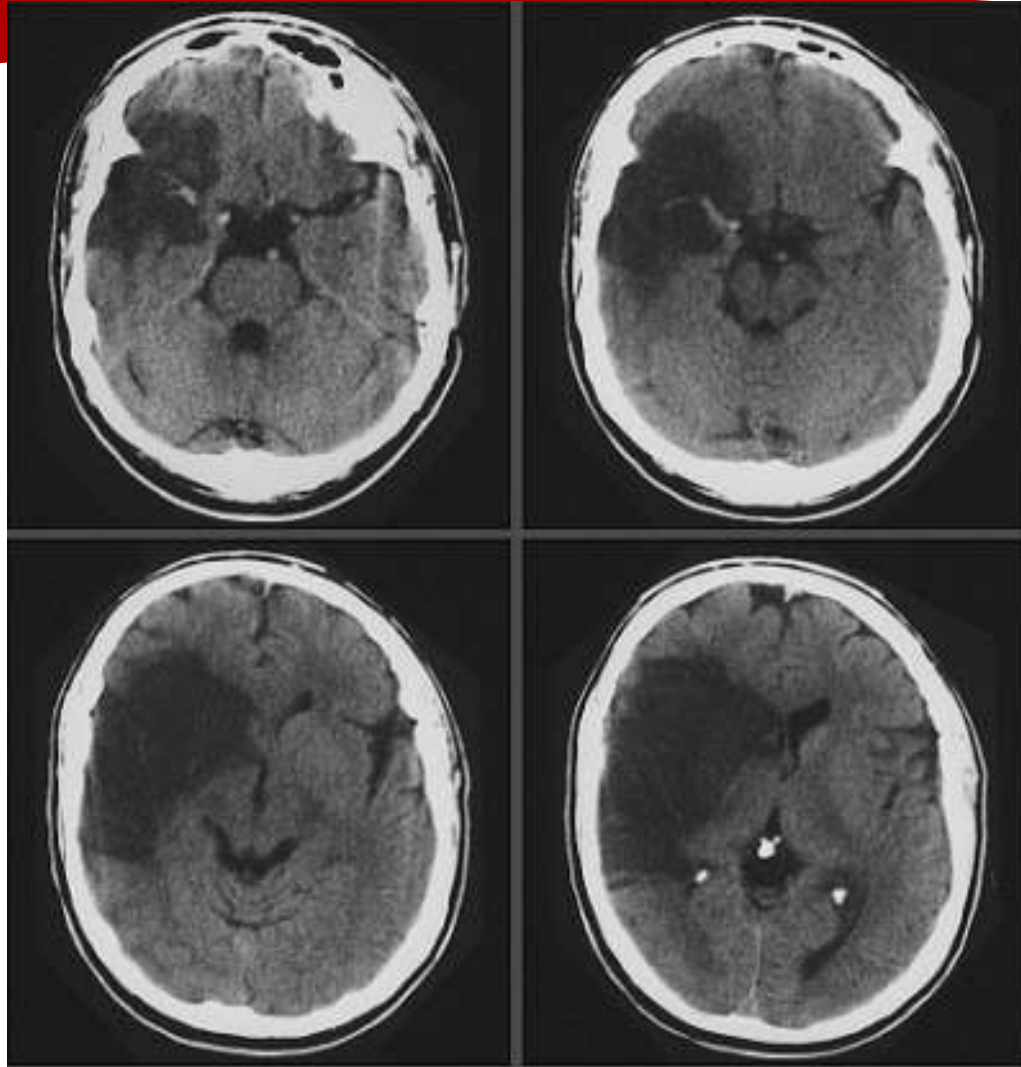


Large penumbra – small infarct core



Small penumbra – large infarct core

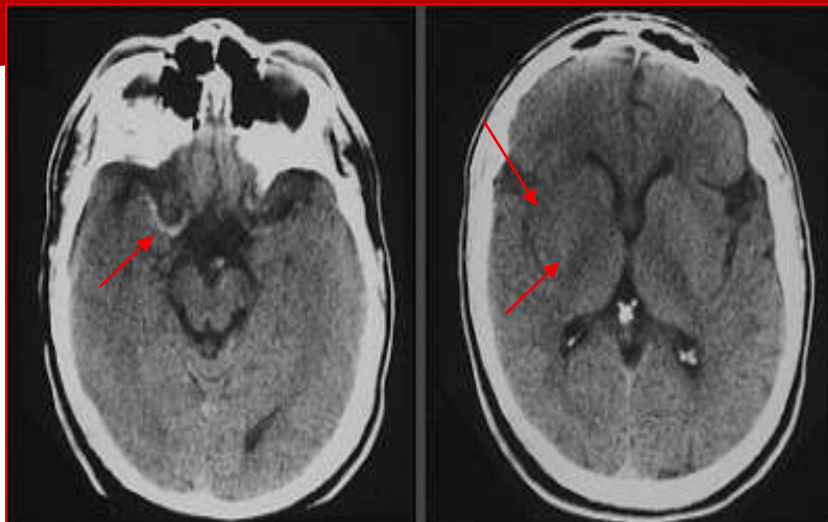
# Head CT after 5 days of stroke onset



# Head CT after 2.5h of stroke onset

## Early signs of ischemia

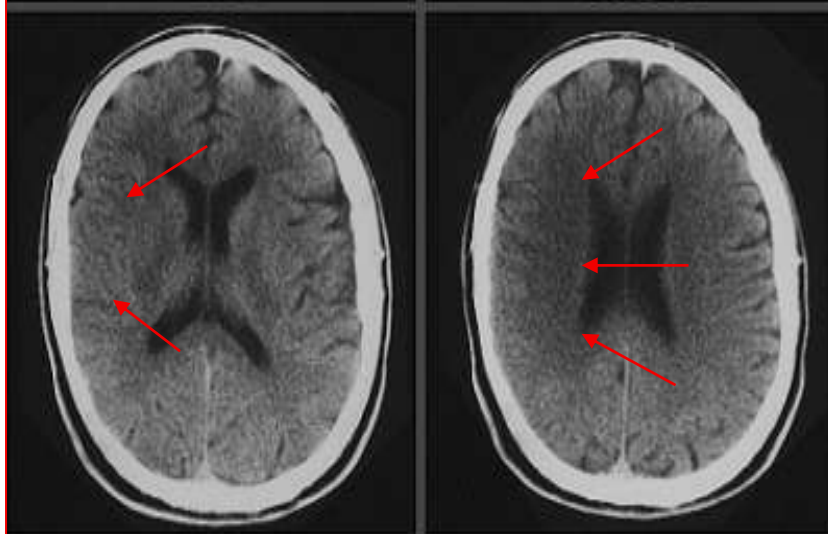
Hyperdense MCA sign



Diminished insular cortex borders

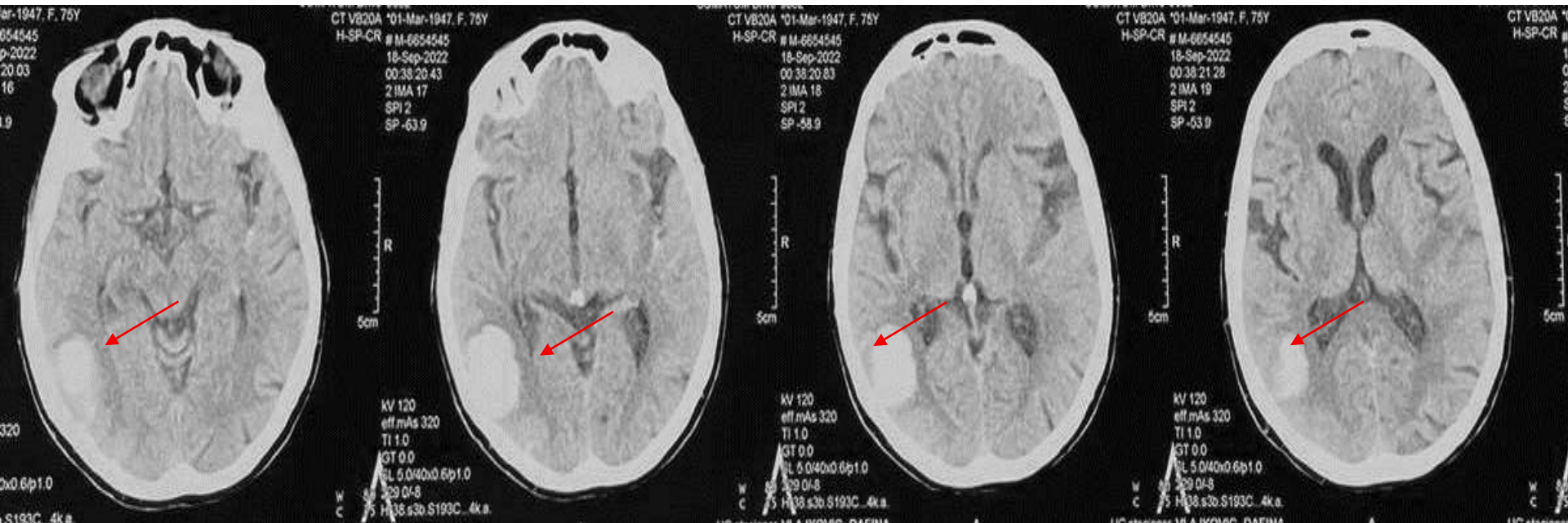
Opsecuration of nc. lentiformis

Gyral flatening



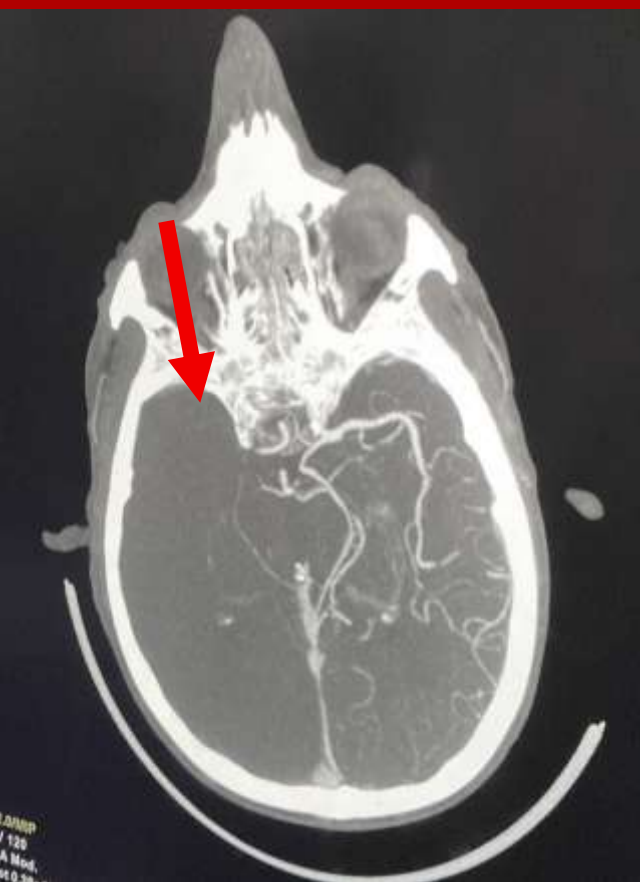
Discrete white matter hypodensity

# Hemorrhage is immediately visible on CT after its occurrence





# CT angiography



MCA occlusion



ICA occlusion



ICA occlusion

# Treatment of acute stroke

- **"Code stroke"** – early recognition of stroke symptoms and urgent driving to specialized hospital
- **Stroke units** – specialized units for managing stroke patients
- **Drugs and therapy procedures** (arterial recanalisation, neuroprotection, prevention of complications, secondary stroke prevention, early physiotherapy)



# How ischemic stroke should be treated?

**Same as acute coronary syndrome!**

**Reperfusion therapy:**

Intravenous thrombolysis (IVT) without/with mechanical thrombectomy (MT)

# Therapy

## Intravenous thrombolysis

- Effective within **first 3-4,5 hours** after stroke onset
- Thrombolysis with recombinant tissue plasminogen activator (rtPA) (intravenous, intraarterial)

### Preconditions

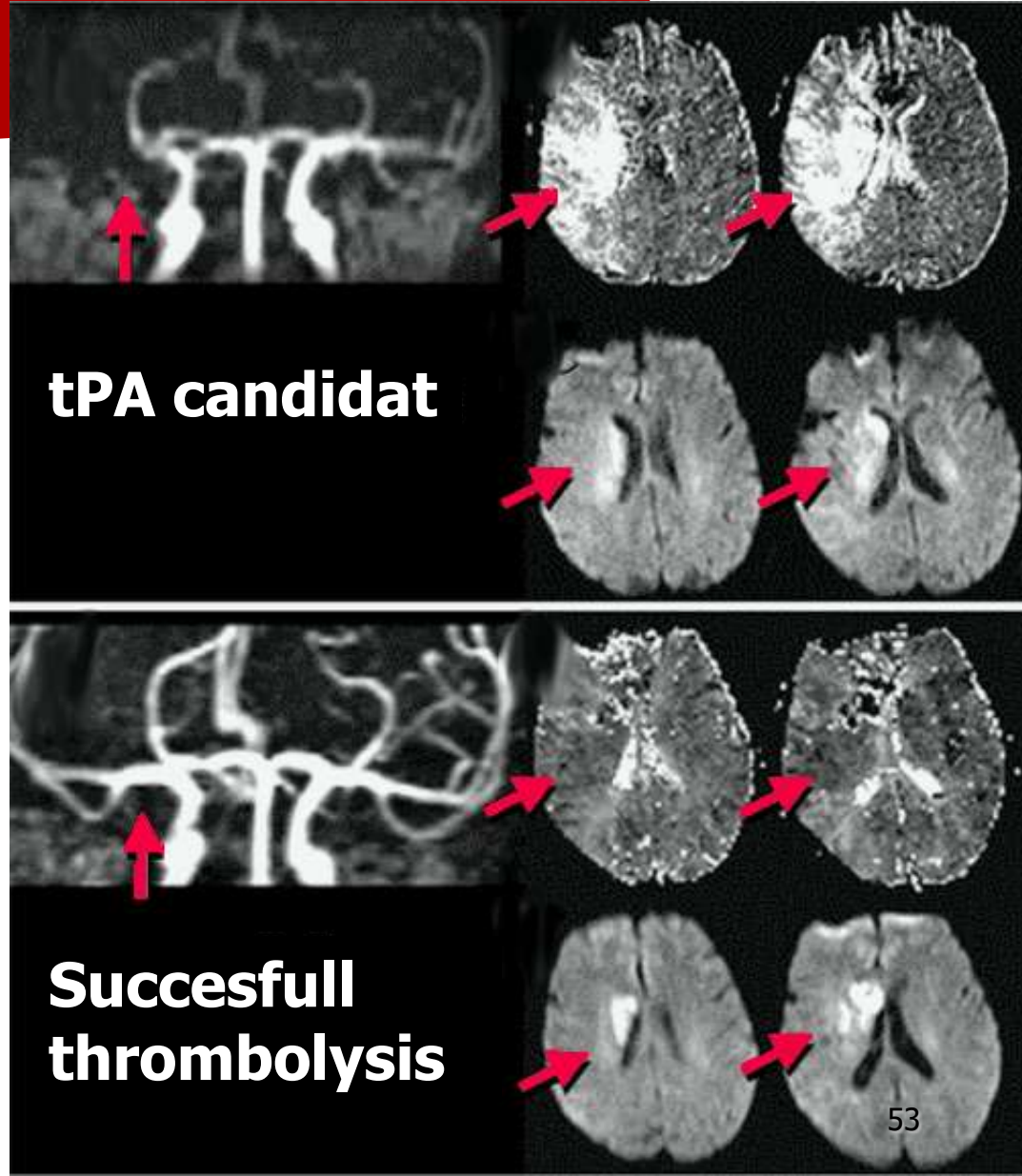
- Ischemic stroke with well-defined time of symptoms onset
- Moderate degree of neurological deficit
- No CT signs of intracranial hemorrhage



# Therapy

## Intravenous thrombolysis

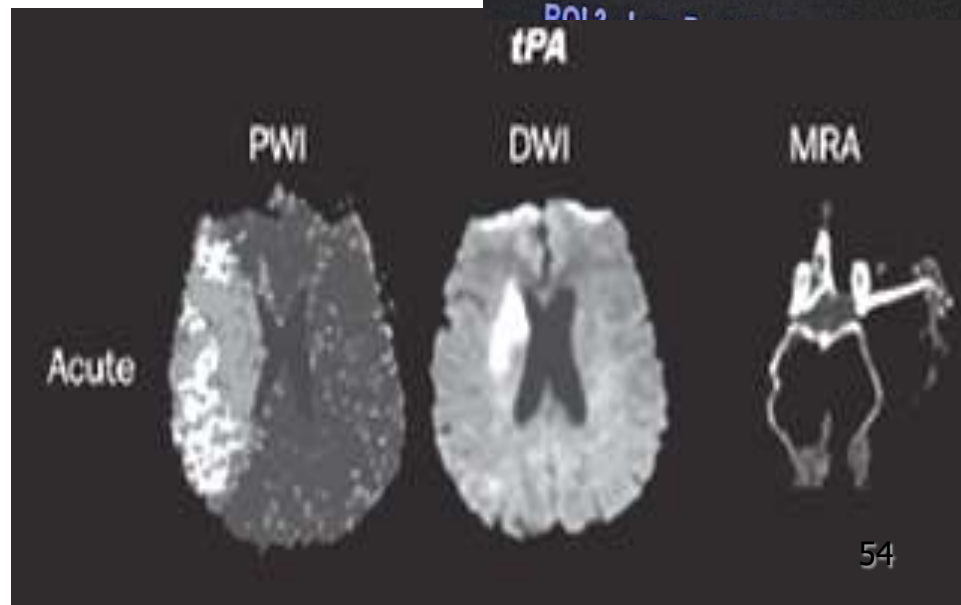
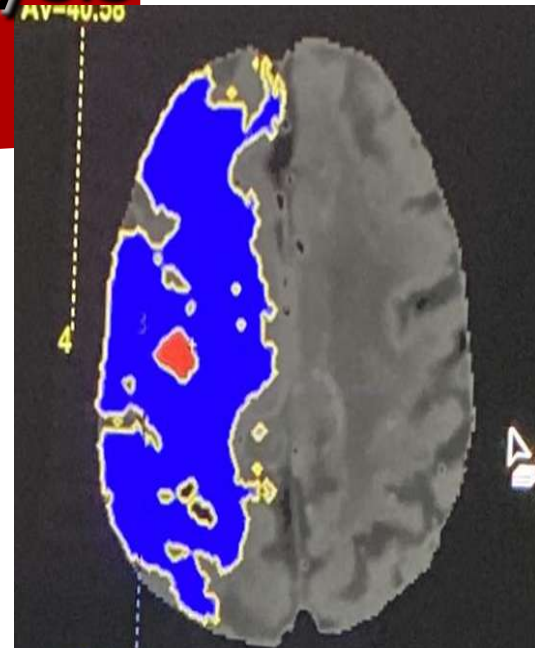
- Numerous exclusion criteria
- Possible haemorrhagic complications (intracerebral haemorrhage!)
- Only 5-10% of all ischemic stroke patients receive thrombolysis!



# Therapy Intravenous thrombolysis

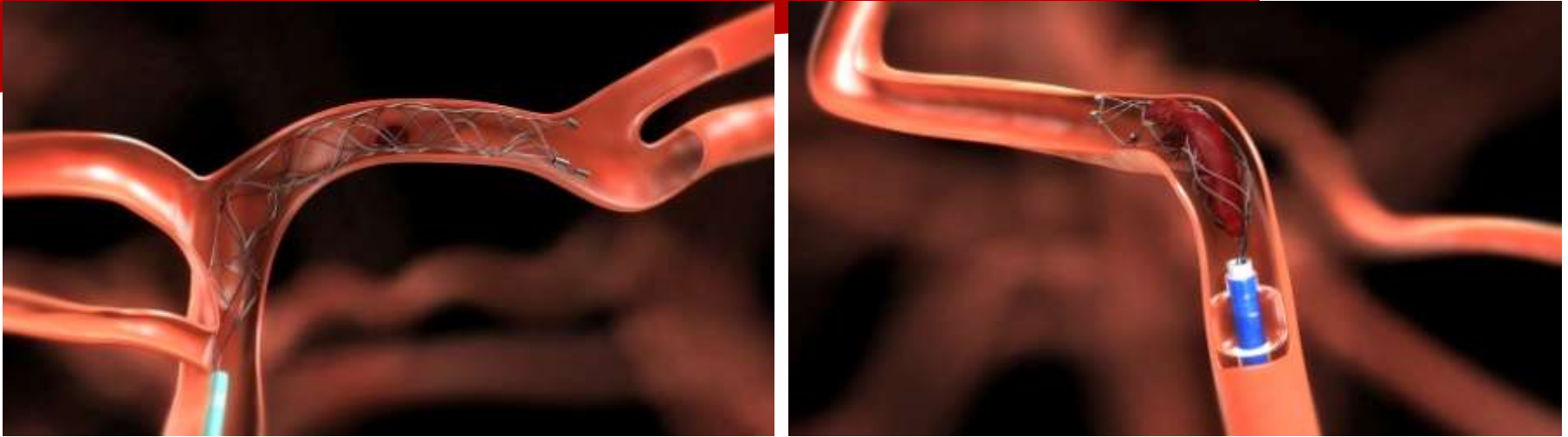
- Possible application in an extended **therapeutic window of 4.5 - 9 hours or after waking up** if a perfusion deficit is confirmed, i.e. penumbra!

It is necessary to perform CT or MRI perfusion for prolonged time window



# Therapy

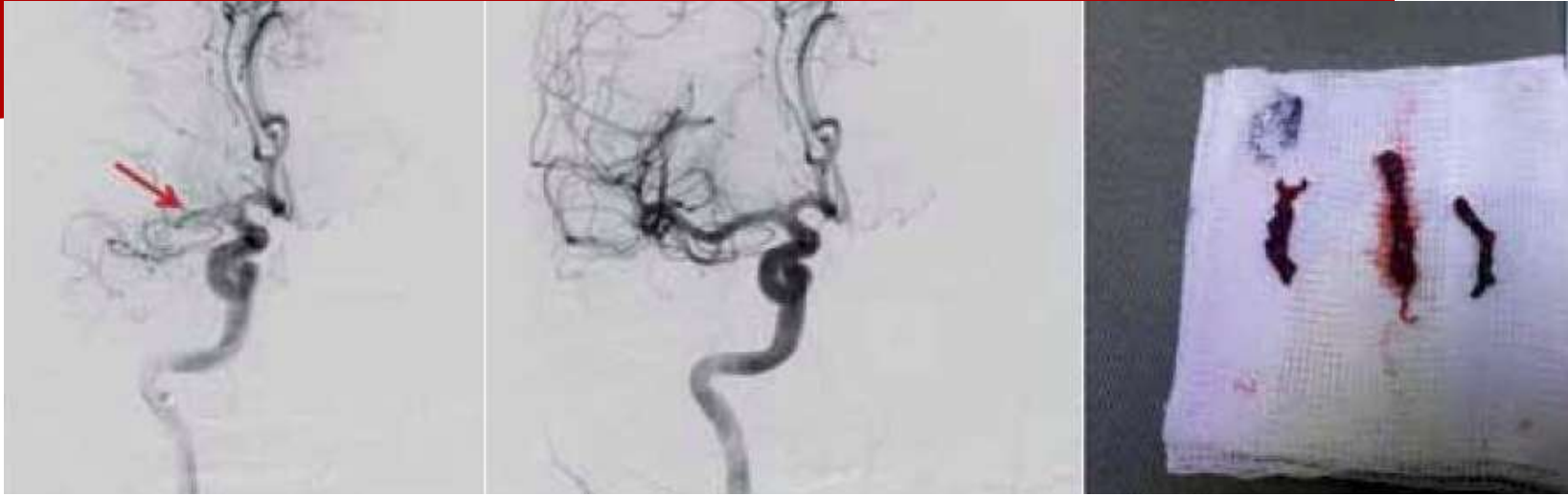
## Mechanical thrombectomy



- **Occlusion of distal ICA or proximal segment of MCA**
- Severe neurological deficit
- Presence of contraindications for IVT
- **Time window is 6-8 hours, in selected group of patients (by CT or MRI perfusion!) even 16-24h**

# Therapy

# Mechanical thrombectomy



## Advantages:

- Rapid arterial recanalization
- Greater efficacy in the large thrombus breakdown
- Less risk of systemic bleeding
- The time window is longer
- Possible application in patients who were recently operated or those with coagulation disorders



# Therapy

## Antiplatelet therapy

- **Aspirin** is prescribed immediately after the exclusion of haemorrhagic stroke (CT!) **within first 24-48 hours**
- In patients who have been given intravenous thrombolysis or mechanical thrombectomy, aspirin is administered after 24 hours of intervention
- The dose of aspirin is **100 - 325 mg**

## **Protection of penumbral neurons and time extension of its viability:**

- early application of general treatment measures
- prevention of brain swelling and edema treatment

- Airway protection and respiratory support
- Avoiding quick lowering of arterial blood pressure
- Treatment of hyperglycemia
- Treatment of high body temperature
- Correction of electrolyte and fluid disturbances
- Brain edema treatment

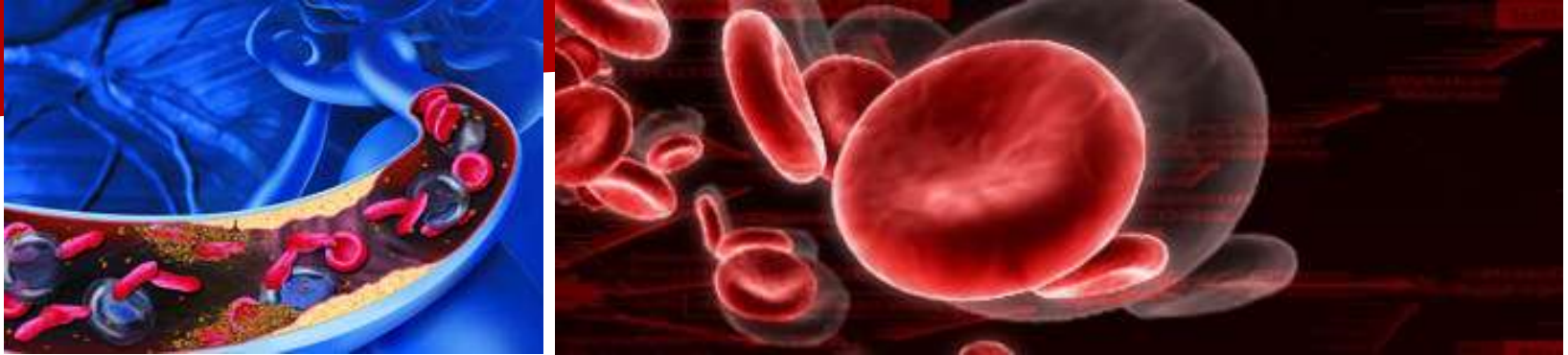
# Primary and secondary prevention



## Risk factor correction

- Regular measurement of BP and its maintenance  $<135/ <85$  mmHg
- Early detection of glucose intolerance
- Treatment of hyperlipidemia (diet, statins)
- Cessation of smoking and excess alcohol consumption
- Regular physical activity, reduction of body weight

# Primary prevention



## ■ **Antithrombotic therapy**

antiplatelet drugs – women > 65 years with risk factors, diabetics

anticoagulant therapy – atrial fibrillation, artefitial valves

## ■ **Surgical therapy** (carotid endarterectomy) – in selected group of patients with asymptomatic high-grade ICA stenosis

# Secondary prevention

- **Antiplatelet therapy** (aspirin 75-325 mg /day, clopidogrel 75 mg/day)
- **Anticoagulant therapy** (heart disease with high risk for embolization) – Vit K antagonists (warfarin, PT INR 2-3,5) or non vit K antagonists (NOAC – apixaban, dabigatran, rivaroxaban)
- **Carotid intervention** (carotid endarterectomy or stentning) - in case of ICA stenosis of 70-99%)



# Any questions ?



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