Malattie Cerebrovascolari

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SAPIENZA
UNIVERSITÀ DI ROMA

The lifetime risk of stroke is 1 in 5 for women 1 in 6 for men

Every two seconds, someone in the world suffers a stroke Every six seconds, someone dies of a stroke Every six seconds, someone's quality of life will forever be changed – they will permanently be physically disabled due to stroke

le vasculopatie cerebrali sono

la seconda causa di morte
e
la prima causa di invalidità

nel mondo occidentale

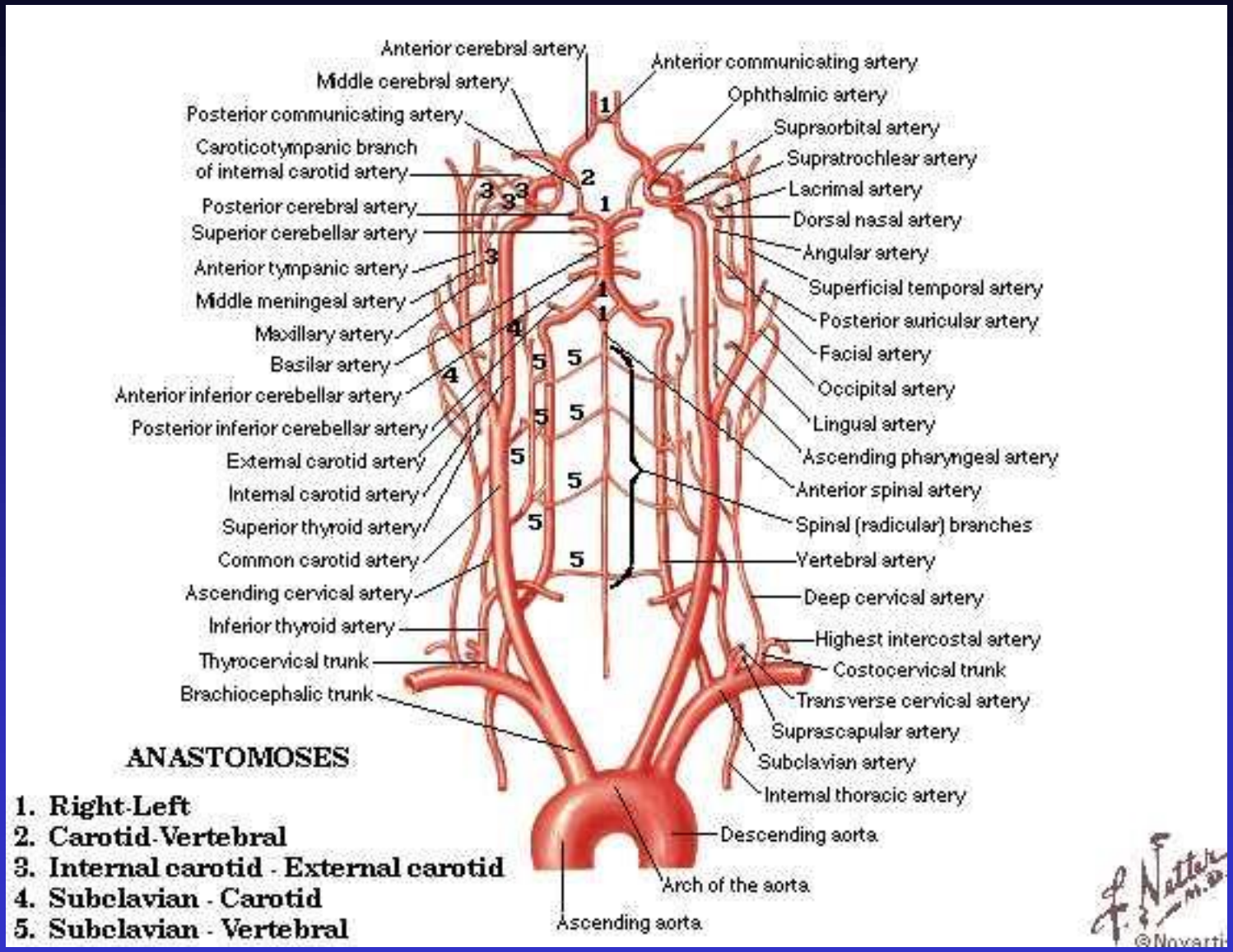
1500 g di neuroni e glia

150 g di glucosio
72 litri di ossigeno

24 h
minuto per minuto

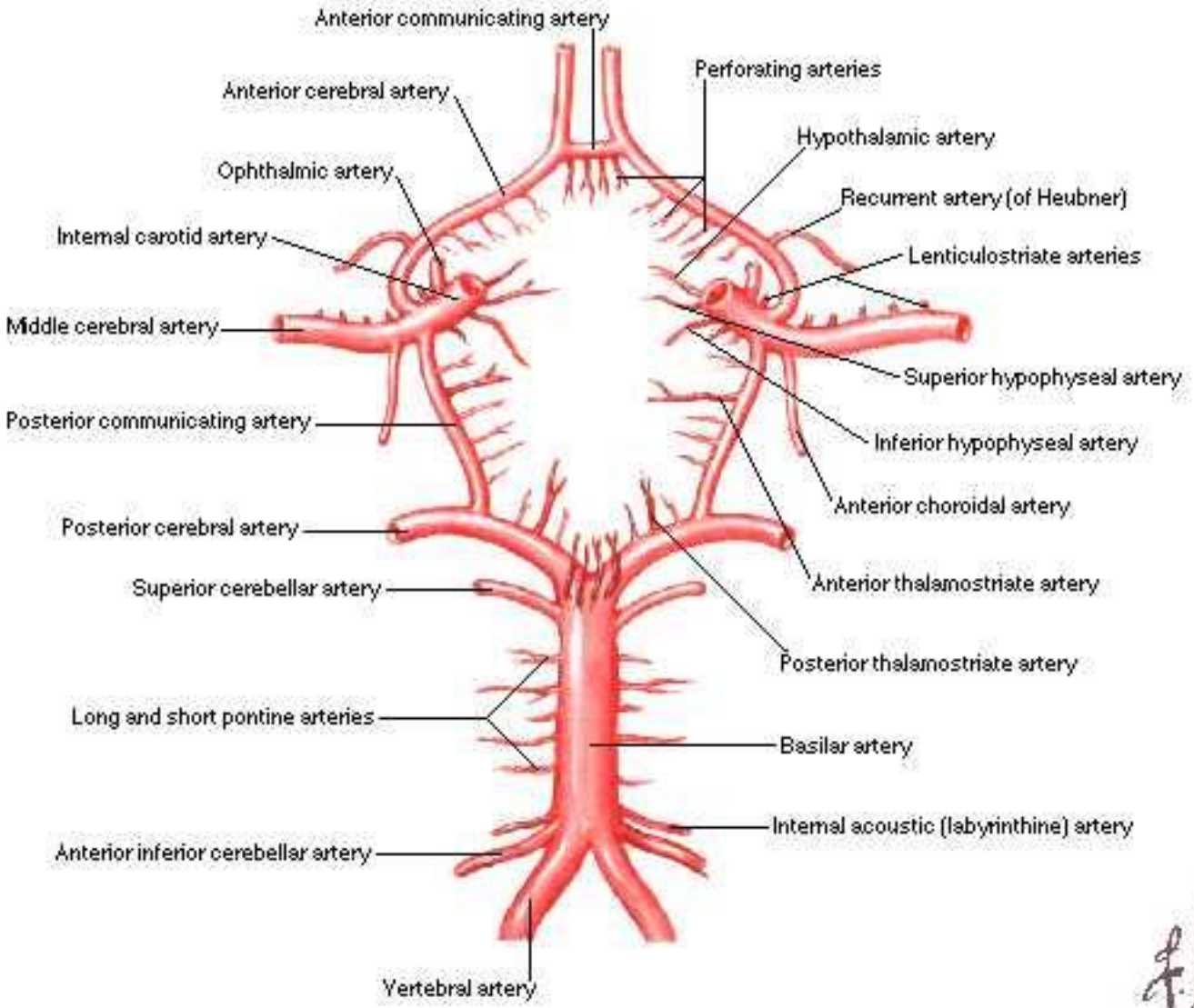
dei 70 cc di sangue che entrano
ad ogni battito cardiaco
nell'aorta ascendente
10-15 vanno al cervello

ogni minuto
350 cc passano
da ogni carotide interna
100-200 cc
dal sistemaa vertebrobasilare


Anterior cerebral artery
Middle cerebral artery
Posterior communicating artery
Caroticotympanic branch of internal carotid artery
Posterior cerebral artery
Superior cerebellar artery
Anterior tympanic artery
Middle meningeal artery
Maxillary artery
Basilar artery
Anterior inferior cerebellar artery
Posterior inferior cerebellar artery
External carotid artery
Internal carotid artery
Superior thyroid artery
Common carotid artery
Ascending cervical artery
Inferior thyroid artery
Thyrocervical trunk
Brachiocephalic trunk
Anterior communicating artery
Ophthalmic artery
Supraorbital artery
Supratrochlear artery
Lacrimal artery
Dorsal nasal artery
Angular artery
Superficial temporal artery
Posterior auricular artery
Facial artery
Occipital artery
Lingual artery
Ascending pharyngeal artery
Anterior spinal artery
Spinal (radicular) branches
Vertebral artery
Deep cervical artery
Highest intercostal artery
Costocervical trunk
Transverse cervical artery
Suprascapular artery
Subclavian artery
Internal thoracic artery
Descending aorta
Arch of the aorta
Ascending aorta
1
2
3
4
5
ANASTOMOSES
1. Right-Left
2. Carotid-Vertebral
3. Internal carotid - External carotid
4. Subclavian - Carotid
5. Subclavian - Vertebral

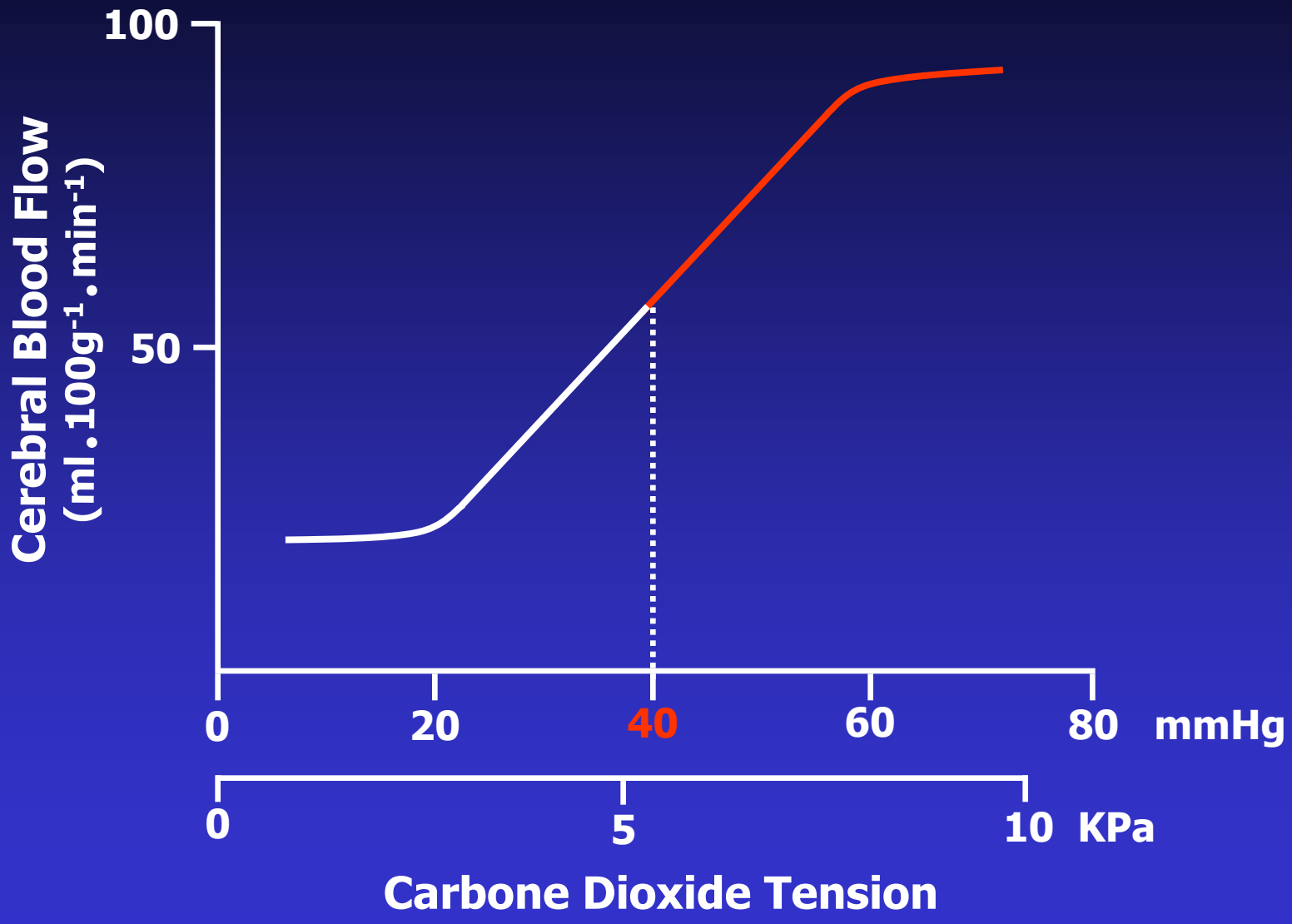
Circle of Willis - Vessels Dissected Out

Inferior View

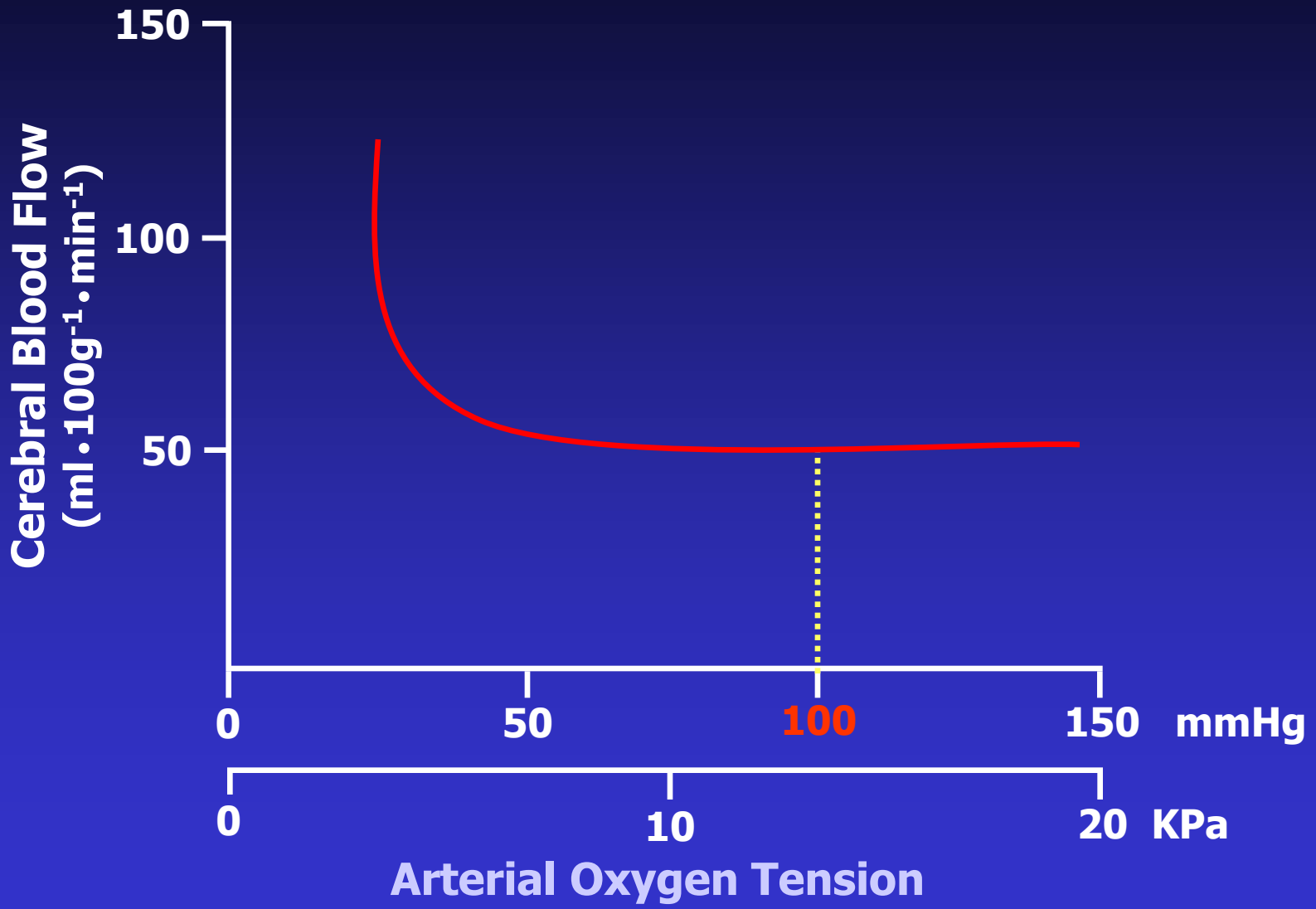


AUTOREGOLAZIONE DEL FLUSSO EMATICO CEREBRALE

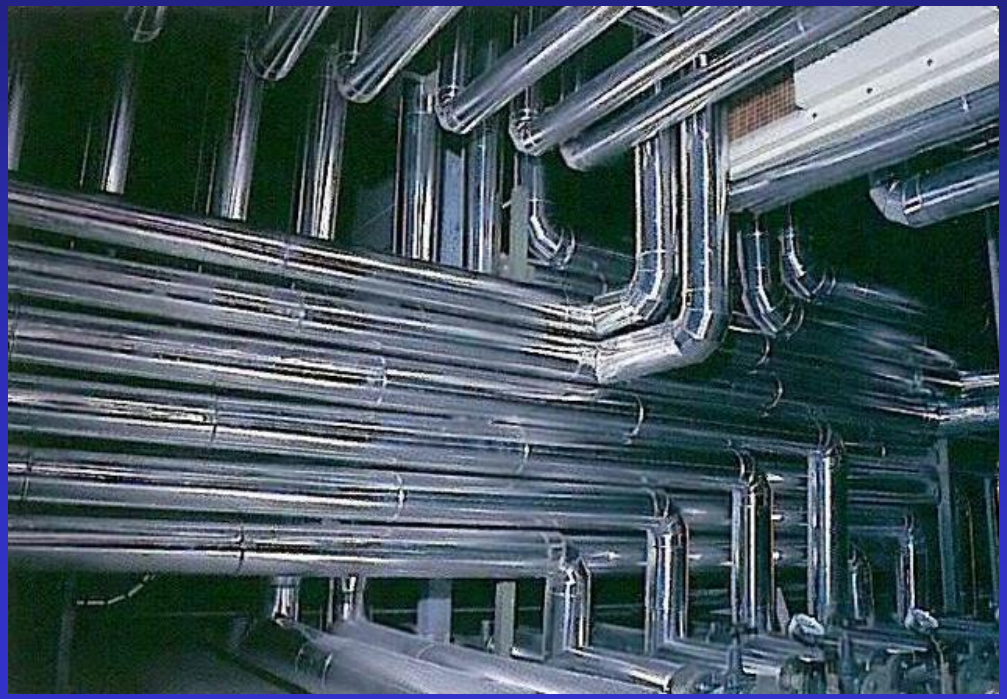
CBF variations in relation to $PaCO_2$ changes



CBF variations in relation to PaO_2 changes



ETIOPATOGENESI



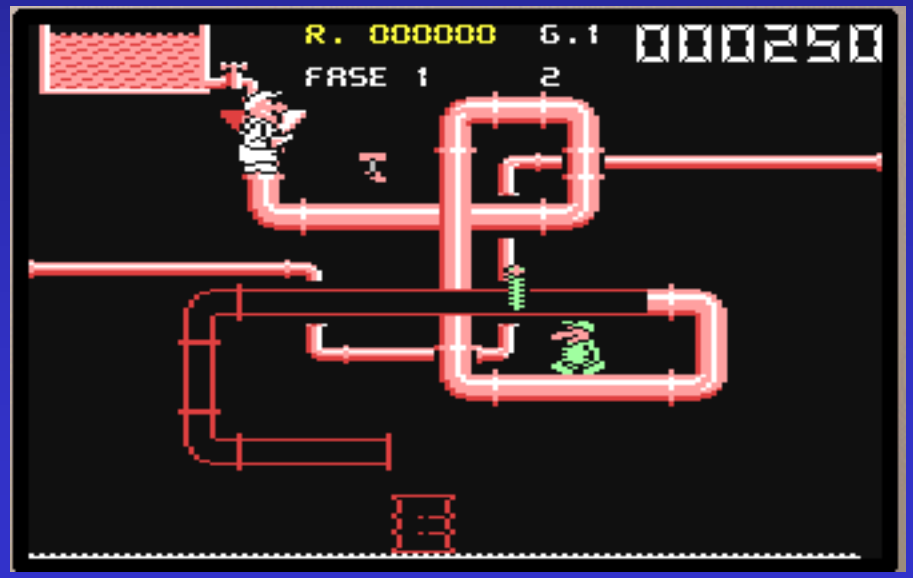
STROKE

Hemorrhage
- **Intracerebral**
- **Subarachnoid**
- **Subdural/epidural**

15%

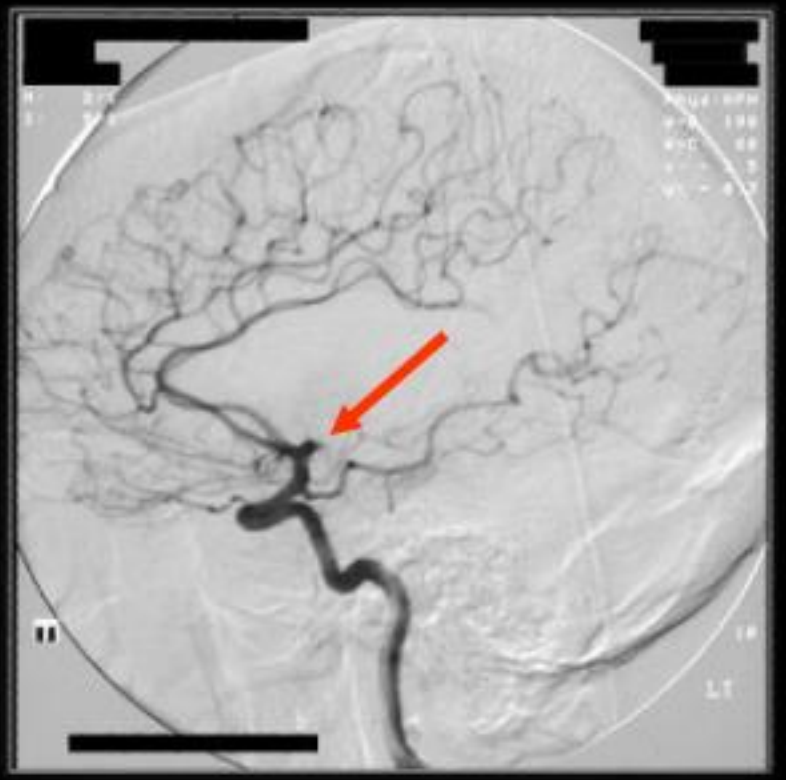
85%

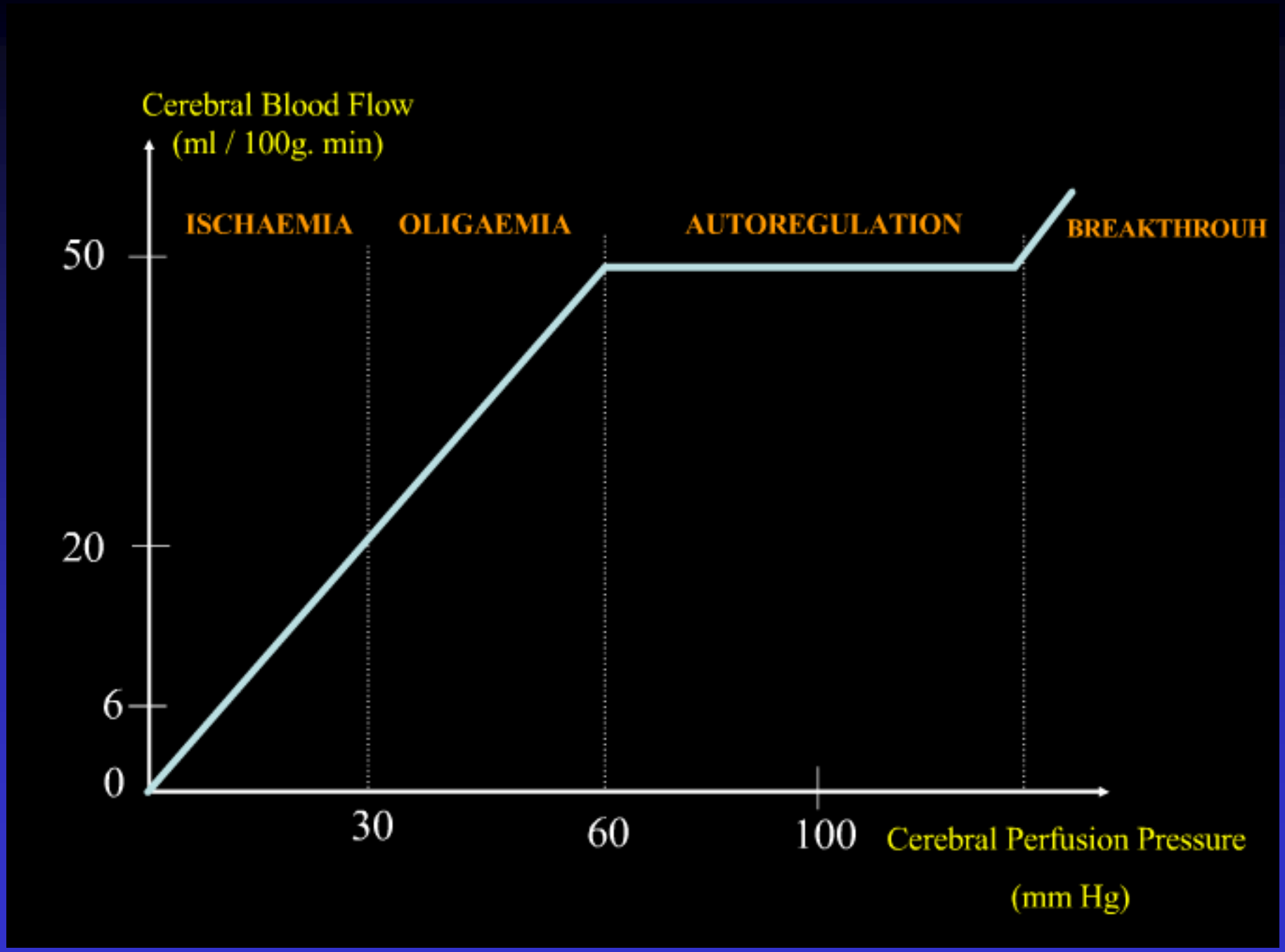
Ischemic Stroke



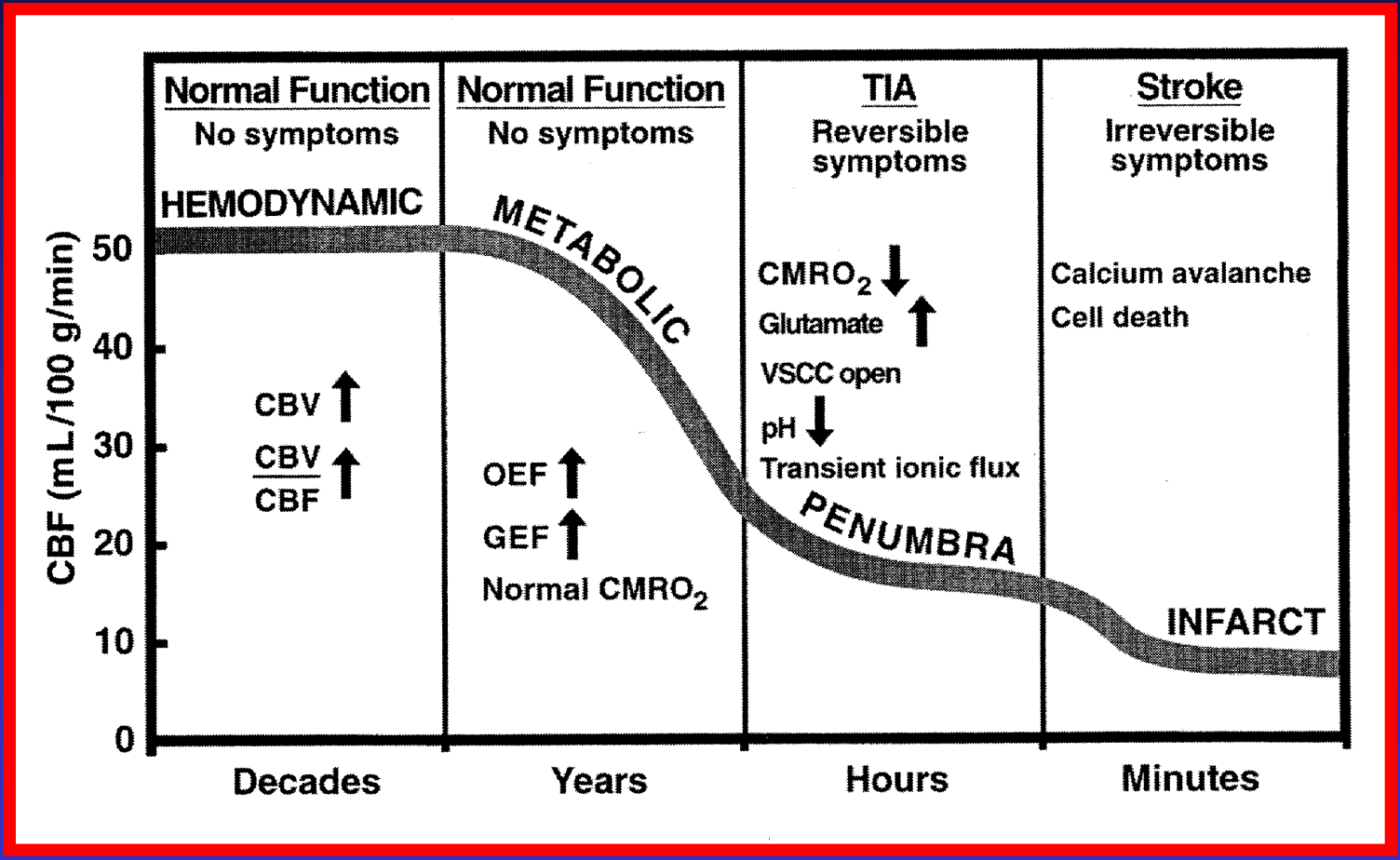
FISIOPATOLOGIA
ISCHEMIA CEREBRALE

Acute MCA occlusion

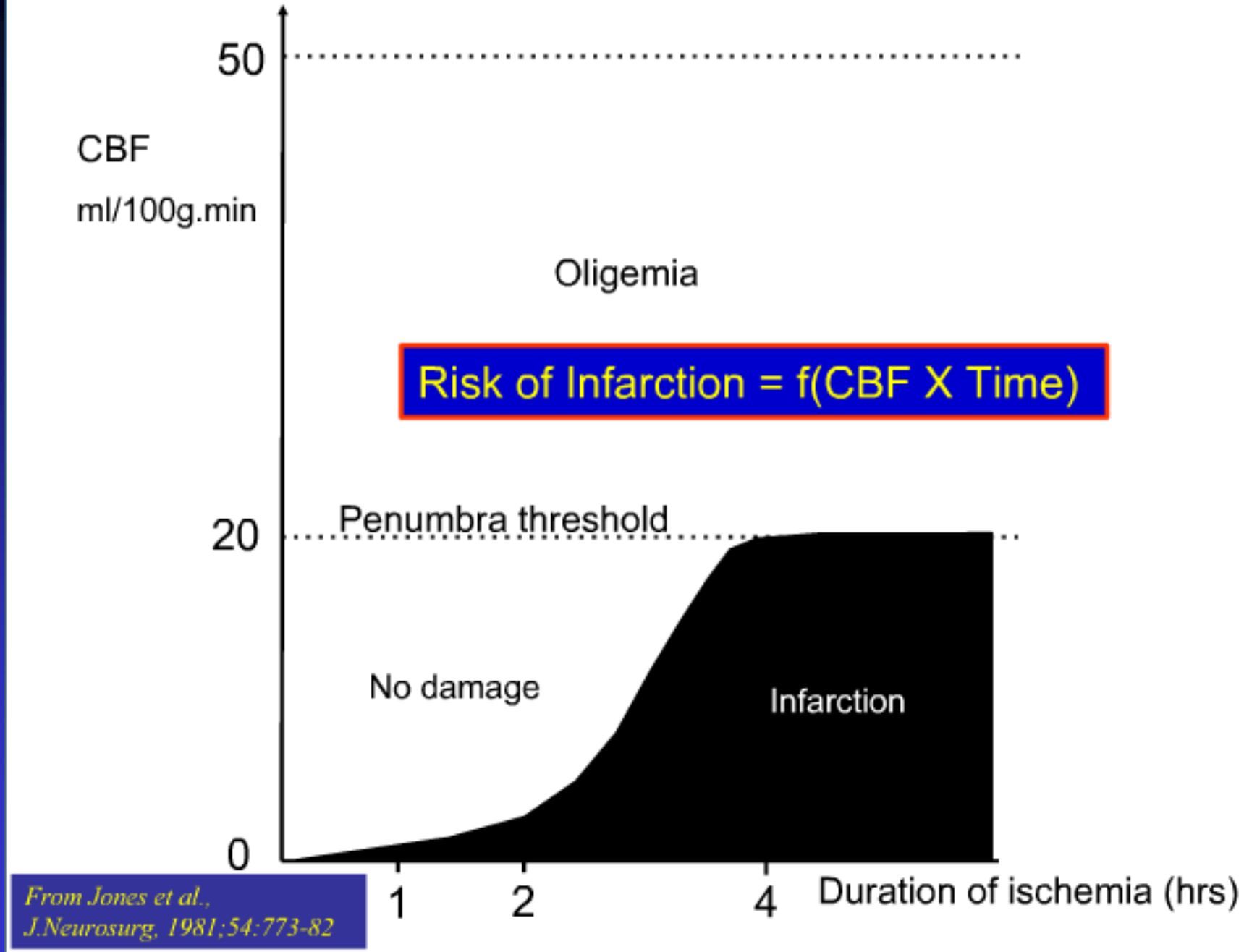



Cerebral Blood Flow
(ml / 100g. min)
ISCHAEMIA
OLIGAEMIA
AUTOREGULATION
BREAKTHROUH
50
20
6
0
30
60
100
Cerebral Perfusion Pressure
(mm Hg)

Cerebral events during progressive vascular constriction

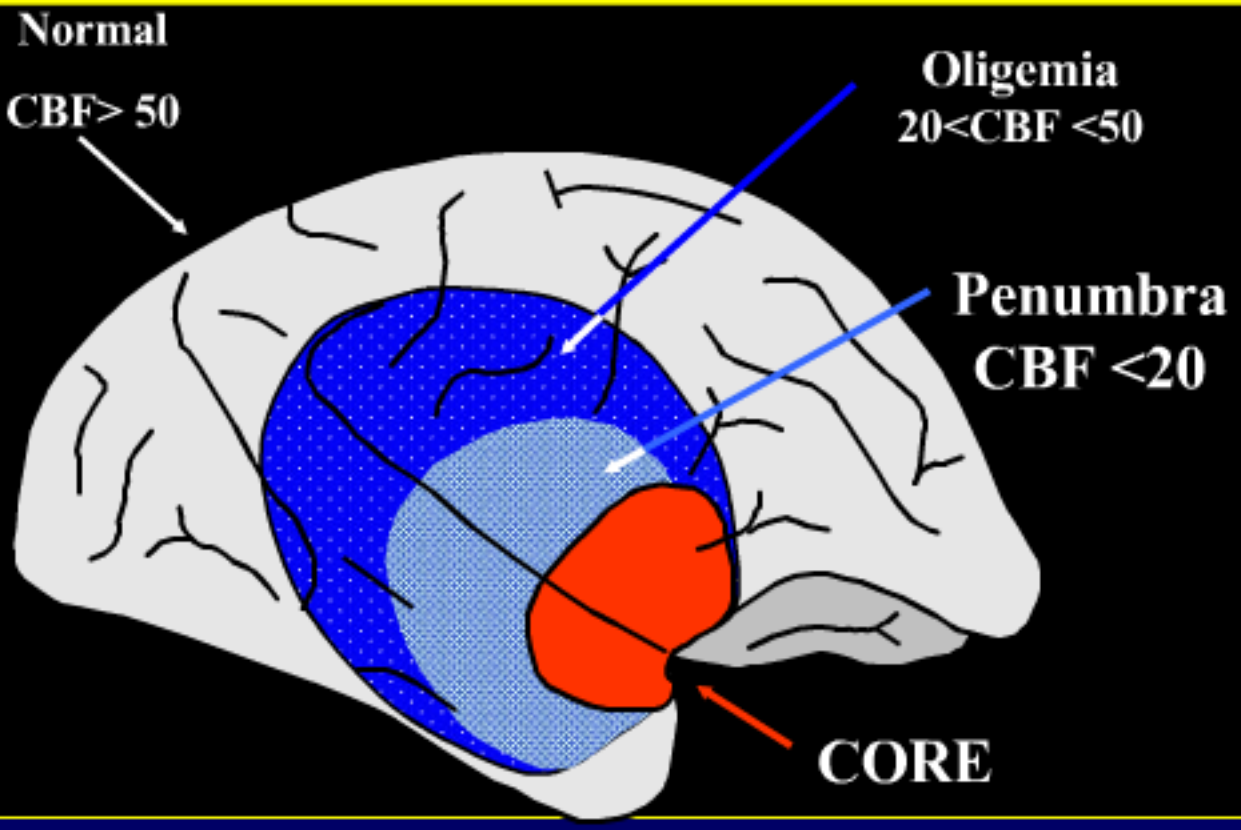


Hakim, 1998


50
CBF
ml/100g.min
Oligemia
Risk of Infarction = f(CBF X Time)
Penumbra threshold
20
No damage
Infarction
0
1
2
4
Duration of ischemia (hrs)
From Jones et al.,
J.Neurosurg, 1981;54:773-82

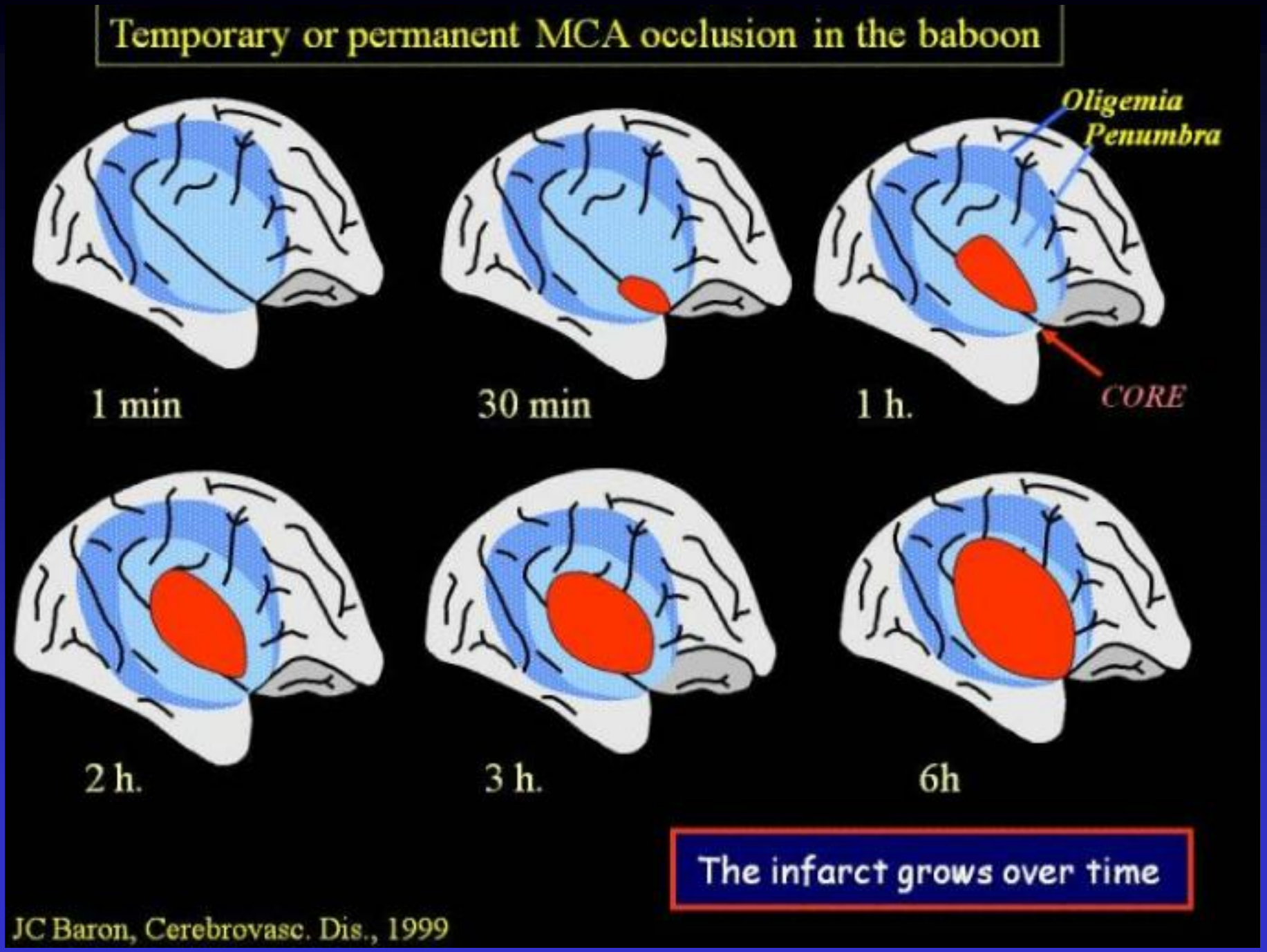
The ischaemic penumbra

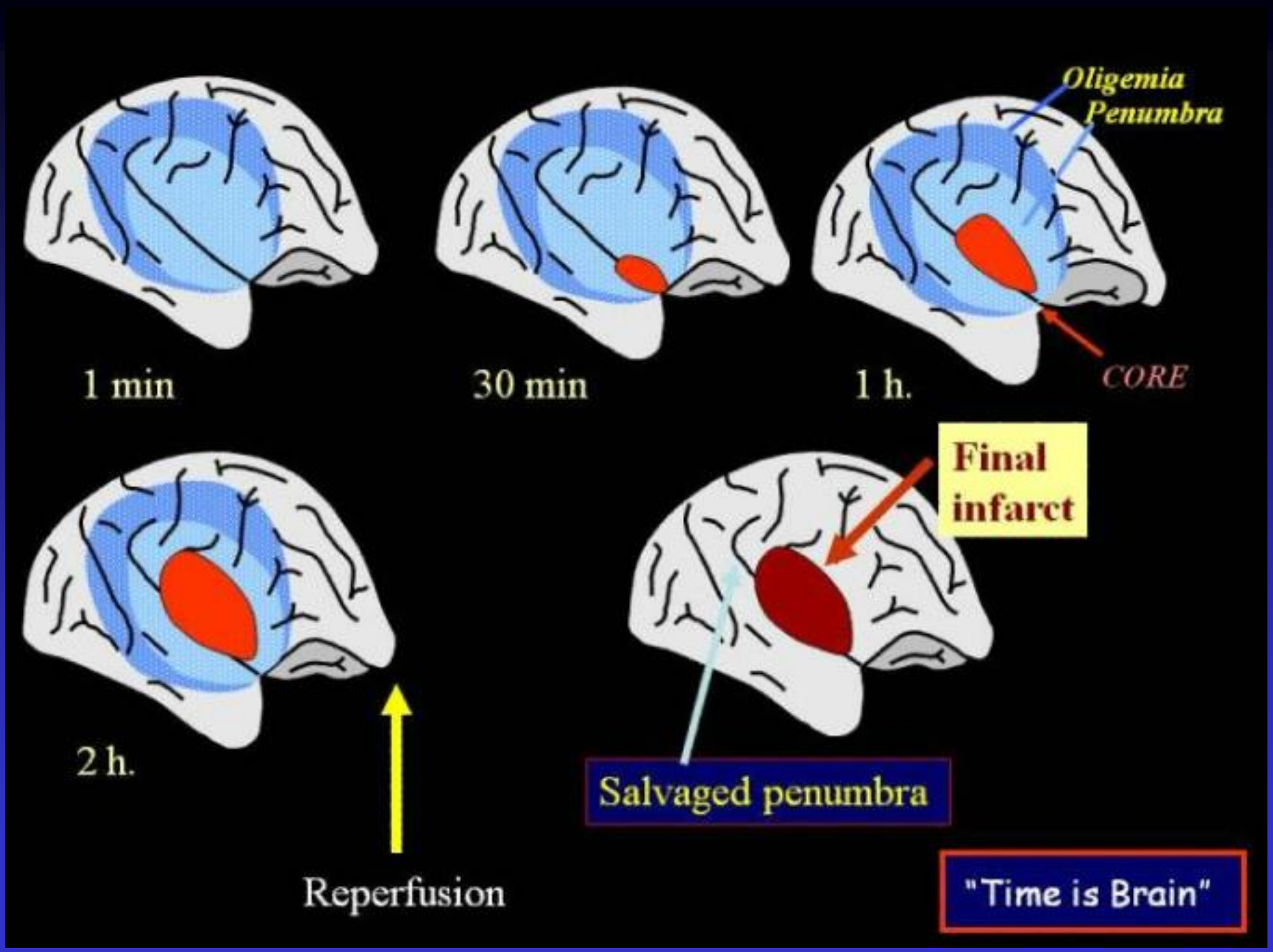
(Symon, Astrup, Lassen, Jones)



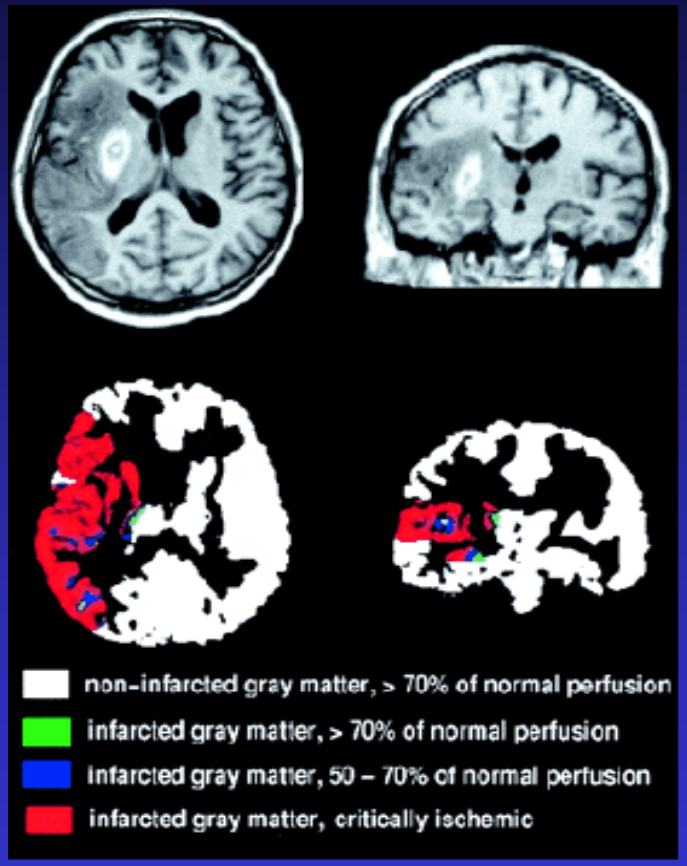
Penumbra

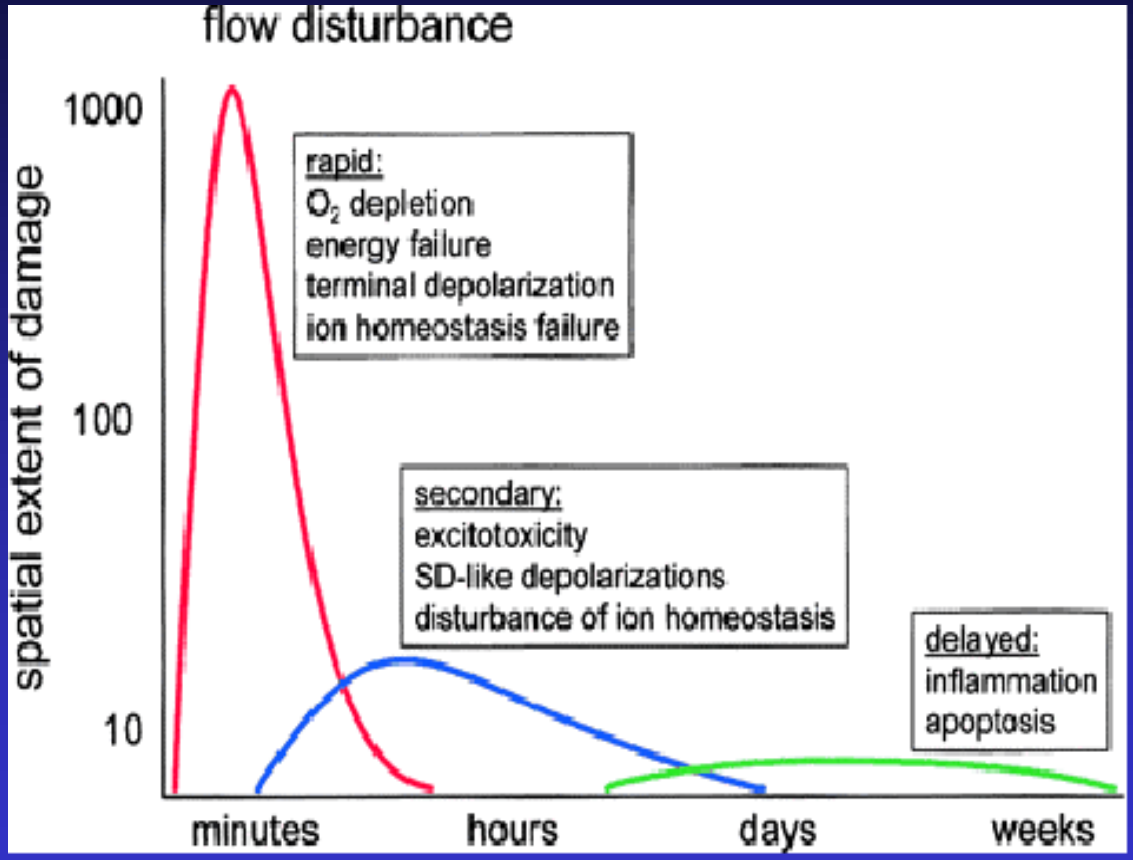
- Severely ischaemic (CBF < 20 mls/100g.min)
- Surrounds the already irreversibly damaged tissue ('Core') and is surrounded by mildly hypoperfused, not at-risk tissue (« Oligemia »)
- Functionally impaired (explains part of the neurological deficit)
- At risk of infarction but will survive if reperfused early


Temporary or permanent MCA occlusion in the baboon
Oligemia
Penumbra
CORE
1 min
30 min
1 h.
2 h.
3 h.
6h
The infarct grows over time
JC Baron, Cerebrovasc. Dis., 1999


Oligemia
Penumbra
1 min
30 min
1 h.
CORE
2 h.
Final infarct
Salvaged penumbra
Reperfusion
"Time is Brain"

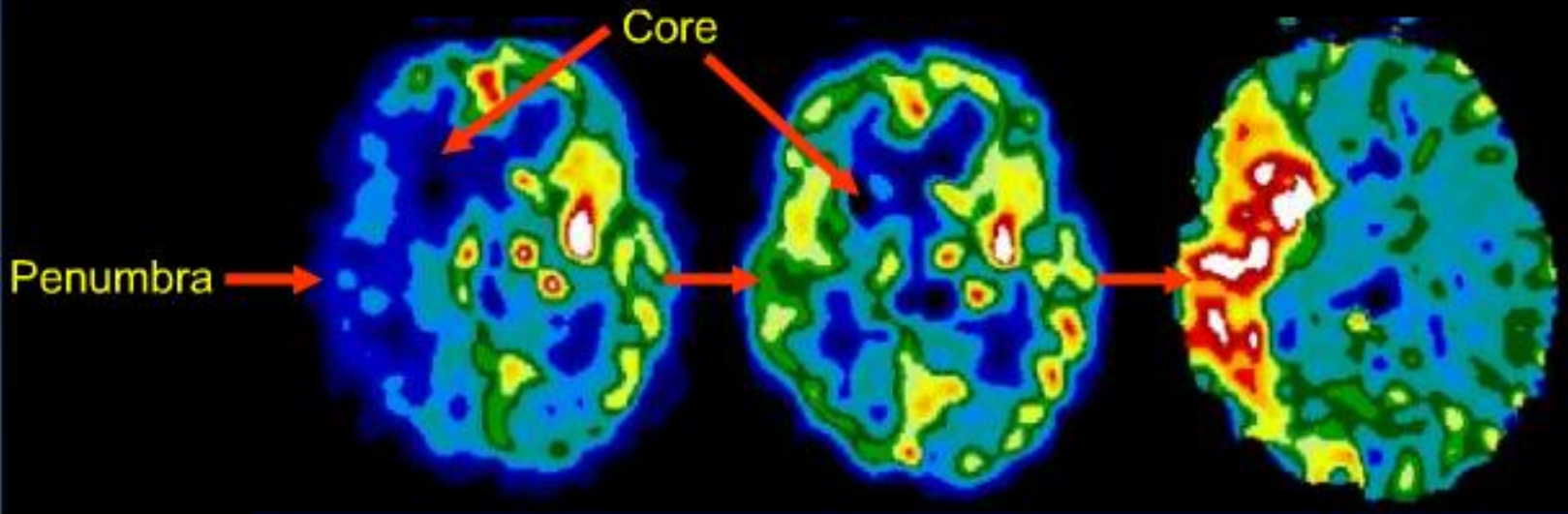
The ischaemic penumbra



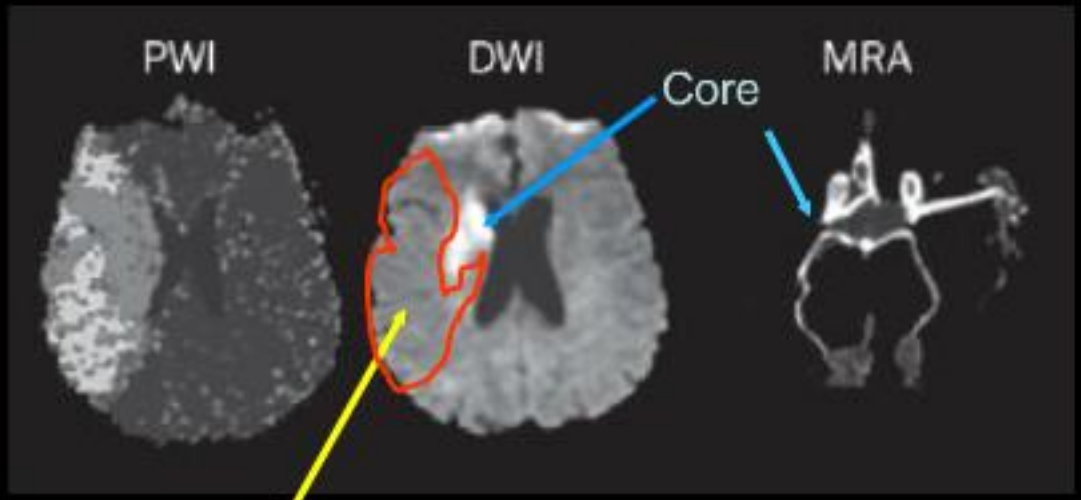


Heiss et al., 1999

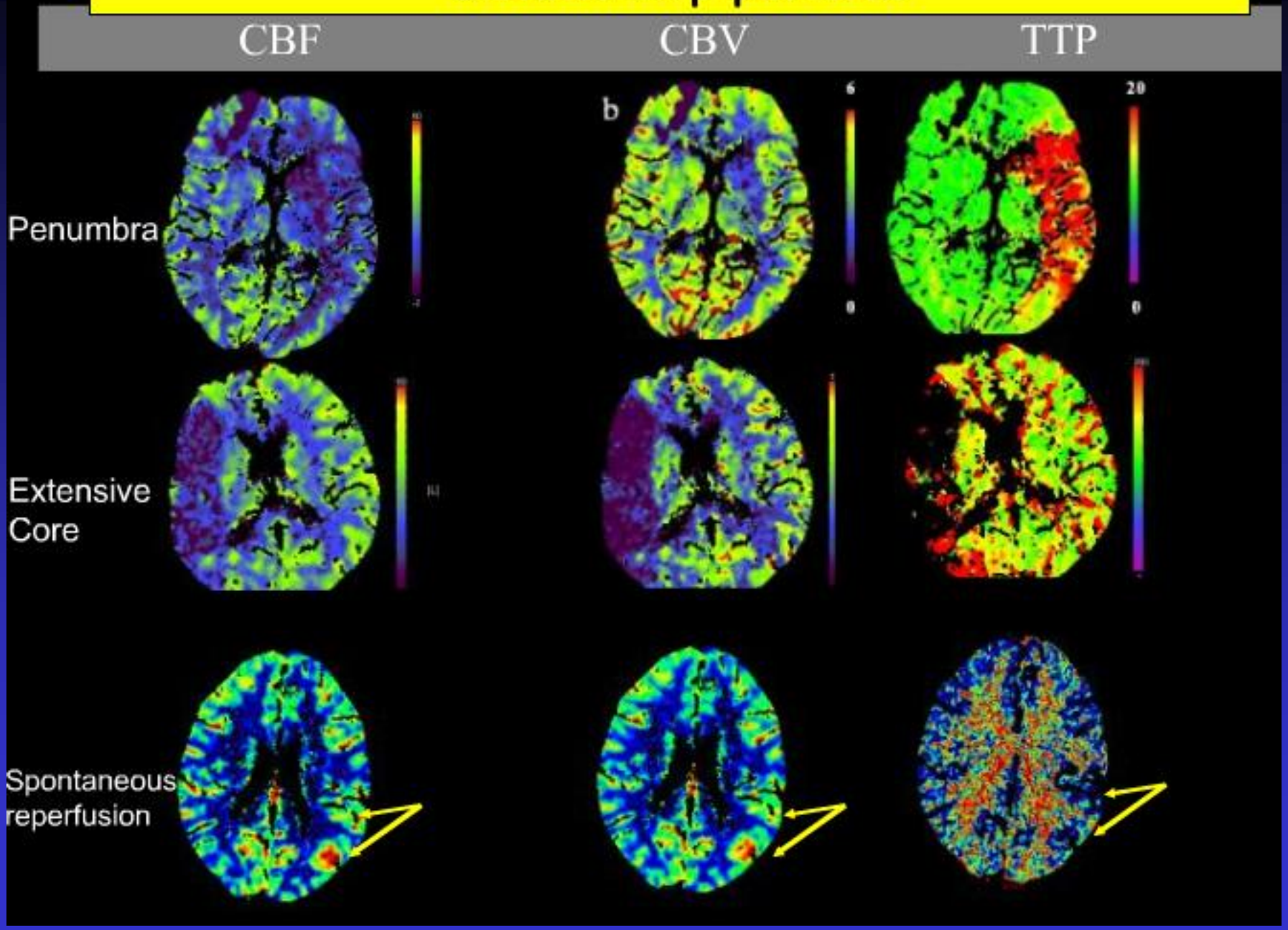
Acute ischaemic stroke



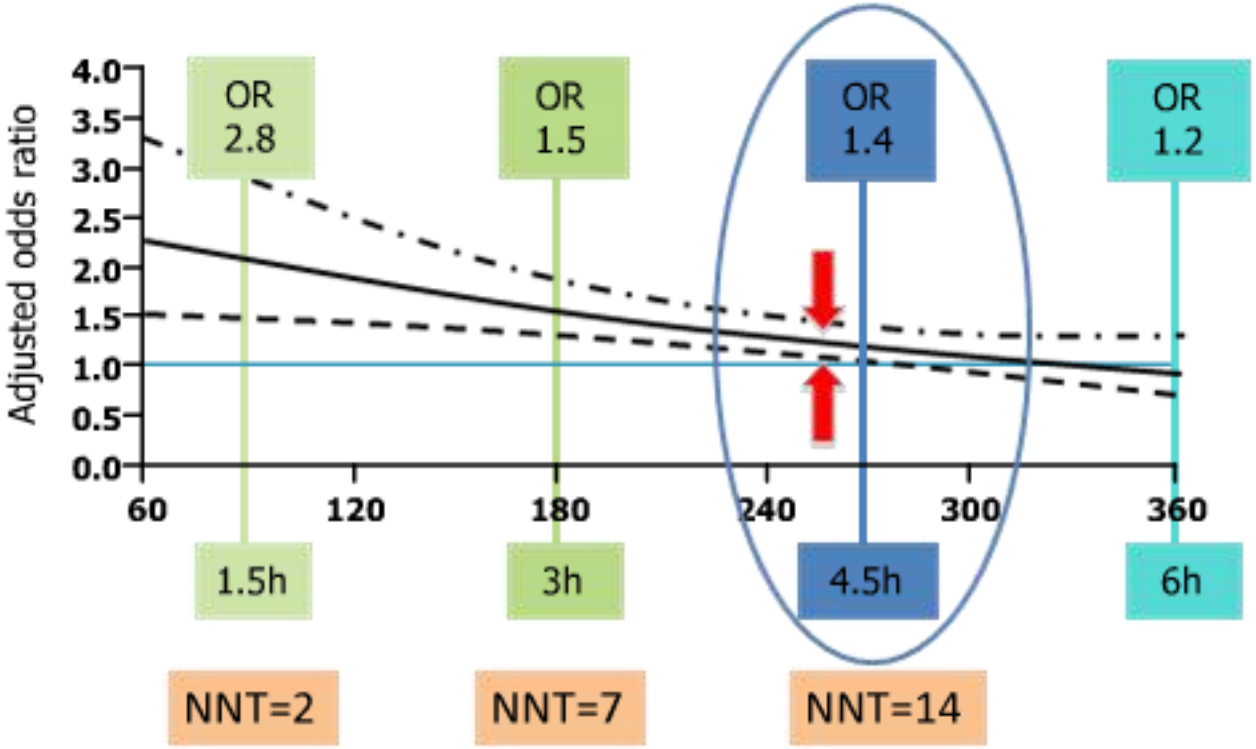
MRI: DWI/PWI and MRA



Distinct CTp patterns



Early treatment remains essential

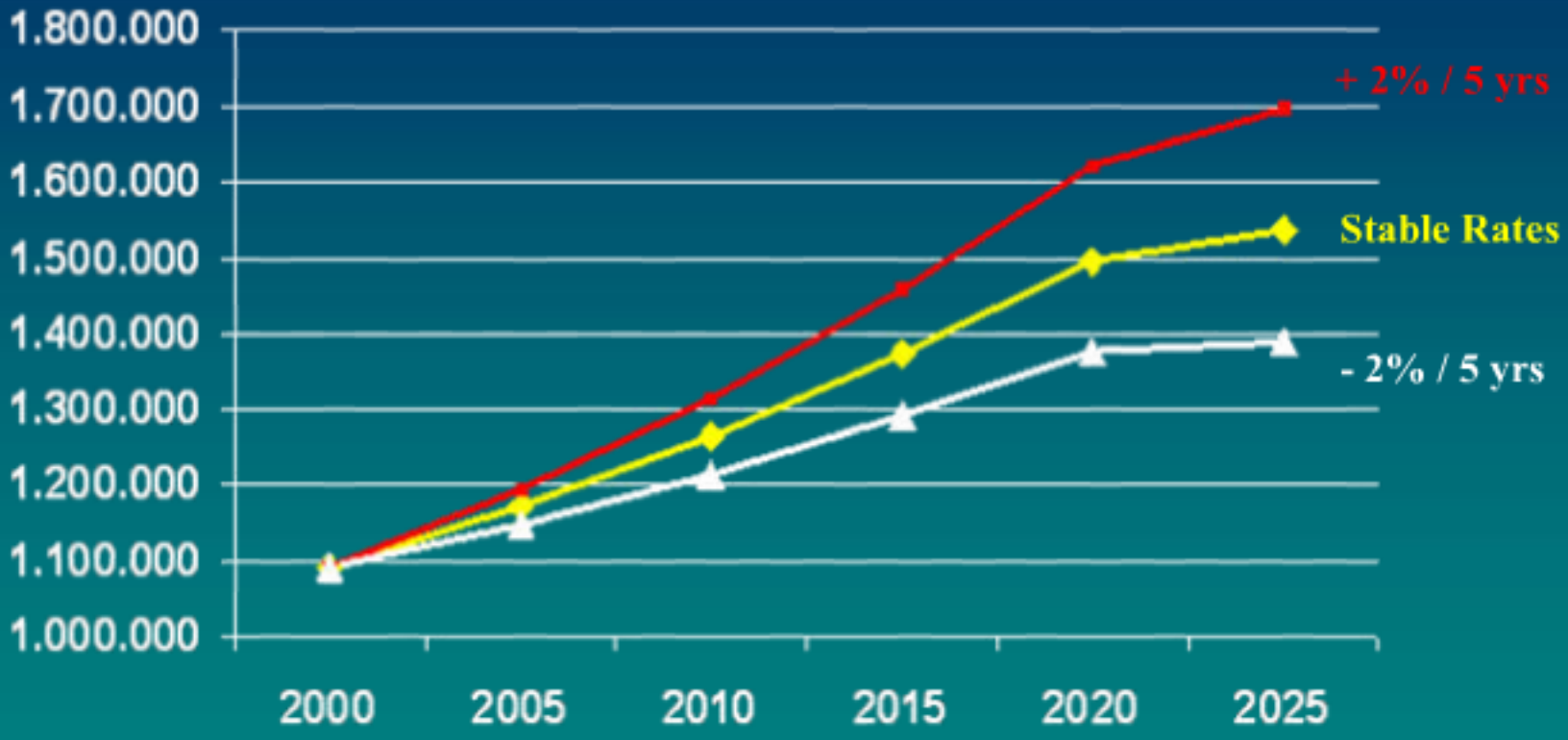


Hacke et al. Lancet 2004

I NUMERI

quanti sono?
chi sono?

Projections of Stroke Events in EU, Iceland, Norway, and Switzerland



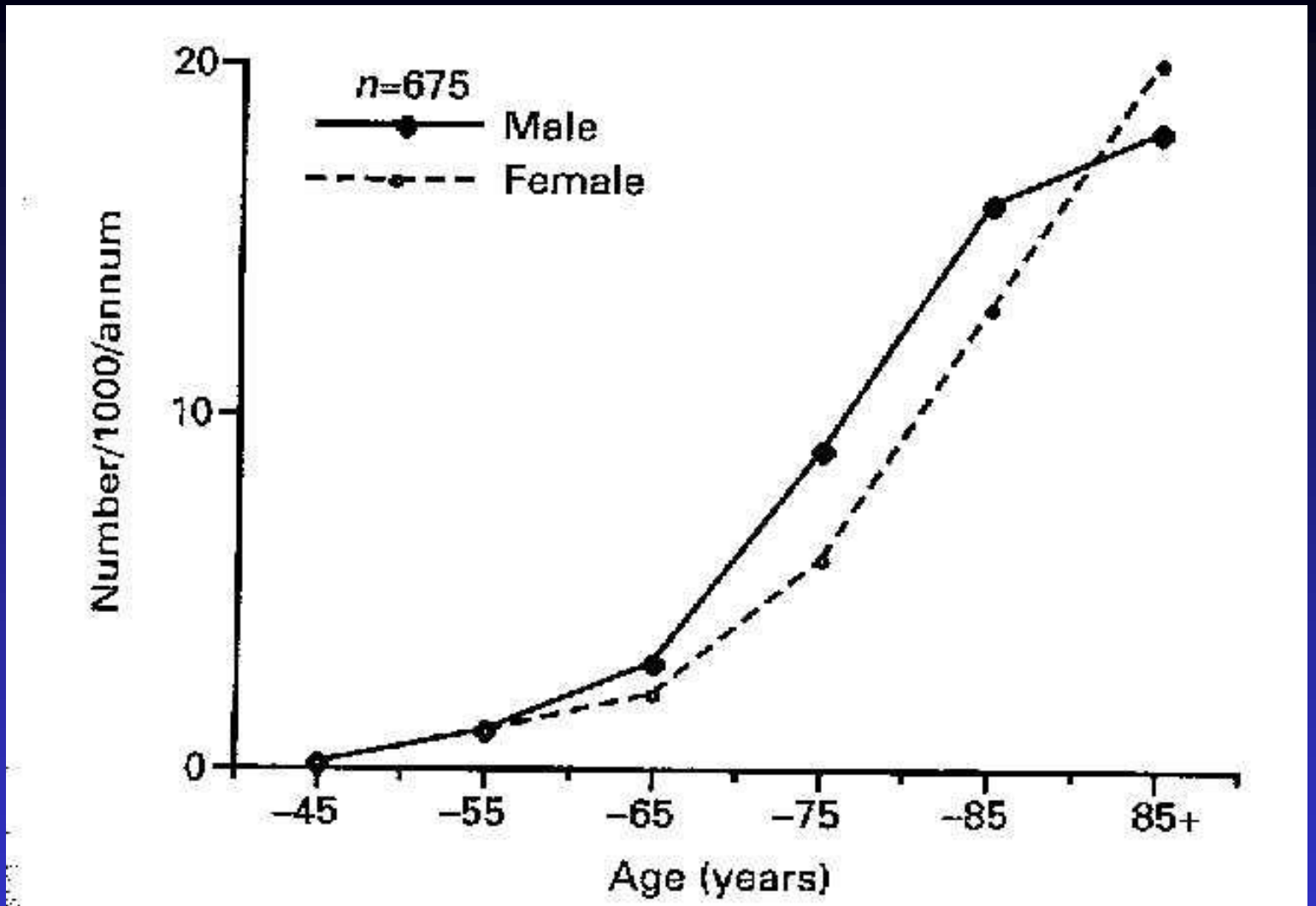


Fig. 27.2. Age- and sex-specific annual incidence of first-ever-in-a-lifetime stroke per 1000 population in Oxfordshire in the mid 1980s (with permission from Bamford *et al.* 1988).

EPIDEMIOLOGY of STROKE

Prevalence

6.5 % — 65-84 years

M 7.4%
F 5.9%

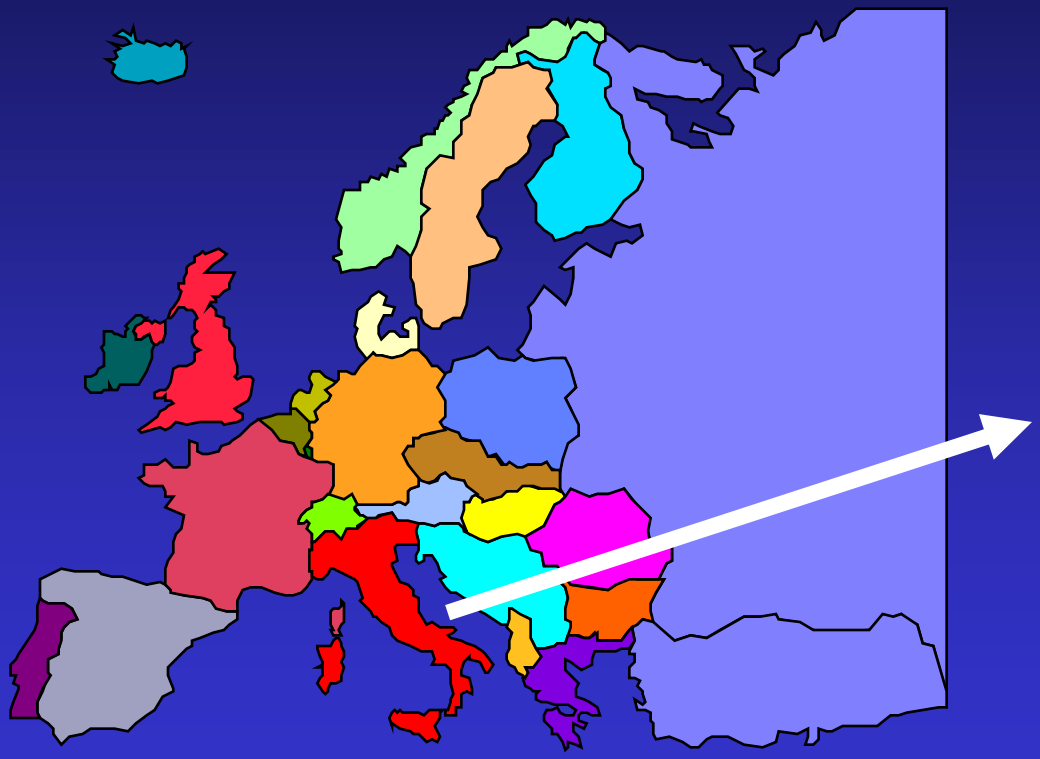
20% haemorragic stroke

80 % ischaemic stroke

Incidence (ischaemic stroke):

4 - 6	new cases /1000	65-69 years
10 -13	new cases /1000	74-84 years

First-ever brain attacks in Italy



75.000 per year

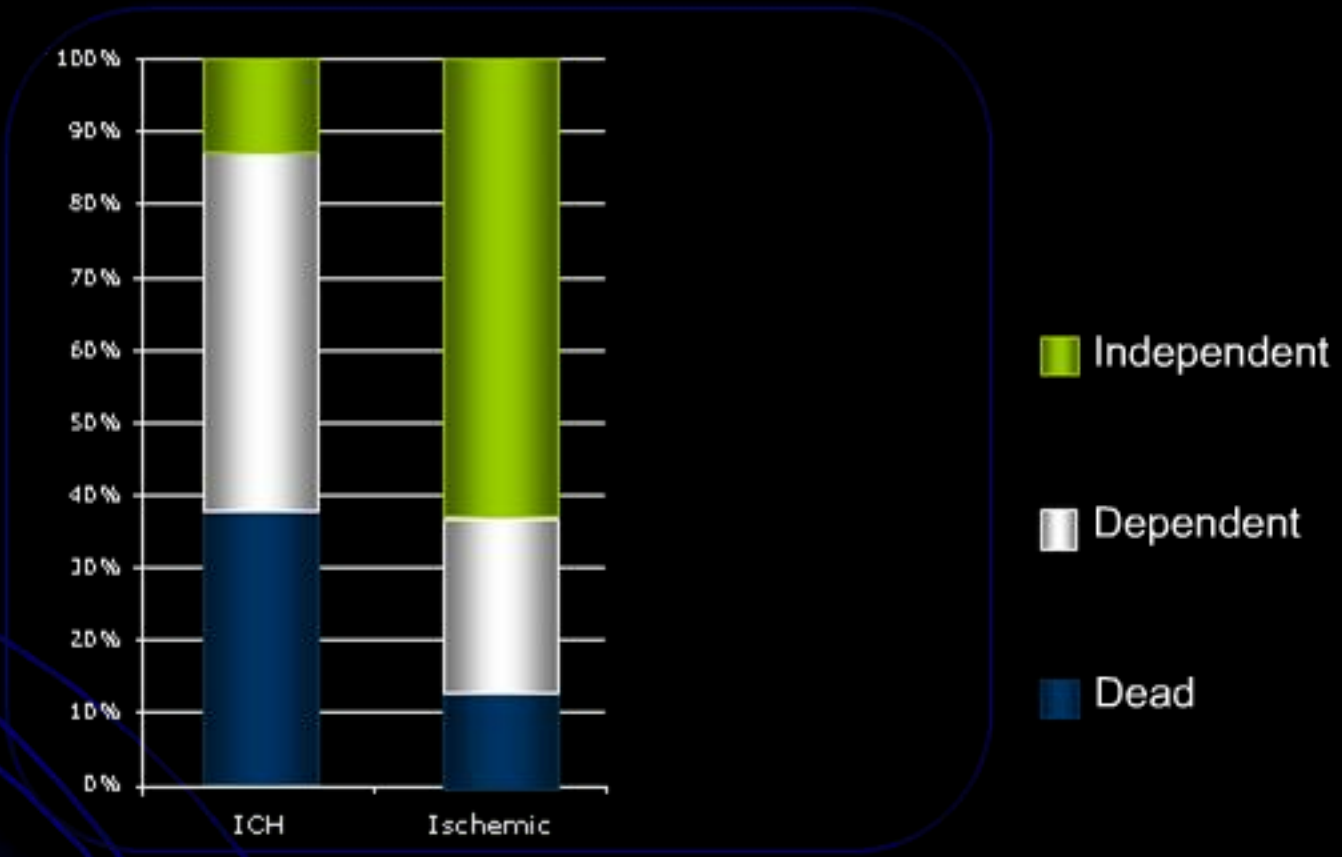
?150.000?

MORTALITA':

CVD in generale 23%

Stroke Ischemico 16%

ICH: worse outcomes than ischemic stroke



American Heart Association. Heart Disease and Stroke Statistics–2005 Update
Qureshi AI et al. N Engl J Med 2001;344:1450-60
Broderick JP et al. Stroke 1999;30:905-15
Broderick JP et al. N Engl J Med 1992;326:733-36

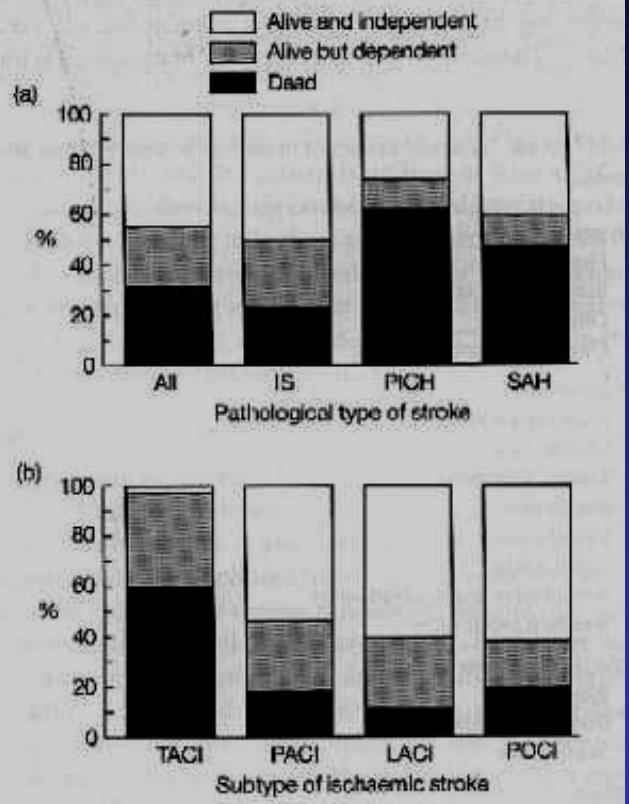
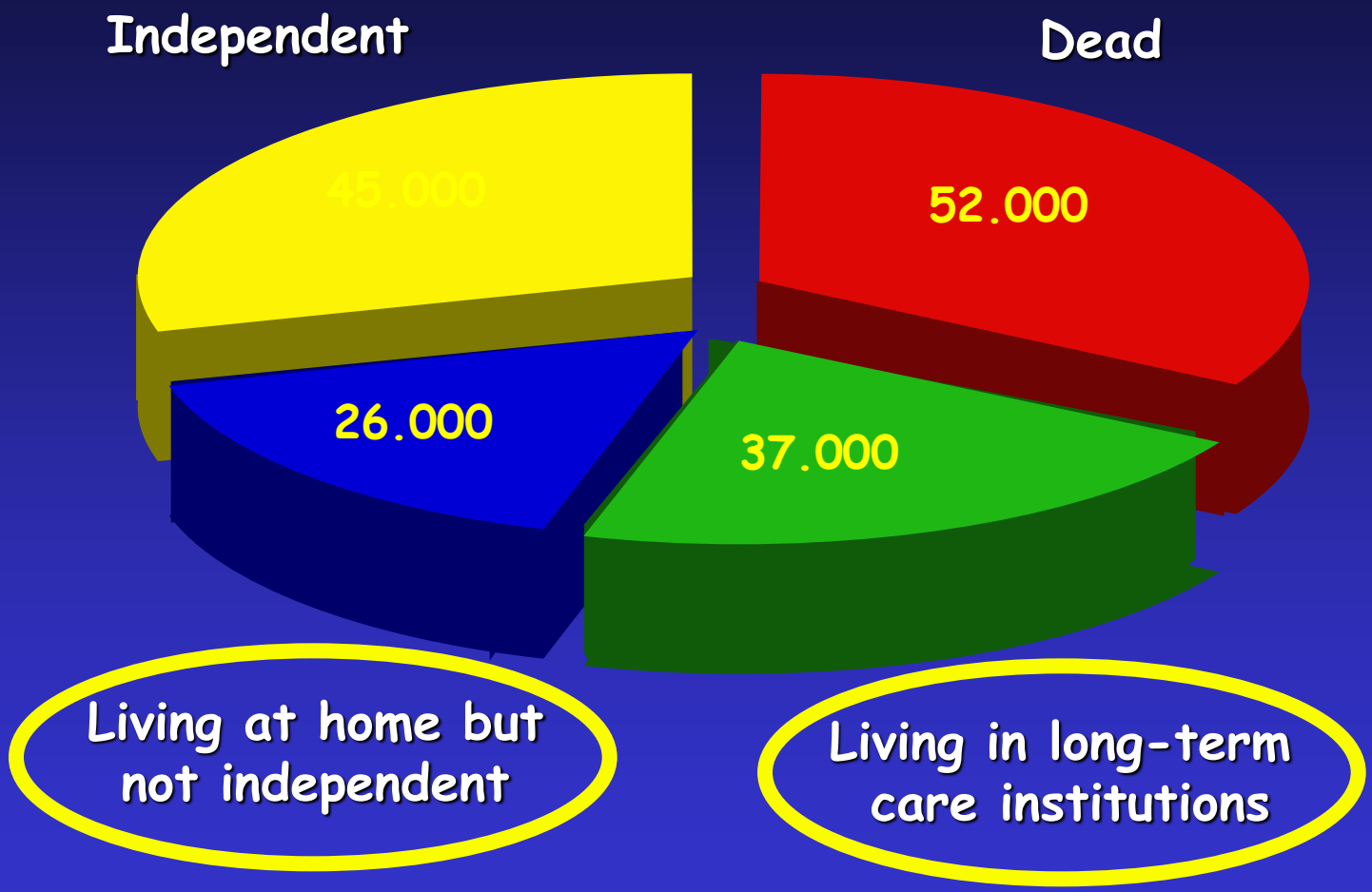


Fig. 27.35. Outcome at 1 year in the 675 first-ever-in-a-lifetime stroke patients in the Oxfordshire Community Stroke Project by (a) pathological type and (b) subtype of ischaemic stroke. IS, ischaemic stroke; PICH, primary intracerebral haemorrhage; SAH, subarachnoid haemorrhage; TACI, total anterior circulation infarct; PACI, partial anterior circulation infarct; LACI, lacunar infarction; POCI, posterior circulation infarction. (From Bamford *et al.* 1990*a*, 1991).

If 150.000 :outcome at 6 months



Severe stroke is more expensive

In Canada the average cost per stroke admission: 21.150 USD

11.550 USD

mild

61.500 USD

severe

Smurawaska et al., Stroke, 1994

Stroke

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Stroke Association℠

A Division of American Heart Association

Helicopter Transfer Offers a Potential Benefit to Patients With Acute Stroke

Molly B. Conroy, Susan U. Rodriguez, Stephen E. Kimmel and Scott E. Kasner

CINCINNATI PREHOSPITAL STROKE SCALE

Facial Droop

Normal:	Both sides of face move equally
Abnormal:	One side of face does not move at all

Arm Drift

Normal:	Both arms move equally or not at all
Abnormal:	One arm drifts compared to the other

Speech

Normal:	Patient uses correct words with no slurring
Abnormal:	Slurred or inappropriate words or mute

Facial Droop

- *Normal*: Both sides of face move equally
- *Abnormal*: One side of face does not move at all

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- *Normal*: Both arms move equally or not at all
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- *Normal*: Patient uses correct words with no slurring
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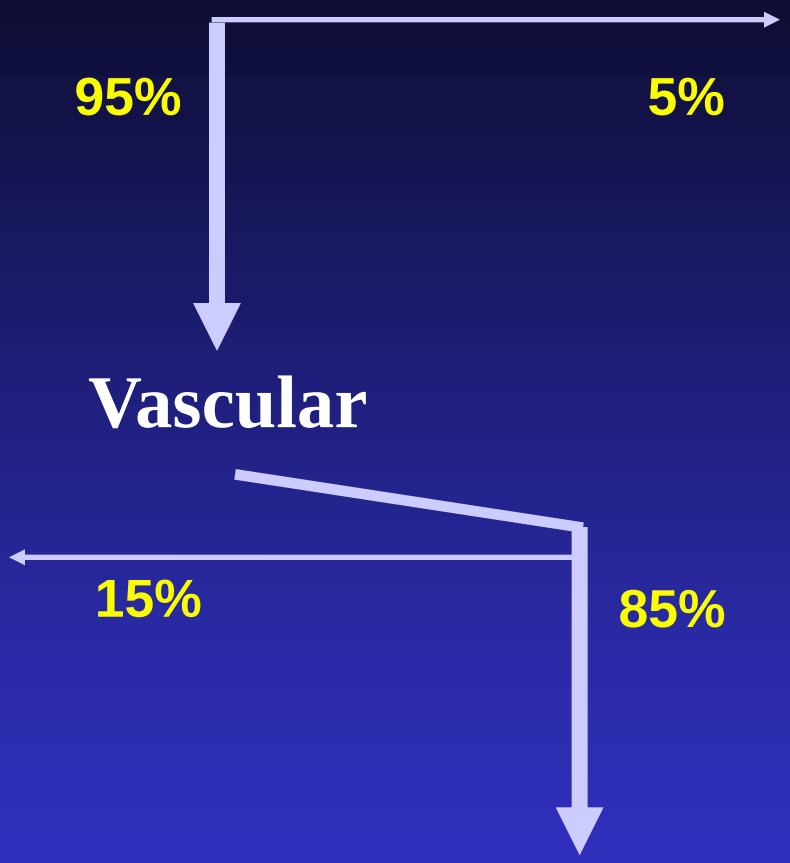
Stroke Scales: NIHSS

UMM UNIVERSITÄTSMEDIZIN MANNHEIM

- 11 parts
- designed to be conducted over 7 minutes
- score range: 0-42
- maximum score actually is 31 for a stroke patient with complete hemiparesis, hemianopia, hemineglect, and aphasia
- severe stroke: NIHSS score > 15-20
- 80% of patients with an NIHSS < 12- 14 will have a good or excellent outcome
- only 20% of patients with an NIHSS > 20-26 will have this similar good or excellent outcome

Diagnostica differenziale nelle CVD

Abrupt Focal CNS Deficit

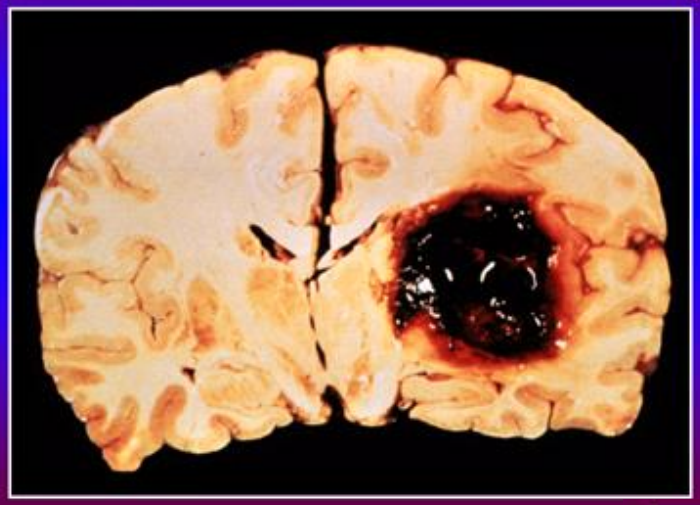


Nonvascular
- Seizure
- Tumor
- Demyelination
- Psychogenic

Hemorrhage
- Intracerebral
- Subarachnoid
- Subdural/epidural

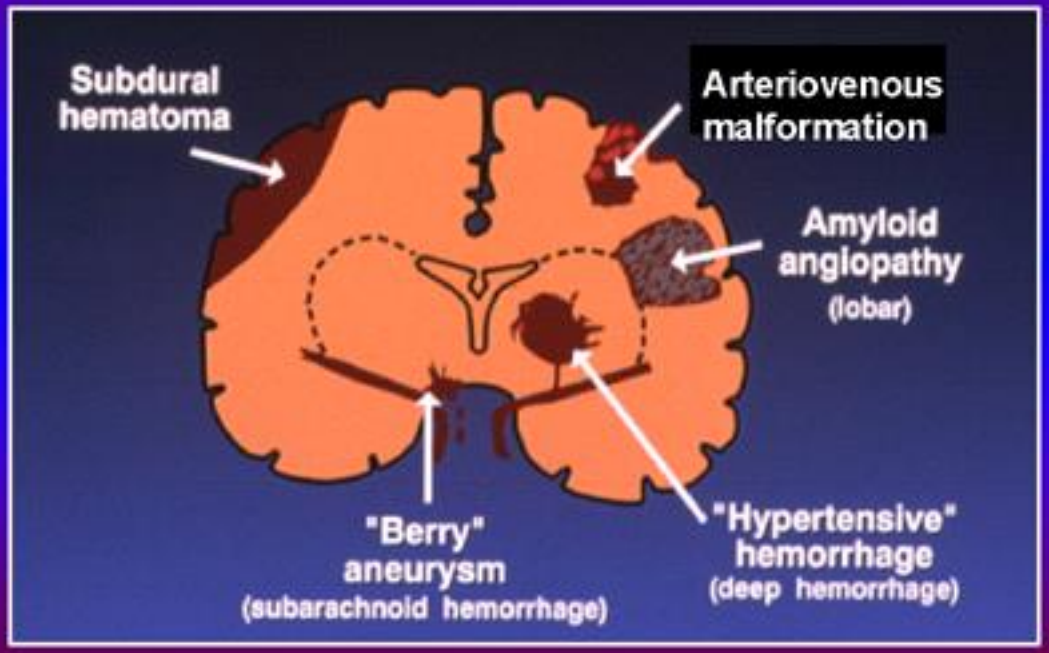
Ischemic Stroke

Hypertensive Intracerebral Hemorrhage

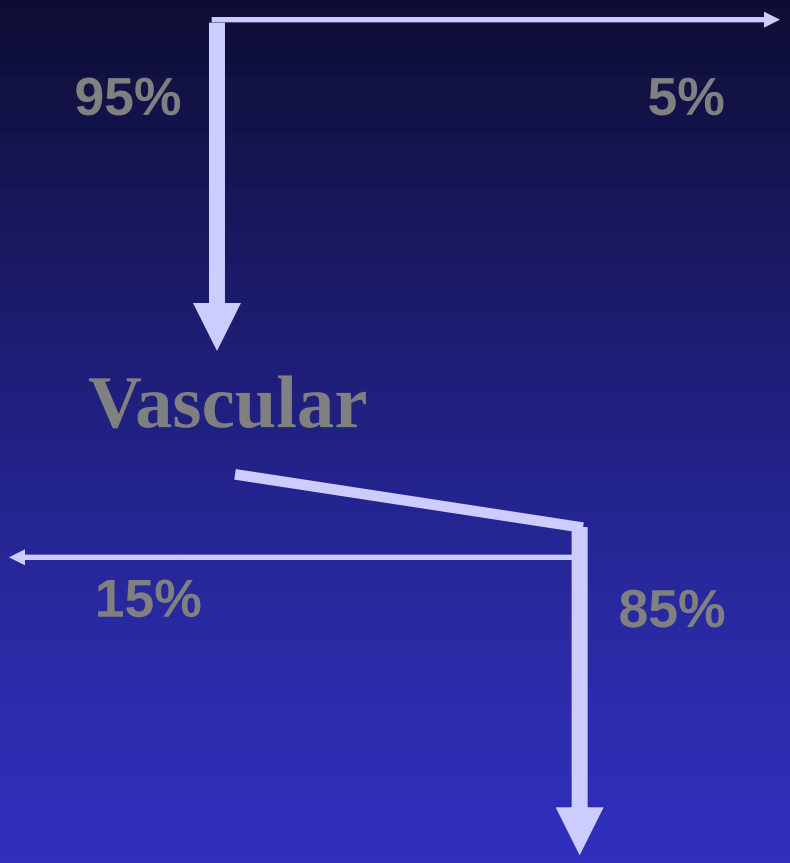


Aneurysmal Subarachnoid Hemorrhage

Types of CNS Hemorrhage



Abrupt Focal CNS Deficit



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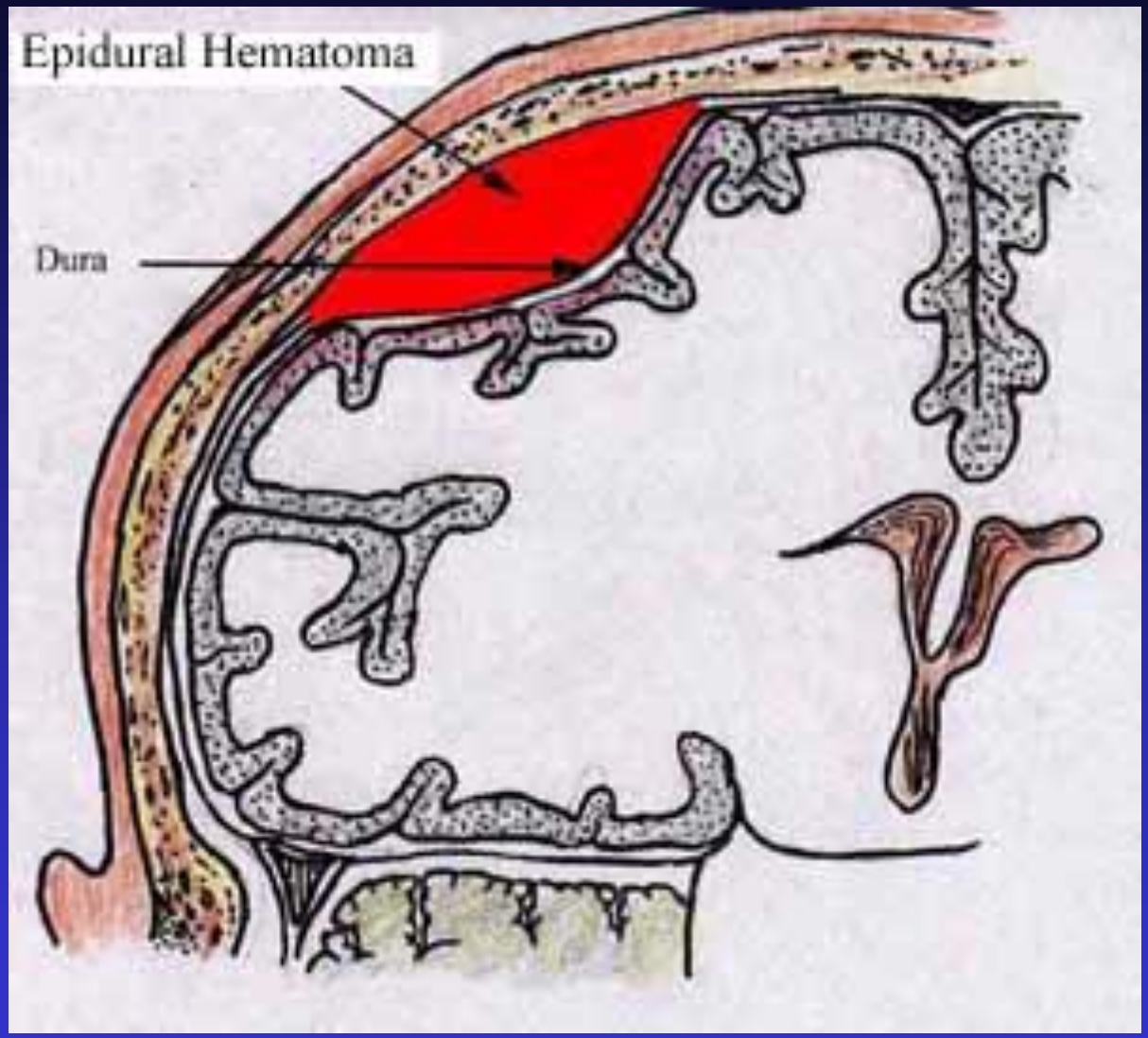
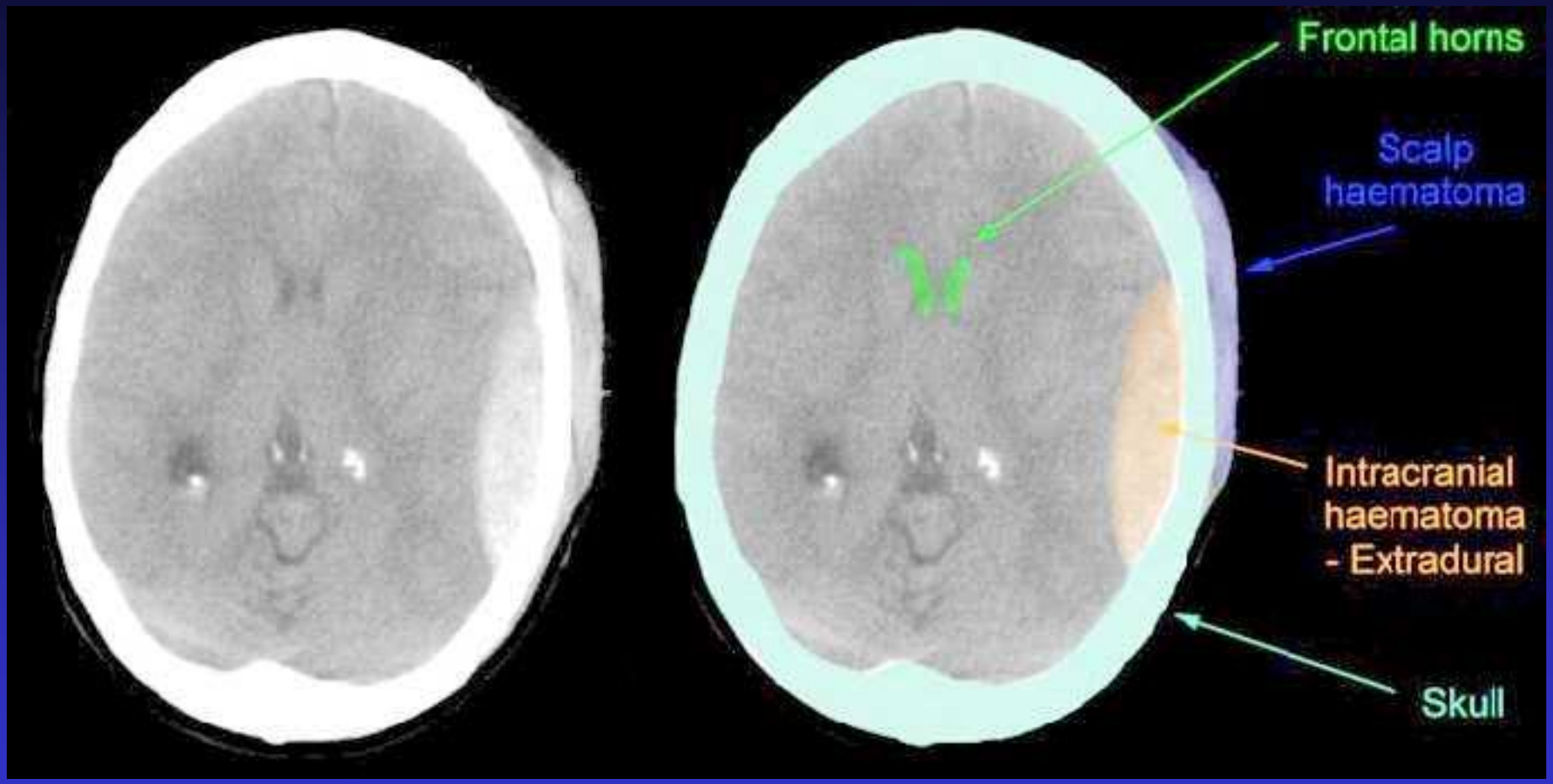
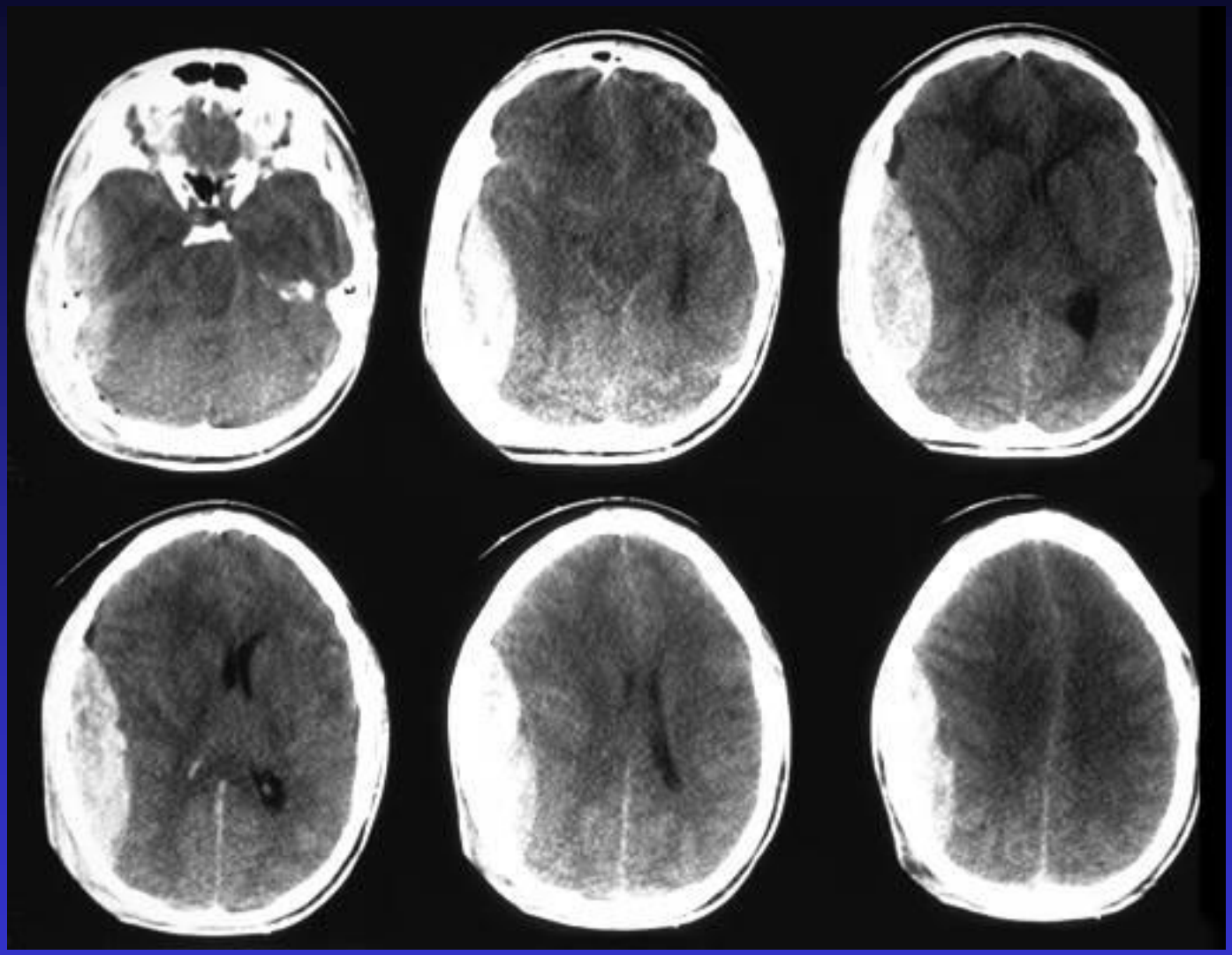
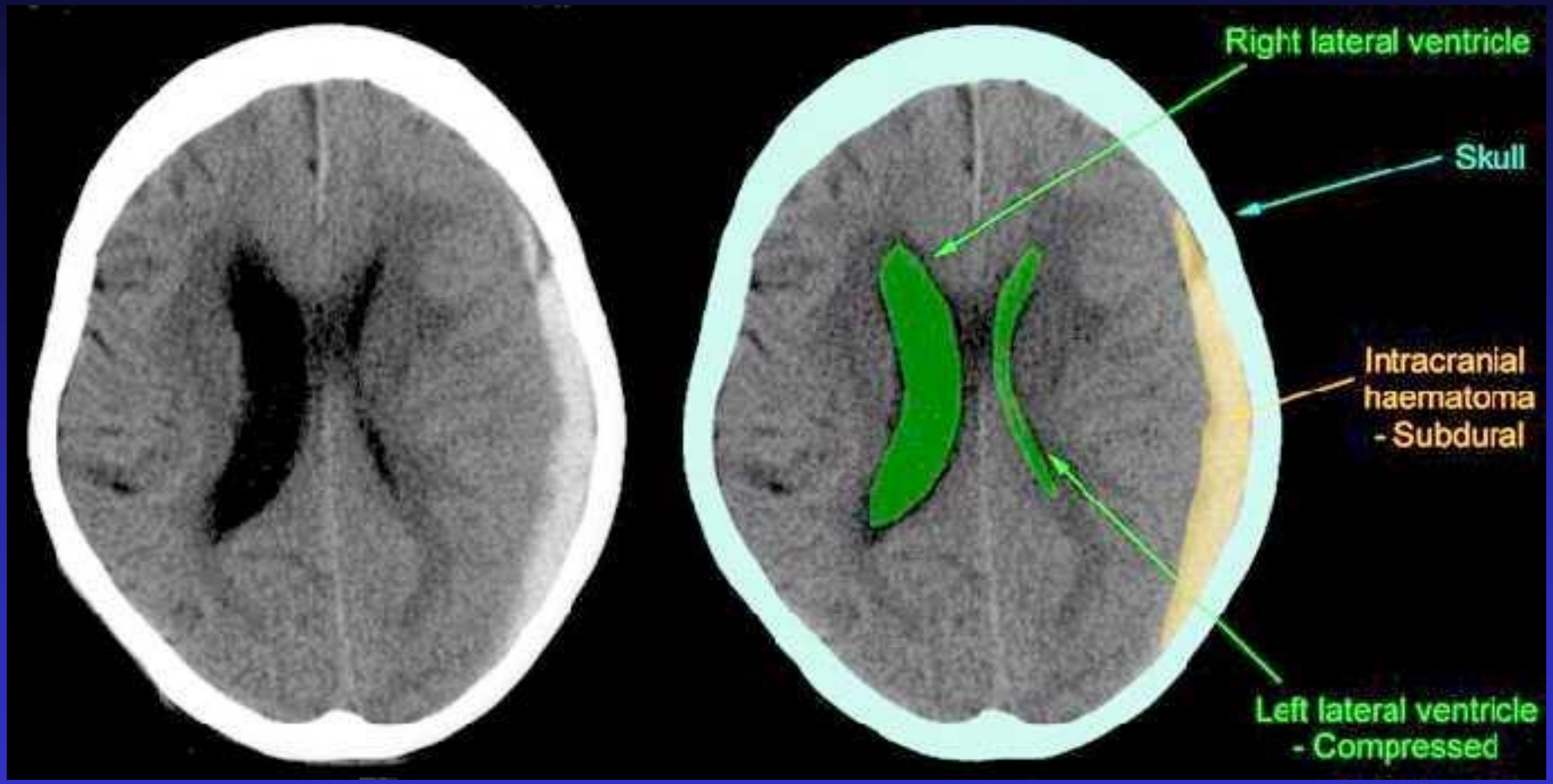
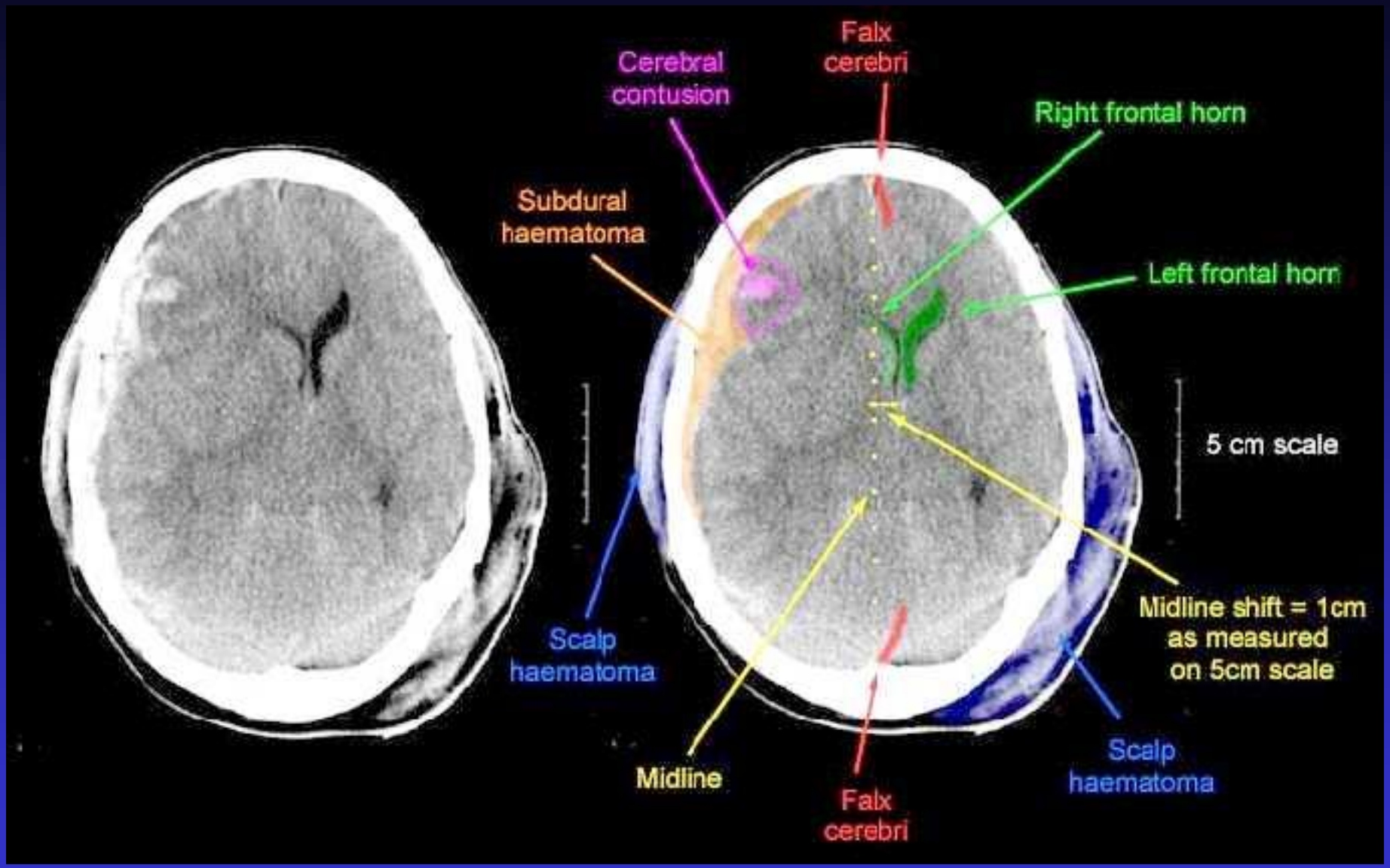

Epidural Hematoma
Dura

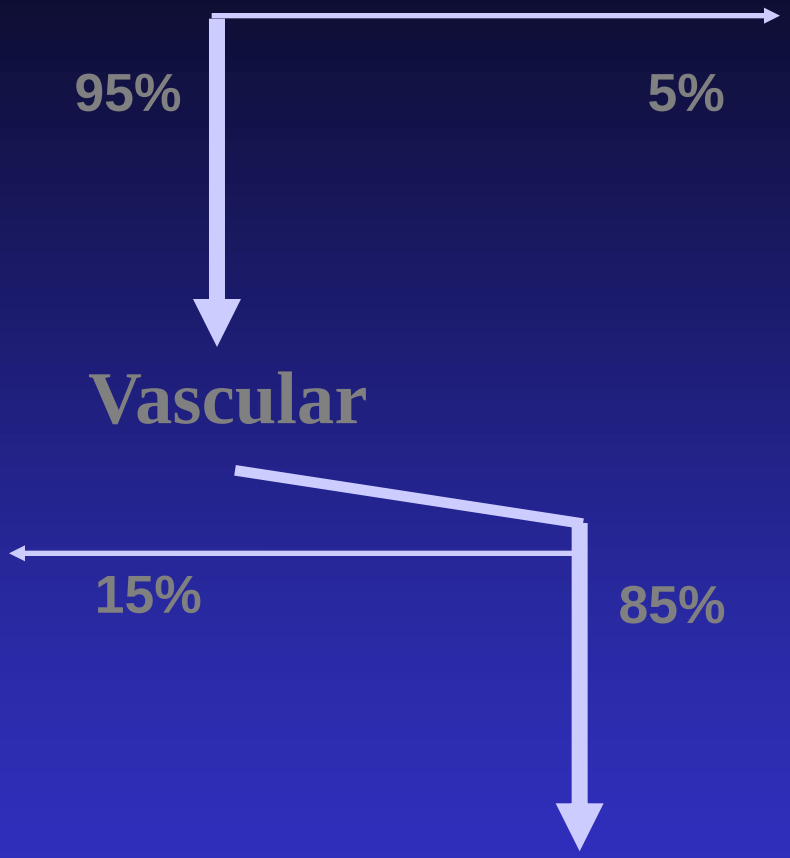

Frontal horns
Scalp haematoma
Intracranial haematoma - Extradural
Skull




Right lateral ventricle
Skull
Intracranial haematoma - Subdural
Left lateral ventricle - Compressed


Falx cerebri
Cerebral contusion
Right frontal horn
Subdural haematoma
Left frontal horn
5 cm scale
Midline shift = 1cm as measured on 5cm scale
Scalp haematoma
Midline
Falx cerebri
Scalp haematoma

Abrupt Focal CNS Deficit



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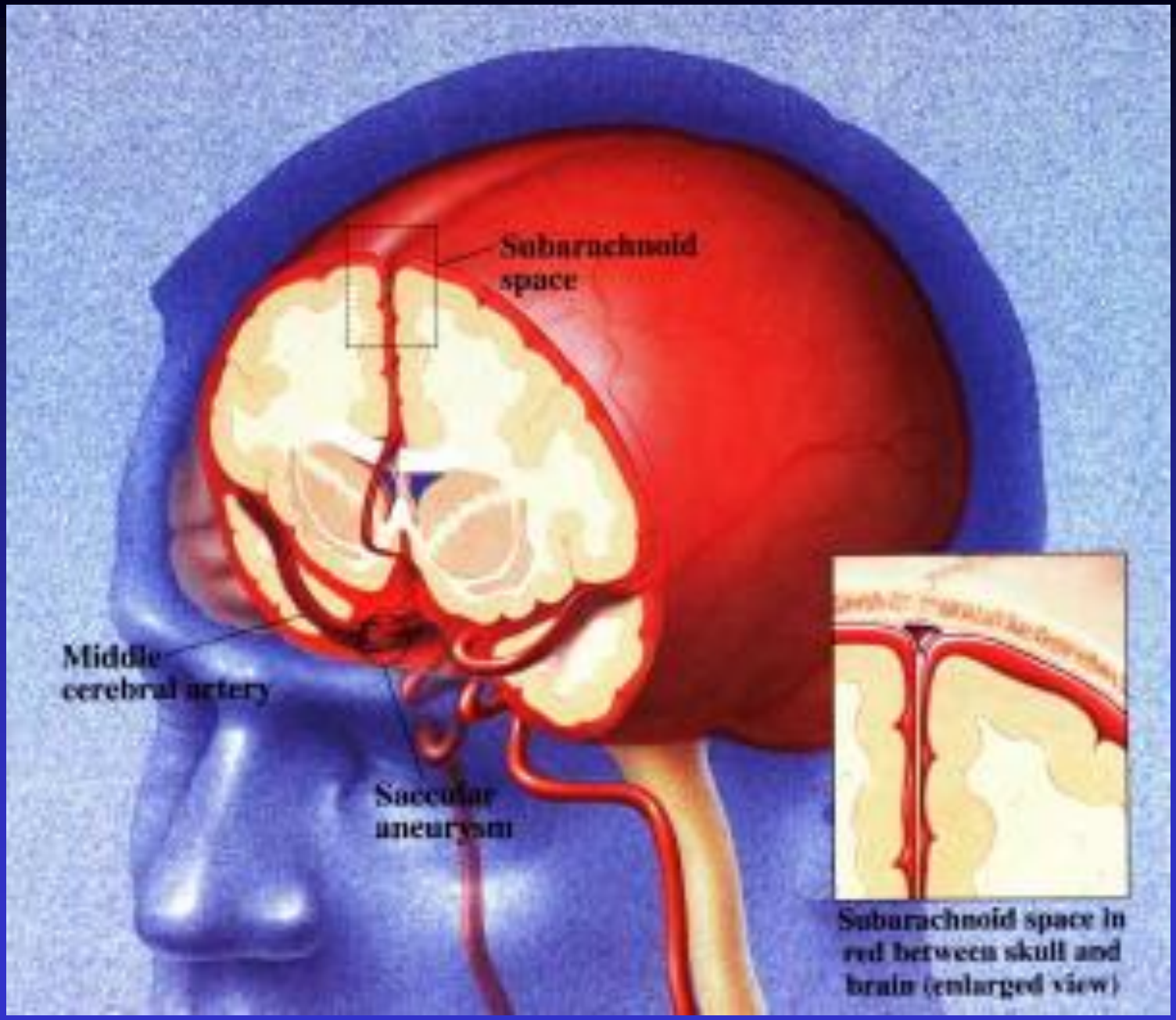

Subarachnoid space
Middle cerebral artery
Saccular aneurysm
Subarachnoid space in red between skull and brain (enlarged view)


©UC Regents

Fig 15

Glasgow Coma Scale

printable version PDF

ACTIVITY	SCORE
Eye Opening	
None	1 = Even to supra-orbital pressure
To pain	2 = Pain from sternum/limb/supra-orbital pressure
To speech	3 = Non-specific response, not necessarily to command
Spontaneous	4 = Eyes open, not necessarily aware
Motor Response	
None	1 = To any pain; limbs remain flaccid
Extension	2 = Shoulder adducted and shoulder and forearm internally rotated
Flexor response	3 = Withdrawal response or assumption of hemiplegic posture
Withdrawal	4 = Arm withdraws to pain, shoulder abducts
Localizes pain	5 = Arm attempts to remove supra-orbital/chest pressure
Obeys commands	6 = Follows simple commands
Verbal Response	
None	1 = No verbalization of any type
Incomprehensible	2 = Moans/groans, no speech
Inappropriate	3 = Intelligible, no sustained sentences
Confused	4 = Converses but confused, disoriented
Oriented	5 = Converses and oriented
	TOTAL (3–15):

World Federation of Neurological Surgeons Grading System for Subarachnoid Hemorrhage - (WFNS) scale

Overview :

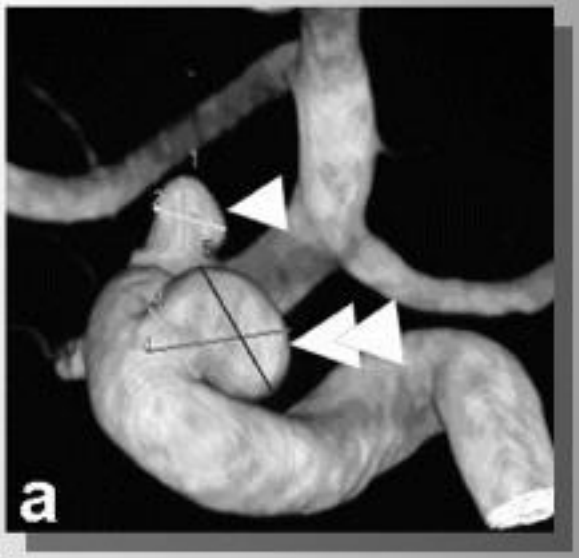
The clinical grading system proposed by the World Federation of Neurologic Surgeons is intended to be a simple, reliable and clinically valid way to grade a patient with subarachnoid hemorrhage. This system offers less interobserver variability than some of the earlier classification systems.

Glasgow Coma Score	Motor Deficit	Grade
15	absent	1
13 - 14	absent	2
13 - 14	present	3
7 - 12	present or absent	4
3 - 6	present or absent	5

*Where a motor deficit refers to a major focal deficit.

Interpretation:
- Maximum score of 15 has the best prognosis
- Minimum score of 3 has the worst prognosis
- Scores of 8 or above have a good chance for recovery
- Scores of 3-5 are potentially fatal, especially if accompanied by fixed pupils or absent oculovestibular responses
- Young children may be nonverbal, requiring a modification of the coma scale for evaluation

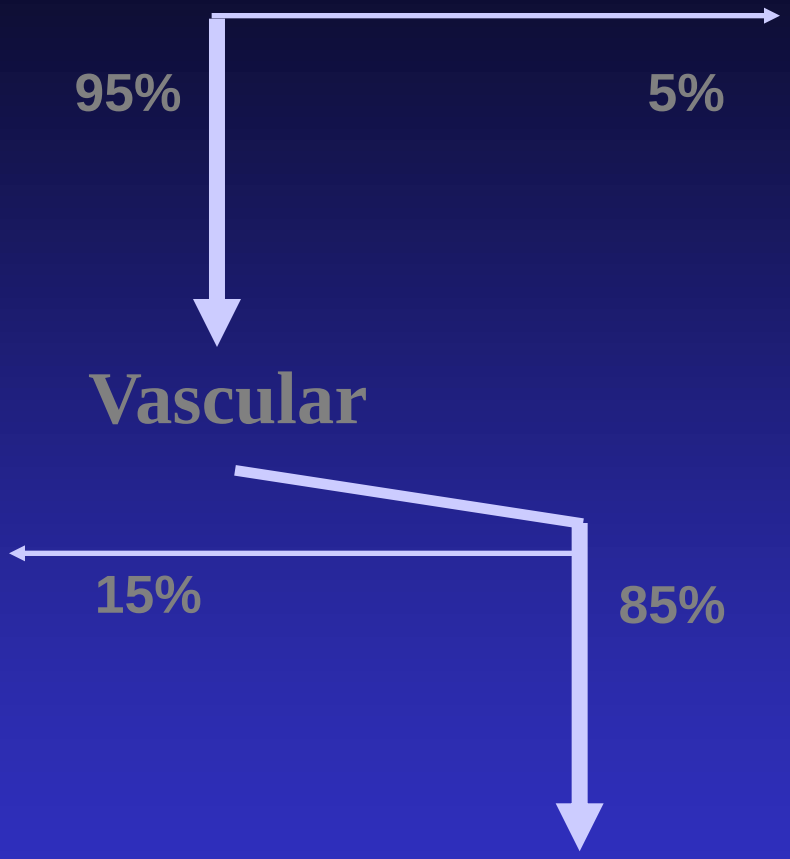
- **Sex ratio:** F/M = 1.3; risk x 4.7, multiple UIA x2 in women
- **Mean age:** 50 yrs
- **Prevalence:** 2 to 5% of the population
- **Multiple:** 35%
- **Risks factors for UIA:**
  - ✓ Smoking X 3-4
  - ✓ Hypertension X 2.5
  - ✓ Alcohol > 150g per week X 2
  - ✓ Familial history > x3 to 5 -1st degree relatives
  - ✓ Connective tissue disease
  - ✓ ADPKD



Rinkel GJ. Natural history, epidemiology and screening of unruptured intracranial aneurysms. ***RevNeurol(Paris)***. *2008;164:781-786*

Raaymakers et al. A. Mortality and morbidity of surgery for unruptured intracranial aneurysms: A meta-analysis. ***Stroke***. *1998;29:1531-1538*

Abrupt Focal CNS Deficit



Nonvascular
- Seizure
- Tumor
- Demyelination
- Psychogenic

Hemorrhage
- Intracerebral
- Subarachnoid
- Subdural/epidural

Where do the bleedings occur?

- Lobar (A) 35%
- Putamen (B) 31%
- Thalamus (C) 18%
- Cerebellum (E) 7%
- Pons (D) 5%
- Caudate 4%

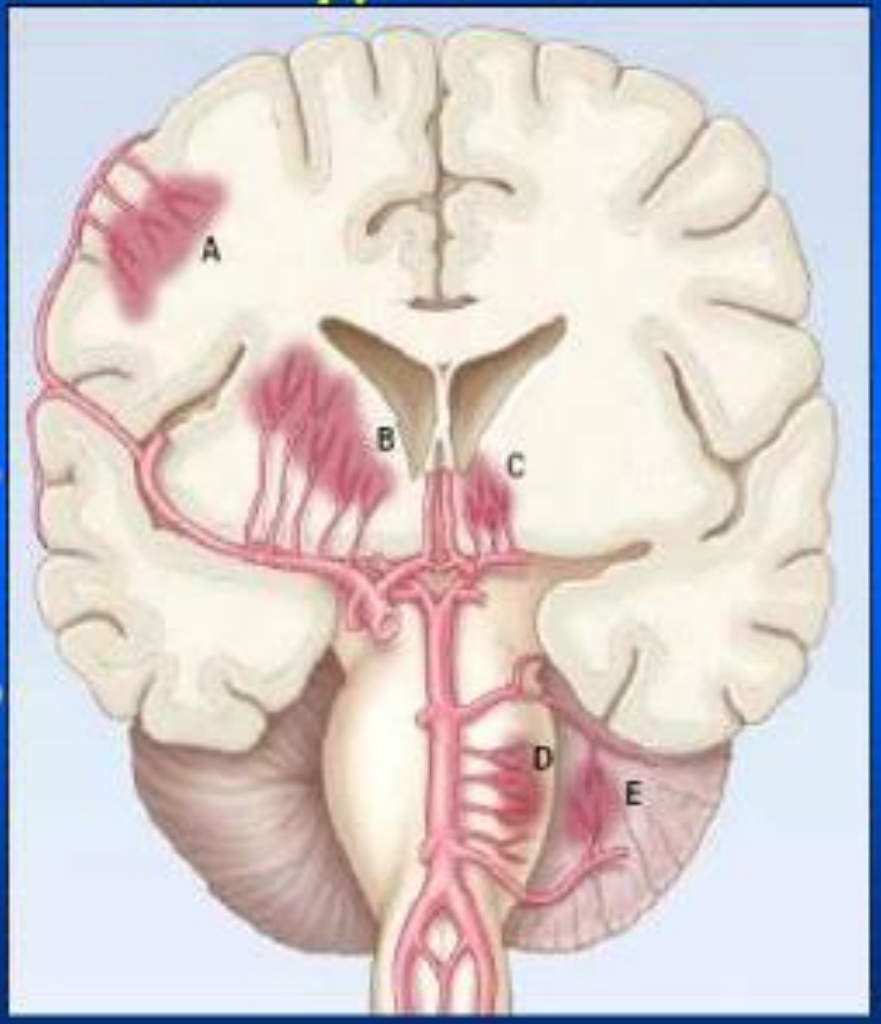
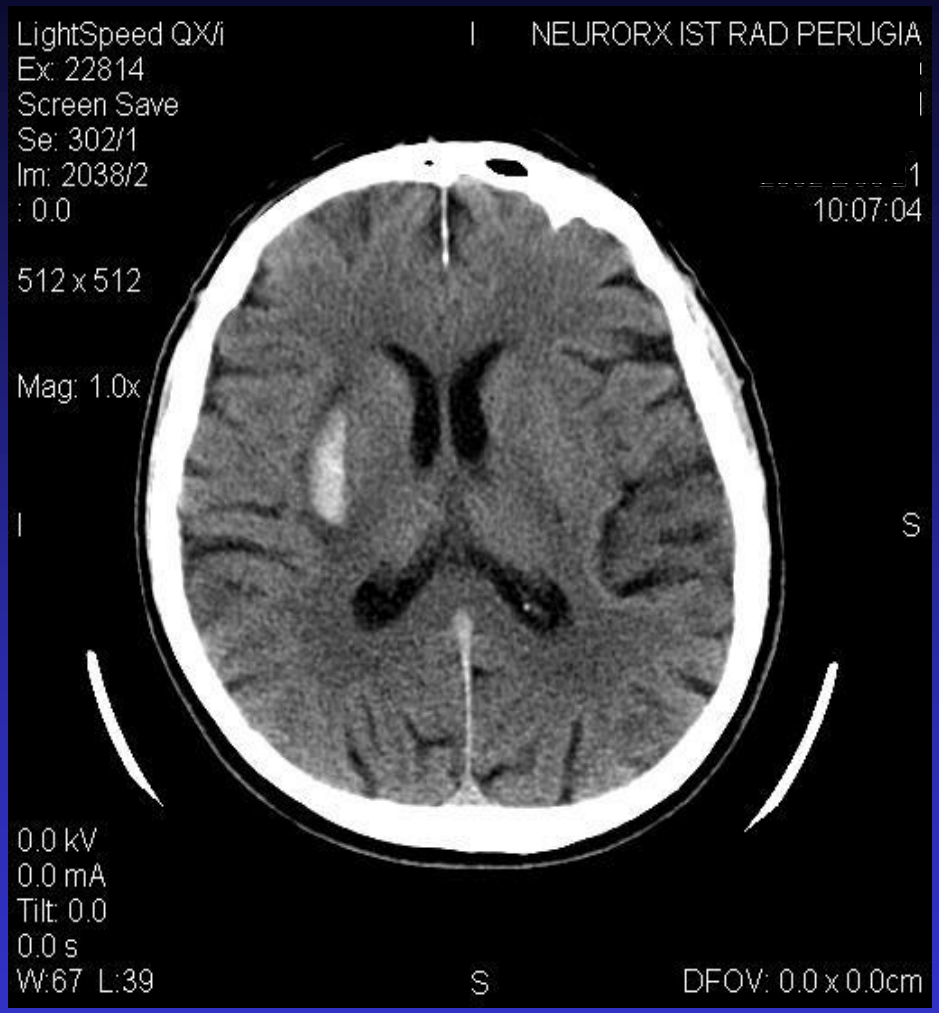


Fig 10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10:07:04
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0.0 kV
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Tilt: 0.0
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W:67 L:39
S
DFOV: 0.0 x 0.0cm

Fig 11

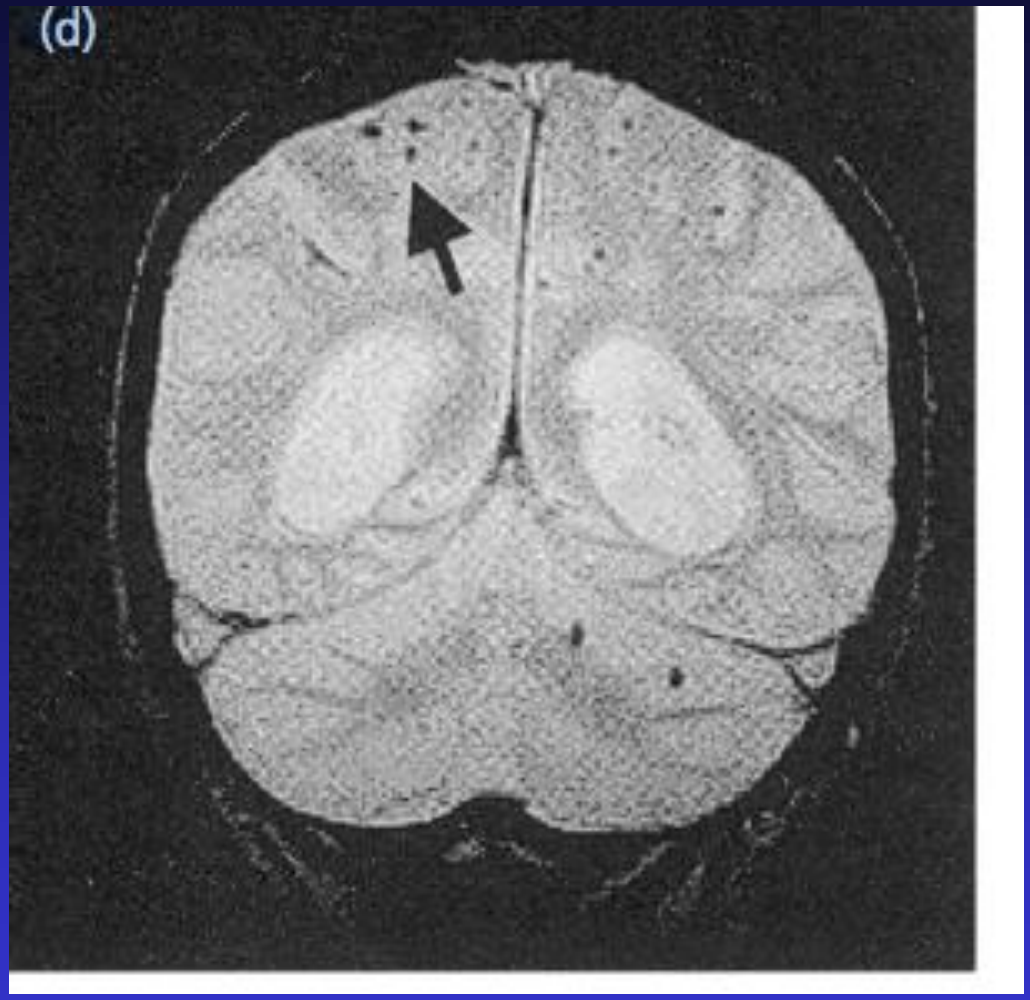
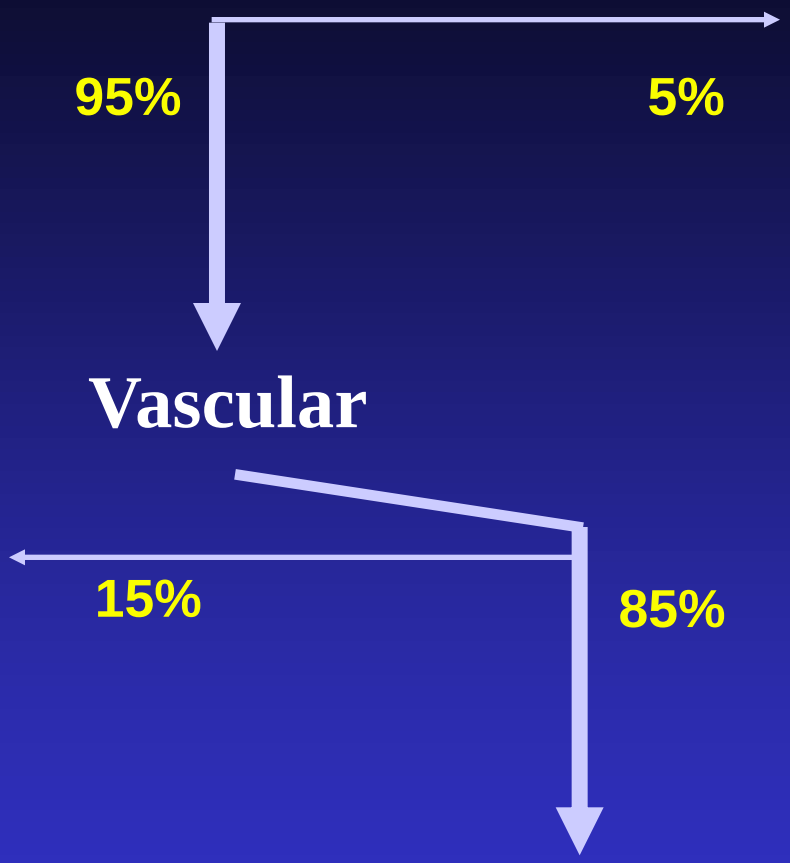

(d)

Table 1.4 Aetiological classification of cerebral haemorrhage

- Subarachnoid haemorrhage
  - Saccular aneurysms
  - Normal angiogram
  - Rare causes
- Primary intracerebral haemorrhage
  - Malformations or changes in cerebral vessels
    - Lipohyalinosis/microaneurysms in perforating arteries
    - Amyloid angiopathy
    - Cerebral arteriovenous malformations
    - Saccular aneurysms
    - Cerebral venous thrombosis
    - Moya–moya syndrome
    - Cerebral arteriovenous malformations
    - Cavernomas
    - Mycotic aneurysms
    - Vasculitis
  - Hypertension
  - Haematological factors
    - Treatment related
      - Anticoagulants
      - Thrombolysis
      - Antiplatelet agents
    - Haemophilia
    - Leukaemia
    - Thrombocytopenia
  - Drugs
    - Alcohol
    - Amphetamines
    - Cocaine
  - Other causes
    - Cerebral tumours

Abrupt Focal CNS Deficit

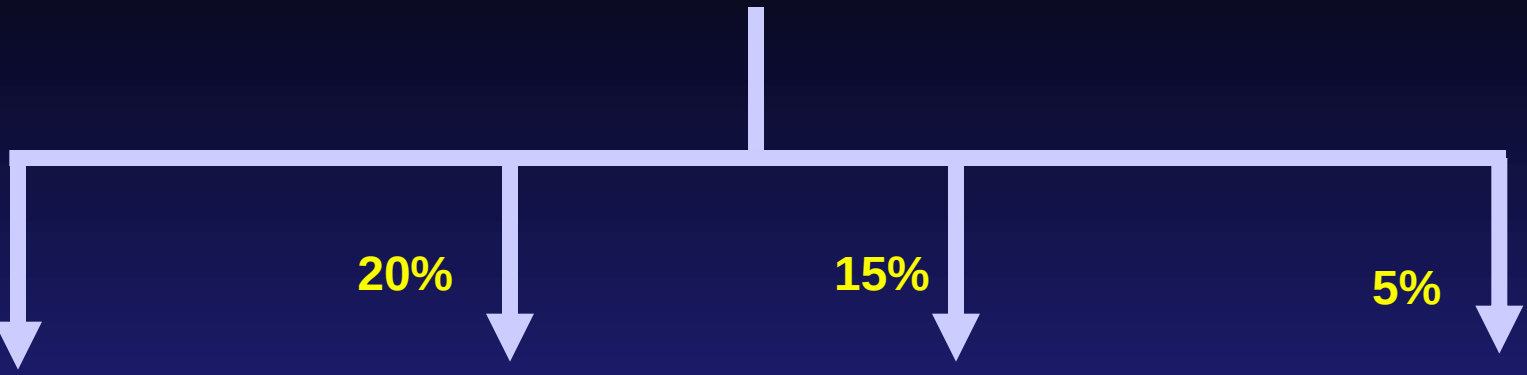


Nonvascular
- Seizure
- Tumor
- Demyelination
- Psychogenic

Hemorrhage
- Intracerebral
- Subarachnoid
- Subdural/epidural

Ischemic Stroke

Ischemic Stroke



60%

Atherosclerotic Cerebrovascular Disease

20%

Penetrating Artery Disease ("Lacunes")

15%

Cardiogenic Embolism

- Atrial Fibrillation
- Valve Disease
- Ventricular thrombi
- Many others

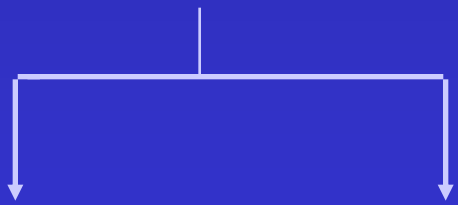
5%

Other, Unusual Causes

- Prothrombotic states
- Dissections
- Arteritis
- Migraine
- Vasospasm
- Drug abuse
- Many more

Intracranial Microatheroma

Large Artery Atheroma



Hypoperfusion

Arteriogenic Emboli

Table 1.1 Pathophysiological classification of stroke[a]

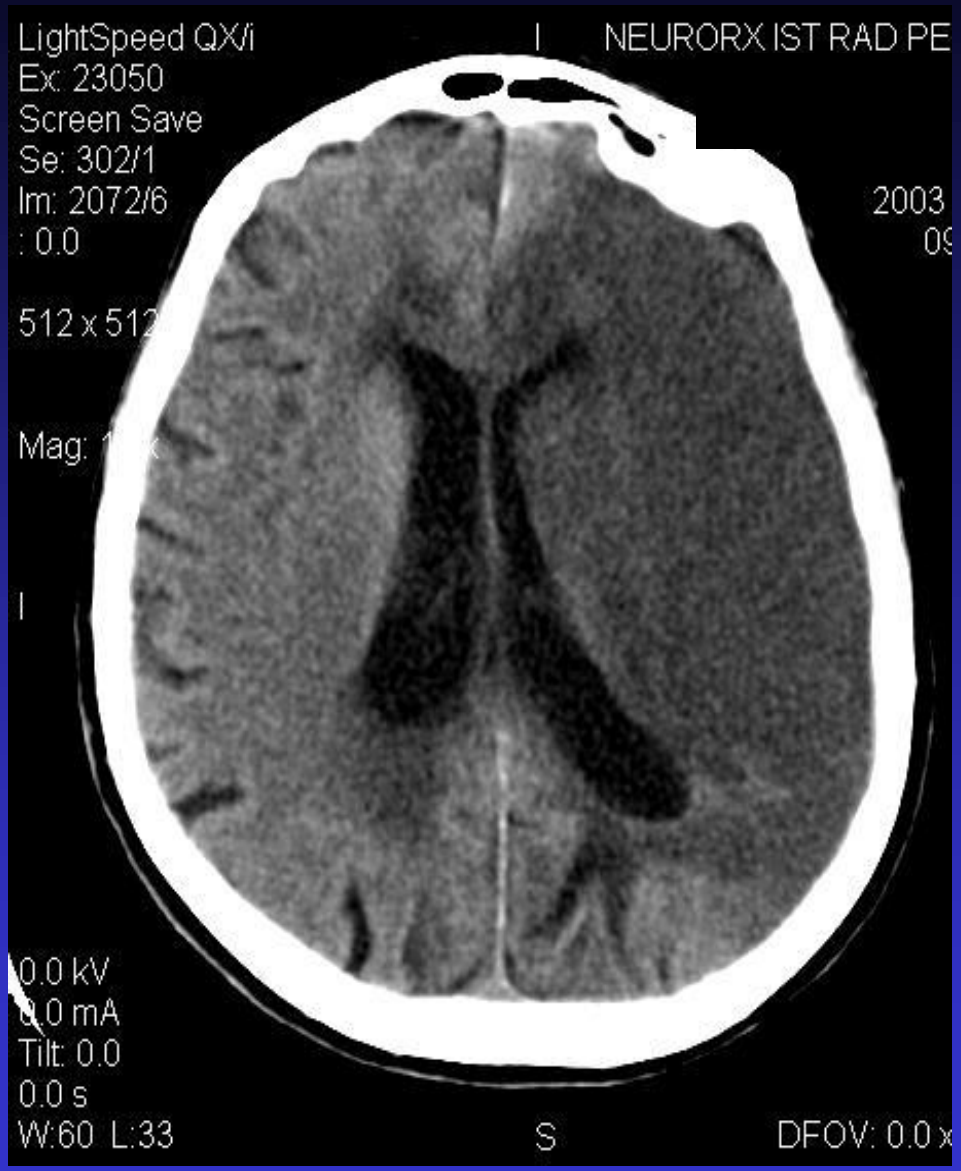
Ischaemic stroke
Large artery
Cardioembolic
Lacunar (small vessel disease)
Other determined aetiology
Undetermined aetiology
Multiple possible aetiologies
Cerebral haemorrhage
Primary subarachnoid haemorrhage
Primary intracerebral haemorrhage
Definitions
Large artery stroke: Occlusion or stenosis (>50%) in large extracranial or intracranial cerebral artery (carotid, vertebral, basilar, anterior cerebral, middle cerebral, posterior cerebral), with ischaemia in that arterial territory.
Cardioembolic stroke: One or more of the following conditions: Mechanical prosthetic heart valve, atrial fibrillation, myocardial infarction within last 2 months, dilated cardiomyopathy/congestive heart failure at stroke onset, endocarditis, sick sinus syndrome, atrial myxoma, left ventricular thrombus.
Lacunar stroke: Lacunar syndrome (pure motor stroke, pure sensory stroke, ataxic hemiparesis, clumsy hand dysarthria) with either no lesion on brain imaging or a deep infarct (≤1.5 cm diameter) in a location consistent with the clinical syndrome.

[a] This classification is based on, but modified from, the TOAST and Stroke Data Bank classifications.

Fig 26

Fig 27

Fig 28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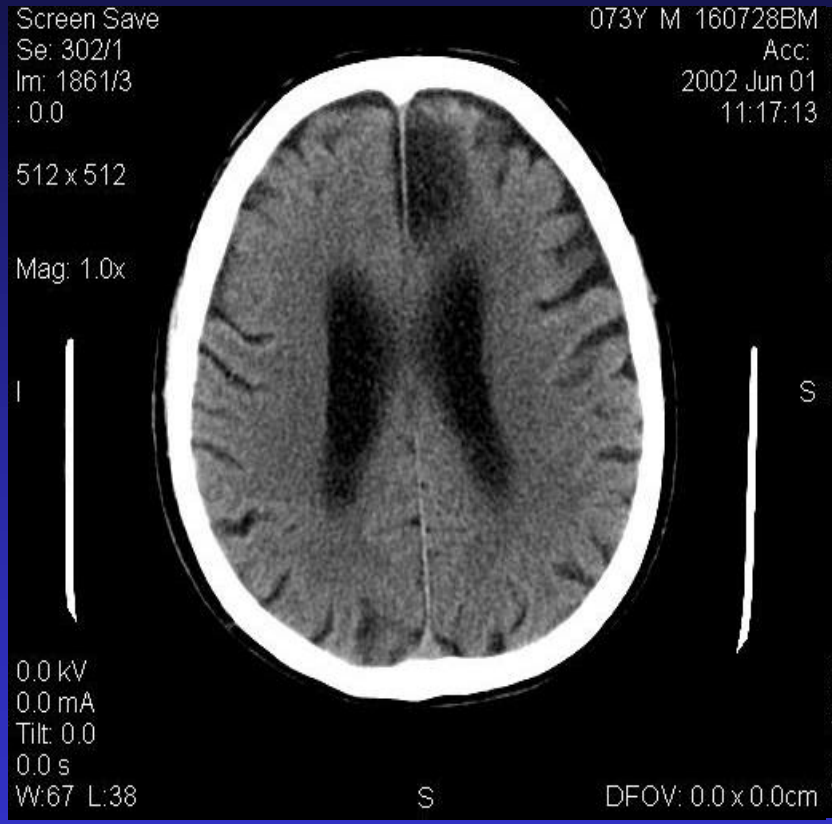
Ex: 23050
Screen Save
Se: 302/1
Im: 2072/6
: 0.0
512 x 512
Mag:
I
NEURORX IST RAD PE
2003
0.0 kV
0.0 mA
Tilt: 0.0
0.0 s
W:60 L:33
S
DFOV: 0.0 x

Fig 32

a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Im: 1861/3
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512 x 512
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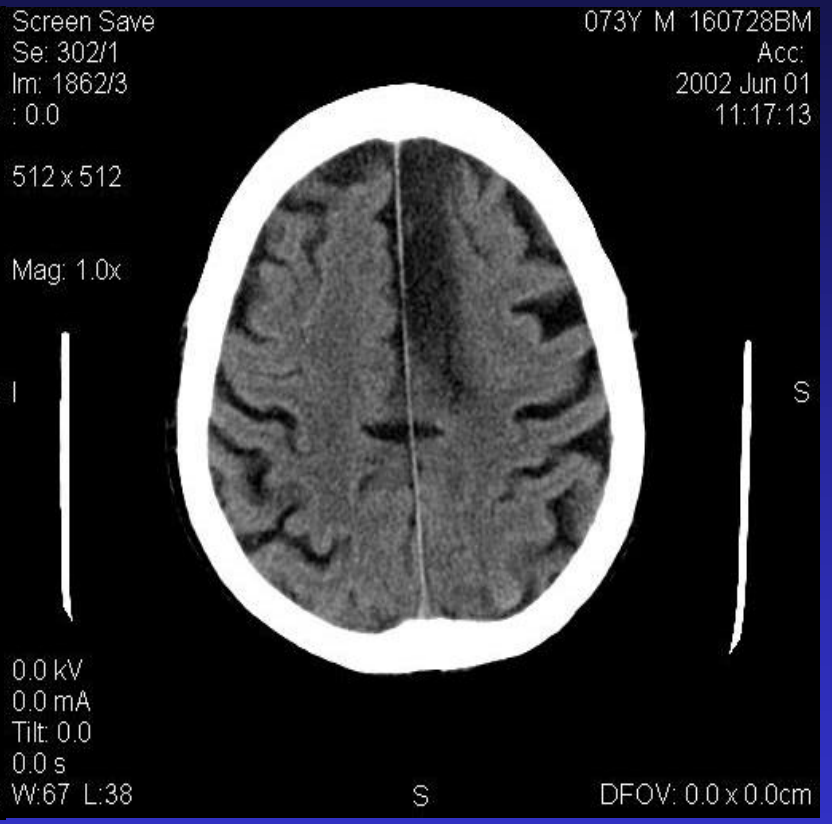
073Y M 160728BM
Acc:
2002 Jun 01
11:17:13
I
S
0.0 kV
0.0 mA
Tilt: 0.0
0.0 s
W:67 L:38
S
DFOV: 0.0 x 0.0cm

b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Tilt: 0.0
0.0 s
W:67 L:38
S
DFOV: 0.0 x 0.0cm

Fig 29


Screen Save
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512 x 512
Mag: 1.0x
063Y F 250938ME
Acc:
2001 Oct 01
16:49:38
I
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0.0 kV
0.0 mA
Tilt: 0.0
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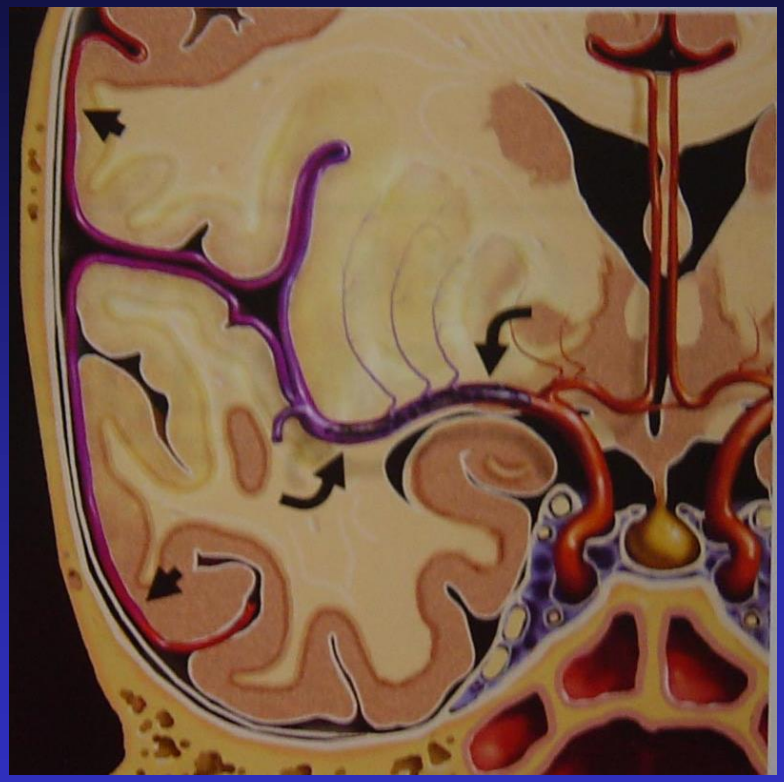
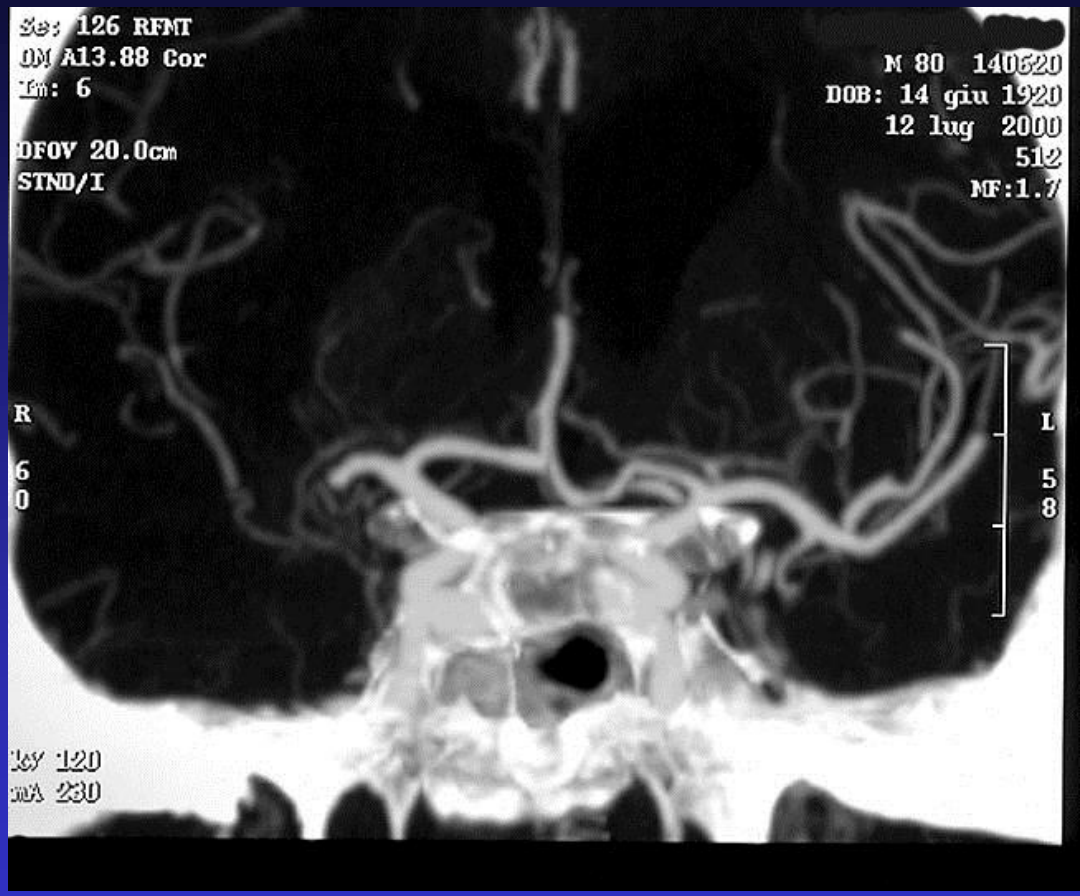
W:76 L:41
S
DFOV: 0.0 x 0.0cm

Fig 51

a



b



Ostruzione prossimale della cerebrale media

Fig 31

a

b

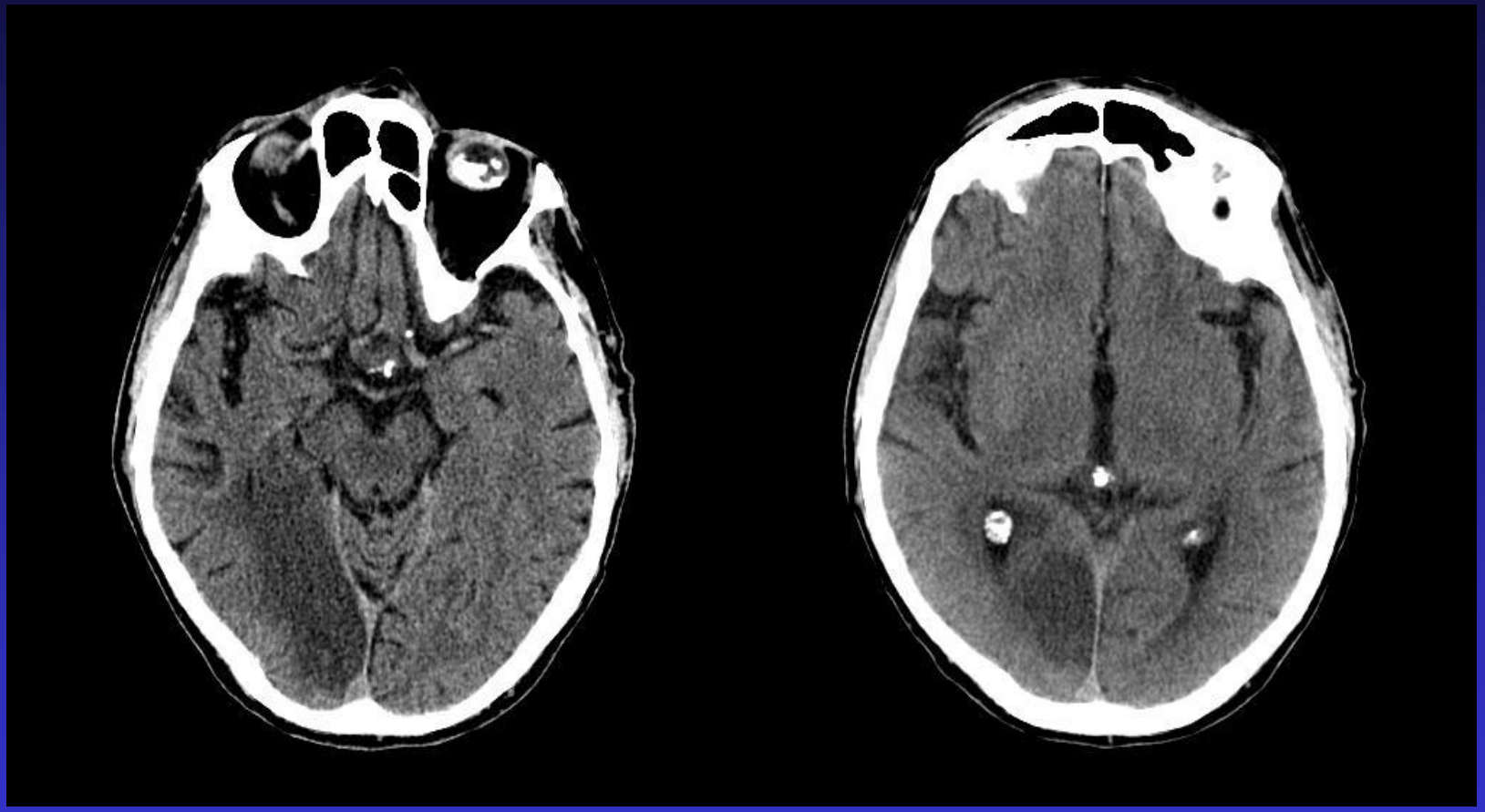
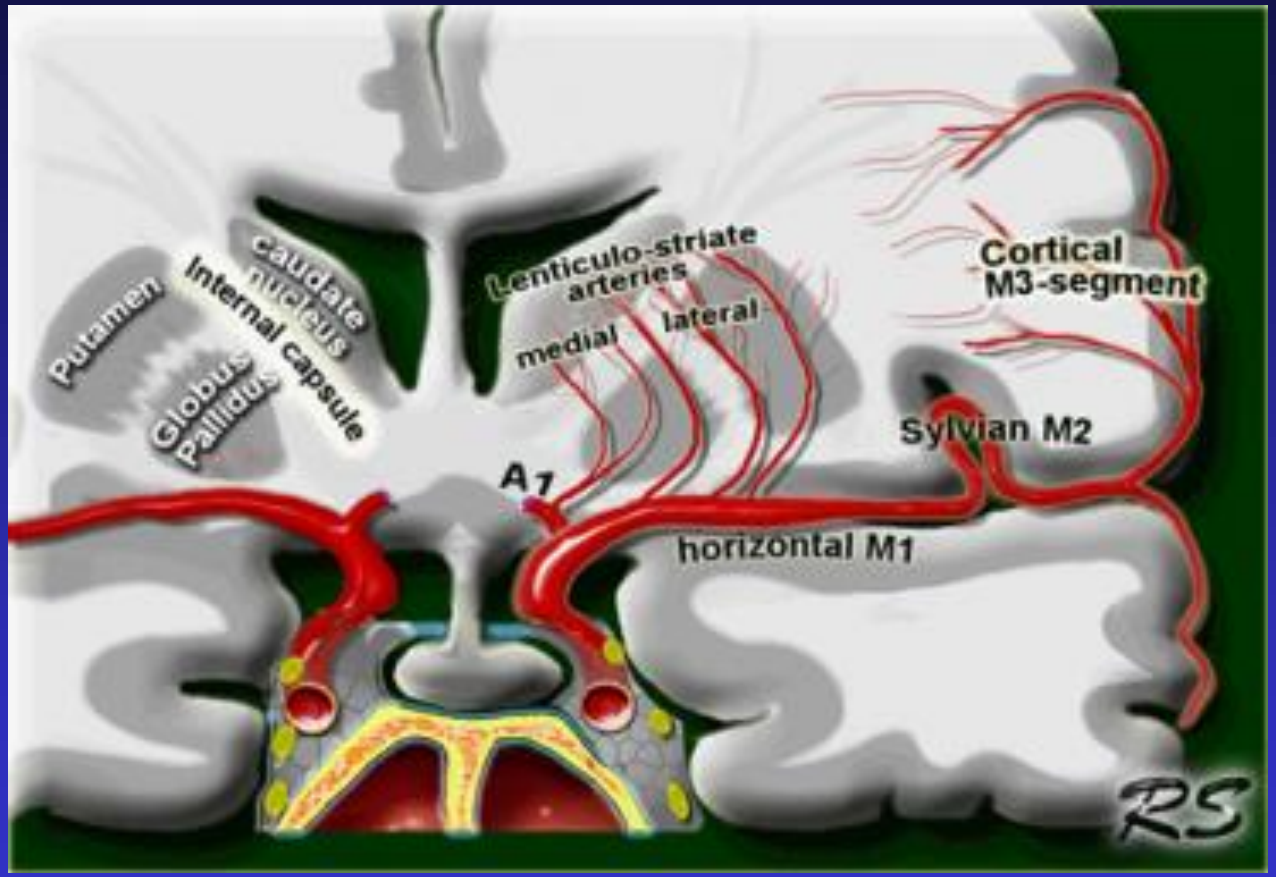
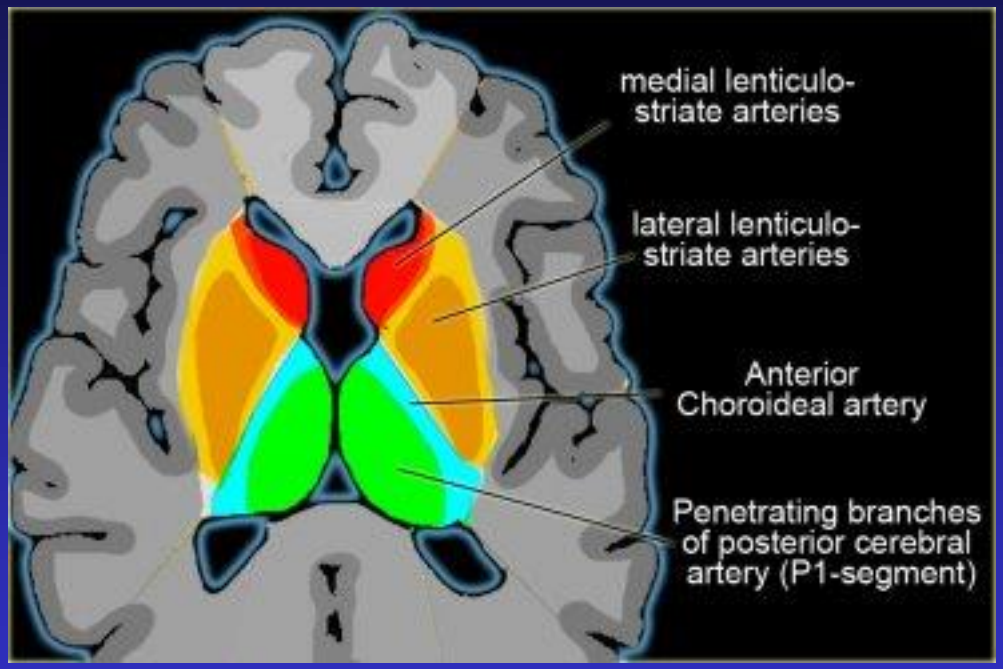


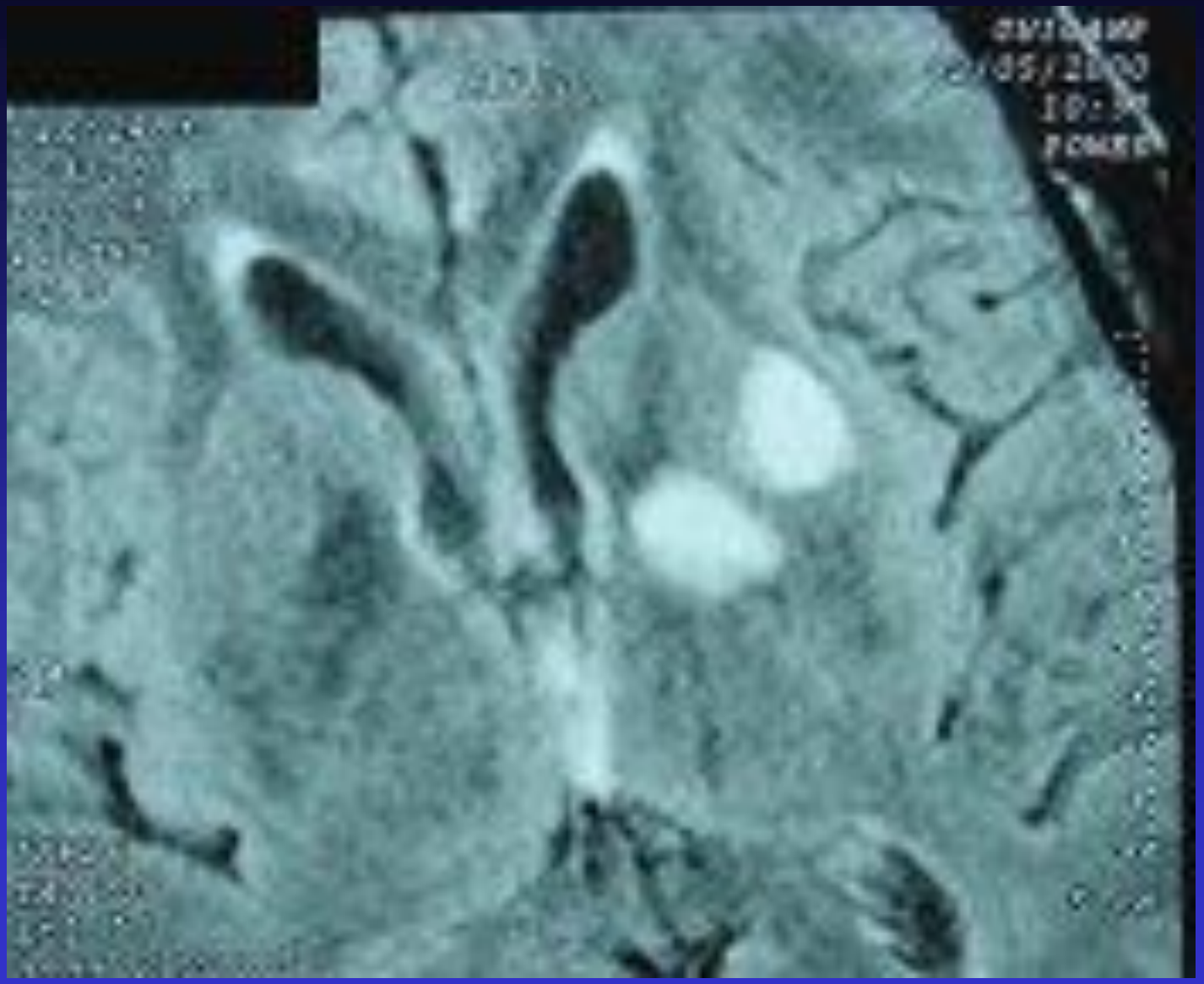
Fig 25

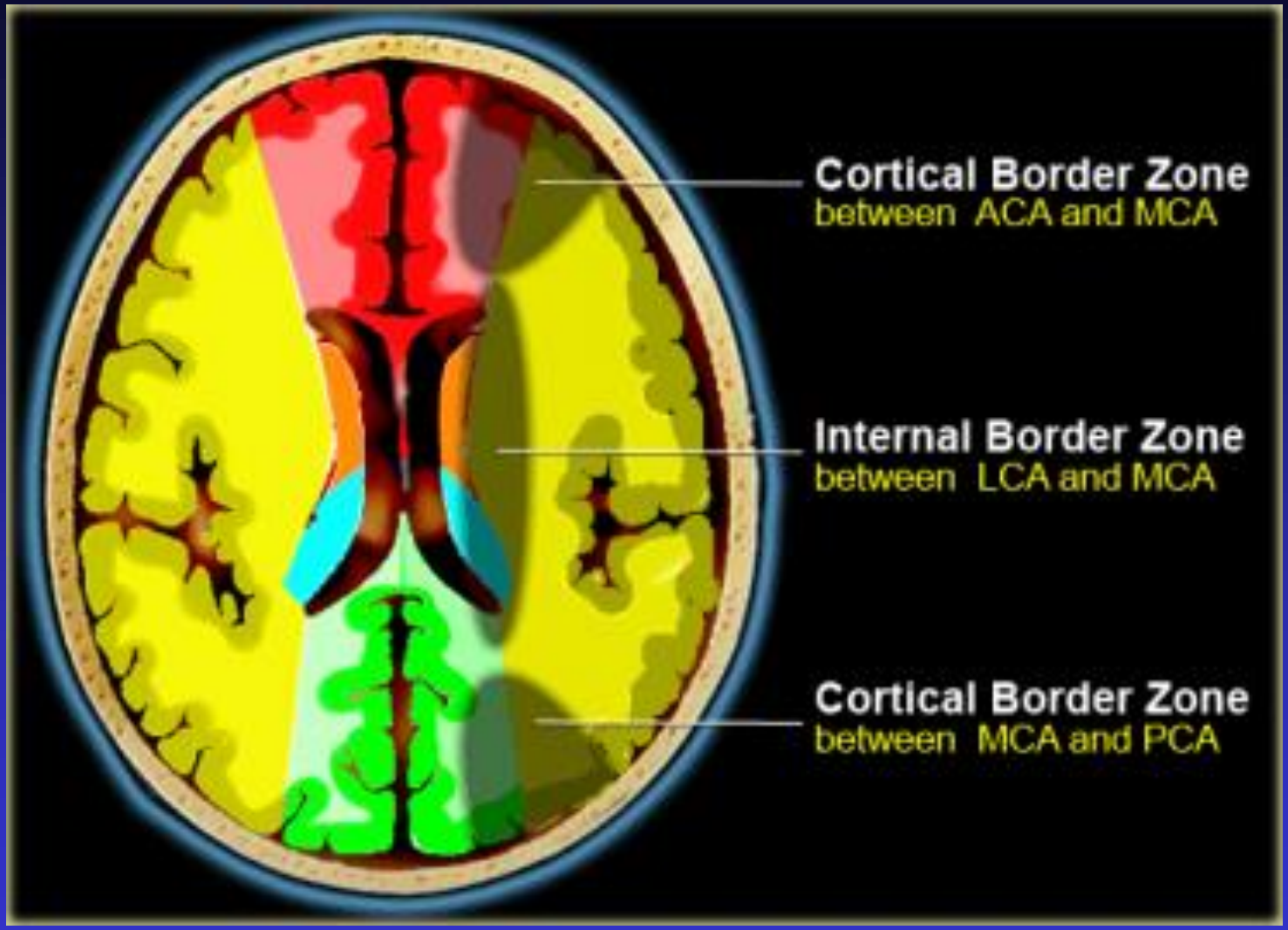
a

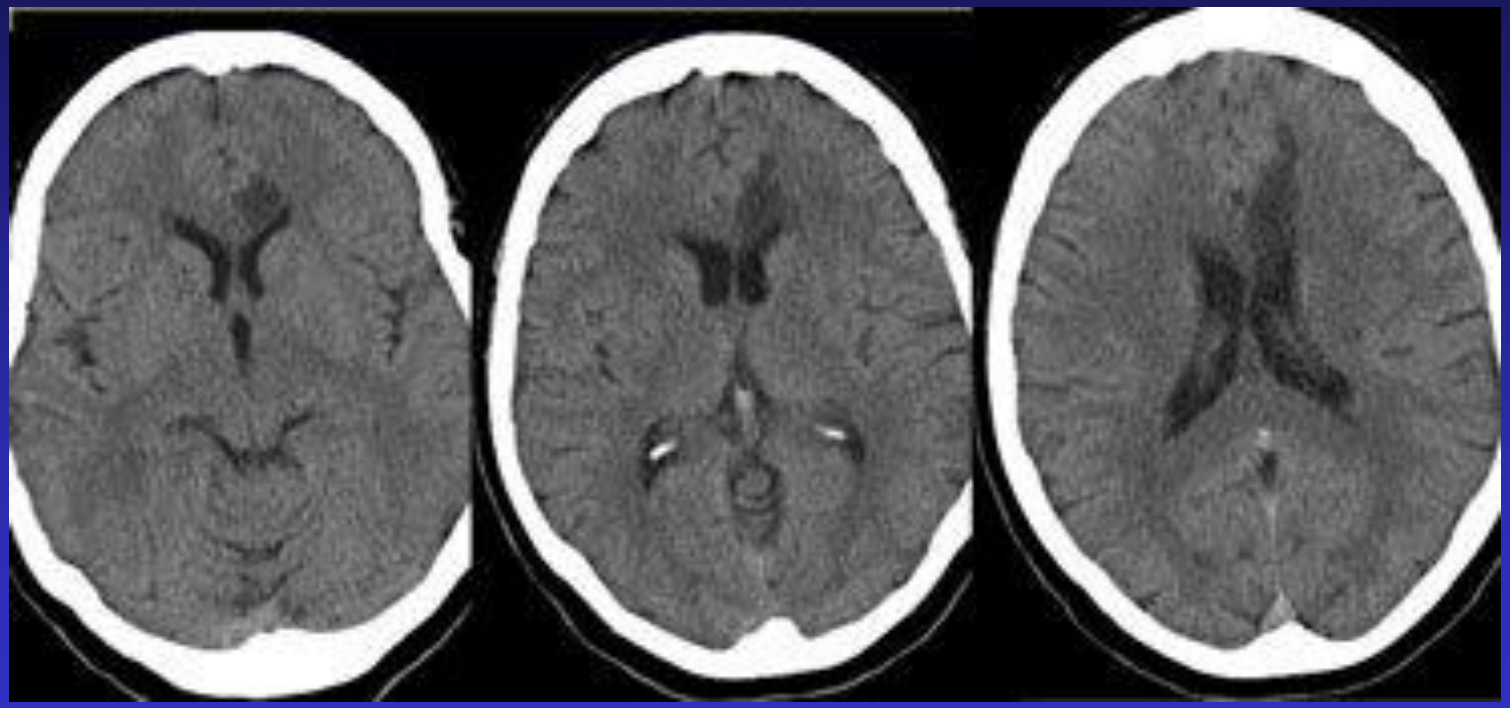
b

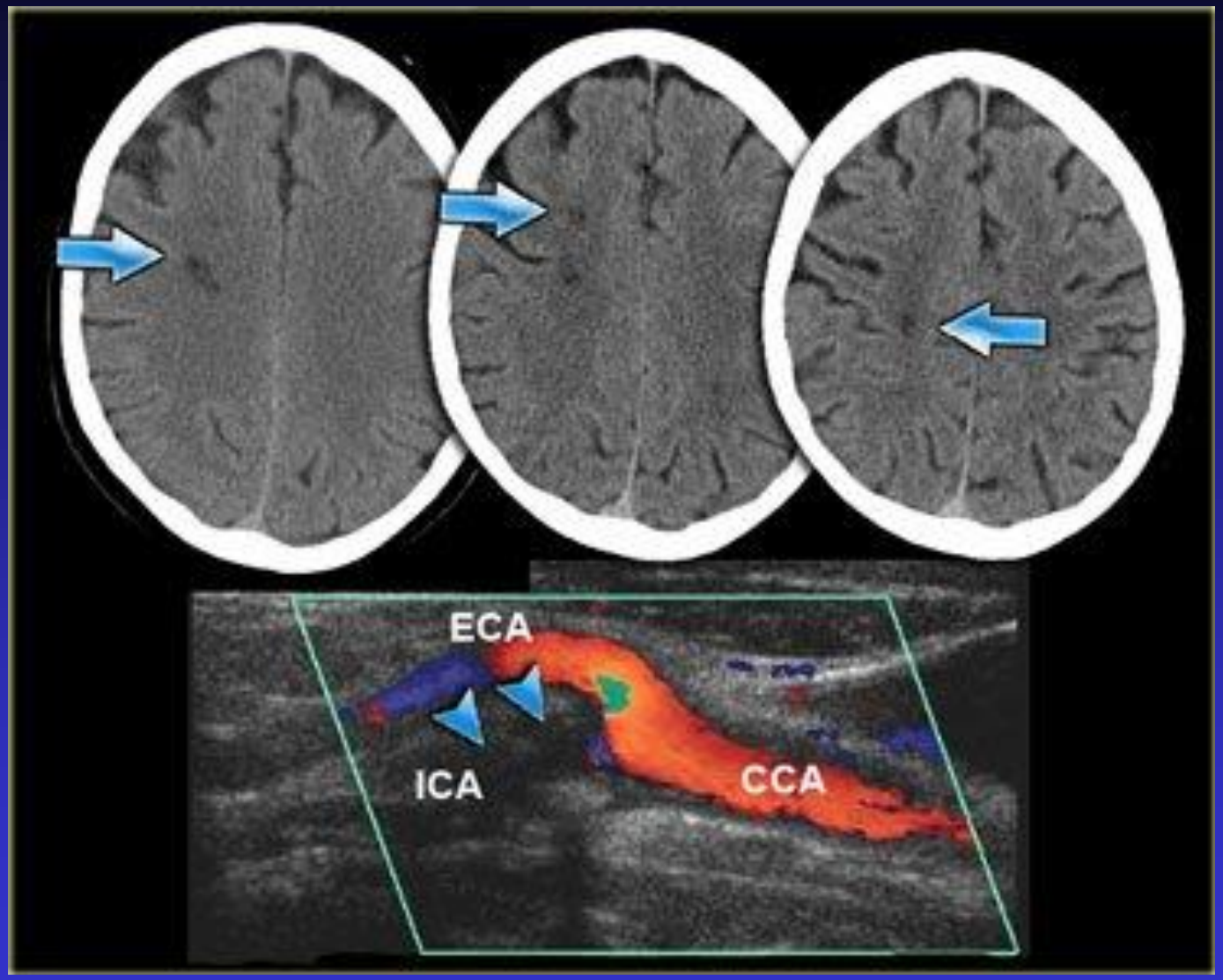

Putamen
Internal capsule
caudate nucleus
Globus Pallidus
Lenticulo-striate arteries
medial
lateral
Cortical M3-segment
Sylvian M2
A1
horizontal M1
RS


medial lenticulo-striate arteries
lateral lenticulo-striate arteries
Anterior Choroideal artery
Penetrating branches of posterior cerebral artery (P1-segment)

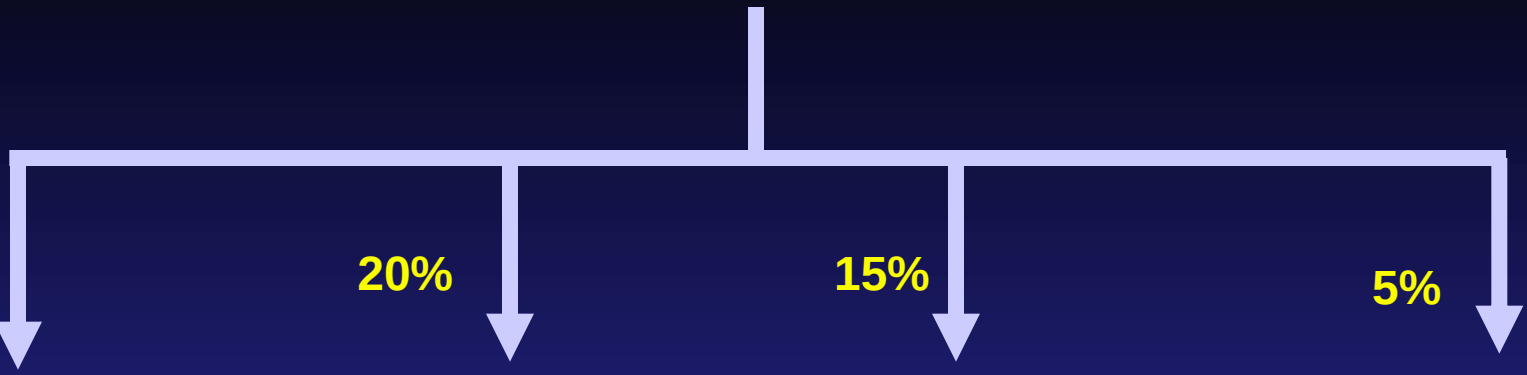



Cortical Border Zone
between ACA and MCA
Internal Border Zone
between LCA and MCA
Cortical Border Zone
between MCA and PCA




ECA
ICA
CCA

Ischemic Stroke



60%

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20%

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- Vasospasm
- Drug abuse
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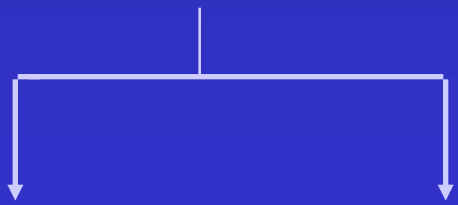
Intracranial Microatheroma

Large Artery Atheroma



Hypoperfusion

Arteriogenic Emboli

INQUADRAMENTO DIAGNOSTICO CLINICO

1. Anamnesi
2. Definizione dei sintomi
3. Diagnosi di sede
4. Sindromi cliniche
5. Diagnosi di causa
6. Identificazione dei fattori di rischio
7. Esame obiettivo generale

INQUADRAMENTO DIAGNOSTICO CLINICO

Obiettivi generali della raccolta anamnestica sono:

- definizioni delle caratteristiche temporali e topografiche dei sintomi
- inquadramento diagnostico differenziale
- identificazione dei fattori di rischio e patologie concomitanti
-Riconoscimento di cause insolite di ictus

INQUADRAMENTO DIAGNOSTICO CLINICO

Caratteristiche cliniche dell' ictus ischemico ed emorragico

Ictus ischemico:

* deterioramento a gradini o progressivo
* segni neurologici focali corrispondenti ad un territorio vascolare
* segni indicativi di una lesione focale corticale o sottocorticale

Ictus emorragico:

* precoce e prolungata perdita di coscienza
* cefalea importante
* rigidità nucale
* segni neurologici focali che non corrispondono ad un territorio vascolare

Can you tell which part of the brain is damaged?

- Clinical examination can help you do this
- Different types of stroke

Stroke Prognosis

	Death at 1 yr	
• Primary ICH	62 %	Worst
• TACI	60%	
• PACI	16%	
• LACI	11%	Least worst
• POCI	19%	

Stroke Classification (Bamford)

- Total Anterior Circulation Infarct (TACI)

  Combination of new higher cerebral dysfunction (eg, dysphasia); homonymous visual field defect; and ipsilateral motor and/or sensory deficit of at least two areas of face, arm and leg.

- Partial Anterior Circulation Infarct (PACI)

  Two of the three components of the TACI syndrome with higher cerebral dysfunction alone, or with a motor/ sensory deficit more restricted than those classified as LACI

Stroke Classification (Bamford)

- Posterior Circulation Infarct (POCI)

  Ipsilateral cranial nerve palsy with contralateral motor and/or sensory deficit;bilateral motor and/or sensory deficit; disorder of conjugate eye movement; cerebellar dysfunction without ipsilateral long tract deficits; or isolated homonymous visual field defect.

- Lacunar Infarct (LACI)

  Pure motor > 2/3 face, arm, leg Pure sensory > 2/3 face, arm, leg Pure sensorimotor > 2/3 face, arm, leg Ataxic hemiparesis, No higher dysphasia or visuospatial or hemianopia or vertebrobasilar problems

TACI	Presenza di tutti i seguenti: - Deficit di una funzione corticale superiore, ad es. afasia, discalculia, deficit visuo-spaziali - Deficit sensitivo/motorio controlaterale alla lesione - Emianopsia controlaterale alla lesione
PACI	Presenza di uno dei seguenti: - Presenza di due dei tre componenti necessari per la diagnosi di TACI - Deficit di una funzione corticale superiore isolato - Deficit sensitivo/motorio più ristretto di quello necessario per la diagnosi di LACI (ad es. deficit che interessa un solo arto, o faccia e mano, ma non tutto l'arto)
POCI	Presenza di almeno uno dei seguenti: - Paralisi di uno o più nervi cranici e deficit sensitivo/motorio controlaterale - Deficit sensitivo/motorio bilaterale - Deficit dei movimenti oculari coniugati - Emianopsia isolata - Deficit cerebellari
LACI	Presenza di uno dei seguenti: - Ictus motorio puro - Ictus sensitivo puro - Ictus sensitivo-motorio - Emiparesi atassica Due dei tre distretti (faccia, braccio e gamba) devono essere interessati, con coinvolgimento di tutto l'arto interessato. Assenza di segni corticali come definiti per TACI e PACI e di segni posteriori come definiti per POCI

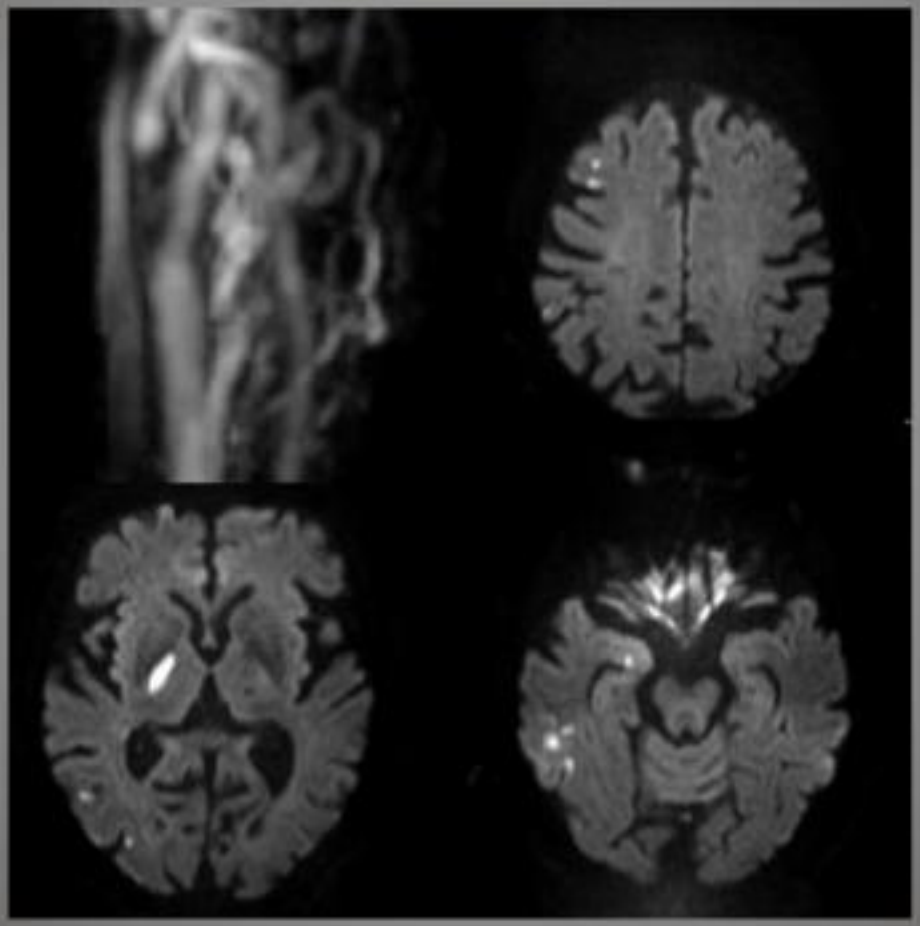
INQUADRAMENTO DIAGNOSTICO CLINICO

Diagnosi di causa

Criteri TOAST validi per i sottotipi di ictus ischemico

- Aterosclerosi dei vasi di grosso calibro
- Cardioembolia (possibile/probabile)
- Occlusione dei piccoli vasi
- Ictus da cause diverse
- Ictus da cause non determinate

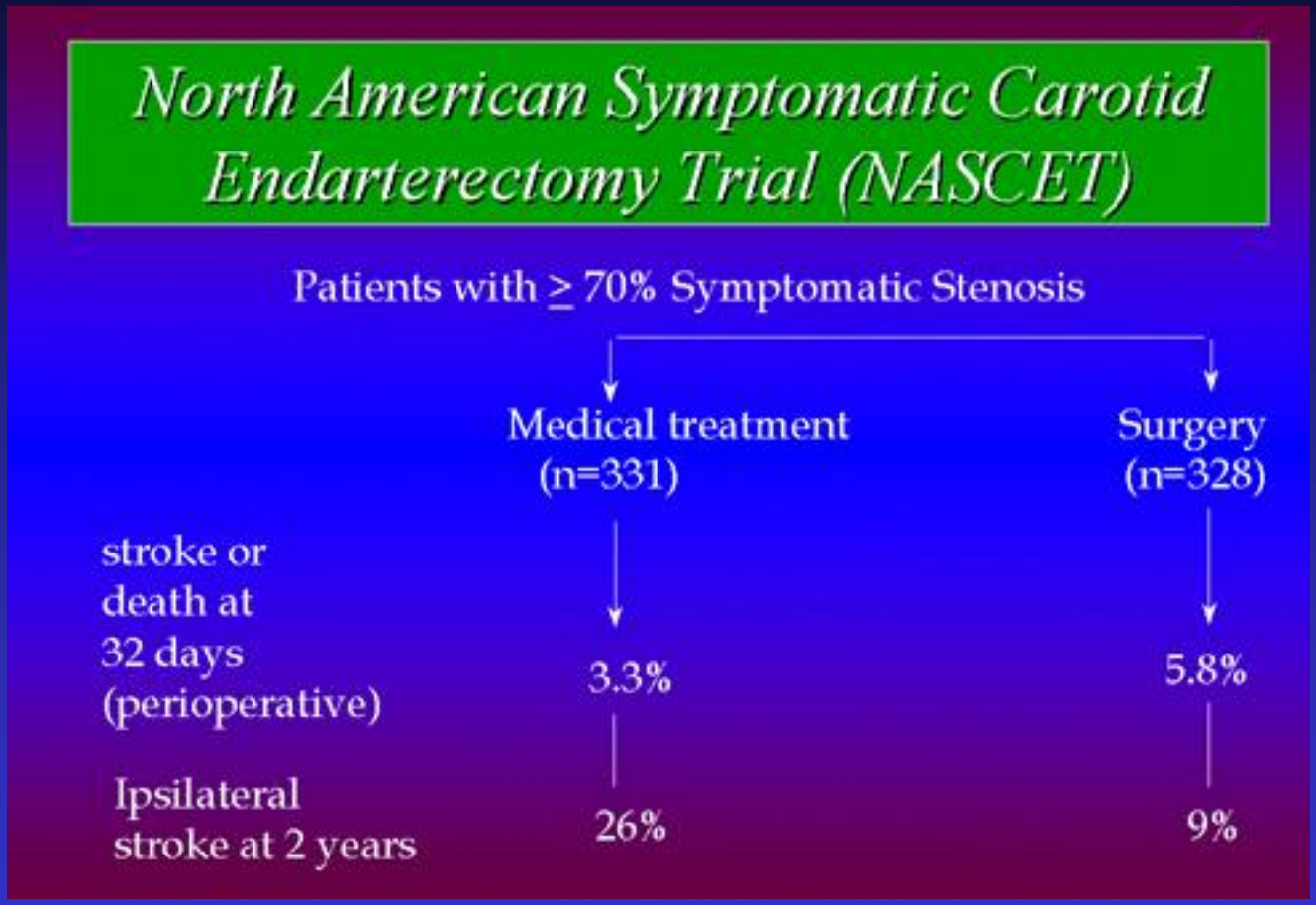
Embolies on stenosis

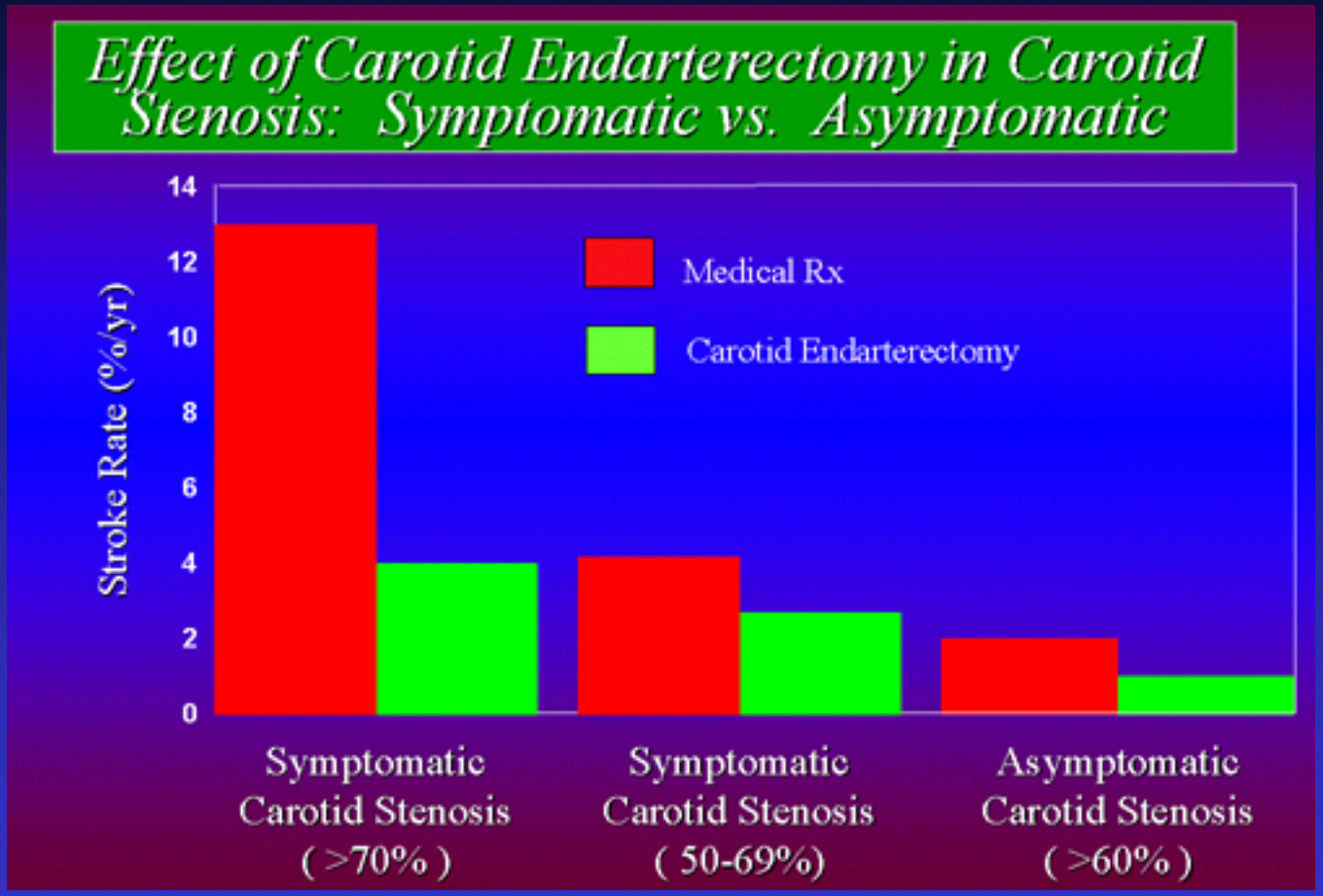


Baird AE, Lövblad KO, Schlaug G, Edelman RR, Warach S. Multiple acute stroke syndrome: marker of embolic disease? Neurology. 2000 Feb 8;54(3):674-8.

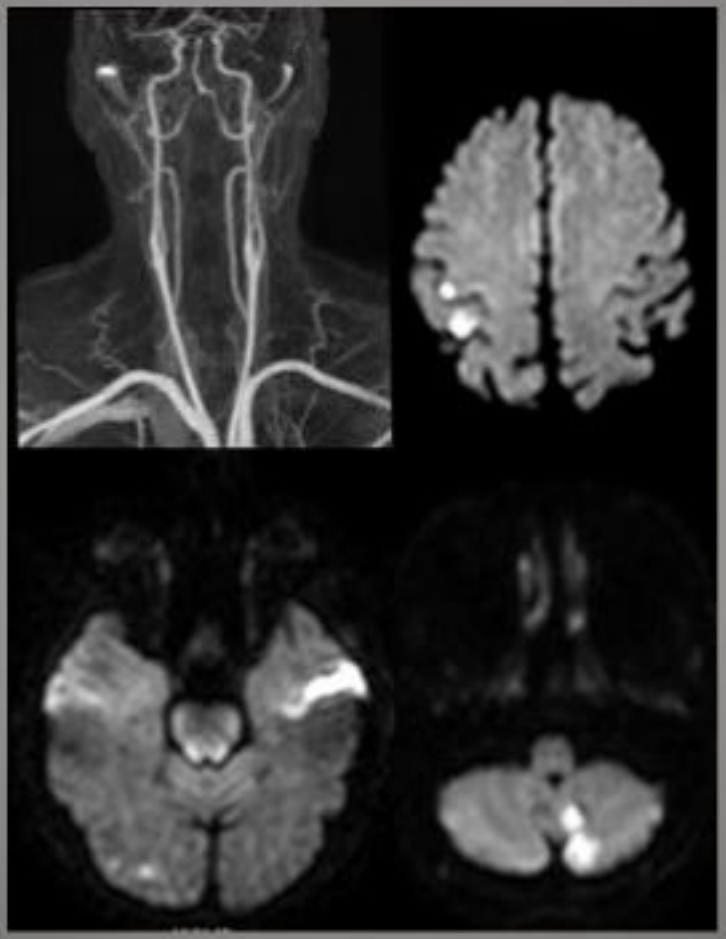

Critical Internal
Carotid Stenosis

North American Symptomatic Carotid Endarterectomy Trial (NASCET)



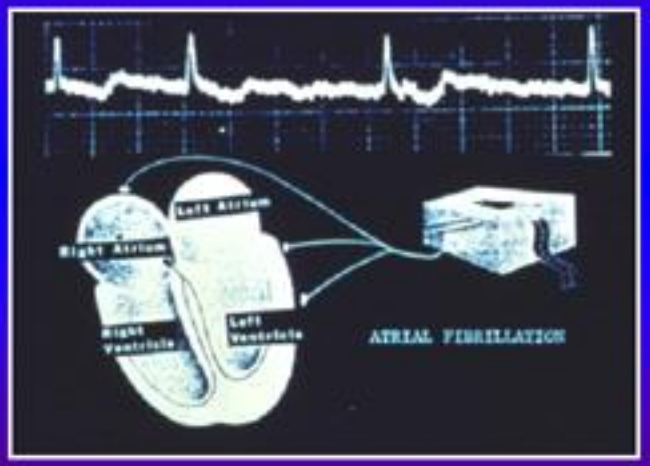

Effect of Carotid Endarterectomy in Carotid Stenosis: Symptomatic vs. Asymptomatic
Stroke Rate (%/yr)
14
12
10
8
6
4
2
0
Medical Rx
Carotid Endarterectomy
Symptomatic Carotid Stenosis (>70%)
Symptomatic Carotid Stenosis (50-69%)
Asymptomatic Carotid Stenosis (>60%)

Cardiac Emboli

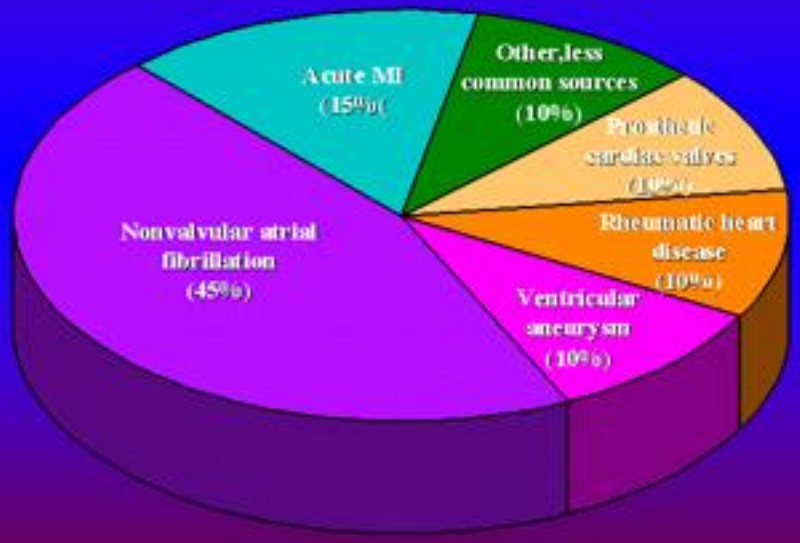


Baird AE, Lövblad KO, Schlaug G, Edelman RR, Warach S. Multiple acute stroke syndrome: marker of embolic disease? Neurology. 2000 Feb 8;54(3):674-8.

Atrial Fibrillation (AF) Predisposes to Stroke



c Embolism



Stroke Prevention in Atrial Fibrillation

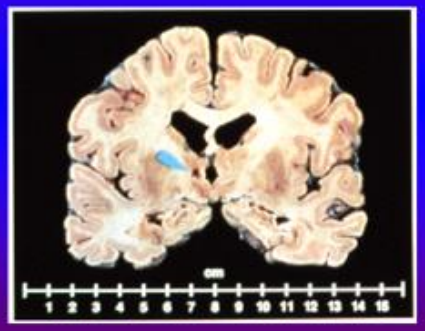
- Mean Onset Age 64, 2.2 Million People
- 35% Have Stroke During Lifetime
- 5% /Yr Stroke Rate
- 100,000 Strokes/Yr in U.S.

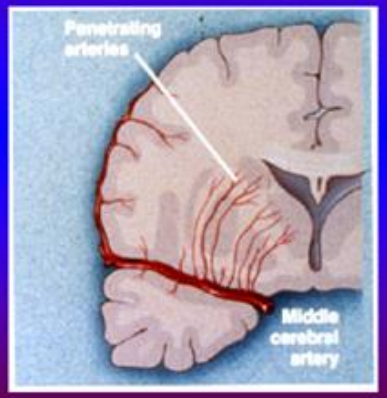
AF is a marker of 2 million Americans with a six-fold increased risk of stroke.

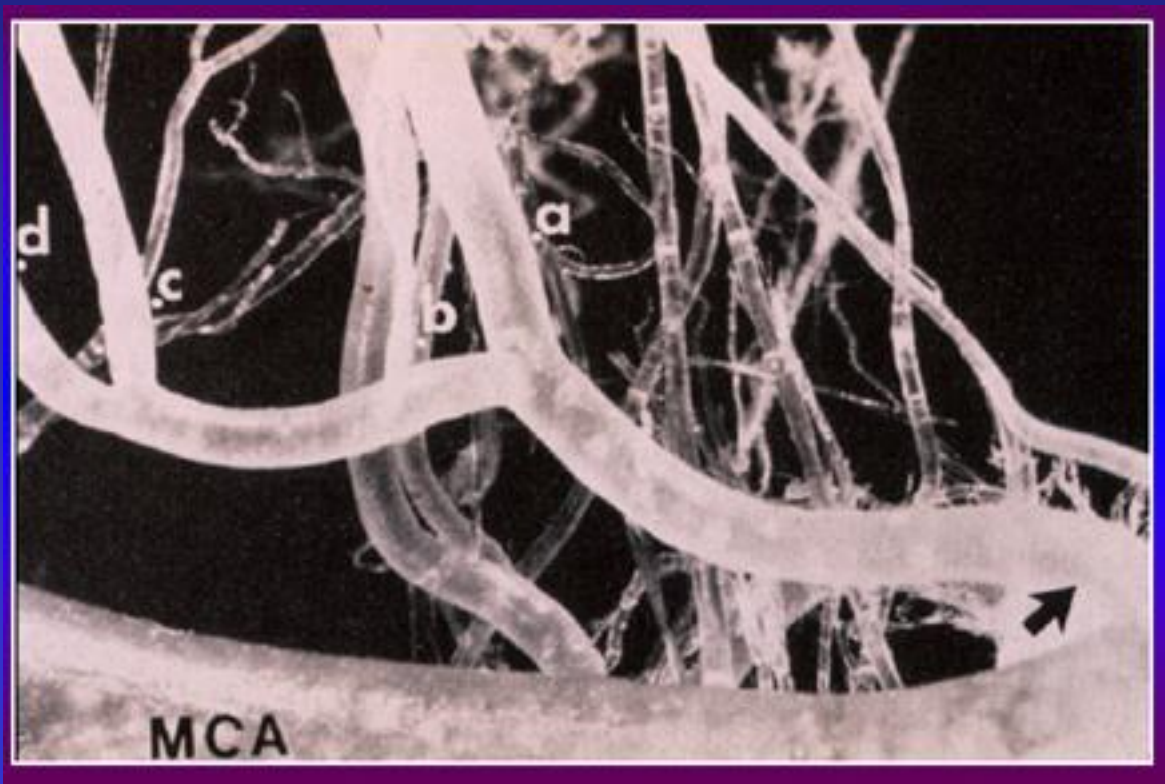
Antithrombotic Therapies for Stroke Prevention in Atrial Fibrillation: Meta-analysis of 16 Randomized Trials

	# Trials	# Participants	Relative Risk Reduction (95% CI)
Adjusted-dose warfarin vs. placebo	6	2900	62% (48,72)
Aspirin vs. placebo	6	3119	22% (2,38)
Adjusted-dose warfarin vs. aspirin	5	2837	36% (14,52)

Lacunar Stroke

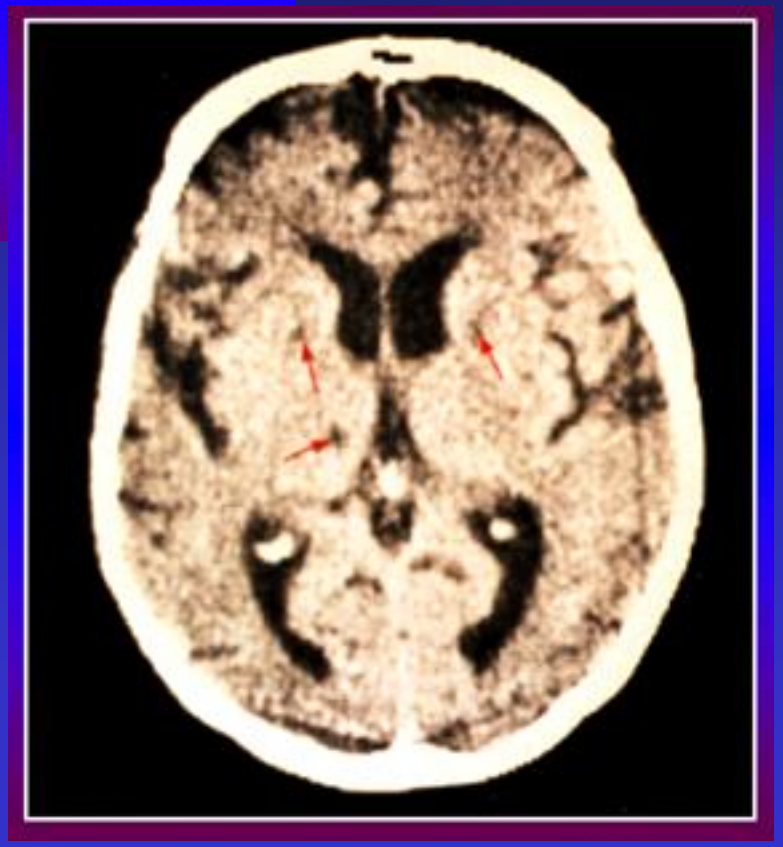






Lacunar Infarcts (Small Subcortical Strokes): Summary

- Diagnosis: Clinical syndrome (e.g., pure motor or pure sensory) plus CT/MRI confirmation
- Risk factor management: Hypertension, diabetes
- Carotid stenosis: Present in only 10%
- Rate of occurrence: High (10% yr)
- Antiplatelet agents probably effective



INQUADRAMENTO DIAGNOSTICO DI LABORATORIO

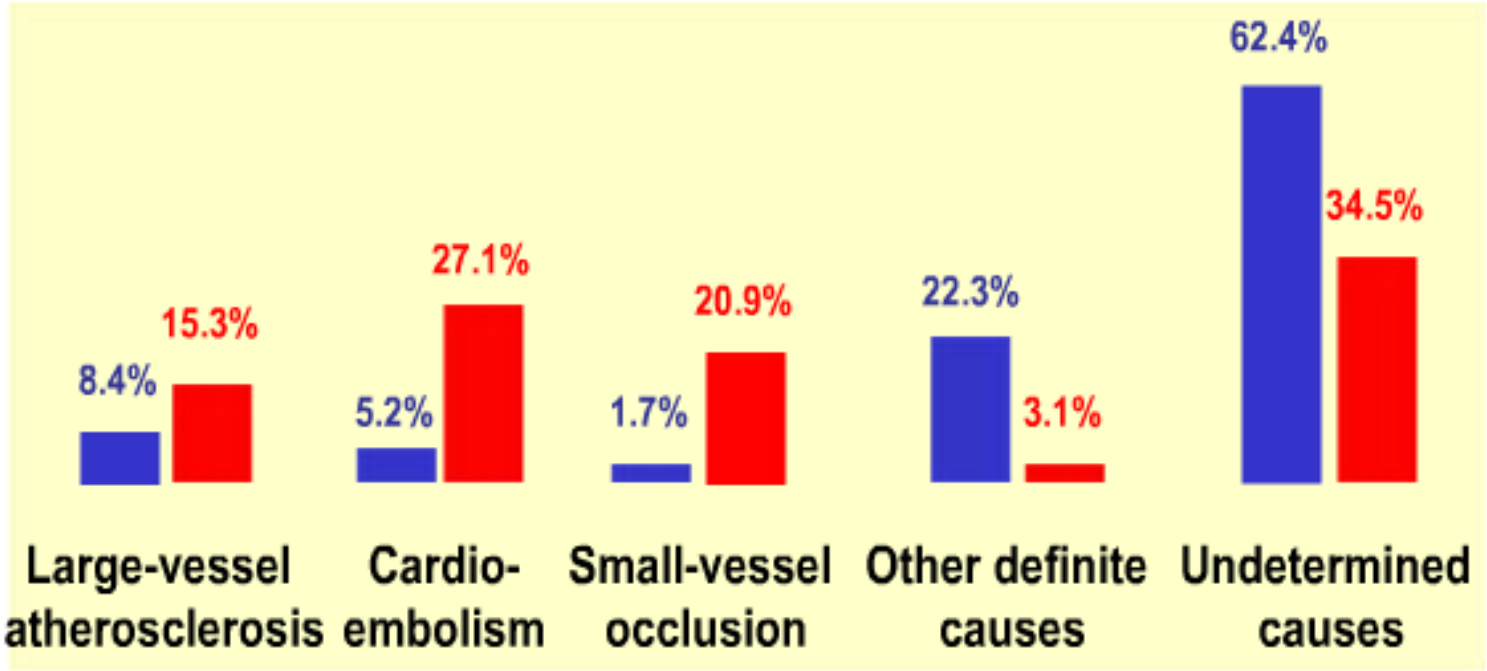
- Esami ematochimici di routine
- Coagulazione (INR, aPTT, PT, fibrinogeno)

Nell' ictus "giovanile"

* Ricerca di Autoanticorpi (aCLA, aB2glicoproteina…)
* Dosaggio Omocisteina
* Biologia molecolare dei fattori della coagulazione (Fattore V di Leiden, omozigosi MTHFR, alterazioni proteina C e S…)

Causes

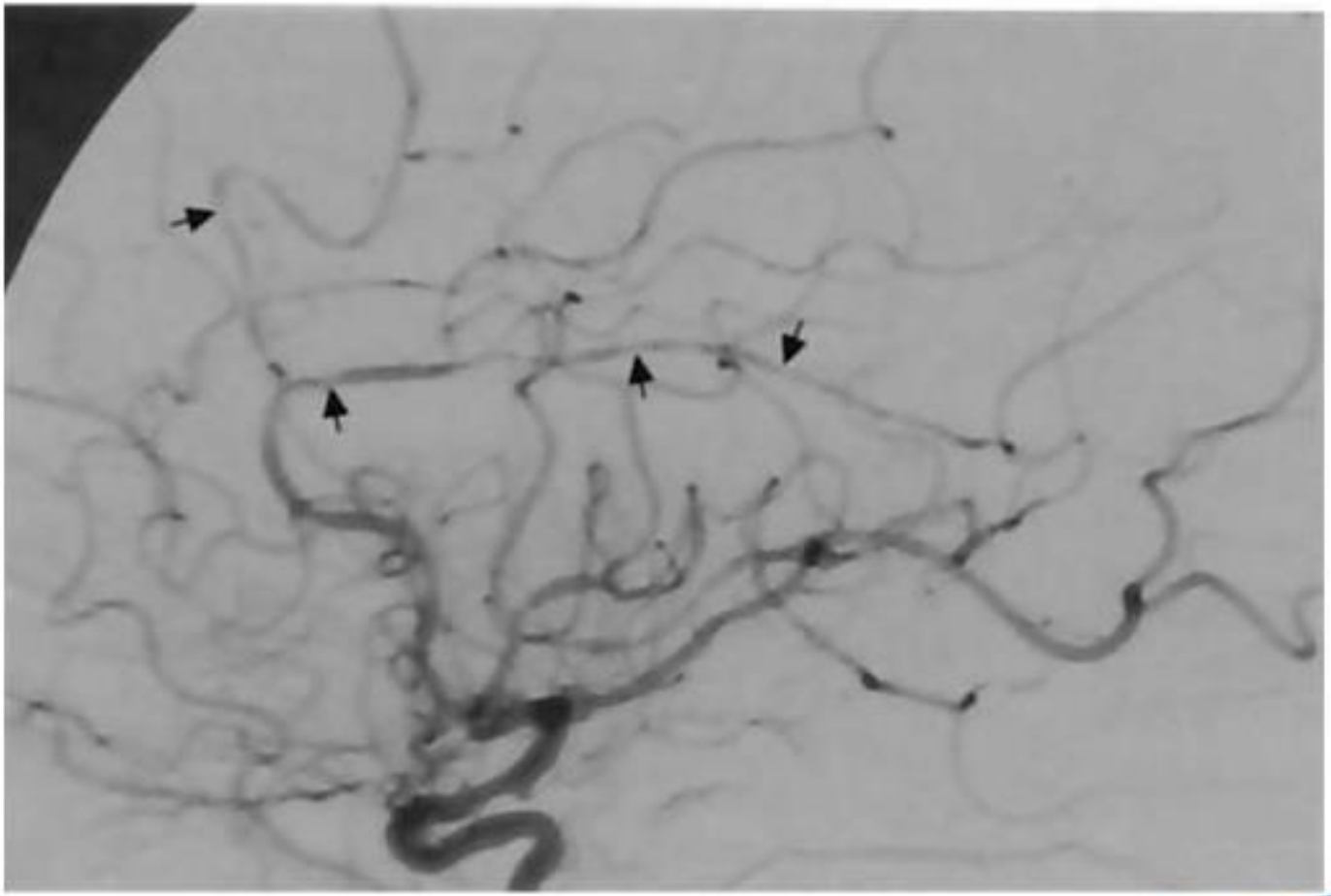
Comparison of the breakdown of causes by age-category



287 ischemic stroke patients aged 15-45 y (mean 36). (Leys et al, Neurology, 2002)

177 ischemic stroke patients aged > 40 y (mean 75). (Hénon et al, Neurology, 2001)

Other definite causes



Stroke evaluation
Important points in history

- Onset
  - Record time & rate of onset
- Risk factors
  - Previous stroke, TIA
  - Hypertension
  - PVD
  - Hyperlipidaemia
  - Smoking
  - Alcohol

Stroke evaluation
Important points on examination

- Pulse rate & rhythm
- Blood pressure
- Heart sounds
- Neck bruits
- Peripheral pulses
- Fundoscopy

Stroke evaluation
Neurological assessment

- Conscious level
- Eye movements
- Limb power
- Communication
- Trunk Control
- Gait
- Swallowing
- Mental Test Score
- Visuospatial function
- Visual fields
- Sensory testing

Stroke evaluation
Important points in investigation

- CT scan
- Plasma viscosity
- Glucose
- Lipids
- Haemoglobin
- White count
- Platelets
- ECG
- Echocardiogram
- NIVA neck scan
- Blood pressure
- Syphilis serology
- Auto-antibodies
- Clotting factors

INQUADRAMENTO DIAGNOSTICO RADIOLOGICO

TC cerebrale

La TC cerebrale è indicata in urgenza per:

* la diagnosi differenziale tra ictus ischemico ed emorragico ed altre patologie non cerebrovascolari

* l'identificazione di eventuali segni precoci di sofferenza ischemica encefalica (segno dell' iperdensità ACM, ipodensità precoce)

INQUADRAMENTO DIAGNOSTICO RADIOLOGICO

Risonanza magnetica

La RM convenzionale in urgenza non fornisce informazioni più accurate della TC.

Le tecniche di DWI e PWI in RM consentono un più accurato inquadramento patogentico e pronostico.

INQUADRAMENTO DIAGNOSTICO NEUROSONOLOGICO

Eco-color Doppler dei tronchi sopraortici (TSA)

Si tratta di una metodica semplice, non invasiva, a basso costo, abbastanza accurata capace di individuare una patologia stenosante od occlusiva dell'arteria carotide interna (ACI).
Può identificare anche un'eventuale dissecazione della carotide o dell'arteria vertebrale.
Tramite l'utilizzo del Doppler transcranico (TCD) si può valutare il circolo intracranico, l'eventuale stenosi e circoli di compenso.

Who Should Undergo Ultrasonography?

- Recommended: Patients with TIA or ischemic stroke who would be candidates for endarterectomy if high-grade, ipsilateral carotid stenosis was detected.
- Optional:
  - A) Brainstem ischemia
    - Assess for cerebrovascular athero, influencing lipid-lowering Rx.
    - Detect vertebral occlusion or subclavian steal.
    - Isolated occipital ischemia can be carotid.
  - B) Asymptomatic cervical bruit
    - Assess for plaque (lipid-lowering Rx) or stenosis ($\pm$ endarterectomy).
    - Serial monitoring for increasing stenosis (controversial).
  - C) Preoperative major vascular/CABG surgery (controversial).
    - Asymptomatic stenosis predicts perioperative stroke, but how to best prevent is unclear.

Who Should Undergo Echocardiography?

- Recommended:
  - A) Patients with TIA or ischemic stroke with clinical evidence (hx,exam, EKG, CXR) of heart disease.
  - B) Patients (esp. under age 60) with TIA or ischemic stroke of uncertain cause.

  If there is no clinical evidence of heart disease and a likely cause for stroke, echocardiography is not mandatory.
- Optional:
  - A) Patients with atrial fibrillation to help risk-stratify based on ventricular function (left atrial thrombi rarely detected).
  - B) Some recommend echo routinely for TIA/ischemic stroke to assess for coexistent ischemic heart disease.

Who Should Undergo Transesophageal Echocardiography (TEE)?

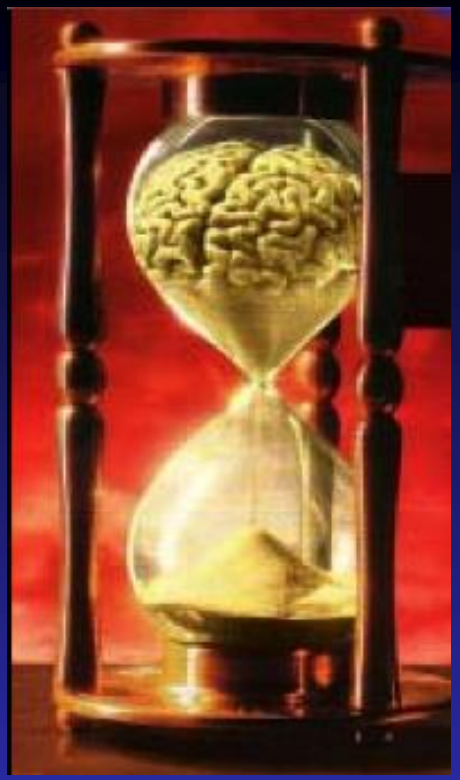
- Recommended:
  - A) Patients with ischemic stroke or TIA with suspected embologenic heart disease in whom precordial echo is poor quality.
  - B) Young (<60) patients with ischemic stroke or TIA of uncertain cause.
  - C) Patients of any age with multiple episodes of ischemic stroke or TIA of unclear cause, especially occurring on antiplatelet therapy.
- Optional:
  - A) Patients with atrial fibrillation to detect left atrial thrombi (unclear management implications).
  - B) Any patient with ischemic stroke or TIA of uncertain cause.
  - C) To detect aortic arch atheroma when diagnosis would change Rx.

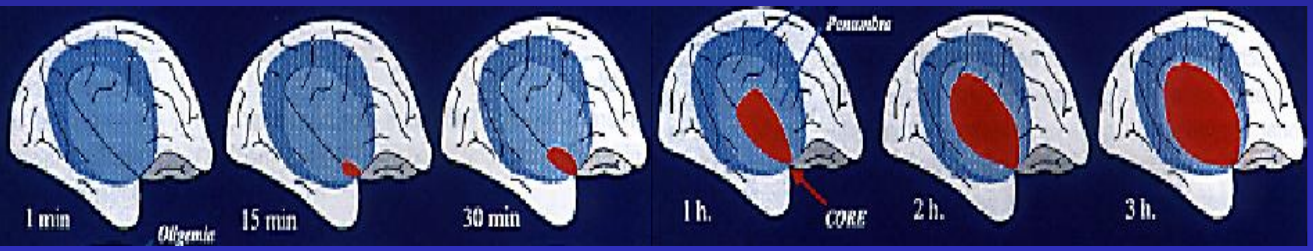
TERAPIA

Therapeutic Strategies in Acute Ischemic Stroke

- Reperfusion
  - << Recanalization
    - << thrombolysis
  - << Increase collaterals
    - << Supportive care
- Neuroprotection
  - << Supportive care
- Avert clot propagation
  - << Aspirin
- Prevent complications
  - << Supportive care

Time is brain



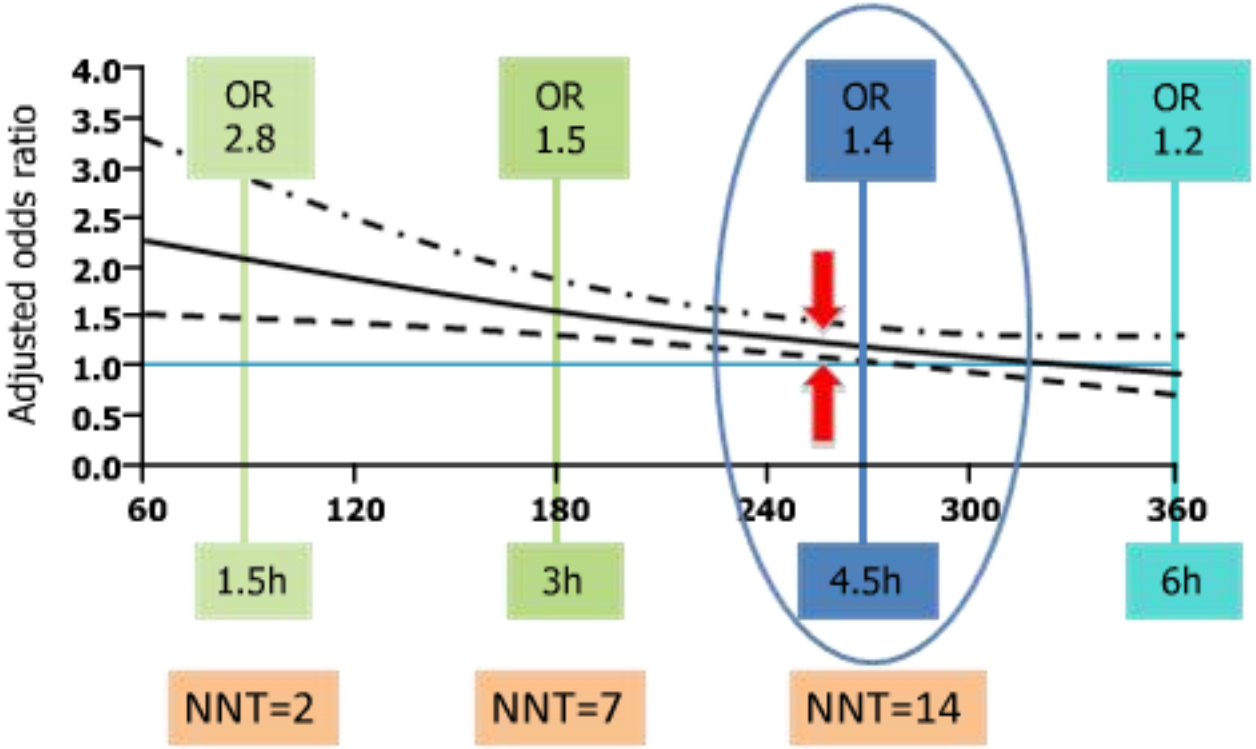


NNT=2

NNT=7

NNT=14

Early treatment remains essential



Hacke et al. Lancet 2004

Limiting or reversing ongoing acute ischemia (4.5-hour window)

intra-venous t-PA
0.9 mg/kg IV, 10% IVP, the remainder infused over 1 hour
6% risk of significant bleeding
experienced clinicians

intra-arterial thrombolysis
large vessel occlusions
within 3 to 6 hours of onset
t-PA (5 to 25 mg IA)
urokinase (250,000 to 1,000,000 units IA)
local clot extraction (Merci® device)

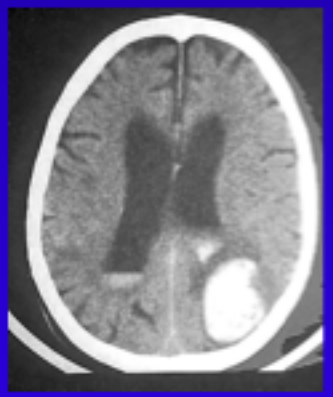
Major Treatment Guidelines for Using t-PA in Stroke Patients

a) Monitor neurological status >

infusion: every 15'
first 6h: every 30'
up to 16h: every 60'

If headache, hypertension, nausea or vomiting >CT scan

If HT > check coagulation + neurosurgeon



b) Monitor BP >

0-2h: every 15'
2-6h: every 30'
6-16h: every 60'

1.	DBP > 140 mmHg	nitroglycerine/ s.nitroprusside
2.	SBP > 220 or DBP 121-140 mmHg	labetalol/urapidil/clonidine
3.	SBP 180-220 or DBP 105-120	labetalol

c) No antiplatelets or anticoagulants for 24 hrs

Major Treatment Guidelines for Using t-PA in Stroke Patients

Inclusion Criteria

- Ischemic stroke in any circulation
- Ability to unambiguously establish the time of onset
- Ability to begin t-PA therapy within 4.5 hours of symptom onset
- Head CT scan without any evidence of hemorrhage or other complicating diseases
- Age 18-80

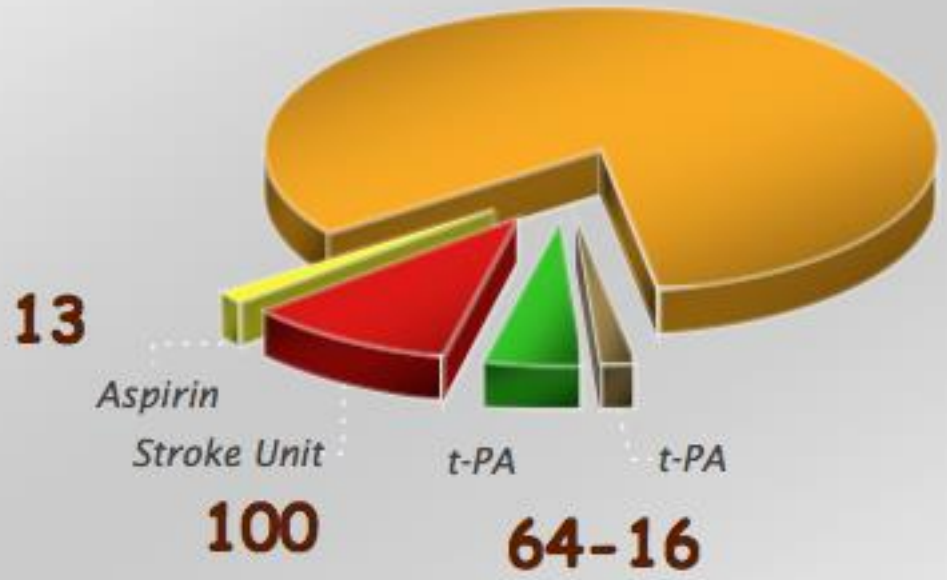
Major Treatment Guidelines for Using t-PA in Stroke Patients

Exclusion Criteria

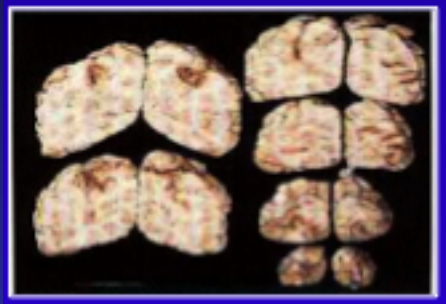
- Rapidly improving or minor symptoms
- Coma or stupor; Seizure at the onset.
- Major surgery or invasive procedure within the past 2 weeks
- GI or genitourinary hemorrhage within the past 3 weeks
- Noncompressible arterial puncture or biopsy within the past week
- Glucose <50 mg/dl or > 400 mg/dl; Known bleeding diathesis
- Pretreatment SBP > 185 or DBP > 110, despite simple measures
- Evidence of active pericarditis, endocarditis, septic emboli, recent pregnancy, lactation, or inflammatory bowel disease
- Active alcohol or drug abuse

Impact of Established Acute Ischemic Stroke Treatments

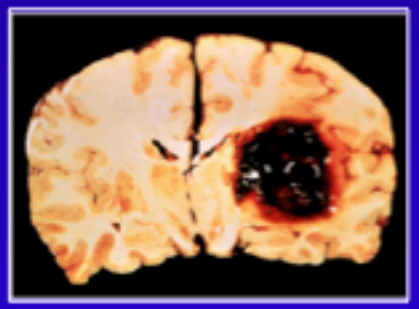
Benefit every 1000 patients treated



Stroke Units have a positive effect on all stroke patients



irrespective of
stroke type
(ischemic or hemorrhagic)



and
admission time
to the hospital!

<4.5h → t-PA

>4.5h ✗ t-PA

Most frequent neurological & medical complications

Neurological

- ✓Stroke progression
- ✓Brain Edema
- ✓Recurrences
- ✓Depression
- ✓Delirium

Medical

- ✓Dehydration
- ✓Respiratory infection
- ✓Urinary tract infection
- ✓Gastrointestinal bleeding
- ✓Deep vein thrombosis

- ✓Hypertension/Hypotension
- ✓Cardiac complications
- ✓Hyperglycemia
- ✓Fever
- ✓Hypoxia

CRITERIO " TEMPO "

il TIA

lo STROKE

Transient Ischemic Attack (TIA)

- "Warning strokes:" transient focal ischemia
- Duration: <24 hrs (usually 5 to 10 minutes)
- May occur with any cause of ischemic stroke
- TIA patients have 10 times the risk of ischemic stroke:
  - Risk highest in first 3 months after TIA
  - 35% stroke risk with 3-5 years after TIA
- An opportunity to prevent stroke

Definition and Evaluation of TIA

A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease

10-15% of patients have a stroke within 3 months, with half occurring within 48 hours.

Acute treatments for TIA also have evolved, with new data supporting early rather than delayed carotid endarterectomy for TIA patients with carotid stenosis.

Easton, 2009

Common Manifestations of TIA

Carotid system TIA

- Unilateral weakness
- Unilateral sensory symptoms
- Aphasia
- Monocular vision loss

Vertebrobasilar system TIA

- Bilateral weakness
- Bilateral sensory symptoms

- Diplopia
- Vertigo
- Ataxia without weakness
- Dysphagia

only in combination; not as isolated symptoms

Definition and Evaluation of TIA

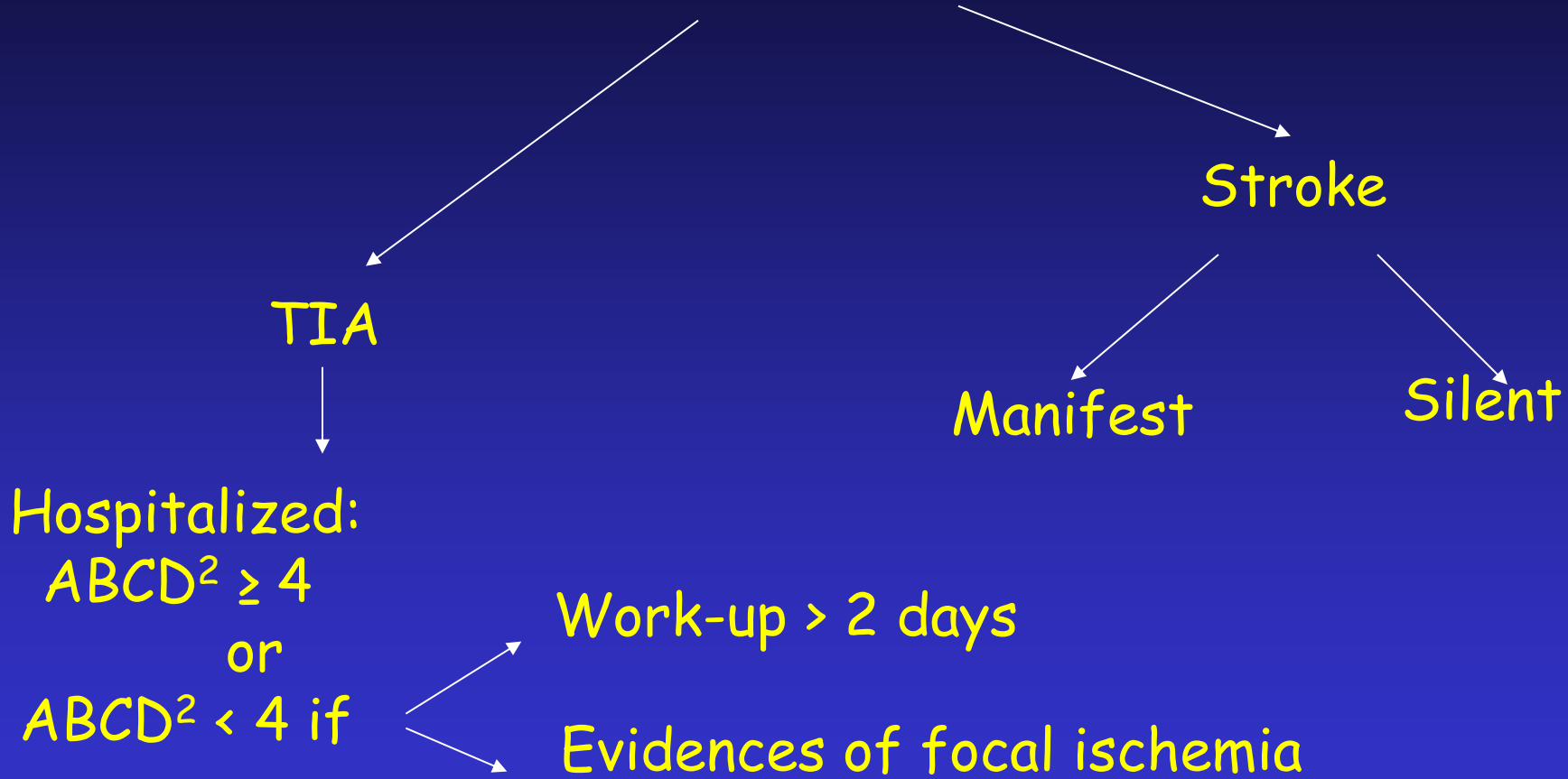
A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease

Table 3. Frequency of DWI Abnormality in Patients With Transient Neurological Episodes of Different Durations: Pooled Data From 10 MRI Studies Enrolling 818 Patients[45]

Duration of Symptoms, h	DWI Hyperintensity
0–1	33.6
1–2	29.5
2–3	39.5
3–6	30.0
6–12	51.1
12–18	50.0
18–24	49.5

Easton, 2009

Acute neurovascular syndrome



(American Stroke Association - May, 2009)

Acute neurovascular syndrome

TIA

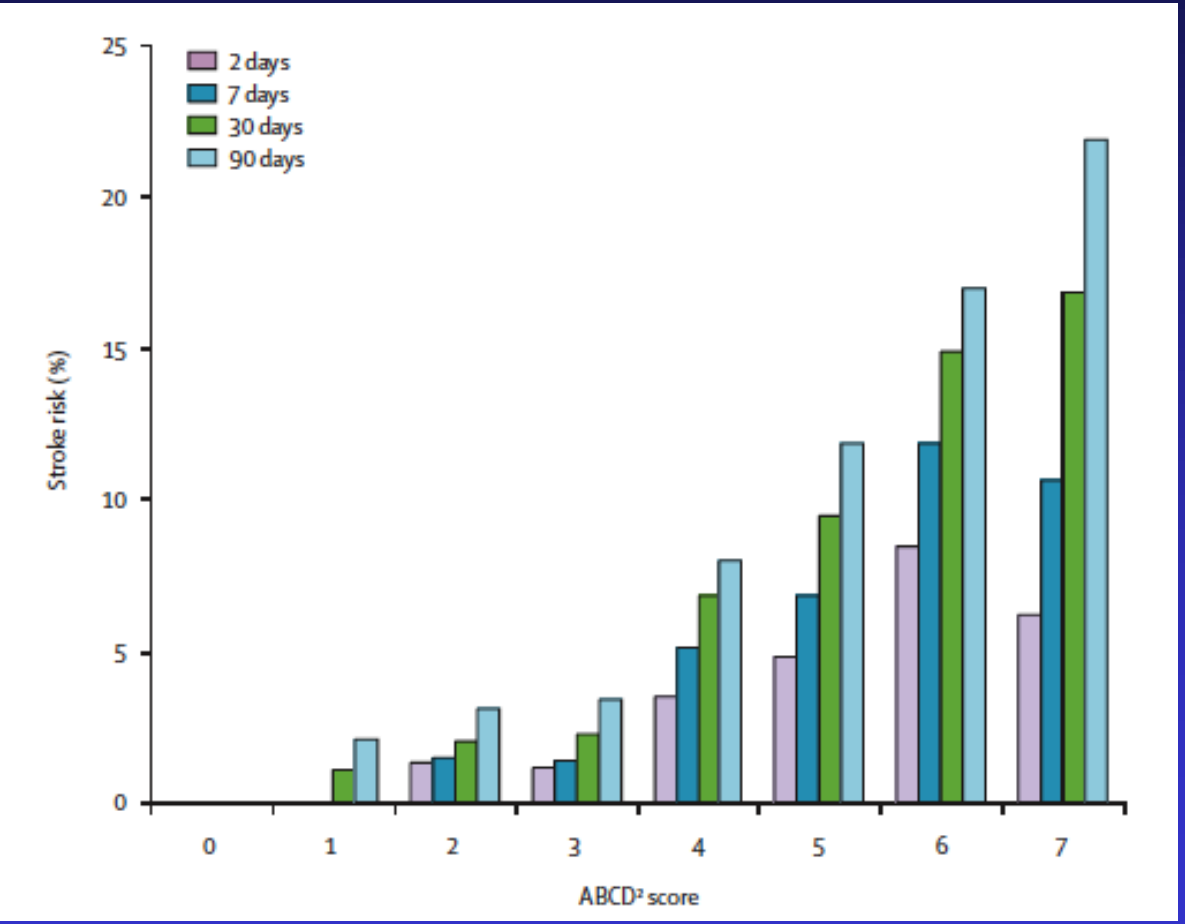
Hospitalized:
$ABCD^2 \geq 4$
or
$ABCD^2 < 4$ if

- Work-up > 2 days
- Evidences of focal ischemia

Age ≥ 60?	☐ Yes +1
BP ≥ 140/90 mmHg at initial evaluation?	☐ Yes +1
Clinical Features of the TIA:	○ Unilateral Weakness +2 ○ Speech Disturbance without Weakness +1
Duration of Symptoms?	○ 10-59 minutes +1 ○ ≥ 60 minutes +2
Diabetes Mellitus in Patient's History?	☐ Yes +1

(American Stroke Association - May, 2009)

Validation and refinement of scores to predict very early stroke risk after TIA



Claiborne, 2007

Does ABCD2 Score Below 4 Allow More Time to Evaluate Patients With a Transient Ischemic Attack?

1176 patients with definite or possible TIA or minor stroke

24.7% (n291)

criteria for emergency treatment: presence of symptomatic internal carotid stenosis 50%, symptomatic intracranialstenosis 50%, or a major cardiac source of embolism.

ABCD2 ≥ 4 (31.6%, n157) ABCD2 <4 (19.7%, n134)

ABCD2 score

Sensitivity 54.0% (95% CI, 48.2 to 59.7)

Specificity 61.6% (95% CI, 58.4 to 64.8)

Amarenco, 2009

Does ABCD2 Score Below 4 Allow More Time to Evaluate Patients With a Transient Ischemic Attack?

In conclusion, no patients with ipsilateral symptomatic carotid stenosis 50% or with atrial fibrillation should be missed or overlooked regardless of ABCD2 score.

Based on our data, when triaging patients based on ABCD2 score above or below 4, clinicians should perform immediate (within 24 hours) carotid ultrasound examination (or default angiographic CT scan) and an electrocardiogram in patients with a TIA before deciding to postpone the workup beyond the 24-hour window.

Amarenco, 2009

*Evaluation of TIA and Ischemic Stroke**

Step I:
- CBC, platelet count, PT, PTT, RPR
- Chemistry profile (glucose, cholesterol)
- ECG
- CT Scan

Step II:
- Carotid ultrasound
- Echocardiography
- Rhythm (Holter) monitoring if suspicious symptoms

Step III:
- Arteriography or MR angiography
- Magnetic resonance imaging
- Special coagulation testing
- Transesophageal echocardiography

* for patients > 50 years old

Major Risk Factors for Cerebrovascular Atherosclerosis

FACTOR	INCREASED RISK
◆ Hypertension	X 5-10
◆ Smoking	X 2
◆ Diabetes	X 2
◆ Hyperlipidemia	X 1.5
◆ Obesity	X 1.5

TIA
a basso rischio
ad alto rischio

Predicted effect of treatment

Based on RCTs of long-term treatment

Most patients	Relative Risk Reduction
Aspirin	20%
Statin	20%
Blood pressure lowering	30%
Some patients	
Warfarin	50%
CEA within 2 weeks	75%
(Aspirin + Clopidogrel	?)
Total	>80%

Hackam DG, Spence JD. Stroke 2007.

Yusuf S. Lancet 2002; 360:2-3.

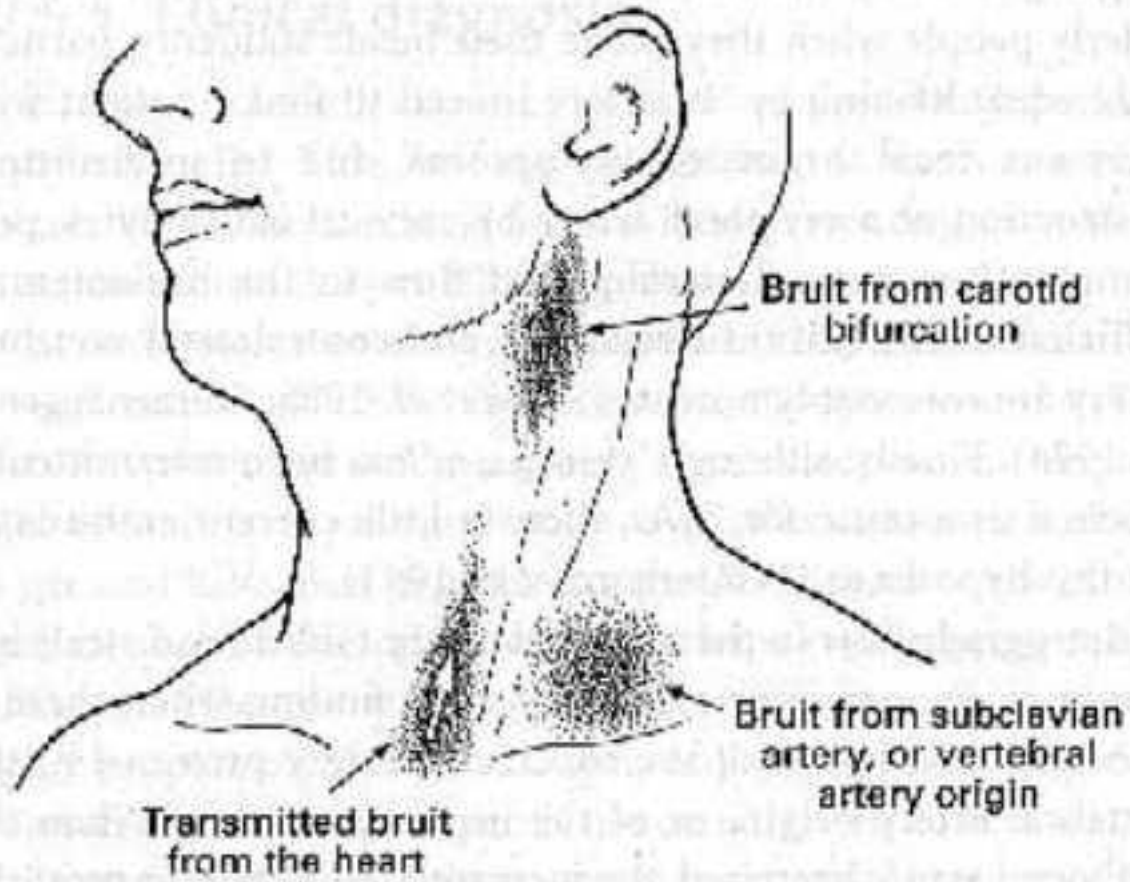


Fig. 27.23. The localization and implications of cervical bruits in various places. Note that a bruit arising from the carotid bifurcation is high up under the angle of the jaw and that supraclavicular bruits can be due to either subclavian or vertebral artery origin stenosis.

TIA: quod agendum?

If I developed right arm weakness and speech disturbance lasting thirty minutes…….
……what would I do?

- Take an aspirin and a statin
- Immediately phone two friends
  - A vascular neurologist
  - Someone to stay by me the next 48 hr
- Ask the second friend to drive me to hospital
- Request carotid and brain imaging
  - Immediately if working hours
  - Next morning if out of hours
- Confirmation of diagnosis and treatment plan
- If I lived near the hospital I would go home as soon as possible. I would make sure the second friend knew what to do if I developed further symptoms
- If I lived far away or I did not have a second friend… ☹…. I would ask to be admitted to the Acute Stroke Unit for 24-48 hours

Acute Neurovascular Syndrome is an emergency

Main causal risk factors for recurrent stroke & other major vascular events

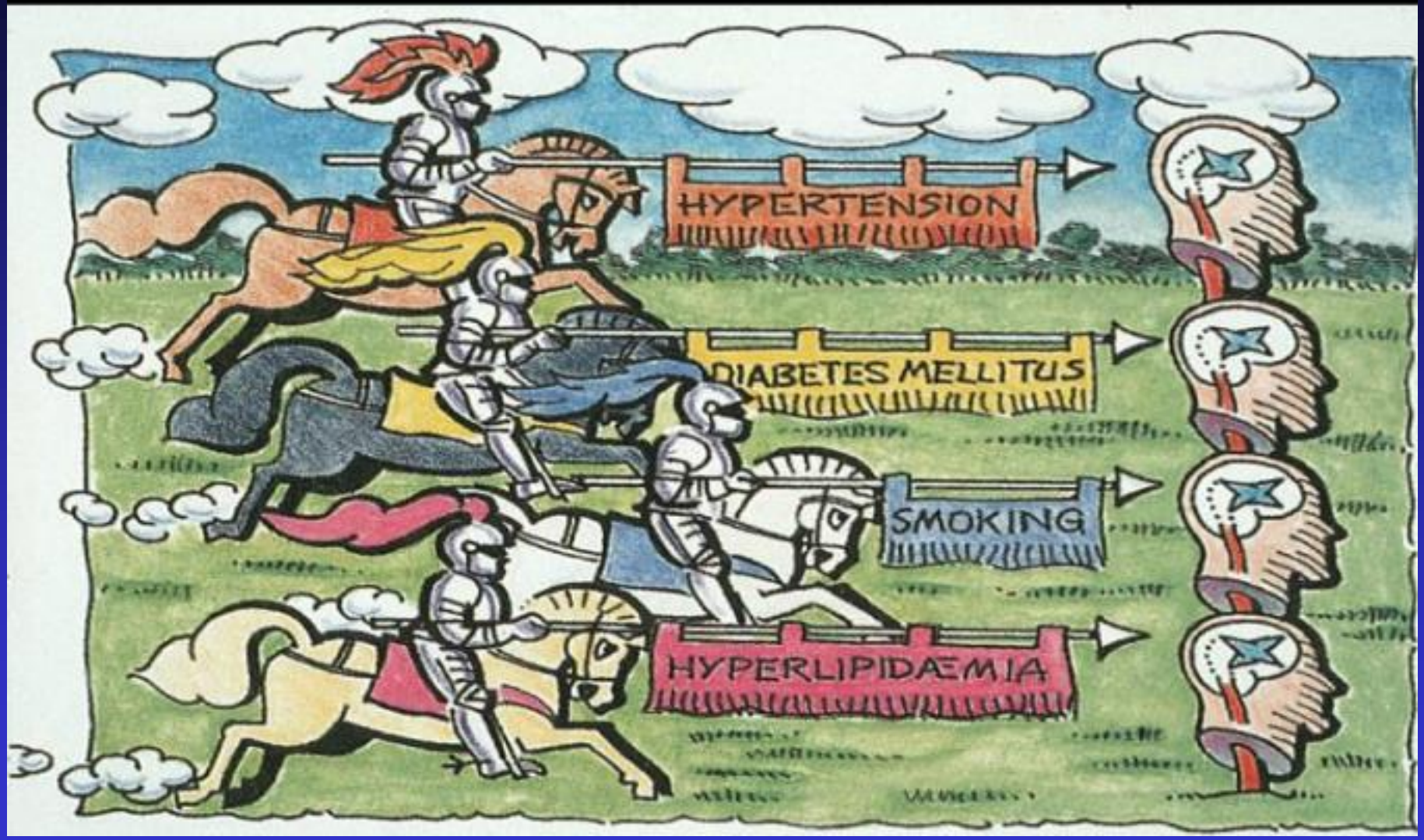
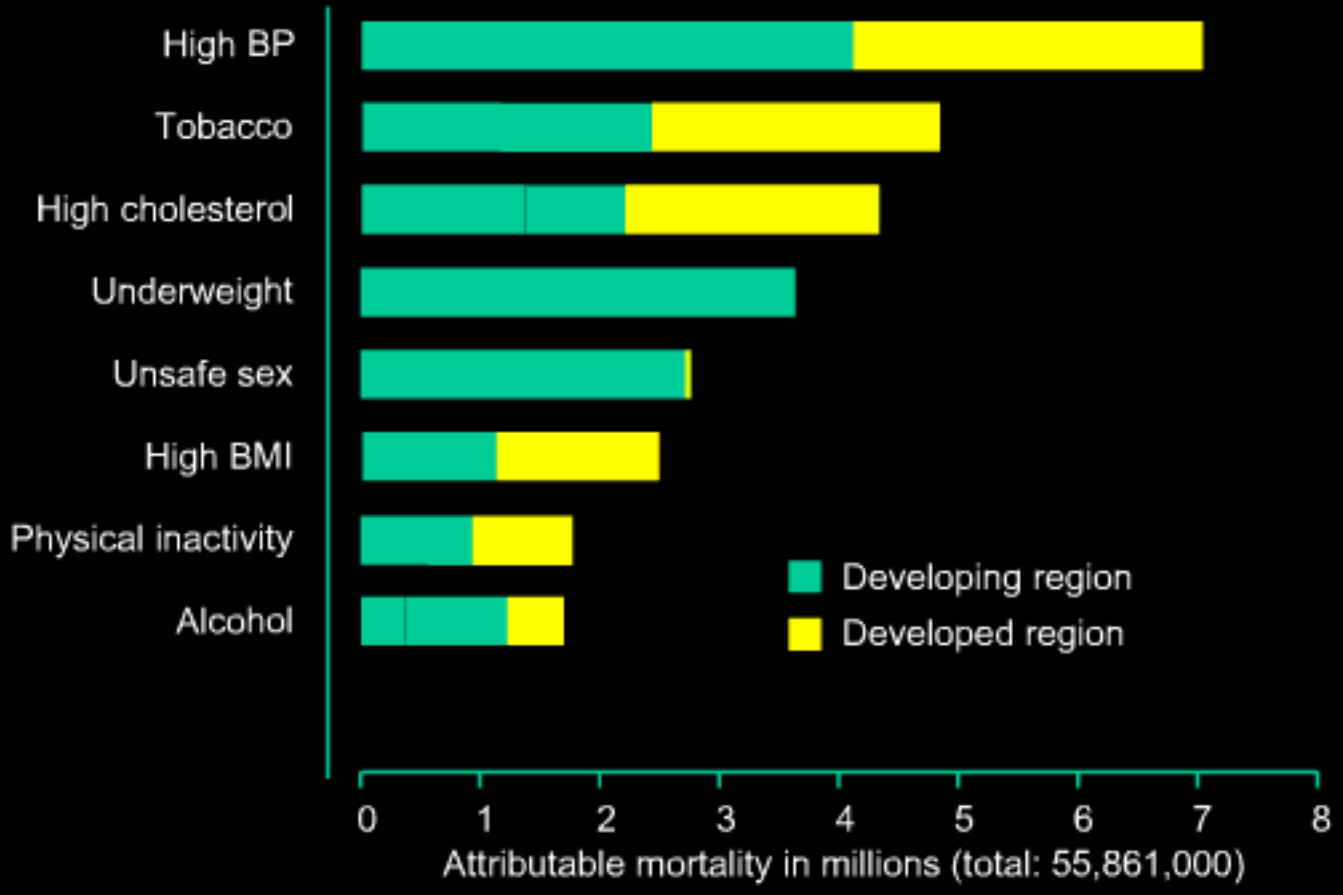


Table 1.3 Approximate relative risks associated with well recognized risk factors for stroke[a]

Risk factor	Relative risk for stroke
Age (55–64 versus >75 years)	5
Blood pressure: 160/95 versus 120/80 mmHg	7
Smoking (current status)	2
Diabetes mellitus	2
United Kingdom social class (I versus V)	1.6
Ischaemic heart disease	3
Heart failure	5
Atrial fibrillation	5
Past TIA	5
Physical activity (little or none versus some)	2.5
Oral contraceptives	3

[a] The estimates of relative risk given are representative figures derived from a number different studies of each risk factor.

Global Mortality 2001:
Impact of Hypertension, Smoking, Cholesterol and Diabetes



Lopez et al. Lancet 2006;367:1747-57

Summary

- The risk of recurrent stroke and other major vascular events can be reduced effectively by:
  - Sustained blood pressure lowering
    - 10mmHg systolic reduction → 34% RRR
  - Sustained blood cholesterol lowering
    - 1 mmol/l (39 mg/dL) LDL-C reduction → 20% RRR

  and *possibly* also reduced by:
  - Optimal control of blood glucose among diabetics
    - 0.9% HbA_{1C} reduction → RRR: 7% (-6% to 19%)
  - Smoking cessation
  - ↑ physical activity (≥ 30 min/day) & ↓ body weight (BMI < 25 kg/m^2)
  - ↓ Alcohol and salt, ↑ dietary fruit and vegetables, and ? folic acid