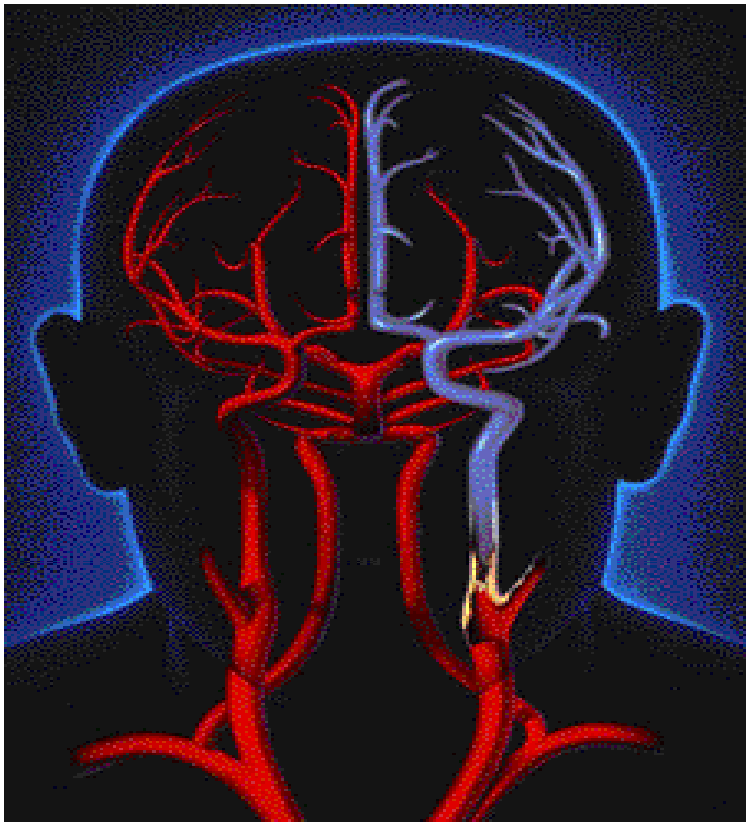
Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

THROMBOLYSIS



In Acute Ischaemic Stroke

5 Acute Trusts - 6 Primary Care Trusts – Ambulance Trust – 4 Local Authorities

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

‘Time is brain’
and..
‘Competence is Brain’

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

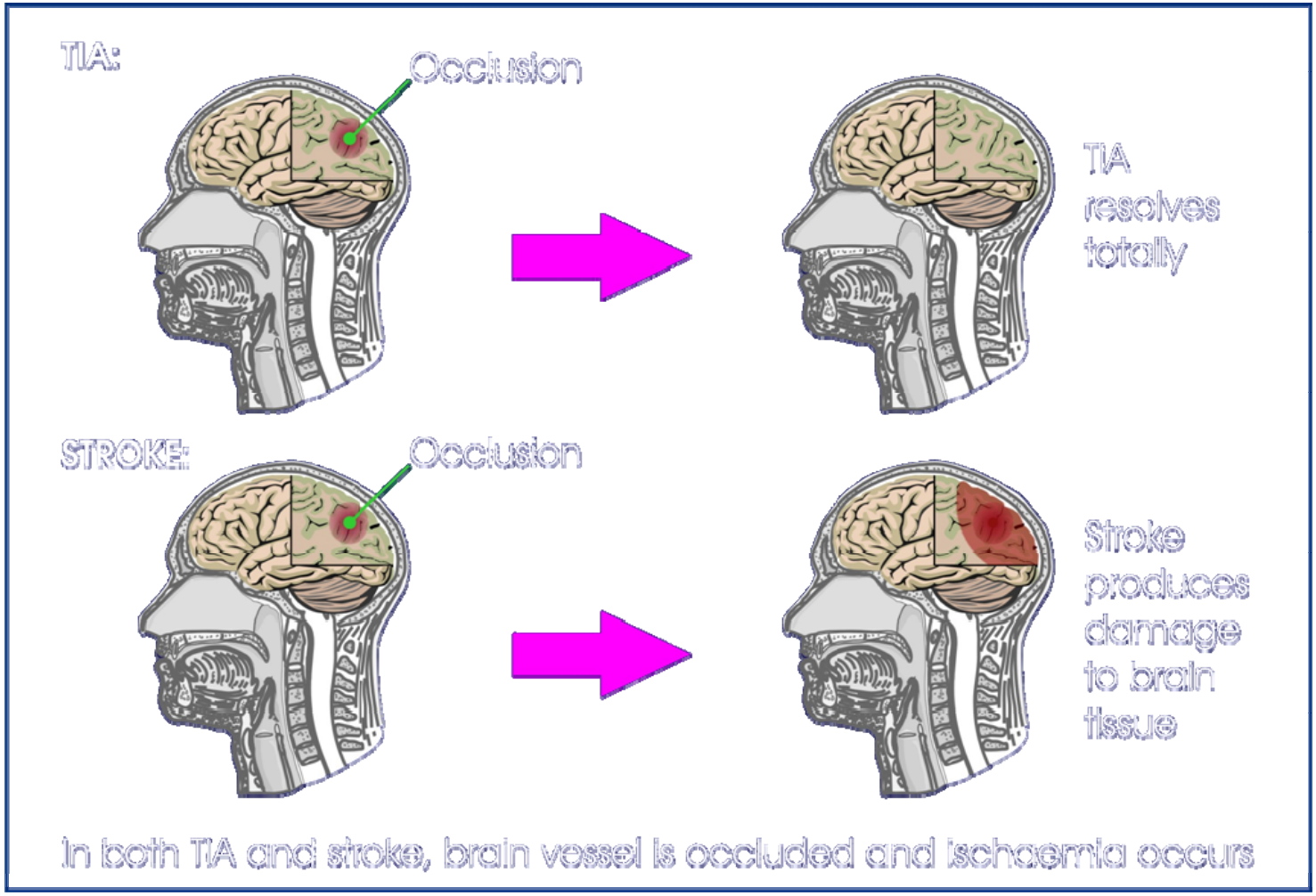
Definition of a stroke

"A focal (or at times global) neurological impairment of sudden onset and lasting more than 24 hours (or leading to death) and of presumed vascular origin."

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

TIA or Stroke

NHS

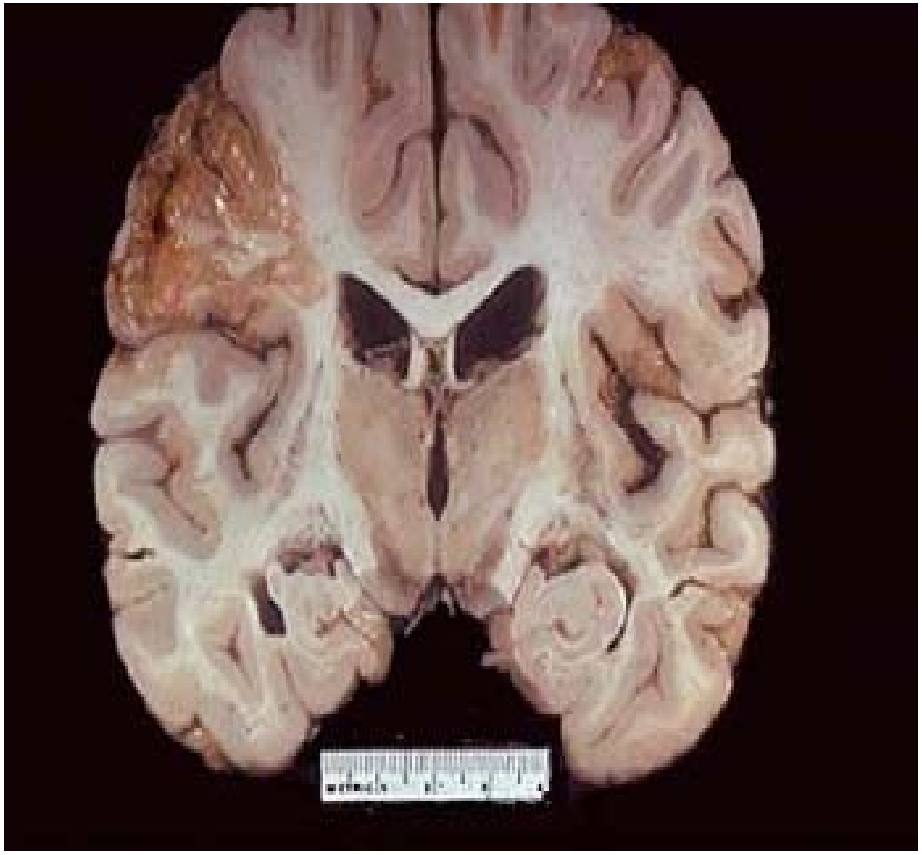


Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

What it is all about..

NHS

Ischaemic 85%



Haemorrhagic 15%

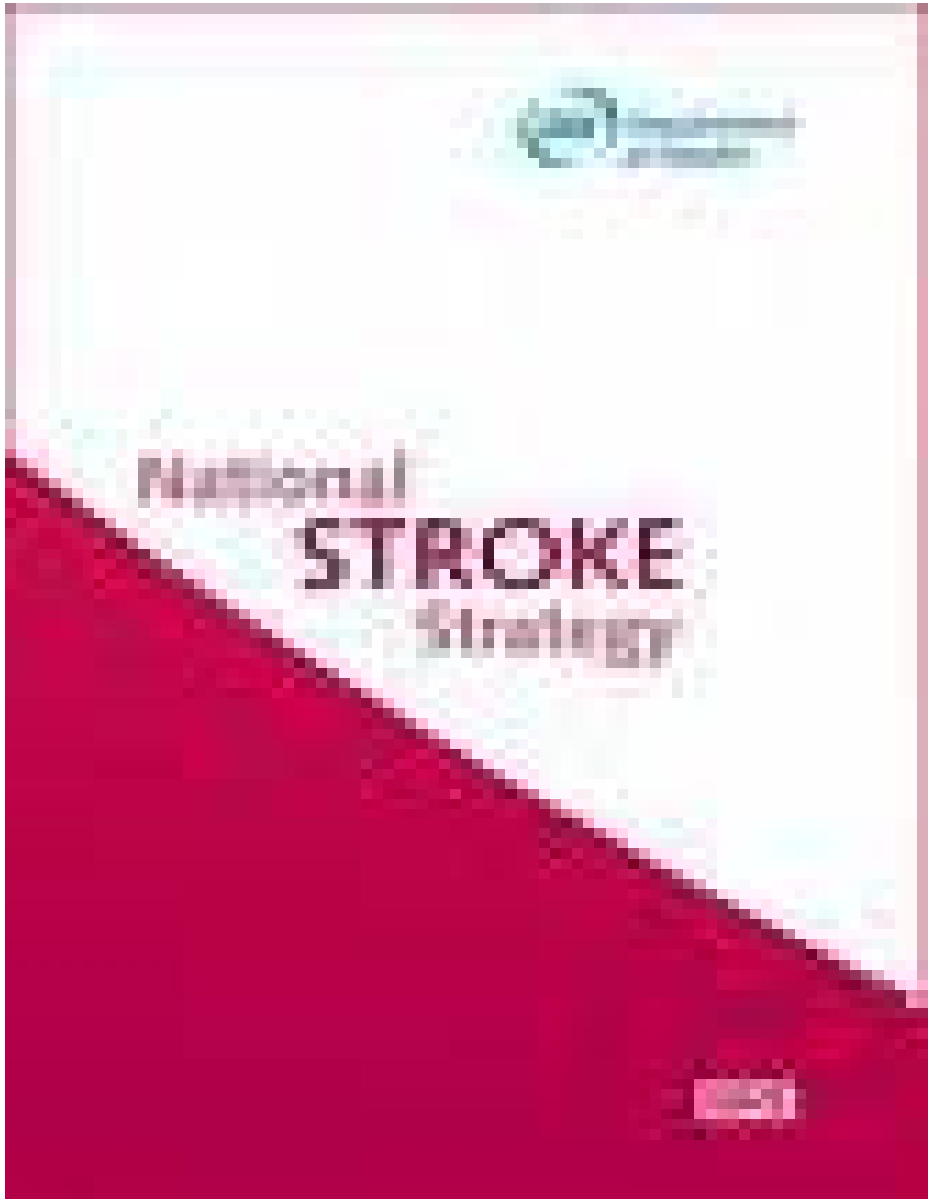
Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

Consider that..

NHS

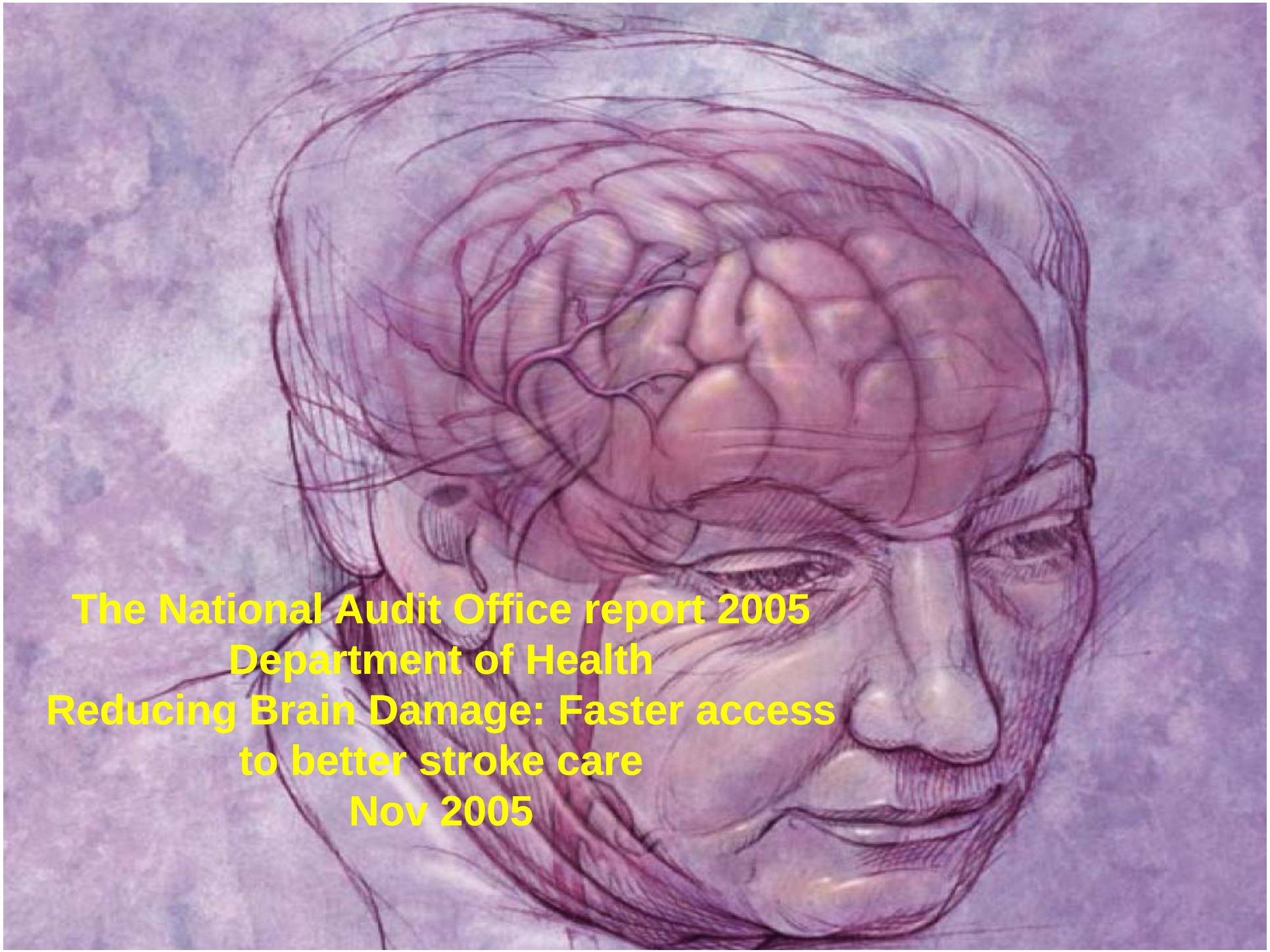
- Every 5 minutes someone in the UK has a stroke.
- Stroke is the 3rd biggest killer and a leading cause of severe adult disability in the UK.
- Almost 1:4 men and 1:5 women aged 45 can expect to have a stroke if they live to 85.
- More than 3 times as many women die from stroke than breast cancer in the UK.
- For every £50 spent on cancer research and £20 on heart disease research, only £1 is spent on stroke research.

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA



NHS

5 Acute Trusts - 6 Primary Care Trusts – Ambulance Trust – 4 Local Authorities


The National Audit Office report 2005
Department of Health
Reducing Brain Damage: Faster access
to better stroke care
Nov 2005

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

Costs to the economy

NHS

- There are at least 300,000 people in England living with moderate to severe disabilities as a result of stroke.
- Stroke care costs the NHS about £2.8 billion a year in direct care costs
  - more than the cost of treating coronary heart disease
  - and £1.8 billion in lost productivity and disability.
- Additionally, the annual informal care costs are around £2.4 billion.
- Total costs £5-7 billion

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Costs to the economy

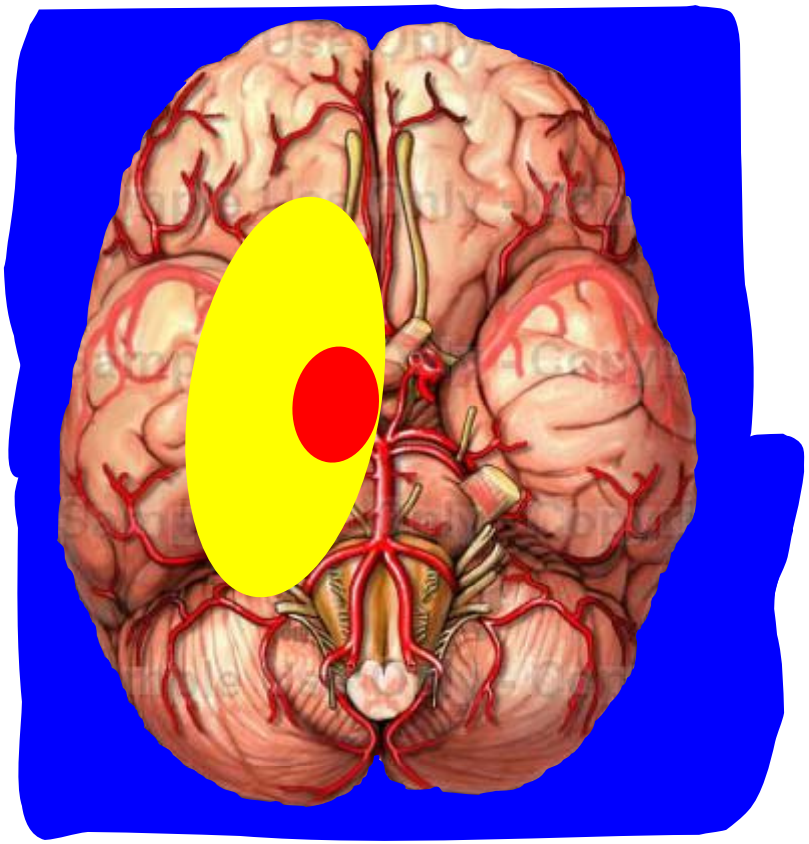
- In leading hospitals in Australia around 9% of patients are thrombolysed and about 40% of these patients then fully recover from their strokes.
- Rates of Thrombolysis in England are <1%.
- Achieving Thrombolysis in 9% of patients with AIS could generate net savings to the NHS of over £16 million a year, with more than 1,500 patients fully recovering from their strokes each year who

  would not otherwise have done so

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Stroke Development & Time



Onset of Stroke

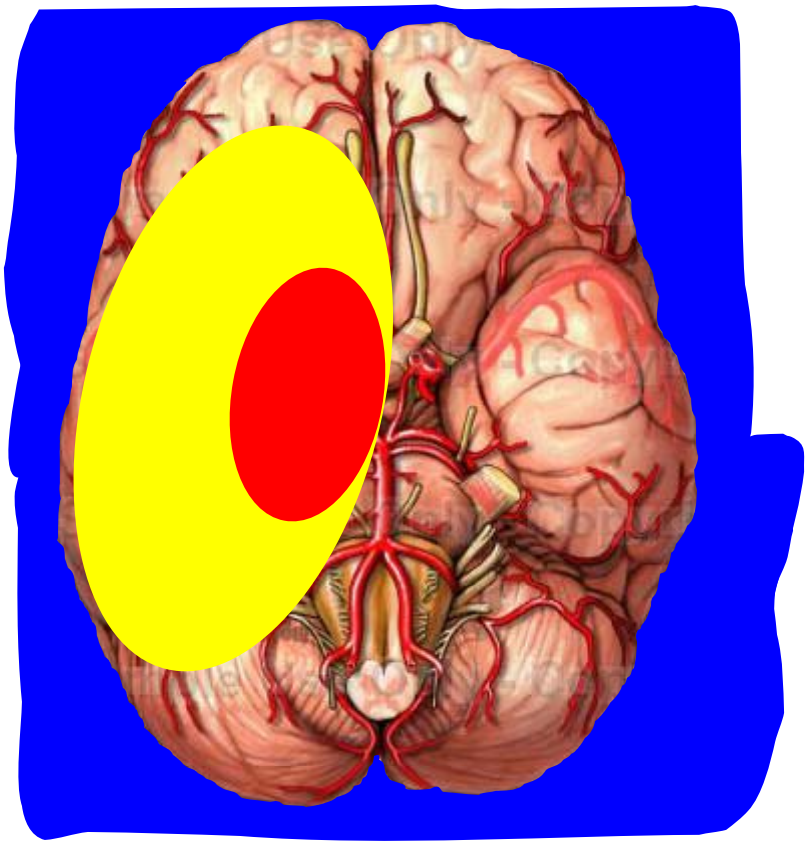
Infarct

Penumbra

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Stroke Development & Time



6 Hours into Stroke

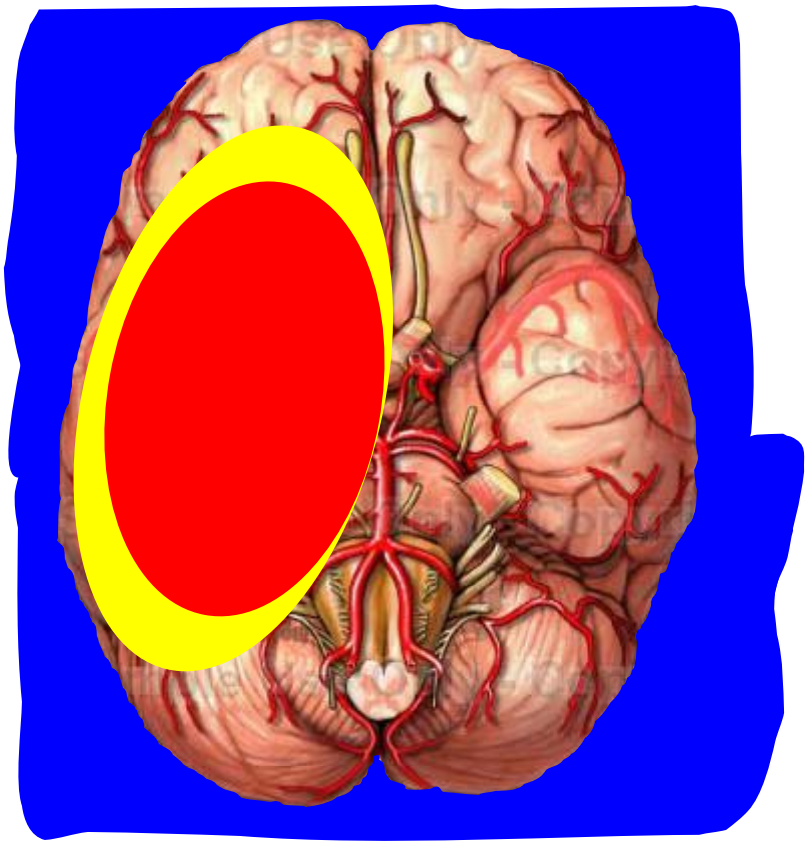
Infarct

Penumbra

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Stroke Development & Time



24 Hours into Stroke

Infarct

Penumbra

Stroke Strategy

- Rapid specialist care concentrated in centres of excellence.

- 10% of patients having access to Thrombolysis treatment.

- Hub and spoke model of care – provision of hyper acute stroke care at a specialist unit before decanting for rehabilitation closer to home.

- Virtual Networks – utilisation of telemedicine to expedite the delivery of Thrombolysis where appropriate

(DOH) Mending Hearts & Brains 2006

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

Stroke Strategy

NHS

- Ambulance trusts should manage patients with a suspected stroke as a Category A call - FAST and PRE-ALERT

- All patients with suspected stroke should be transferred immediately to a hospital providing acute stroke services

  - Stroke triage system
  - Provision of expert clinical assessment
  - Timely imaging
  - Delivery of Thrombolysis (24hrs)
  - 24hr availability of brain scanning
  - Opinion of a Consultant stroke specialist available as required

(DOH) Mending Hearts & Brains 2006

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

Stroke Strategy

NHS

- Patients with suspected stroke should receive an immediate structured clinical assessment in A&E

- All patients with suspected stroke should be scanned as rapidly as possible (Next available slot/60 mins – out of hours)

- All stroke patients should have access to high quality stroke specialist care

- Specialist neurointensive care should be rapidly available through collaboration and commissioning where needed.

(DOH) Mending Hearts & Brains 2006

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Questions

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Cerebral Circulation and patho-physiology

Risk Factors for AIS

Modifiable	Non-Modifiable
Transient Ischaemic attack	Age
Hypertension	Gender
Cardiac function (AF)	Ethnicity
Dyslipoproteinaemia	Familial history
Smoking	
Diabetes	
Alcohol	
Cocaine	

Larry B. Goldstein; Robert Adams,et al. *Stroke.* 2001;32:280-99

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

Background

NHS

- Brain tissue cannot survive without O_2 and glucose. Although only 2% of total body weight the brain accounts for 25% of O_2 consumption

- Within 10 seconds of ischaemia there is loss of consciousness, 20 seconds electrical activity ceases, after a few minutes irreversible brain damage begins (Brain damage also occurs when brain goes without glucose for 10-15 minutes)

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

Background

NHS

- Normal blood flow is 55ml/100g/min of brain tissue.

- Reduction to about 20ml/100g/min causes neurons to stop generating electrical signals.

- Reduction to about 10ml/100g/min results in **infarction** and lead to a **stroke**.

Cerebral Blood Supply

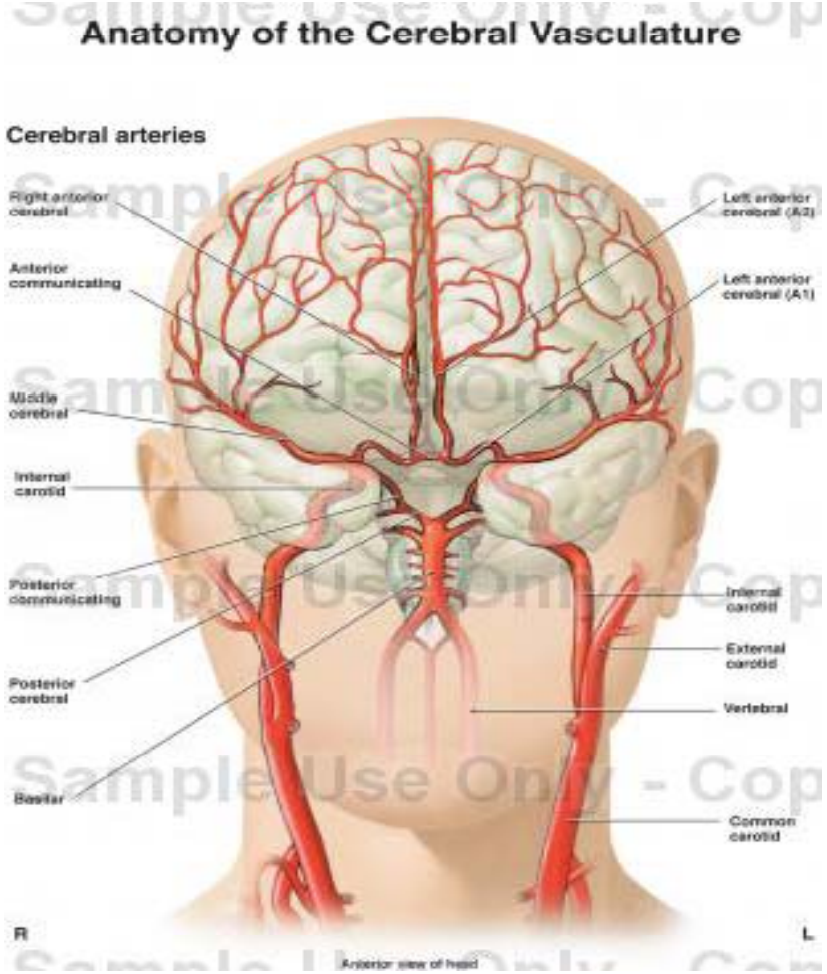
The arterial blood supply to the brain is derived from two pairs of vessels

- Anterior - Internal Carotid Arteries (80%)
- Posterior - Vertebral Arteries (20%)

Cerebral Blood Supply

Internal carotid artery gives rise to :

- Anterior cerebral arteries (ACA)
- Middle cerebral arteries (MCA)
- Anterior choroidal artery (AchA)
- Posterior communicating artery (PCA)



Cerebral Blood Supply

- Anterior cerebral arteries supply

  blood to:

  - medial surfaces of the frontal and parietal lobes, cingulate gyrus, basal ganglia, and corpus callosum.

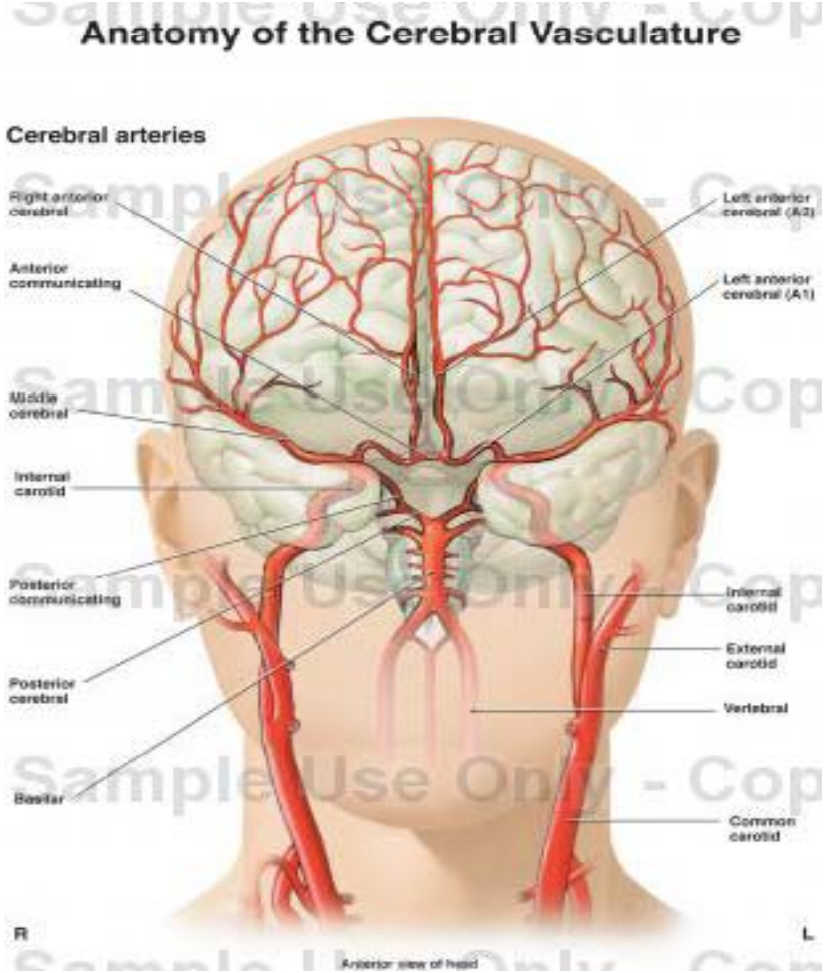
- Middle cerebral arteries supply blood to:

  - lateral surfaces of the frontal, occipital, temporal and parietal lobes and lenticulostriate arteries

Cerebral Blood Supply

Vertebral arteries gives rise to :

- Basilar cerebral artery (BCA)
- Posterior cerebral arteries (PCA)
- Anterior inferior communicating artery (AICA)



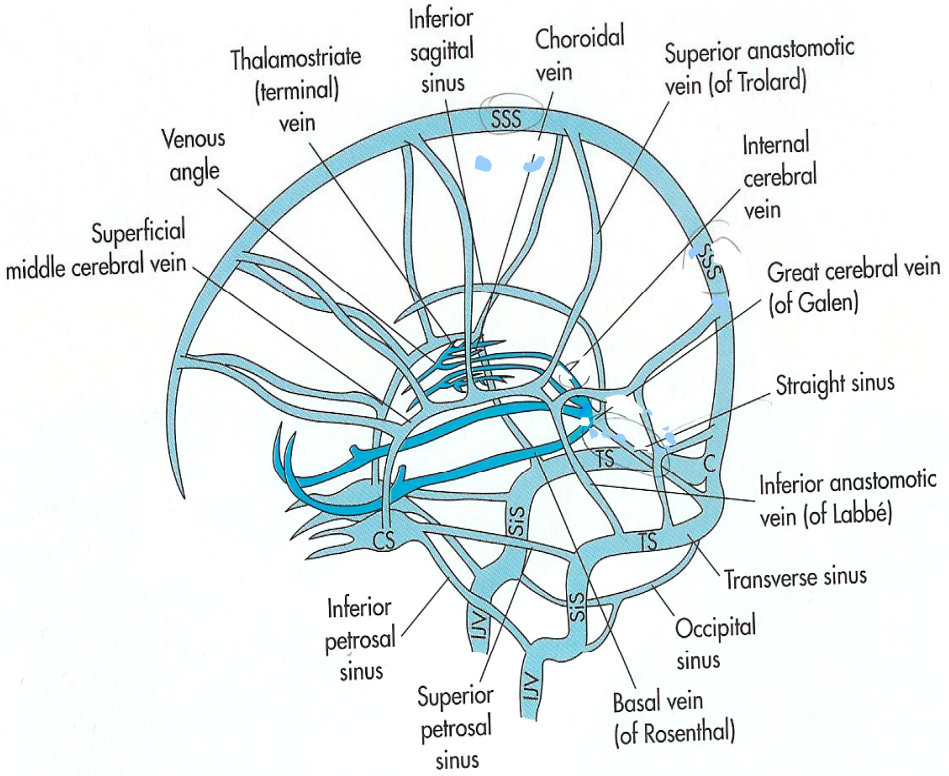
Cerebral Blood Supply

- Basilar cerebral artery supply blood to:
  - Internal ears, pons & cerebellum
- Also gives rise to the Posterior cerebral arteries. Supply blood to:
  - Midbrain, occipital lobe & medial surfaces of the temporal lobe

Cerebral Veins

- Cerebral veins are divided into Superficial and Deep groups.

- They eventually empty into the internal jugular veins and then to the right atrium of the heart



Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

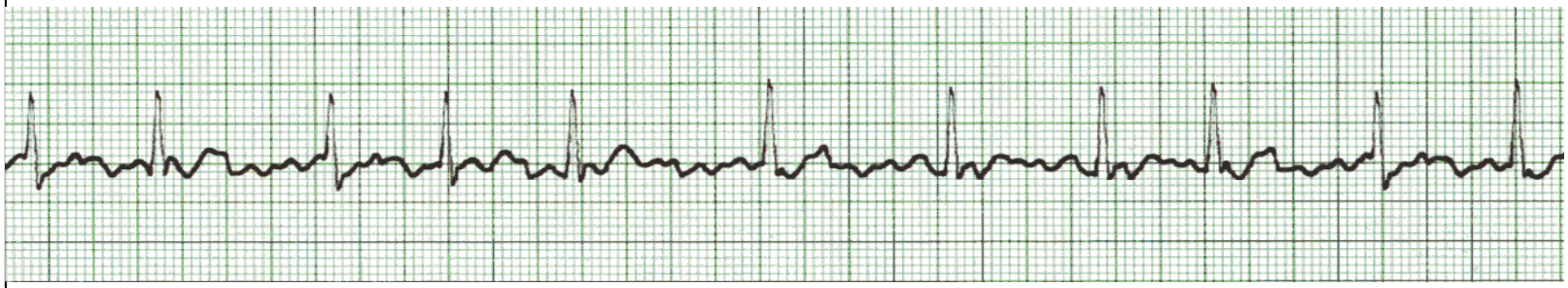
Questions

Aetiology of Stroke

Cardio embolic

- AF, mural thrombus, patent foramen ovale, infective endocarditis

- AF, which is found in less than 5% of the general public, is found in around 25% of patients admitted with stroke.



Aetiology of Stroke

- Atherothromboembolic
  - Carotid / vertebral atheroma, cerebral artery occlusion, carotid dissection
  - The development of atheroma within the carotid and vertebral arteries is the same as in any other artery. Patients presenting with stroke due to arterial disease are likely to have evidence of Ischaemic heart disease and/or peripheral vascular disease.

Aetiology of Stroke

- Small Vessel Disease
  - Hypertensive arterial disease, diabetic vasculopathy, vasculitis
  - Small vessel disease resulting from occlusion of small arteries in the brain, is most frequently associated with hypertension, diabetes and dyslipoproteinaemia. Occasionally, it can result from micro-emboli in the heart or carotid arteries

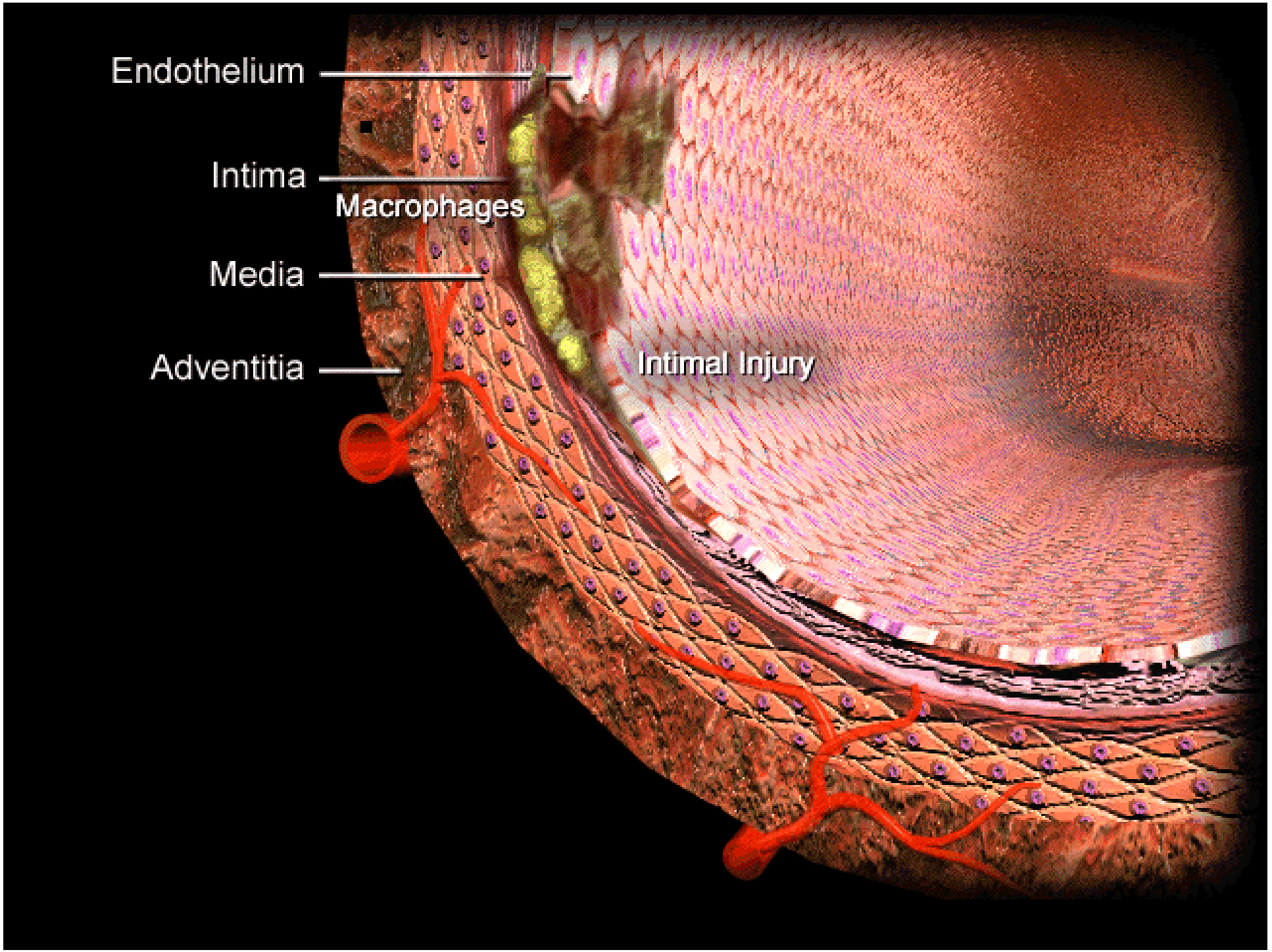
Aetiology of Stroke

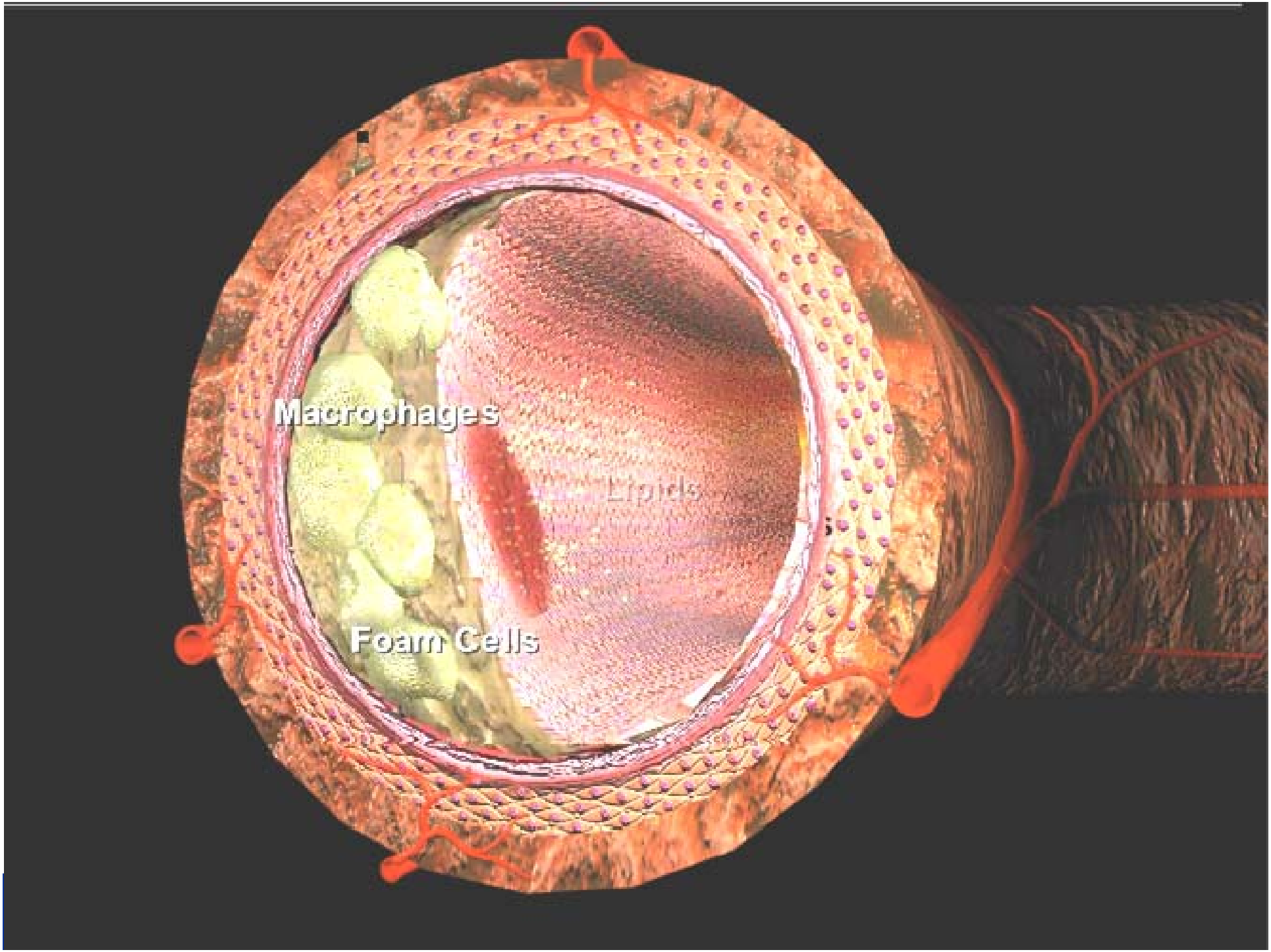
- Haemorrhagic
  - Hypertensive arterial disease, Amyloid angiopathy, Arteriovenous malformation, Aneurysm
  - In ICH, pressure from the space-occupying blood clot causes damage to brain tissue. Rupture from a large vessel will often be rapidly fatal. Hypertension is the main underlying cause of ICH. SAH most commonly arises from a congenital aneurysm of a major vessel. It is one of the more common reasons for stroke in younger adults.

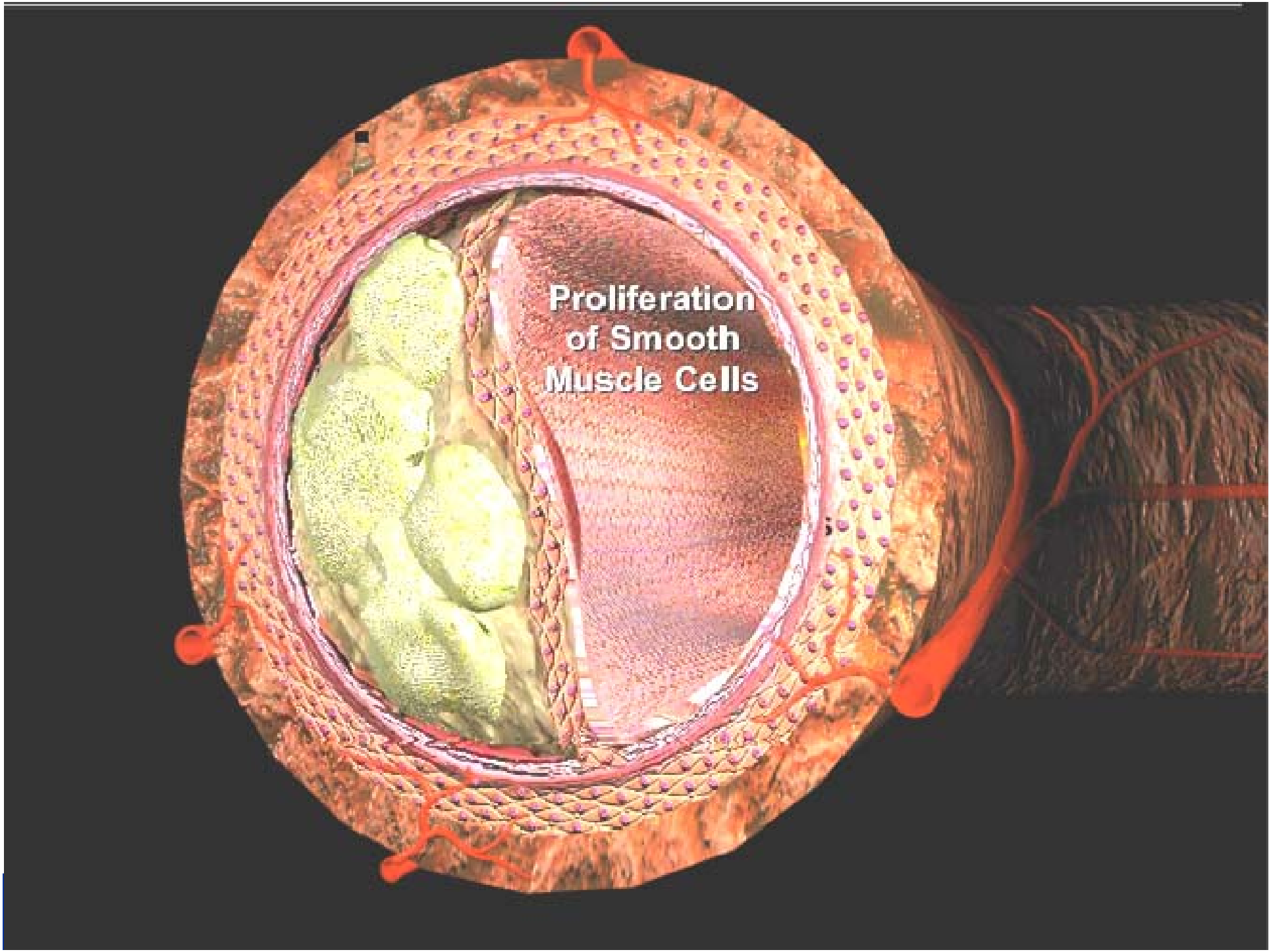
Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Atherosclerosis


Endothelium
Intima
Macrophages
Media
Adventitia
Intimal Injury


Macrophages
Lipids
Foam Cells


Proliferation
of Smooth
Muscle Cells

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Questions

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Diagnosis of Acute Ischaemic Stroke

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

Diagnosis of Acute Ischaemic Stroke

NHS

Introduction

- Stroke should be considered a “brain attack” with emphasis placed upon rapid diagnosis, evaluation and treatment. Remember “Time is brain”
- Early recognition by patient or bystander is essential
- Emergency medical services must be called immediately
- Emergency medical services must perceive stroke as a similar emergency to AMI and trauma

Diagnosis of Acute Ischaemic Stroke

Goals of diagnosis

- Determine that neurological symptoms are due to stroke and exclude non-vascular reasons for symptom
- Determine the type of stroke e.g. haemorrhagic or Ischaemic
- Determine the location of brain injury to assess the size of the stroke
- Determine the most likely cause of the vascular lesion
- Detect any acute neurological or medical complications

Diagnosis of Acute Ischaemic Stroke

Differential diagnosis of acute stroke

- Ischaemic stroke
- Haemorrhagic stroke
- Craniocerebral trauma
- Brain abscess
- Encephalitis
- Brain tumours
- Seizure
- Hypoglycaemia
- Migraine headache

Diagnosis of Acute Ischaemic Stroke

Differential diagnosis of acute stroke

FEATURES SUGGESTING HAEMORRHAGIC STROKE	FEATURES SUGGESTING ISCHAEMIC STROKE
•Early and prolonged loss of consciousness •Prominent headache, nausea and vomiting •Retinal haemorrhages •Nuchal rigidity •Focal signs do not fit the anatomic •pattern of a single blood vessel	•Stepwise deterioration or progressive worsening •Waxing and waning of findings •Focal neurologic impairments in the pattern of a single blood vessel •Signs point to a focal cortical or sub cortical lesion

Diagnosis of Acute Ischaemic Stroke

Clinical features of stroke

TIME COURSE AND EVOLUTION	•Sudden or rapid onset •Reach maximal intensity within 24 hrs
FOCAL NEUROLOGICAL SYMPTOMS	•Headache •Nausea and vomiting •Altered mental status (syncope, seizure, coma) •Hypertension and abnormal vital signs •Nuchal rigidity
GLOBAL SYMPTOMS AND SIGNS	•Cognitive impairments (i.e.. Aphasia, neglect, etc.) •Weakness or lack of coordination of limbs •Facial weakness •Numbness of limbs and/or face

Diagnosis of Acute Ischaemic Stroke

Diagnostic tools

- Variety of diagnostic tools available, and should be performed urgently
- Medical history may reveal risk factors, stroke type and area of brain affected
- Physical examination will help uncover underlying pathology
- CVS assessment might provide evidence of cause or detect cardiovascular complications
- Computed tomography is most reliable way to differentiate haemorrhagic stroke from Ischaemic stroke

Diagnosis of Acute Ischaemic Stroke

CT scanning

- Most important initial diagnostic study

- Current gold standard for ruling out haemorrhagic stroke. It is:

  Widely available, non-invasive, quick, relatively inexpensive, relatively easy to interpret

But limitations because:

Ability to detect cerebral infarction depends upon size, location and age of lesion. Infarcts smaller than 5 mm may escape detection, only around 5% are visible within the first 12 hours of stroke onset

Diagnosis of Acute Ischaemic Stroke

MRI scanning

- MRI has some advantages over CT scanning:

  It is more sensitive to changes in tissue structure
  It provides a more accurate and earlier measure of cerebral infarction

- However, it also has some limitations:

  It is more expensive than CT
  It is less widely available
  It requires special expertise

Mortality and Disability

(30 days)	TACI	PACI	LACI	POCI
Death	39	4	2	7
Dependant	56	39	36	31
Independent	4	56	62	62

Bamford et al Lancet 1991

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Questions

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

Elements of patient Pathway

NHS

- Pre-hospital
- Emergency Department
- Radiology
- Acute Stroke Unit

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Pre-Hospital Stroke Care

Paramedic Responsibilities

- Ambulance response – Cat A
- Patient assessment – FAST
- Blood glucose – hypo/hyperglycaemia
- Appropriate hospital pre-alert – saying "FAST positive stroke patient" – A&E / stroke team (dedicated bleep?)
- Correct positioning of stroke patient - conscious (semi-sitting) unconscious (stable side position, paralysed limb uppermost)
- Patient relative (if possible) – time of onset / consent

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Paramedic Responsibilities

Potential eligibility for Thrombolysis

- FAST positive
- Onset within last 2 hours
- Aged 18 – 80
- Conscious or easily rousable
- No seizures / fits
- BM > 3mmols
- Not on Warfarin

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Does FAST work ?

	Element	Paramedic	Neurologist
• Face	F	68	70
• Arm	A	96	95
• Speech	S	79	77
• Time	T		

% recorded signs in 217 patients with confirmed stroke [1]

Paramedics correct in 144/183 (79%) using FAST Test [2]

1. Mohd Nor et al *Stroke* 2004 2. Harbison et al *Stroke* 2003

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

FAST

Face - Ask the patient to smile or show teeth and look for NEW lack of symmetry

Arm - Ask the patient to lift their arms together and hold for 5 seconds. Does one arm drift or fall down. The arm with motor weakness will drift downwards compared to the unaffected limb

Speech - Ask the patient to repeat a phrase. Assess for slurring or difficulty with the words or sentence

Time - Time to call 999, stroke is a medical emergency

JRCALC , Specific Treatment Options 2006

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Emergency Department

Emergency Department

Assessment

- Confirm time of onset
- Exclude hypoglycaemia
- Define neurological deficit (ROSIER)
- IV access – bloods (FBC, clotting, glucose, U&E, PT, aPTT, INR, cardiac enzymes + ECG)
- NIHSS
- Medications (Warfarin)
- Assess patient weight
- Request Urgent CT scan
- Complete Thrombolysis checklist
- Inform patient / relative potential candidate for Thrombolysis

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

ROSIER

Date/time of symptom onset _ _ _ _ _ _ _ _ _ _

GCS E= V= M= BP BM

(if BM <3.5mmols treat urgently and reassess once blood glucose normal)

Has there been loss of consciousness or syncope Y(-1) N(0) ✓

Has there been seizure activity Y(-1) N(0) ✓

Is there a NEW ACUTE onset or on awakening from sleep

Asymmetric facial weakness	Y(1)	✓	N(0)
Asymmetric arm weakness	Y(1)	✓	N(0)
Asymmetric leg weakness	Y(1)	✓	N(0)
Speech disturbance	Y(1)	✓	N(0)
Visual field deficit	Y(1)	✓	N(0)

Total score _____(-2 to +5)

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

NIHSS

- The NIHSS assesses neurological impairment such as:
  - Paresis
  - Aphasia
  - Level of consciousness
  - Sensory symptoms
  - Facial and gaze palsy
  - Dysarthria and hemi-neglect

  It shows good inter-rater reliability and validity, which can be increased by video-assisted training and self assessment
- It has a score range from 0 to 42; death is not coded

Brott et al. *Stroke* 1989; 20 (7): 864–870.
Lyden et al. *Stroke* 1994; 25 (11): 2220–2226.
Spilker J, Kongable G. *Stroke Intervent* 2000; 2: 7–14.

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

NIHSS is the most commonly used assessment tool for stroke Thrombolysis

NIH Stroke Scale

This form is to help you calculate the total NIHSS score. File in medical notes after use.

Patients Name: **Date:**

1a. Level of Consciousness (LOC)	0	Alert – keenly responsive
	1	Drowsy – arousable by minor stimulation to obey, answer or respond
	2	Stuporous – requires repeated stimulation to attend or is obtunded and requires strong or painful stimulation to make movements (not stereotyped)
	3	Comatose – responds only with reflex motor or autonomic effects or totally unresponsive, flaccid
1b. LOC Questions	0	Answers both correctly
	1	Answers one correctly **Patient is asked to state the month and his/her age**
	2	Both incorrect
1c. LOC Commands	0	Obeys both correctly
	1	Obeys one correctly **Patient is asked to open & close eyes, grip & release normal hand**
	2	Both incorrect
2. Best Gaze	0	Normal
	1	Partial gaze palsy – gaze is abnormal in one or both eyes, no forced deviation/total gaze paresis
	2	Forced deviation – or total gaze paresis not overcome by oculophalic manoeuvre
3. Visual Fields	0	No visual loss (or in coma)
	1	Partial hemianopia
	2	Complete hemianopia
	3	Bilateral hemianopia – including cortical blindness
4. Facial Palsy	0	Normal
	1	Minor – flattened nasolabial fold, asymmetry on smiling
	2	Partial – total or near total paralysis of lower face
	3	Complete – absent facial movement in upper and lower face on one or both sides
5. Best Motor (Right Arm)	0	No drift – holds limb at 90 degrees for full 10 seconds
	1	Drift – drifts down but does not hit bed
	2	Some effort against gravity
	3	No effort against gravity
	4	No movement
6. Best Motor (Left Arm)	0	No drift – holds limb at 90 degrees for full 10 seconds
	1	Drift – drifts down but does not hit bed
	2	Some effort against gravity
	3	No effort against gravity
	4	No movement
7. Best Motor (Right Leg)	0	No drift – holds limb at 45 degrees for full 5 seconds
	1	Drift – drifts down but does not hit bed
	2	Some effort against gravity
	3	No effort against gravity
	4	No movement
8. Best Motor (Left Leg)	0	No drift – holds limb at 45 degrees for full 5 seconds
	1	Drift – drifts down but does not hit bed
	2	Some effort against gravity
	3	No effort against gravity
	4	No movement
9. Limb Ataxia	0	Absent (or in coma)
	1	Present in one limb
	2	Present in two or more limbs
10. Sensory	0	Normal
	1	Partial loss – patient feels pinprick is less sharp or is dull on affected side
	2	Dense loss (or in coma) – patient is unaware of being touched on face, arm or leg
11. Best Language	0	No dysphasia
	1	Mild – Moderate dysphasia - obvious loss of fluency or comprehension without significant limitation on ideas expressed or form of expression. Make conversation about provided material difficult or impossible. E.g. examiner can identify picture or naming card from patients response
	2	Severe dysphasia – all communication is through fragmentary expression, great need for inference, questioning and guessing by the listener who carries burden of communication. Examiner cannot identify materials provided from patient response.
	3	Mute – no usable speech or auditory comprehension or in coma
12. Dysarthria	0	Normal articulation
	1	Mild – Moderate dysarthria – patient slurs some words, can be understood with some difficulty
	2	Unintelligible or worse – speech is so slurred as to be unintelligible (absence of or out of proportion to dysphasia)or is a mute/anarthric or in a coma
13. Neglect	0	No neglect or in a coma
	1	Partial neglect – visual, tactile, auditor, spatial or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities
	2	Complete neglect – profound hemi-inattention of hem-inattention to more than one modality. Does not recognise own hand or onents to only one side of space
Total		

Emergency Department

Stroke Mimics

Neurological

- Seizure/post-ictal state
- Complicated migraine
- Subdural Haematoma
- Abscess, tumour or malignancy
- Hypertensive encephalopathy
- Multiple sclerosis (or other demyelinating process)
- Vertigo
- Cranial and peripheral neuropathies

Emergency Department

Stroke Mimics

Neurological (cont)

- Spinal cord or disc disease
- Transient global ischaemia
- Bell's Palsy
- Encephalitis

Metabolic

- Hypo/hyperglycaemia
- Hyponatraemia
- Hepatic encephalopathy

Emergency Department

Stroke Mimics

Metabolic (cont)

- Drug overdose

Other

- Syncope

Emergency Department

What the clinician needs to know

- Has a stroke occurred or are the patient's symptoms due to a different pathology?
- If a stroke has occurred, is it a haemorrhagic stroke or a cerebral infarction
- Is there a treatable underlying aetiology for the patient's acute stroke.
- Is the territory of the Ischaemic insult salvageable or are the tissues already irreversibly infarcted

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Imaging Interpretation

Image Interpretation

What to look for in the first CT scan

There are a number of features that should be looked for in the initial CT scan. These are:

- A spot or tubular structure along the major intracranial vessels particularly at the intracranial bifurcation of the internal carotid artery, along the basilar artery or along the middle cerebral artery, which is hyperdense in relation to the remainder of the vessel or to other vessels. This indicates the presence of a clot within the vessel.

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Image Interpretation

What to look for in the first CT scan

- Early parenchymal hypodensity of the basal ganglia and/or the cortex, possibly associated with sulcal effacement or ventricular compression, indicating the extent of the affected tissue.
- Parenchymal hyper density which may represent parenchymal haemorrhage. Haemorrhages may be difficult to see at this early stage and may appear as a tiny white spot
- Evidence of previous Ischaemic brain damage, the pattern of which may indicate the underlying disease.

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

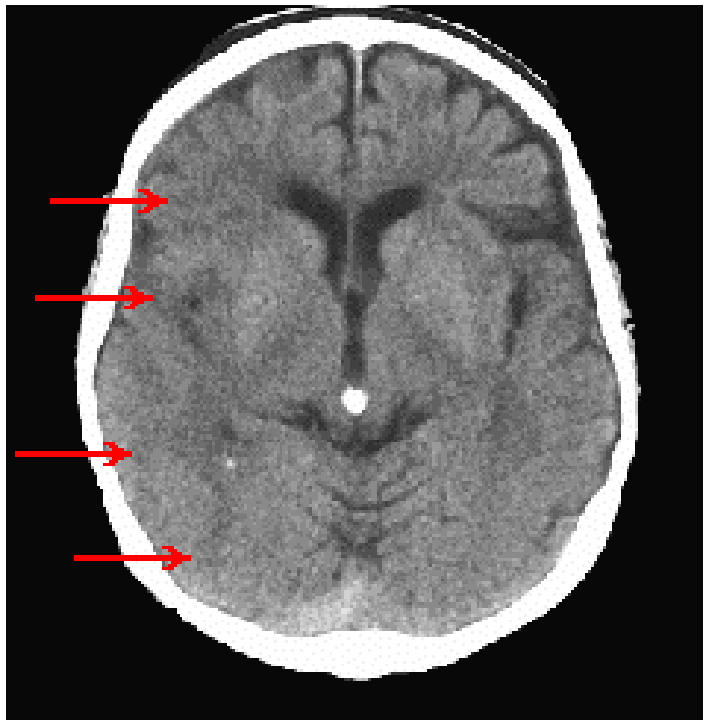
NHS

Image Interpretation

Estimating extent of early Ischaemic damage

If a patient is being assessed for Thrombolysis, there may not be time for quantitative measurement of parenchymal hypodensity.

The investigators of the ECASS trial concluded that patients with hypo-density comprising more than 33% of the MCA territory should not be considered for Thrombolysis



Hypodensity > 33% of MCA Territory

"Early CT Diagnosis of Acute Ischaemic Stroke: A Physicians' Guide" produced by MediCine International plc for Boehringer Ingelheim GmbH

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Image Interpretation

Hyperdense cerebral vessels

A useful early sign of cerebral Ischaemia is the appearance on The CT of hyperdense vessels As clotted blood possesses a higher absorption value on CT than moving blood, any intraluminal clotted blood makes the affected artery stand out against lower density unaffected arteries

"Early CT Diagnosis of Acute Ischaemic Stroke: A Physicians' Guide" produced by MediCine International plc for Boehringer Ingelheim GmbH

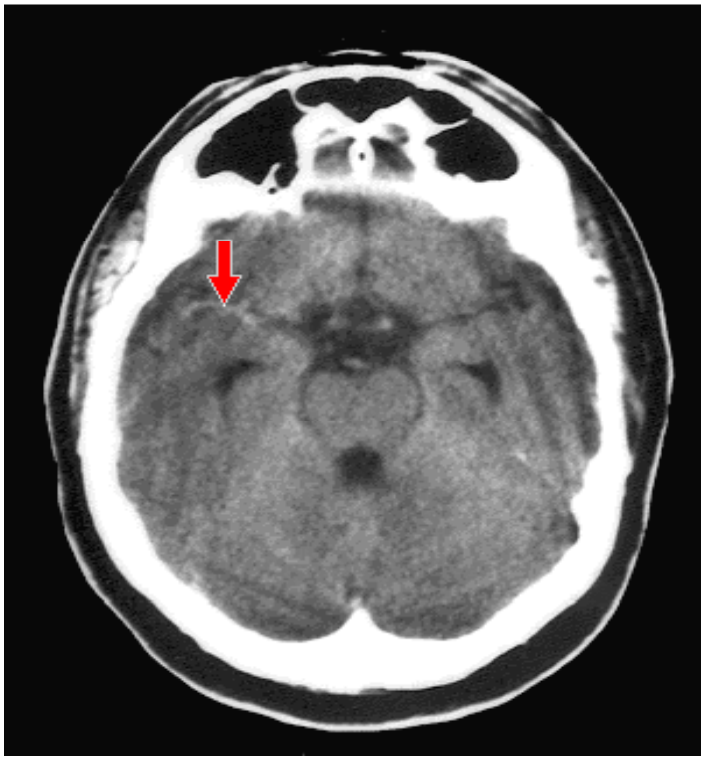
Image Interpretation

Hyperdense middle cerebral artery sign (HMCAS)

The MCA is the commonest vessel to be occluded in cerebral Ischaemia and is considered a reliable early sign of impending infarction

Occasionally, however, a patient with HMCAS may show no infarction Because of good collateral flow

Large HMCAS branch



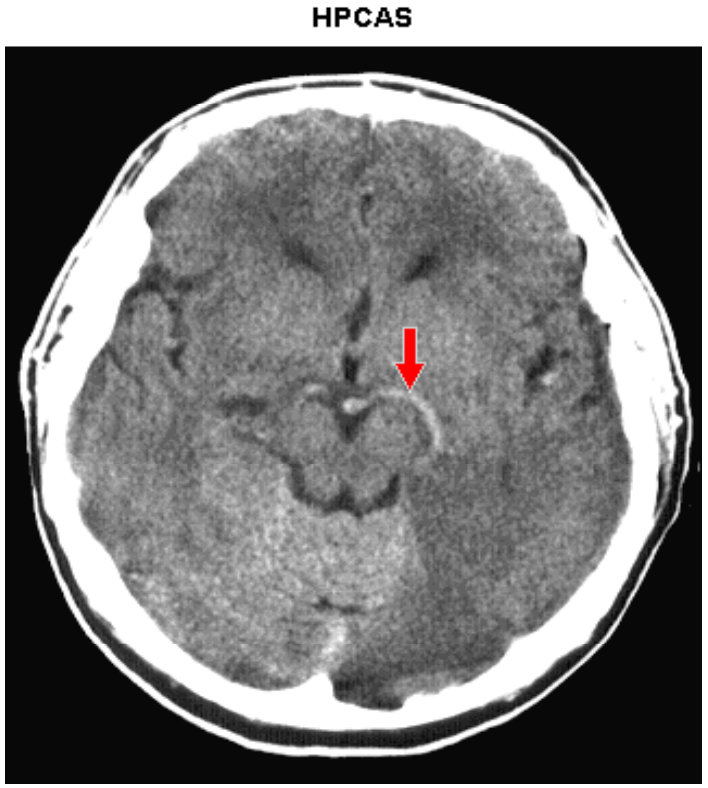
"Early CT Diagnosis of Acute Ischaemic Stroke: A Physicians' Guide" produced by MediCine International plc for Boehringer Ingelheim GmbH

Image Interpretation

Hyperdense posterior cerebral artery (HPCAS) and hyperdense internal carotid artery sign (HICAS)

The HPCAS and HICAS are found much less commonly than the HMCAS

Often the disappearance of the hyperdense sign indicates that recanalisation therapy Has been successful



"Early CT Diagnosis of Acute Ischaemic Stroke: A Physicians' Guide" produced by MediCine International plc for Boehringer Ingelheim GmbH

Image Interpretation

Parenchymal hypodensity as a predictor of neurological outcome

The hypodensity that develops during the first hours after the onset of cerebral ischaemia may be predictive of eventual outcome but it is often very subtle and difficult to define

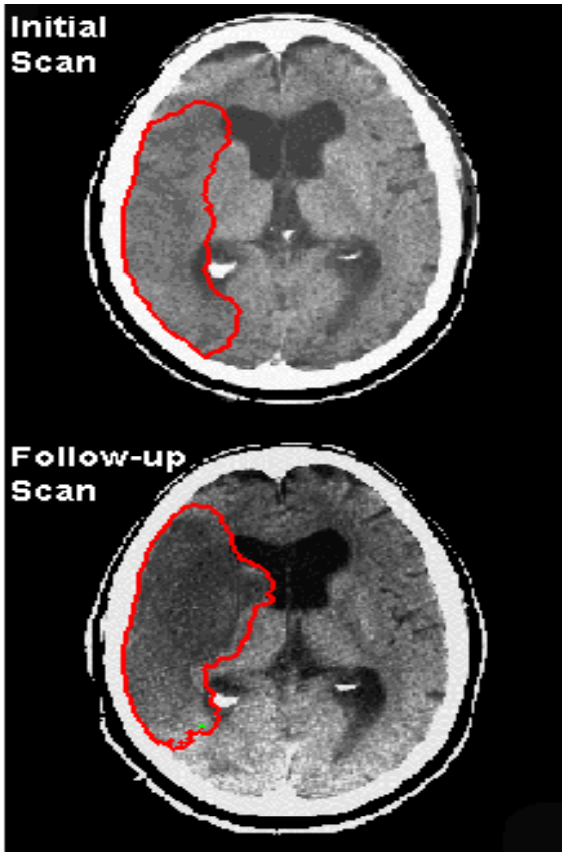
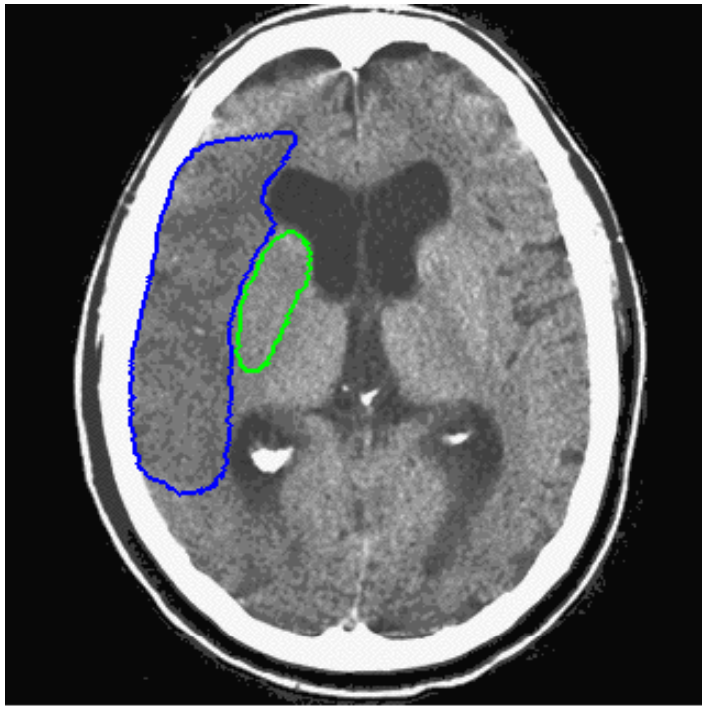


Image Interpretation

Consequences of hypodensity for therapy

Parenchymal hypodensity as shown on CT within 6 hours of stroke onset represents the early stages of necrosis in the core of an Ischaemic infarct

Following stroke the lentiform nucleus frequently appears hypo-dense on CT due to its poor collateral supply



MCA Territory
Lentiform Nucleus

"Early CT Diagnosis of Acute Ischaemic Stroke: A Physicians' Guide" produced by MediCine International plc for Boehringer Ingelheim GmbH

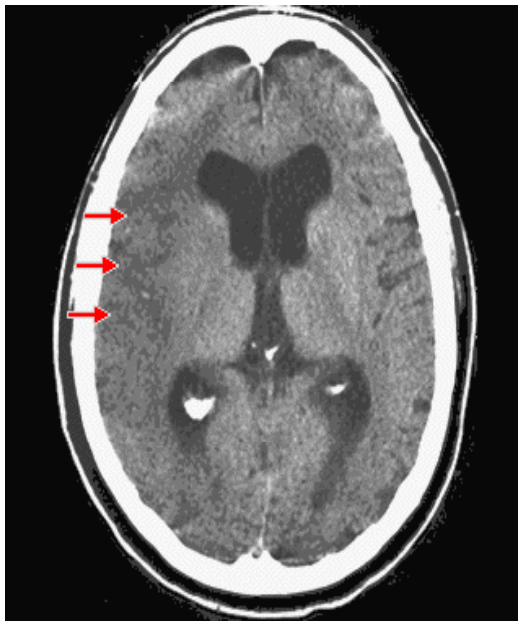
Image Interpretation

Ischaemic brain oedema and CT

Parenchymal hypodensity during the first six hours after stroke is often accompanied by brain swelling

There is often effacement of cortical sulci with loss of grey-white matter differentiation, which can best be detected by comparing the two hemispheres

Effacement of sulci



"Early CT Diagnosis of Acute Ischaemic Stroke: A Physicians' Guide" produced by MediCine International plc for Boehringer Ingelheim GmbH

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

CT or MRI ?

NHS

Non-contrast CT

- Recommended initial neuro-imaging
- CT not ideal, because of difficulty in detecting acute or small infarcts and artifact in the brainstem area
- CT can identify subtle signs of early ischaemia or arterial occlusion

MRI

- Better for detection of acute ischaemia than CT - sensitivity and specificity of diffusion-weighted imaging for detecting acute ischaemia are about 100%
- Diffusion-weighted imaging also provides the additional advantage of visualisation of small lesions, usually poorly visualised on CT

Newer CT methods :

- CT angiography, CT perfusion, and CT cerebral-blood volume imaging can obtain similar information to MRI.

Khaja, M. **Lancet 2007; 369: 319-30**

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Questions

Thrombolysis

Alteplase (rtPA) approved for use in Ischaemic stroke 2002 in Europe

- Randomised trials:
  - NINDS 624pts randomised <3hrs
  - ECASS I 620pts randomised <6hrs
  - ECASS II 800pts randomised <6hrs

- Required registry as condition of licence
  - SITS MOST 4961 pts <3 hrs

NINDS : National Institute of Neurological Disorders and Stroke
ECASS: European Cooperative Acute Stroke Study (as required by EMEA in support of European licence)
SITS-MOST: Safe Implementation of Thrombolysis in Stroke Monitoring Study

Thrombolysis trials

National Institute of Neurological Disorders and Stroke Study (NINDS), 1995

624 patients; onset <3hours, randomised to rt-PA (0.9mg/kg) or placebo

"Compared with patients given placebo, patients treated with t-PA were at least 30 % more likely to have minimal or no disability at 3 months on the assessment scales"

"Symptomatic intra-cerebral haemorrhage within 36 hours after the onset of stroke occurred in 6.4 % of patients given t-PA but only 0.6 % of patients given placebo (P < 0.001). Mortality at three months was 17 % in the t-PA group and 20 % in the placebo group (P = 0.30)."

NINDS Study, NEJM 1995;333:1581-87

NINDS – modified Rankin scores

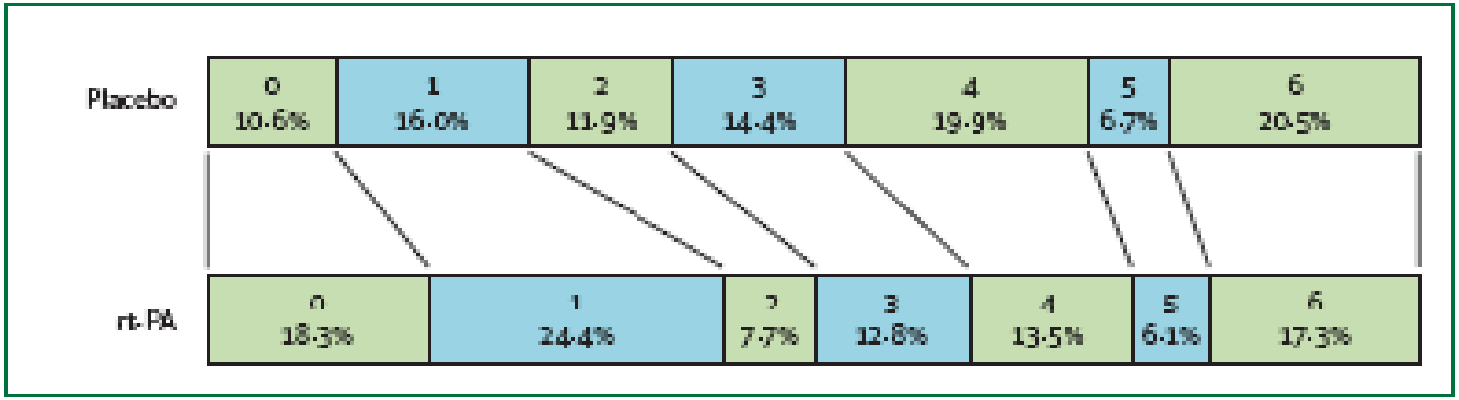


Figure 1: Modified Rankin Scale at 3 months in NINDS rt-PA trial

Data from reference 1. Modified Rankin Scale scores range from 0 (indicating no symptoms) to 6 (indicating death).

0 - No symptoms at all

1 - No significant disability despite symptoms. Able to carry out all usual duties and activities

2 - Slight disability: unable to carry out all previous activities, but able to look after own affairs unassisted

3 - Moderate disability: requiring some help but able to walk unassisted

4 - Moderately sever disability: unable to walk and attend to own bodily needs unassisted

5 - Severe disability: bedridden, incontinent and requiring constant nursing care and attention

6 - Death

Khaja AM, Grotta JC, 2007 Established treatments for acute Ischaemic stroke. Lancet 369:324

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Thrombolysis trials

European Co-operative Acute Stroke Study (ECASS),1995

620 patients, <6 hours of stroke onset. Randomised to rt-PA (1.1mg/kg) or placebo, 18-80 years.

"There was no difference in primary endpoints in the intention to treat analysis but the explanatory analysis of the target population showed a significant difference (p=0.035) in the Rankin Scale in favour of rt-PA treated patients"

"There were no statistically significant differences in the mortality rate at 30 days or in the overall incidence of intracerebral haemorrhages among the rt-PA and placebo treatment arms in either analysis"

ECASS,JAMA 1995;274:1017-25

Thrombolysis trials

European and Australian Co-operative Acute Stroke Study (ECASS II),1998

800 patients, <6 hours of stroke onset. Randomised to rt-PA (0.9mg/kg) or placebo, 18-80 years.

"165 rt-PA patients and 143 placebo-group patients had favourable MRS outcomes (p=0.277). Outcomes were similar whether patients treated within 0-3 hours or 3-6 hours with no difference between treatment groups at day 90 +/-14 days. 85(10·6%) patients died, with no difference between treatment groups at day 90±14 days (43 Alteplase, 42 placebo). Symptomatic intracranial haemorrhage occurred in 36(8·8%) Alteplase group patients and 13 (3·4%) placebo-group patients."

"Despite the increased risk of intracranial haemorrhage, Thrombolysis with Alteplase at a dose of 0·9 mg/kg in selected patients may lead to a clinically relevant improvement in outcome."

ECASS II , Lancet 1998;352:1245-51

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Thrombolysis Registry

Safe Implementation of Thrombolysis in Stroke Monitoring Study (SITS-MOST), 2007

6483 patients were recruited from 285 centres (50% with little previous experience in stroke Thrombolysis) in 14 countries between 2002 and 2006 for this prospective, open, monitored, observational study.

"To compare the safety and efficacy of tissue plasminogen activator (rt-PA) administered in controlled clinical trials to that of rt-PA prescribed in routine clinical practice."

(NB. All SITS-MOST patients were treated within the licence i.e. within 3 hours of onset)

SITS-MOST, 2007 Lancet 369;275-82

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Thrombolysis Registry

SITS-MOST conclusion:

"Alteplase, when used in routine clinical practice, has a safety profile at least as good as seen in randomised controlled trials and is effective when used within 3 hours of stroke onset, even in stroke centres with little previous experience of thrombolytic therapy in acute stroke."

"This trial showed a 3.4 % improvement in direct comparison across the full modified Rankin scale at 3 months with other randomized clinical trials, which showed a 10 % improvement for rt-PA use over placebo."

SITS-MOST, 2007 Lancet 369;275-82

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

SITS Database

S afe

I mplimentation of

T hrombolysis in

S troke

SITS is an academic-driven, non-profit, international collaboration. It is a initiative by the medical profession to certify excellence in acute stroke treatment.

Internet-based interactive Thrombolysis register, to serve as an instrument for clinical centres to follow their own treatment results and compare with other centres in their countries and in the collaborating countries.

www.acutestroke.org

Thrombolysis Registry

Evidence – On-going:

European Cooperative Acute Stroke Study (ECASS) III (Report - Vienna 2008)

To evaluate efficacy and safety of rt-PA between 3 and 4 hours after stroke onset in the European setting.

International Stroke Trial (IST3) (Reporting ? 2010/11)

To determine whether administration of rt-PA within 6 hours of ischemic stroke increases the proportion of independent survivors at 6 months.

SITS Databases

SITS Registries

- SITS – Global registry of all patients irrespective of time to treatment
- SITS-MOST – Registry is closed
- SITS-ISTR – In support of the Asian and far eastern countries licence applications. Patients treated within licence

SITS-MOST, 2007 Lancet 369;275-82

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Thrombolysis

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Thrombolysis

Numbers Needed to Treat for Several Therapies

- Thrombolysis < 6 hours vs placebo in myocardial infarction (MI) to prevent 1 death = 33 (absolute risk reduction (RR) of 3%)
- rt-PA < 3 hours vs placebo to prevent poor outcome (mRS 2–6) based on NINDS alone = 8.4
- rt-PA < 3 hours vs placebo to prevent disability or death (mRS 3–6) based on NINDS, ECASS I+II = 7 (relative odds reduction of 45%)

Ford G, Freemantle N. *Lancet* 1999; 353 (9146): 65; author reply 67–68. Lees KR. *Lancet* 1999; 353 (9146): 65–66; author reply 67–68. Wardlaw et al. *Cochrane Database Syst Rev* 2002; 2: CD000213.

Thrombolysis

Inclusion criteria

- Aged 18 – 80
- Ischaemic stroke with clearly defined time of onset
- Measurable neurological deficit
- Neuroimaging excluding haemorrhage
- Consent

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Thrombolysis

Exclusion criteria

- Evidence of intracranial haemorrhage on pretreatment evaluation
- Suspicion of subarachnoid haemorrhage
- Recent intracranial surgery or serious head trauma or recent previous stroke
- History of intracranial haemorrhage
- Uncontrolled hypertension at time of treatment (e.g., >185mm Hg. systolic or >110 m Hg. diastolic)
- Seizure at the onset of stroke
- Active internal bleeding

Thrombolysis

Exclusion criteria (cont.)

Intracranial neoplasm, arteriovenous malformation, or aneurysm.

- Known bleeding diathesis, including but not limited to
  - Current use of oral anticoagulants (e.g., Warfarin) with elevated INR.
  - Administration of heparin within 48 hours preceding the onset of stroke and an elevated activated partial thromboplastin time (aPTT) at presentation
  - Platelet count < $100x10^9$ per litre

Thrombolysis

Pharmacokinetics

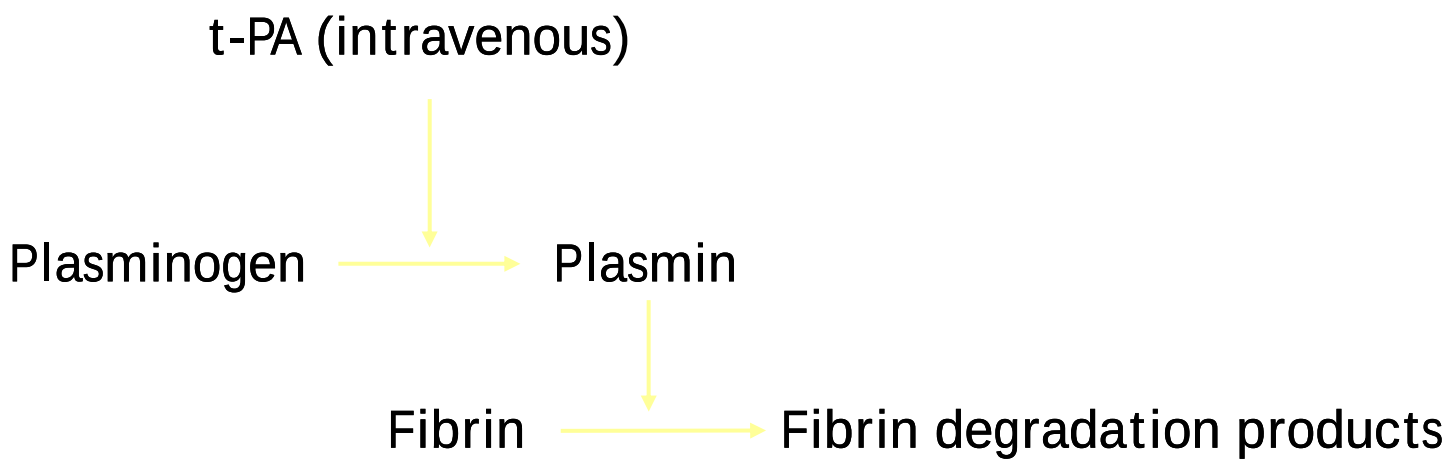
Rapidly cleared from plasma

- Initial distribution phase half life <5mins
- Terminal elimination phase 40 mins

- If infusion stopped
  - 50% cleared from plasma within 5 mins
  - 80% cleared from plasma within 10 mins

Thrombolysis

rt-PA (Actilyse) Mode of action



Thrombolysis

Dosage

- 0.9mg/kg/body weight up to a maximum of 90mg
- Dilute with sterile water to 1mg/ml
- Give 10% of dose as bolus injection
- Give 90% as infusion over 1 hour

Thrombolysis

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Patient Weight					
Stones	Lbs	Kg	Bolus	Infusion	Total Dose
15	10	100kg	9.0mg	81.0mg	90.0mg
14	13	95kg	8.6mg	76.9mg	85.5mg
14	2	90kg	8.1mg	72.9mg	81.0mg
13	5	85kg	7.7mg	68.8mg	76.5mg
12	8	80kg	7.2mg	64.8mg	72.0mg
11	11	75kg	6.8mg	60.7mg	67.5mg
11	0	70kg	6.3mg	56.7mg	63.0mg
10	3	65kg	5.9mg	52.6mg	58.5mg
9	6	60kg	5.6mg	50.4mg	56.0mg
8	9	55kg	5.0mg	44.5mg	49.5mg
7	12	50kg	4.5mg	40.5mg	45.0mg
7	1	45kg	4.1mg	36.4mg	40.5mg
6	4	40kg	3.6mg	32.4mg	36.0mg
5	7	35kg	3.2mg	28.3mg	31.5mg
4	10	30kg	2.7mg	24.3mg	27.0mg

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Post- Thrombolysis

Post-Thrombolysis

First 24hrs of Care:

- Stroke nurse / medic must be present from infusion to safe transfer to ASU
- Thrombolysis observations for 24 hrs as per pathway
- 24-36 hrs repeat CT scan
- No antiplatelets for 24 hrs
- No indication for concomittant heparin
- No IM injections (48hrs), catheterisation or invasive procedure (36hrs) - unless unavoidable
- IV access

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

NHS

Post-Thrombolysis

What can go wrong:

- Early intra-cerebral haemorrhage
- Deteriorating conscious level due to oedema from infarct (but cannot distinguish from haemorrhage clinically)
- Other bleeding (unusual)
- Hypertension (>185/110mmHg)
- Anaphylaxis

Post-Thrombolysis

Pulse, BP, O_2 saturation and conscious level:

Example monitoring of blood pressure;

- Every 15 mins for the first 2 hours (manual BP)
- Every 30 mins for the next 6 hours (automatic BP) = 8 hrs
- Hourly for further 12 hours = 20 hrs
- 2 hourly for 18 hrs = 38 hrs total
- Then 4 hourly (NB - Neurological observations done at same time as BP)

This is to detect hypertension, hypotension, bleeding or early neurological deterioration. (NB. If ICH, BP goes up and pulse goes down)

Post-Thrombolysis

High blood pressure (target maximum BP <185/110mmHg)

If above this range

- Inform Dr if any single reading >230/120mmHg
- Check for pain and treat cause
- Recheck after 5 minutes.
- If BP 230/120mmHg on single reading or >185/110mmHg on two readings 5 minutes apart, suggested management is:

  - Nitrate infusion according to BP (local protocol)
  - Labetalol 10mg IV repeated 10-20 minutes (may mask bradycardia as early sign of raised intracranial pressure)

Post-Thrombolysis

Low blood pressure (target minimum systolic BP >95mmHg)

If below this range

- Stop nitrate infusion
- Check for external bleeding
- Recheck after 5 minutes.
- If BP still below range, suggested management is:

  - Inform Dr
  - Give IV fluids as appropriate (local protocol)
  - Urgent blood for FBC and clotting

Post-Thrombolysis

O_2 Saturations (target minimum 95%)

If lower than this level:

- Sit Patient up
- Supplementary O^2 as necessary
- Inform Dr

Post-Thrombolysis

Conscious level (a ↓ of 2 points or more – taken as significant)

If conscious level score drops by this much, or other reason to suspect neurological deterioration then :

- Stop infusion
- Inform Dr
- Check clotting
- Consider repeat CT scan
- Consider cryoprecipitate

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

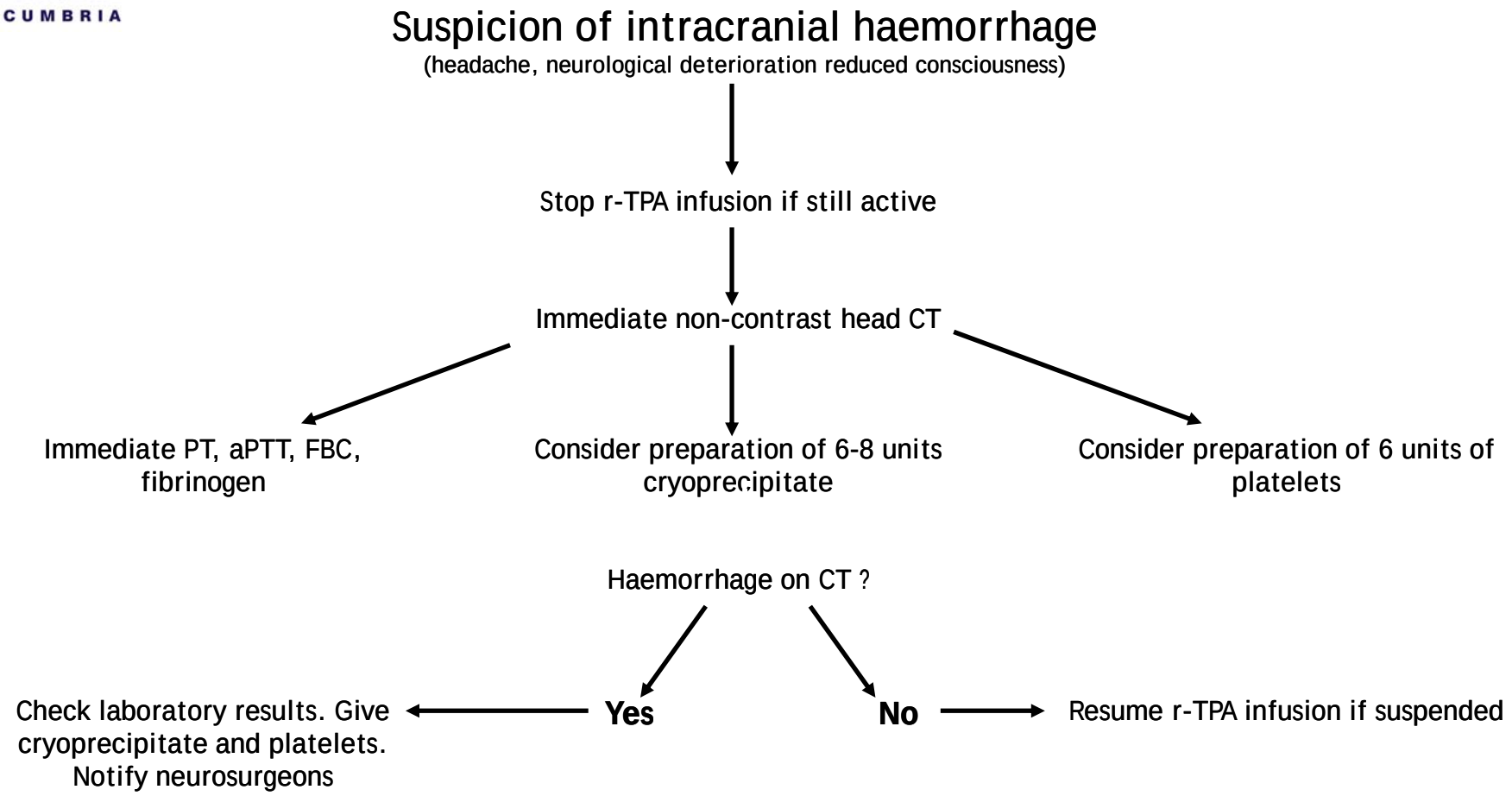
NHS

Post-Thrombolysis

Decreased GCS, signs of raised intracranial pressure / intracranial bleeding :

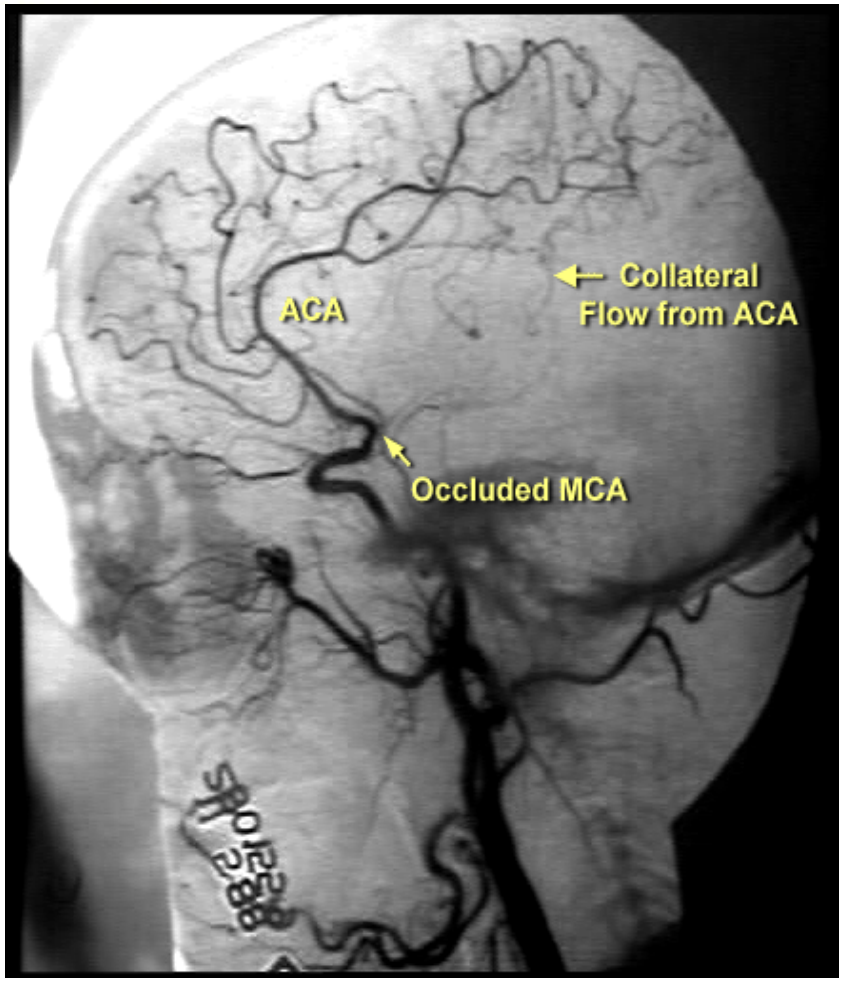
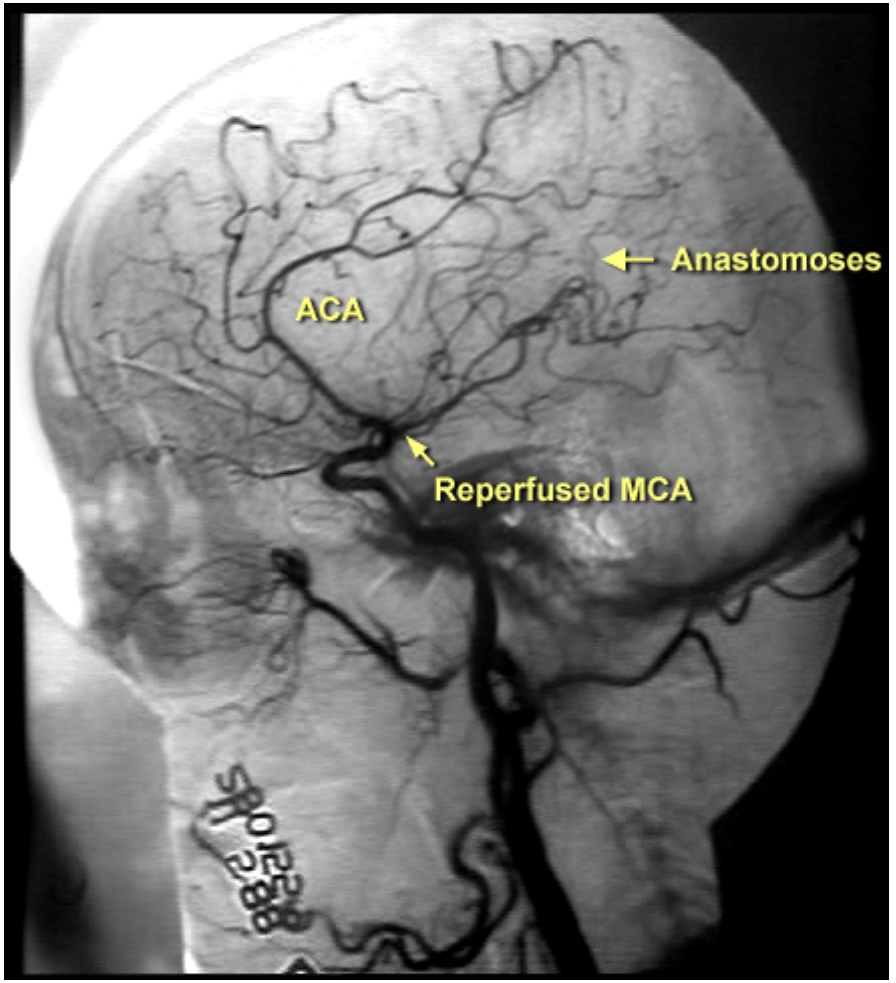
- Unequal pupils
- Drop in consciousness
- Drowsiness
- Nausea, vomiting, sometimes photophobia
- Raising BP & falling pulse

Post-Thrombolysis



Khaja AM, Grotta JC (2007) Lancet 369:324

Cardiac & Stroke Networks LANCASHIRE & CUMBRIA

Reperfusion After Thrombolysis

NHS