

# Stroke – An Overview

Dr Declan O’Kane MD MRCP(UK) DipCompSci(Cantab)  
Consultant Physician VOL

# Stroke - Topics

1. Terminology
2. Prevention – primary and secondary
3. Acute treatment
4. Stroke Units and Teams
5. Future developments

# Terminology

- Cerebrovascular Accident (CVA) – Not a recommended term
  - Accident ? No it is preventable
  - Medical Jargon – Most people understand “stroke”
- ‘Stroke’
  - State side of stroke + disability
  - eg. Left sided Ischaemic Stroke with Right hemiparesis and Right homonymous hemianopia and an expressive dysphasia

# Transient Ischaemic Attack – Definition outdated

- Neurological deficit of presumed vascular origin lasting less than 24 hours
- Most really last minutes
- Brain Infarction occurs with ischaemia > 1 hour
- When does a TIA become a stroke in these days of thrombolysis ?
- Many would suggest limiting time to 1 hour
- Alternative terminologies being discussed – ‘Brain Attack’

# 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

# Stroke Prognosis

## Death at 1 yr

- Primary ICH      62 %      Worst
- TACI              60%
- PACI              16%
- LACI              11%      Least worst
- POCI              19%

# Stroke Prevention

# Transient Ischaemic Attack

- Transient cerebral ischaemia is a sign of impending stroke ( x 13 fold the risk of stroke )
- Data from the Framingham study have shown that the risk of a permanent neurological deficit rises dramatically after a patient has experienced a TIA
- Approximately 60 percent of patients with a completed stroke have had premonitory TIAs.
- TIA May be due to
  - low flow with inadequate collateral blood supply - typically brief, repetitive, stereotyped spells and herald strokes occurring in the territory of the internal carotid artery
  - embolic TIAs are usually single and more prolonged

# Transient Ischaemic Attack

- Aspirin reduces risk of stroke by 15-20%
- Carotid endarterectomy (CEA) should be considered for patients with large vessel atherothrombotic disease in the internal carotid artery that causes low flow or embolic TIAs
- CEA should be done quickly
- Virtually all patients with atrial fibrillation who have a history of stroke or TIA should be treated with warfarin in the absence of contraindications

# 1° Prevention of Stroke

Lifestyle changes - Cigarette smoking,  
alcohol use, Exercise, Diet

Risk Factors – Hypertension, MI, AF,  
Diabetes Mellitus, Hyperlipidaemia,  
asymptomatic carotid artery stenosis

Gorelick et al JAMA 1999;281:1112-1120

# 1° Prevention of Stroke – Blood Pressure

- Most common treatable risk factor
- Direct relationship BP – Stroke
- 5-6 mmHg drop reduces stroke by 42%
- Treatment of Systolic HTN in elderly reduced stroke by 37%
- Especially effective – ACEI and ARBs ?

# 1° Prevention of Stroke – Blood Pressure

- HOPE study (Ramipril) showed 22% reduction more than placebo in vascular death and stroke 32%
- LIFE trial suggested losartan better than Atenolol
- ALLHAT trial – chlorthalidone more effective than Lisinopril or doxazosin ?  
Wrong ACEI

## 2° Prevention of Stroke – Blood Pressure

- PROGRESS TRIAL (6,105 patients)
- Perindopril ± Indapamide vs Placebo
- 28% reduction in stroke (also ICH and MI)
- Normotensive and hypertensive patients benefited
- Average reduction was 9/4 mmHg
- Perindopril group only 5/3 mmHg reduction had no benefit !
- Perindopril ± Indapamide 12/5 mmHg reduction and maximal benefit

# Lipids and 1° Stroke Prevention

- Cholesterol – Stroke relationship not shown until MRFIT trial
- WOSCOPS suggested 10% reduction in stroke but not significant as few events
- 4S trial retrospectively looked at stroke and found 30% reduction in those with Simvastatin
- CARE study showed stroke reduction with Pravastatin
- PROSPER study showed no stroke reduction in elderly patients with Pravastatin
- Added effects of statins – plaque stabilisation, reduction of radical and inflammatory markers and antiplatelet effects

# 1<sup>o</sup> and 2<sup>o</sup> Stroke Prevention and Antiplatelet Therapy

- No clear evidence of aspirin in primary prevention of stroke (unlike MI)
- Secondary Prevention
  - Canadian study 1300 mg aspirin/ day showed 50% reduction in death / stroke in males only
  - Low doses (75 mg, 81 mg) have been suggested to preferentially inhibit platelet TXA<sub>2</sub> and not endothelial PGI<sub>2</sub>
  - Low doses have been shown to be equally effective

# Antiplatelet Therapy

- **Ticlopidine** (Blocks ADP dependant platelet aggregation)
  - Showed significant effect greater than aspirin but toxic - Diarrhoea, rash, neutropaenia
- **Clopidogrel** (action similar to ticlopidine)
  - CAPRIE study of 19,000 showed minimal benefit over aspirin
  - CURE trials of Aspirin + Clopidogrel -Greater efficacy for Acute coronary syndrome with increased bleeding
  - MATCH trial ongoing looking at stroke prevention with combination Aspirin + Clopidogrel

# Antiplatelet Therapy

- Combination of extended release [Dipyridamole](#) and aspirin (25/200 mg twice daily) is recommended
- Glycoprotein IIb/IIIa platelet receptor antagonists, have been used in cardiac revascularisation and are currently being evaluated in ischaemic stroke patients

# Stroke Prevention

- Glucose and electrolytes and LFTS
- FBC ESR
- CXR and ECG
- CT Head
- Cardiac echo
- Carotid ultrasound
- Coagulation screen – young and cryptogenic strokes

# Stroke Prevention

- Smoking - a meta-analysis of 32 studies found that smoking was associated with an increased risk of stroke
- Diet changes (nonhydrogenated unsaturated fats, whole grains, omega-3 fatty acids) reduce coronary artery disease. Evidence for role in preventing stroke lacking
- Individuals with high fibre intake have a 40 to 50 percent reduction in the risk of CHD and stroke compared with low intake
- Antioxidants - Results of a number of randomized trials are now available and show largely no significant clinical benefits on CVD
- Alcohol - Individuals who consume small to moderate amounts of alcohol have lower risks of ischaemic stroke but higher risks of hemorrhagic stroke

# Surgical Prevention of Stroke

Carotid stenosis measured by Carotid ultrasound which combines B-mode and Doppler ultrasound

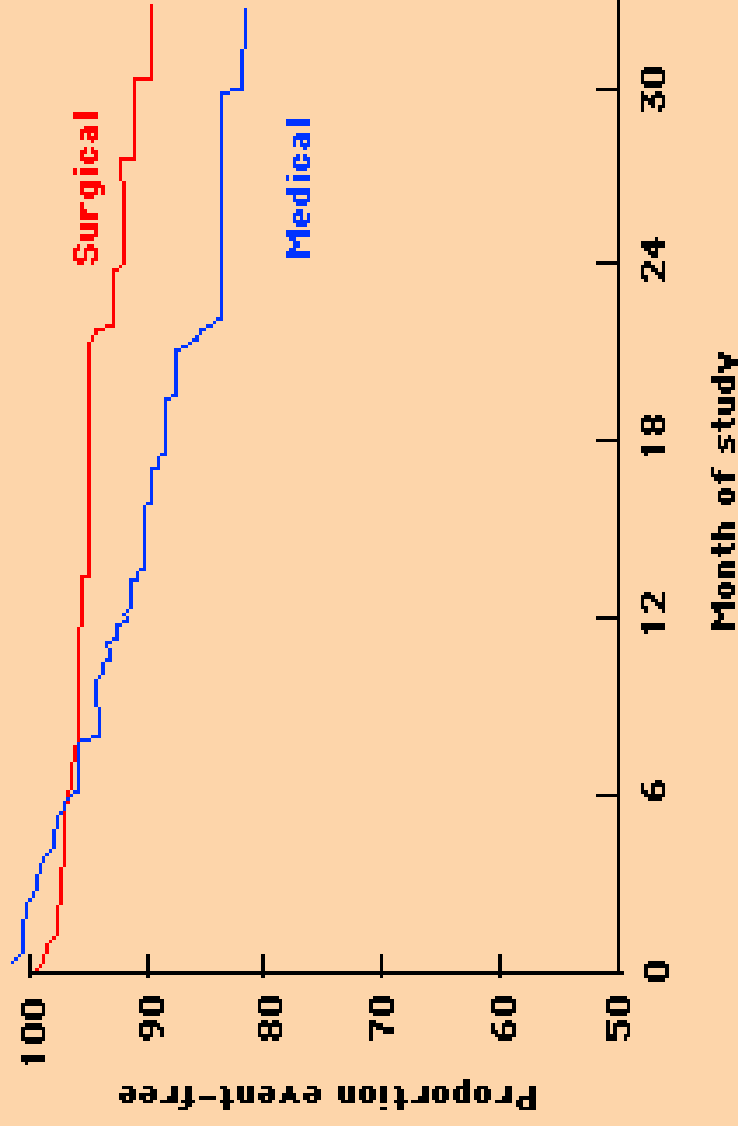
Two major trials, the North American Symptomatic Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST)

Carotid Endarterectomy advocated in fit patients

- with 70% - 99 % stenosis internal carotid artery
- Symptoms suggestive of TIA or non-disabling stroke in the corresponding vascular territory

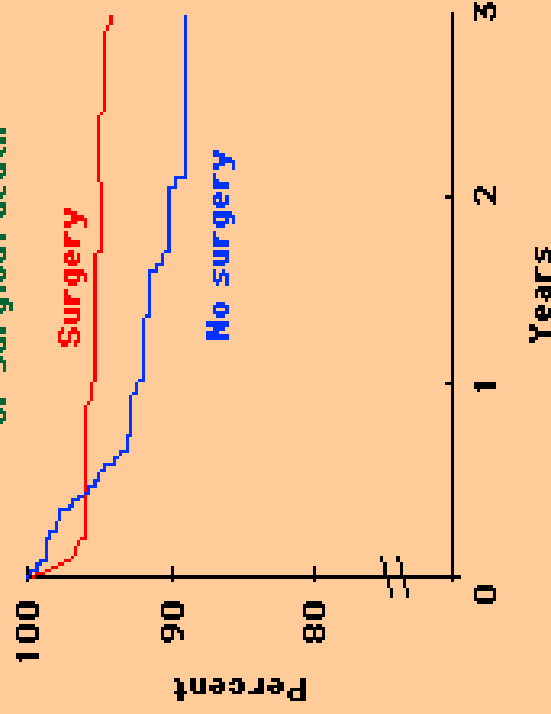
# Surgical Prevention of Stroke in the Elderly

Subset analysis of patients ages 75 and older found that elderly patients with 50 to 99 percent stenosis benefited more from CEA than younger patients - CEA should not be withheld from appropriately selected, fit patients over the age of 75.

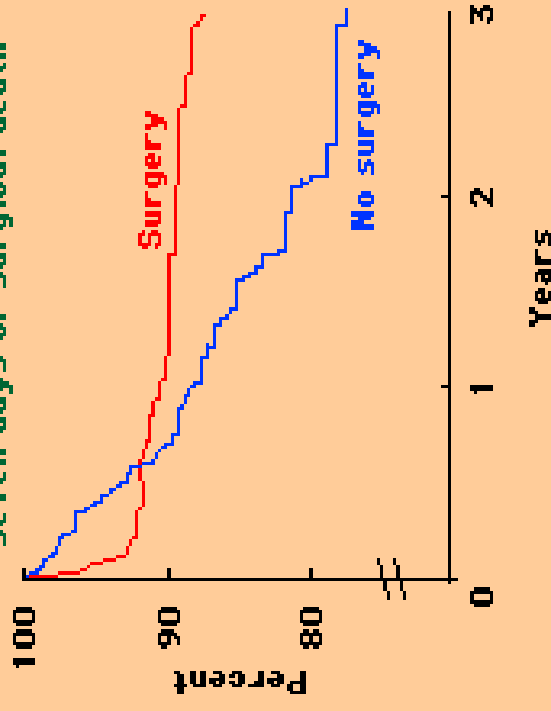


**Carotid endarterectomy reduces major stroke and death in symptomatic patients with severe stenosis** In 659 patients with a prior nondisabling stroke or TIA associated with a carotid stenosis of 70 to 99 percent, carotid endarterectomy significantly reduced the incidence of a major stroke or death at two years ( $p < 0.01$ ). (Data from North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med* 1991; 325:445.)

Disabling or fatal stroke or surgical death



Any stroke lasting more than seven days or surgical death



**Carotid endarterectomy prevents stroke in symptomatic patients with a severe stenosis** The European Carotid Surgery Trial included 778 patients with a history of a stroke, TIA, or retinal infarct who had a severe carotid stenosis (70 to 99 percent). Left panel: The percent of patients free of disabling or fatal stroke was higher with carotid endarterectomy than medical therapy, even when considering surgical death (94 versus 89 percent,  $p < 0.05$ ). Right panel: The percent of patients free of any stroke lasting more than seven days was also higher with carotid endarterectomy than medical therapy, even when considering surgical mortality (87.7 versus 78.1 percent,  $p < 0.01$ ). (Data from European Carotid Surgery Trialist Collaborative Group. *Lancet* 1991; 337:1235.)

# Importance of 'Silent Stroke'

Infarcts with no clinical history of stroke or TIA seen on imaging

In the Rotterdam Scan Study, patients with silent brain infarcts were at significantly increased risk for subsequent stroke

Accumulating evidence that a burden of 'silent stroke' disease found by MRI is to be blamed for many of the features of 'ageing' – cognitive decline, immobility, incontinence, falls etc..??

# Acute treatment of Stroke

# Stroke

- The mortality from the acute event is about 20 percent
- Approximately 50 percent of patients are alive after five years

# Ischaemic Cascade

- Irreversible damage begins at immediately at the core
- The surrounding area (penumbra) may be viable for up to 6 hours
- Process of stroke injury at cellular level called the ischaemic cascade
- ATP depletion, Membrane pumps fail, Calcium mediated cytotoxic reactions and release of excitatory neurotransmitters such as glutamate
- Another target for therapeutic interventions

# Early intervention is Essential

- (*In theory*) Penumbra salvageable with thrombolysis and/ or neuroprotective agents
- Reperfusion injury and ischaemic cascade targeted by neuroprotective agents – nothing useful yet
- IV thrombolysis (t-PA) given within 3 hours improves functional outcome and reduces neurological impairment

# Thrombolysis of Stroke

- **NINDS trial** — The NINDS (National Institute of Neurological Disorders and Stroke) [alteplase](#) (t-pa) stroke study is the only large, randomized trial that documented benefit from the treatment of acute ischaemic stroke with intravenous thrombolytic therapy. The success of the trial is widely believed to reflect its strict exclusion criteria and its treatment of patients within three hours of the onset of symptoms.
- Thrombolysis after 3 hours is disastrous
- Streptokinase increased mortality

# Thrombolysis of Stroke

1. Inclusion criteria for intravenous tPA use in acute stroke include the following:
2. More than a minimal neurological deficit (greater than minimal weakness, isolated ataxia, isolated sensory deficits, or isolated dysarthria)
3. Stroke symptoms must be present for at least 30 minutes and not significantly improve before treatment. Symptoms must be distinguishable from an episode of generalized ischaemia (i.e. syncope), seizure, or migraine disorder.
4. Time of onset <3 hours
5. No CT scan evidence of ICH

# Thrombolysis of Stroke

NINDS trials, the rate of symptomatic ICH (ie, clinical worsening due to new ICH) 24-36 hours after treatment was 6.4% with tPA versus 0.6% without tPA.

Three-month mortality was not significantly different between the two groups, despite a 10-fold increase in symptomatic intracerebral haemorrhage

After 12 months, patients treated with alteplase were at least 30 percent more likely to have minimal or no disability, although mortality rates did not differ significantly between the two treatment arms

# NINDS recommended Targets

- Door to Doctor 10 minutes
- Access to Neurological expertise 15 minutes
- Door to CT completion 25 minutes
- Door to CT interpretation 45 minutes
- Door to treatment 60 minutes
- Admission to monitored bed 3 hours

# Thrombolysis – Exclusion Criteria

Rapidly improving neurological signs

Systolic blood pressure (SBP) greater than 185 mm Hg or diastolic blood pressure (DBP) greater than 110 mm Hg or aggressive (continuous intravenous) treatment required to lower BP to this range

Seizure at stroke onset

Symptoms suggestive of subarachnoid haemorrhage

Suspected acute pericarditis

## Thrombolysis – Exclusion Criteria

Stroke or serious head trauma within 3 months

Major surgery or serious bodily trauma within 2 weeks

History of a prior ICH

Intracranial neoplasm

Arteriovenous malformation or aneurysm

GI or urinary tract hemorrhage within 21 days

Arterial puncture at a noncompressible site or lumbar puncture within 1 week

Concomitant oral anticoagulant (INR > 1.7)

# Thrombolysis – Exclusion criteria

- Platelet count  $<100 \times 10^9/L$
- Prothrombin time (PT)  $>15$  (INR  $>1.7$ )
- Activated partial thromboplastin time (aPTT) elevated beyond reference range
- Glucose  $<50$  mg/dL or  $>400$  mg/dL
- Positive pregnancy test (in woman of childbearing age)
- Blood should be sent for type and screen in case transfusions are required

# Thrombolysis - Scanning

- Non contrast head CT scan
- An immediate head CT scan is imperative.
- Any Haemorrhage is an absolute contraindication to thrombolysis.
- Early signs of major infarction on initial CT scan (eg, mass effect, oedema, hypodensity involving more than one third of the middle cerebral artery territory) are a reason for caution in the use of thrombolytic therapy, because the risk of haemorrhage is increased.

# Thrombolysis – Practical Aspects

1. Arrange for an emergency head CT scan and laboratory studies.
2. Monitor BP at least every 15 minutes before tPA. If SBP greater than 185 mm Hg or DBP greater than 110 mm Hg on 2 successive readings, treat with intravenous labetalol bolus (or other suitable agent).
3. BP must be under these parameters to administer tPA.
4. Establish intravenous access for hydration and thrombolytic therapy.
5. Mix tPA as soon as the patient is deemed to be a potential candidate for treatment
6. Monitor for improvement of neurological deficits.
7. Place a Foley indwelling catheter and nasogastric tube, if necessary, prior to starting tPA.
8. During and after tPA infusion, monitor BP at least every 15 minutes for 2 hours.

## Complications – Intracerebral Haemorrhage

ICH may be signaled by acute hypertension, headache, neurological deterioration, and nausea or vomiting.

If ICH is suspected, obtain an emergent head CT scan and obtain PT, aPTT, platelet count, and fibrinogen.

If ICH is present on CT scan, evaluate lab studies and administer, if needed, 6-8 units of cryoprecipitate containing fibrinogen and factor VIII, 6-8 units of platelets, and/or fresh frozen plasma.

Neurosurgery Haematology

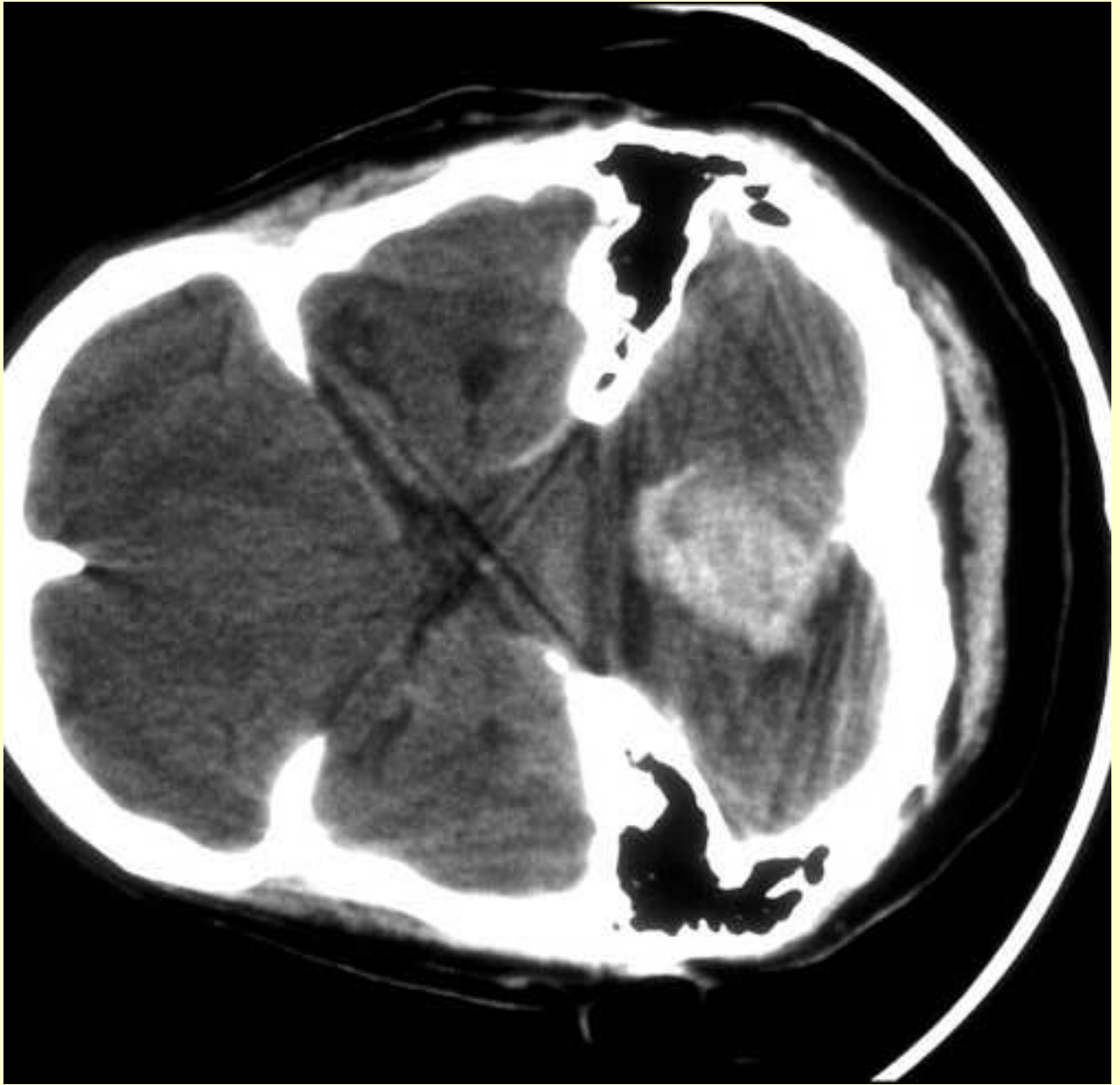
Haemorrhage



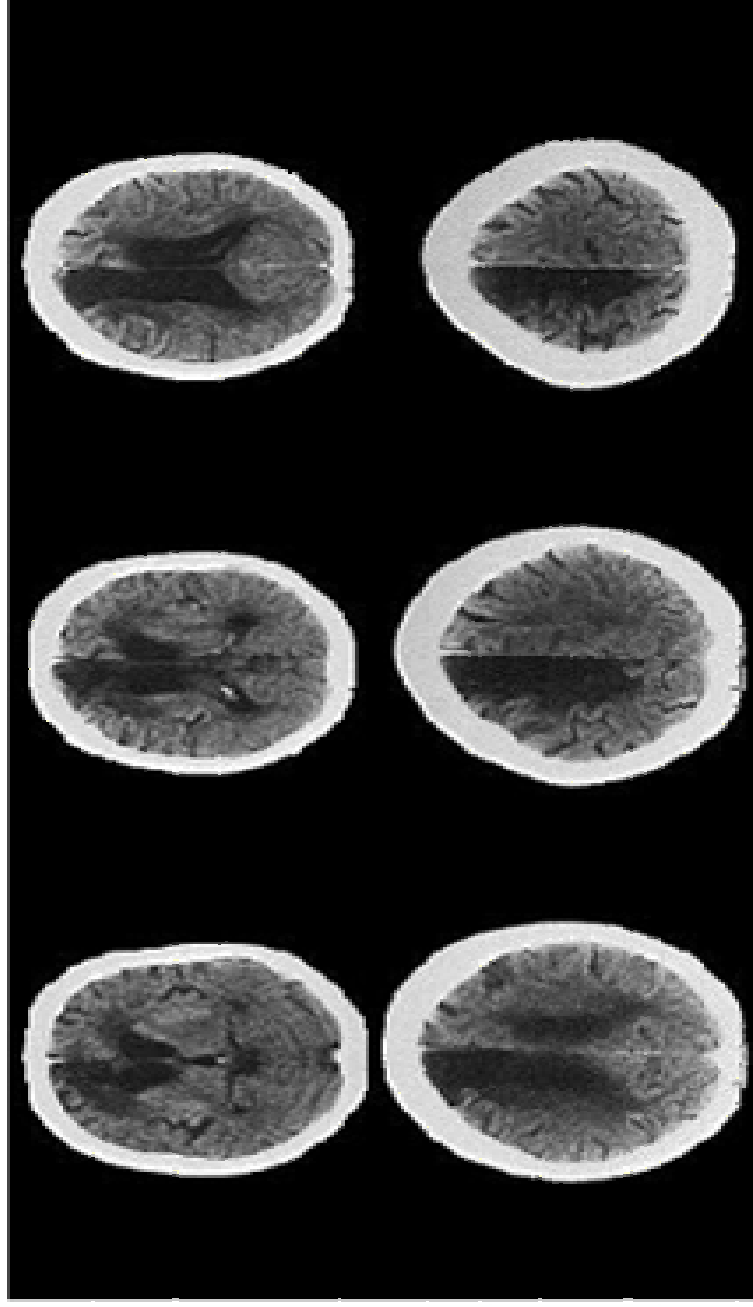
# Summary - Thrombolysis of Stroke

- Current evidence suggests thrombolysis is Beneficial
- Currently Thrombolysis for acute ischaemic stroke is best given as part of a clinical trial
- Requires significant organizational resources pre-hospital and then rapid assessment CT/ Radiologist/ Labs /Experienced physician
- Patients need to know to recognise early signs of stroke and get help early
- In USA they advertise 'CALL 911 for stroke'

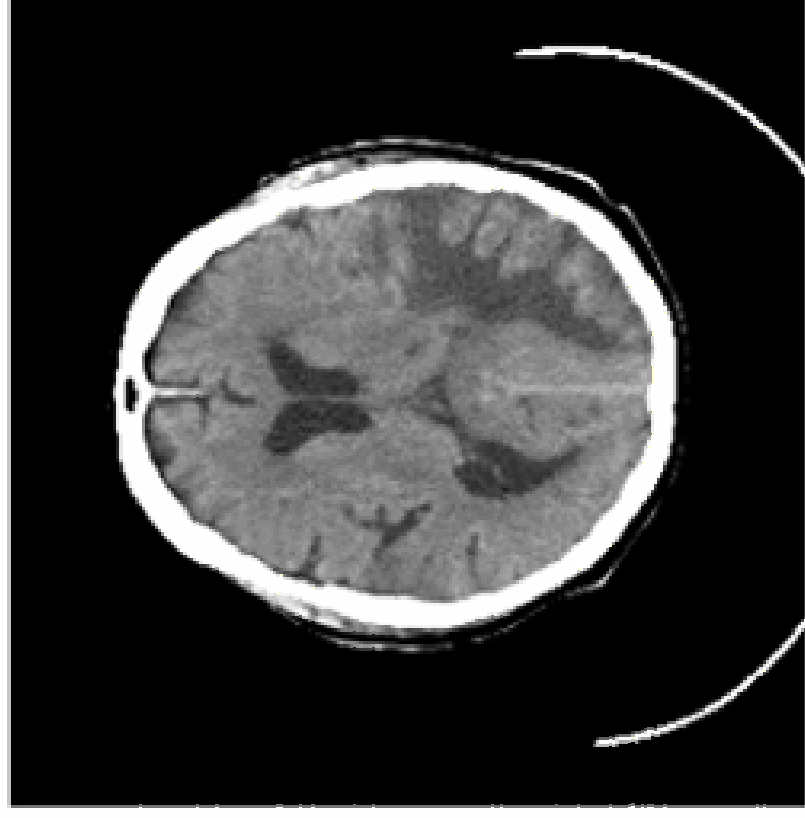
# CT scans



# Anterior Cerebral Artery Ischaemic Stroke



# Ischaemic Stroke In Posterior Branch Of Middle Cerebral Artery



# Medical Acute Stroke Management

- Consider Thrombolysis – as discussed
- Aspirin 300 mg initially and then 75 mg od
- Blood pressure medications stopped for first week though evidence is controversial.
- Relative Hypotension reduces blood flow around stroke area
- Treat severe persisting hypertension
- Warfarin started day 10 if indicated

# Common Stroke Unit Issues

- IV fluids – avoid 5% Dextrose and excess fluid administration
- Swallowing
  - Nil orally initially
  - SALT assessment + IV fluids
  - Temporary NG feed if appropriate
  - PEG placement if appropriate
  - Try to ensure nutrition in all patients

# Common Stroke Unit Issues

- O<sub>2</sub> if SaO<sub>2</sub> < 90 % or hypotensive
- Avoid hyperthermia – PR/PO  
Paracetamol if necessary
- Blood glucose – maintain normoglycaemia
- Antidepressants – shown to be useful in stroke related depression
- Anticonvulsants where needed

# Stroke Unit and Rehabilitation Team

Stroke recovery is really about having a good  
Caring dedicated experienced rehab team

- Medical
- Nursing
- Occupational therapy
- Physiotherapy
- Social Work for discharge planning
- Speech and Language Therapy
- Dietician
- Voluntary Services

# Rehabilitation Team

- Weekly meeting
  - Set goals
  - Determine recovery eg Barthel
  - Share information
  - Discharge planning

# Future Developments

# Future Developments

- Carotid angioplasty and carotid stent placement have also been considered for patients with atherothrombotic lesions that are thought to be responsible for low flow TIAs
- There are as yet no controlled studies that have adequately defined the role of carotid angioplasty and stent placement in the treatment of carotid disease.
- Intraarterial thrombolysis

# Future Developments – Neuroprotective agents

## Neuroprotective Agents

Drug	Action
Fiblast	Basic fibroblast growth factor
*Aptiganel hydrochloride	NMDA receptor ion-channel blocker
*Selfotel	NMDA receptor antagonist
*GV 150526	NMDA receptor glycine site blocker
YM90K	AMPA receptor antagonist
*Tirilazad	Fe <sup>3+</sup> -generated free radical scavenger
Pergorgotein	Polyethylene glycol superoxide dismutase
*Enlimomab	Granulocyte adhesion blocker
*Lubeluzole	Na <sup>+</sup> -channel blocker
Riluzole	Na <sup>+</sup> -channel blocker
*Phosphenytoin	Na <sup>+</sup> -channel blocker
SNX111	N type Ca <sup>++</sup> -channel blocker
*Nimodipine	L type Ca <sup>++</sup> -channel blocker
*Clomethiazole <sup>3</sup>	Potentiates GABA
BMS-204352	Ca <sup>++</sup> -dependent K <sup>+</sup> -channel agonist
*Citicoline	Phospholipid precursor

\*Completed trial in stroke patients did not demonstrate beneficial effect on the primary study endpoint.

# Future Developments - Mechanical thrombolysis in acute stroke

Endovascular Photo Acoustic recanalization  
(EPAR) catheter

