

Acute brain ischaemia

Organ specific problems

Update August 2010

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LEARNING OBJECTIVES

After studying this module on Acute brain ischaemia, you should be able to:

1. Distinguish the possible causes of stroke
2. Differentiate an ischaemic from a haemorrhagic stroke
3. Manage complications in a stroke patient
4. Identify and initiate timely treatment options

FACULTY DISCLOSURES

The authors of this module have not reported any associated disclosures.

DURATION

7 hours

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INTRODUCTION

The cerebrovascular event rate is as high as the coronary vascular event rate. Stroke is, after cardiovascular disease and cancer, the third most common cause of death in industrialised countries. The yearly incidence is estimated to be between 100 and 200 per 100,000. Furthermore, stroke is the most important cause of morbidity and long-term disability in Europe as well as in other industrialised countries. This imposes an enormous economic and social burden.

Stroke is a major cost to society in both human and economic terms

Increasing pathophysiological knowledge and the expansion of therapeutic options have dramatically changed the management of stroke patients over the last ten years. As a result, acute stroke is now recognised as a medical emergency.

Stroke is an emergency

Many diagnostic and therapeutic advances have been accomplished and assessed; promising approaches are under way, while others have been abandoned for lack of effect. Despite tremendous research efforts, only four aspects of *acute* stroke therapy have been shown to improve patient outcomes in acute ischaemic stroke in trials of sufficient quality:

- Stroke care in specialised units (Stroke units)
- Platelet inhibitors such as acetylsalicylic acid within 72 hours
- Intravenous thrombolysis within 4.5 hours
- Hemicraniectomy within 48 hours (see reference below)



Donnan GA, Fisher M, Macleod M, Davis SM. Stroke. *Lancet* 2008; 371(9624): 1612-1623 Review. PMID 18468545

The intensivist is involved in stroke care when cardiovascular (e.g. blood pressure instability or arrhythmia) or respiratory dysfunction (e.g. pneumonia or compromised airway) has developed. Moreover, there are certain types of ischaemic stroke and conditions related to stroke that are often treated in the intensive care unit (ICU).

- Large, space-occupying hemispheric infarct
- Space-occupying cerebellar infarct
- Basilar artery thrombosis
- Septic embolic infarction secondary to bacterial endocarditis
- Stroke associated with cardiothoracic surgery
- Pre- and post-intervention care of stroke-related angiography.

In addition to providing supportive therapy, arranging appropriate imaging and specific therapies, the intensivist may have to evaluate cerebral circulation and oxygenation at the bedside by clinical assessment and specific investigations such

as transcranial Doppler and intracranial pressure (ICP)/cerebral perfusion pressure (CPP) measurement.

In some specialised ICUs, multimodal neuromonitoring involving electroencephalography (EEG), evoked potentials (EP), invasive microdialysis, invasive oxygen tension, and invasive cerebral blood flow (CBF) assessments might be applied. A good understanding of the stroke process can facilitate better performance and provision of good quality care in the ICU. You may find it useful to review the following references before starting this module.



European Stroke Organisation (ESO) Executive Committee; ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovasc Dis* 2008; 25(5): 457–507. PMID 18477843

Update January 2009. View PDFs, Slideshows and Teaching Tools on <http://www.eso-stroke.org>

Rothwell PM, Coull AJ, Giles MF, Howard SC, Silver LE, Bull LM, et al; Oxford Vascular Study. Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study). *Lancet* 2004; 363(9425): 1925-1933. PMID 15194251

Adams HP Jr, del Zoppo G, Alberts MJ, Bhatt DL, Brass L, Furlan A, et al. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. *Stroke* 2007; 38(5): 1655–1711. PMID 17431204

<http://stroke.ahajournals.org/cgi/content/full/38/5/1655>

<http://www.eusi-stroke.com>

<http://www.americanheart.org>

1. IMMEDIATE TASKS

The main aim of acute management is to:

- Resuscitate, treat and monitor factors that influence the functional outcome and mortality of the stroke patient. These include circulation, oxygenation, body temperature and blood glucose.
- Immediately assess the indication for acute revascularisation.
- Determine the possible cause of the stroke. This will facilitate institution of optimal secondary prophylaxis, with the aim of preventing early recurrences.
- Assess the optimal management location –emergency department (ED), stroke unit (SU) or ICU.

Appropriate triage of stroke patients and the decision to admit a patient to the ICU can best be achieved through the collaboration of neurologists and intensivists. Your management will be most effective if you develop and practise a logical routine along the lines indicated below.

Immediate assessment and treatment

First line assessment and treatment are closely inter-related and include the following tasks:

- Securing the airway and optimising oxygenation
- Haemodynamic stabilisation and fluid administration
- Basic monitoring (including rapid determination of blood glucose)
- Clinical history
- Physical examination (see also Task 2)
- Treatment of patient discomfort (such as agitation, vomiting, etc) that may lead to or increase intracerebral pressure
- Initiation of diagnostic procedures and interventions (see also Task 3).

NOTE

The ABC of resuscitation clearly takes precedence and some procedures may occur in parallel. For example, while taking the patient's history or starting the physical examination, a nurse or other assistant may draw blood, initiate a standard crystalloid infusion, and establish electrocardiogram (ECG) monitoring and pulse oximetry.

Assessment

Clinical history

Taking the clinical history is important to:

- Decide whether it is really a stroke?
- Determine whether the patient is within the time window for reperfusion therapy.

- Obtain clues to the mechanism of the stroke (course of symptoms, risk factors). This may aid the later technical investigative procedures.
- Avoid potential complications of your acute therapy.

In relation to the therapeutic window you should be aware that time is limited and that history taking has to be focused.

History taking and physical examination are crucial but do not delay specific treatment

Consider the following items in history taking:

Focus the questioning

- When did the first symptoms occur? Did the patient awake with symptoms/signs?
- How have the symptoms evolved since onset? How rapidly have symptoms developed?
- Has the patient ever had a stroke before? Has she/he any vascular risk factors?
- What medication is the patient taking?
- Is the patient suffering from diabetes or hypertension?
- Are there contraindications to thrombolytic treatment or anticoagulation?

[Link to PACT module on Basic clinical examination](#)

NOTE

History taking from the patient may be time-consuming, difficult or even misleading in cases of aphasia, severe dysarthria or reduced level of consciousness. Consider early involvement of relatives or other eye witnesses in your history taking. Find out who is the next of kin as they will be important for future management and treatment decisions.

[Link to PACT module on Ethics](#)

Physical examination

The initial physical examination should be brief and focused in order to save time (i.e. no more than 5-10 min). An orienting examination in the acute setting should include:

Focus the neurological examination

- Level of consciousness, orientation in time and place
- Cranial nerves: pupils, visual fields, oculomotor function, facial weakness, gag/corneal reflex, tongue deviation, shoulder elevation
- Higher cortical dysfunction (aphasia, neglect, apraxia)
- Muscle tone, limb pareses/reaction to pain (in patients with reduced consciousness)
- Coordination, gait
- Gross sensory loss, reaction to pain stimulus
- Reflexes: biceps, triceps, knee and ankle jerk, plantars (Babinski).

NOTE

Further, general examination must include: auscultation of heart (arrhythmias, murmurs?) and lung (pulmonary oedema?), cardiovascular status (murmurs over carotid or femoral arteries, pulses).

In patients with severely impaired level of consciousness, the neurological examination will be limited. Nevertheless, examination of pupils, other brainstem reflexes, and the reflex status along with observation of spontaneous activity and reaction to painful stimuli (asymmetry?) may provide enough information for the suspicion of stroke and the possible location of the insult.

For further information regarding clinical findings and their interpretation see Task 2.

Q. You are aware that 5-10 minutes after occlusion or hypoperfusion of a cerebral vessel, neuronal damage is irreversible. What, therefore, can be the justification for acute medical treatment? Why not rather direct your attention to organising rehabilitative measures, dependent on the patient's disability?

A.

- During the first hours of ischaemic stroke, the core of irreversibly damaged tissue is surrounded by the so-called penumbra, an area of functionally impaired but still viable brain tissue, supplied with blood from collaterals. The transformation of this area into infarction due to secondary neuronal damage may be prevented by early vessel reperfusion.
- There are several other factors which influence the mortality and the late functional outcome of the stroke patient during the first two days after stroke onset. These factors can easily be monitored and treated and include haemodynamic stability, blood oxygenation, glucose metabolism and body temperature.
- There are several possible underlying and secondary illnesses and complications in stroke patients that have to be recognised and treated promptly in order to prevent secondary neuronal damage.
- Secondary prevention has to be implemented correctly and rapidly, especially in the case of a transient ischaemic attack.

To some extent you can confirm your suspicion of stroke in patients by simple neurological examination even before cranial computed tomography (cranial CT) and other tests have been performed (see Task 3). However, you cannot distinguish ischaemic from haemorrhagic stroke by clinical examination alone; for that determination a CT or an MRI (if performed with no time delay) is needed.

Treatment



In the next five patients you see with possible stroke, create a diagnostic and therapeutic strategy for their immediate management. Determine whether they would be candidates for reperfusion therapy; if yes – which intervention, if not – why not?

Airway and breathing

The maintenance of adequate ventilation, oxygenation and CO₂ removal is an important prerequisite for the preservation of the metabolic activity in the penumbra.

Avoid hypoxia at all costs

Q What kind of respiratory problems might be expected in stroke patients?

A:

- Hypoventilation due to impaired respiratory drive
- Coma
- Lesions of respiratory centres in the brainstem and upper spinal cord
- Upper airway obstruction due to oropharyngeal muscular dysfunction
- Aspiration due to impaired airway protection
- Neurogenic pulmonary oedema (very rare)
- Later stage: (aspiration) pneumonia.

Q Which stroke patients are at special risk of airway and oxygenation disturbances and consequently require continuous respiratory monitoring?

A. These problems may be expected in patients with brainstem infarction, large hemispheric infarctions or space occupying lesions.



Torbey MT, editor. Neurocritical Care. Cambridge: Cambridge University Press; 2010. ISBN: 978-0-521-67689-2

Critical Care of Acute Stroke. In: Ropper AH, Gress DR, Diringner MN, Green DM, Mayer SA, Bleck TP. Neurological and Neurosurgical Intensive Care. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2004. ISBN: 0-7817-3196-8. p. 208

Fisher M, editor. Stroke Therapy. 2nd ed. Boston: Butterworth Heinemann; 2001. ISBN: 0-7506-7236-6. p. 225.

The following manoeuvres should be effected without delay:

- Administer oxygen via nasal cannula or face mask when oxygen saturation is <96%.

THINK: What is the physiological basis for maintaining an oxygen saturation of >96%? You may wish to refer to the following reference and reflect on the evidence for the suggested approach.



Rønning OM, Guldvog B. Should stroke victims routinely receive supplemental oxygen? A quasi-randomized controlled trial. *Stroke* 1999; 30 (10): 2033–2037. PMID 10512903

- Avoid and/or treat aspiration
- Place the patient in a secure position (see Task 4)
- Consider intubation in patients with reduced level of consciousness and oropharyngeal muscular dysfunction
- Intubate and ventilate if other measures do not normalise oxygenation and ventilation rapidly and adequately and for airway protection.

About 5% of acute stroke patients require intubation and mechanical ventilation. These interventions in association with the severity of the underlying disease generally carry a poor prognosis. Mechanical ventilation should be aimed at providing optimal oxygenation and avoidance of an elevation in PaCO₂ or a high PEEP level in order not to increase intracranial pressure (ICP).

In the less acute setting, clinical observation and measurement of oxygen saturation by pulse oximetry may be all that is required for respiratory monitoring; if connected to a breathing system, use capnography.

Circulation

Adequate cerebral perfusion is crucial to preserve the penumbra, where cerebral autoregulation is impaired and the cerebral blood flow (CBF) is passively dependent on mean arterial pressure (MAP); post-stenotic flow requires stable circulatory conditions.

The control of blood pressure is a major issue. If the pressure is too high this may exacerbate reperfusion injury to the penumbra and lead to increased oedema, cellular hypoxia or haemorrhagic transformation. If the pressure is too low, CBF in the penumbra can decrease to a level causing irreversible neuronal damage; additionally, this can cause vessels in intact brain regions to dilate, which can then lead to a potential 'steal-effect', further promoting ischaemia in the penumbra.

The approach to circulatory monitoring and treatment of the stroke patient involves:

- Electrocardiography (ECG)
- Frequent non-invasive blood pressure measurement (if the patient is not intubated)
- Insertion of a peripheral venous cannula.

Other monitoring:

- When necessary, particularly if the patient is intubated and ventilated, consider continuous invasive blood pressure measurement.

NOTE Local guidelines often preclude arterial puncture/cannulation before thrombolysis and similar caution is required for other invasive investigations outlined below.

- In selected cases, transthoracic (TTE) or transoesophageal (TEE) echocardiography
- In selected cases, insertion of a central venous catheter to measure central venous pressures or administer vasoactive drugs
- When indicated (e.g. cardiac or septic shock), insertion of catheters for cardiac output monitoring (pulmonary artery or femoral artery thermodilution catheters).

Q. What do you find in the acute stroke patient?

A.

- More than 70% of acute stroke patients are hypertensive
- ECG may show atrial fibrillation (AF), which may suggest an embolic mechanism but may also occur secondary to ischaemic stroke
- Many other bradycardic and tachycardic arrhythmias, including third degree atrioventricular (AV) block or ventricular fibrillation may be seen, especially in hemispheric strokes involving the right insular cortex.

Q. How should you react?

A.

- Tolerate moderate hypertension of 160-220/95-120 mmHg
- Avoid and treat hypotension and/or blood pressure collapse
- Treat arrhythmias that compromise maintenance of adequate blood pressure.



European Stroke Organisation (ESO) Executive Committee; ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovasc Dis* 2008; 25(5): 457–507. PMID 18477843

Update January 2009. View PDFs, Slideshows and Teaching Tools on <http://www.eso-stroke.org>

<http://www.eusi-stroke.com>

Ischaemic stroke. In: Waldmann C, Soni N, Rhodes A, editors. *Oxford Desk Reference: Critical Care*. Oxford: Oxford University Press; 2008. ISBN: 978-0-199-22958-1. p. 370

Q. Give arguments as to why hypertension should or should not be accepted in the acute stroke patient, since in the acute phase a haemorrhagic stroke cannot be excluded?

A. Excessive hypertension may exacerbate acute cerebral bleeding; however 'only' 15% of acute strokes are haemorrhagic. The blood pressure targets for intracerebral haemorrhage (ICH) should be:

- upper recommended limit of 160/95 mmHg in patients without known hypertension. If treatment is necessary, target blood pressure 150/90 mmHg
- upper limit of systolic blood pressure of 180 mmHg if known hypertension and, if treatment is necessary, target blood pressure is 160/100 mmHg.

Most haemorrhagic strokes occur in hypertensive patients, whose cerebral blood flow autoregulation is impaired and whose blood pressure should therefore not be lowered too aggressively. Mean BP reduction should always be limited to <20% of baseline.

[Link to PACT module on Hypertension](#)

Link to **ESICM Flash Conference**: Giuseppe Citerio, Monza, Italy. Blood pressure in brain haemorrhage and stroke: how high is too high? Summer conference, Dublin 2010

NOTE **There are some conditions where these rules for blood pressure management are not applicable e.g.** known or suspected aortic dissection, hypertensive encephalopathy, subarachnoid or intracerebral bleeding, severe heart failure, acute myocardial infarction or unstable angina. In these situations, a compromise has to be achieved.

Basic monitoring

Q. List the priorities for monitoring and justify your choices.

A.

Monitoring	Reason
Arterial blood pressure	Avoid and treat hypotension. Do not treat moderate hypertension.
Pulse oximetry	Provide optimal oxygenation.
ECG	Detect atrial fibrillation, tachycardic or bradycardic rhythms.
Clinical observation	Detect neurologic deterioration or improvement. Detect respiratory or cardiovascular dysfunction.
Blood glucose	Treat hypo- and hyperglycaemia.
Body temperature	Treat fever aiming for normothermia.

NOTE **Due to the time pressures, diagnostic procedures have to be initiated** as soon as possible. You may have to interrupt your clinical assessment to carry out an essential cranial CT. Emergency laboratory tests and monitoring can be performed in parallel (see above).

2. CLINICAL DIAGNOSIS

The history facilitates determination of the possible cause of stroke, especially if technical diagnostic tests are not immediately available. It is also essential for assessment of the reperfusion time window.

Clinical assessment

Clinical examination is important in localising the stroke, determining the extent of the lesion, evaluating prognosis, and assessing overall stability of the patient.

Assessments influence:

- The therapeutic options in the acute phase (e.g. no thrombolysis in extending infarction within the 3-6 hour window)
- Hospital management (e.g. decision about transfer to the ICU)
 - Ideally, all stroke patients should be treated on a stroke unit
 - Indications for admission to the ICU include
 - Respiratory failure
 - Cardiovascular instability
 - Coma
 - Seizures which are not quickly controlled
 - Elective intubation for diagnostic/therapeutic procedures.

Quantitative assessment facilitates observation of the evolution of the lesion (e.g. spontaneous or therapy associated improvement, secondary deterioration).

Q. Why perform such a thorough clinical assessment when a cranial CT is available?

A. Cranial CT in the early phase of ischaemic stroke, and therefore within the therapeutic window can often be negative. Imaging studies always have to be interpreted within the overall clinical context to guide treatment decisions.

Clinical symptoms and signs vary with the brain territory involved. However, some symptoms are frequent:

- Hemiparesis, hemihyperaesthesia
- Aphasia, apraxia, dysarthria, neglect
- Partial or complete hemianopsia
- Disturbances of consciousness, confusion
- Diplopia, vertigo, nystagmus, ataxia.

NOTE **When you are confronted with a patient presenting** with one, or a combination of these symptoms, consider: **Is it really a stroke?**

These symptoms can also be caused by other pathologies, such as inflammatory processes, tumours, some metabolic disorders and intoxications. These possibilities will, in part, need other acute diagnostic and therapeutic investigations.

NOTE

Stroke is a medical emergency demanding rapid appropriate treatment, and has to be confirmed or ruled out immediately!

Differential diagnosis

Stroke is a sudden or rapidly developing neurological deficit. The differential diagnostic considerations below can be of help.

The principal condition to identify in the differential diagnosis of acute stroke is **intracerebral haemorrhage (ICH)**.

Clinical findings favouring the diagnosis of ICH include:

- Onset during a hypertensive crisis
- Progression of symptoms within minutes
- Early, excessive vomiting
- Early/immediate loss of consciousness
- Acute onset of headache.



Intracerebral haemorrhage. In: Waldmann C, Soni N, Rhodes A, editors. Oxford Desk Reference: Critical Care. Oxford: Oxford University Press; 2008. ISBN: 978-0-199-22958-1. p. 366

The diagnosis cannot, however, be confirmed by history and clinical examination alone. Neuroimaging (CT/MRI) is urgently required.

Other differential diagnoses of ischaemic stroke include:

- **Subarachnoid haemorrhage:** sudden occipital headache, meningism, detection of subarachnoid blood on cranial CT and/or in cerebrospinal fluid (CSF).
- **Neoplasm:** neurological deficit developing over many days/months, sometimes with acute exacerbation: e.g. due to worsening oedema or haemorrhage in brain tumours.
- **Sinus (sagittal) venous thrombosis:** early seizures, headache, typical risk factors (head or neck trauma, prior or current malignancy, diabetes, dehydration, prior or current hypercoagulability).
- **Meningitis/vasculitis:** fever, meningism, typical CSF findings.
- **Multiple sclerosis:** symptoms that usually develop over days but in rare cases, symptoms and neurological deficits may develop within hours.
- **Postictal paresis:** Todd's paresis.
- **Migraine**
- **Eclampsia (peripartum).**

Mechanism and localisation of stroke

Prior to reading the next section you may wish to refresh your memory of the normal anatomy of the brain and the deficits likely to follow occlusion of individual cerebral vessels. A useful reference in this regard is:

The mechanism of stroke can often be determined by history taking and clinical examination



Caplan LR. *Caplan's Stroke: A Clinical Approach*. 4th ed. Philadelphia: Saunders Elsevier; 2009. ISBN: 978-1-4160-4721-6

The following mechanisms and types of stroke do not always lead to conditions that have to be treated by the intensivist, however, secondary deterioration in the acute case is always possible.

Microangiopathic or lacunar stroke

The mode of onset and clinical course of lacunar infarcts often differ from those originating elsewhere:

- Preceding transient ischaemic attacks (TIAs) (15-20%) generally occur shortly (several days) before onset of infarction, tend to occur in clusters and are more stereotypical compared with large vessel TIAs.
- Insidious onset and a gradually progressive, 'stuttering' course.
- Lacunar lesions are small and may become symptomatic in regions with a high density of axons and with multiple extensions, e.g. the cerebral peduncles and the brainstem. They may present as:
 - Pure motor stroke
 - Pure sensory stroke
 - Sensory-motor stroke
 - Ataxic hemiparesis
 - Dysarthria-clumsy-hand syndrome.

Systemic embolism

A history of cardiac disease may be mentioned by the patient, relatives or referring doctor. This may involve: mechanical or cardiac valve dysfunction, atrial fibrillation, left atrial and/or ventricular thrombus, dilated cardiomyopathy, recent myocardial infarction (<4 weeks), left ventricular aneurysm, sick sinus syndrome, infective myocarditis, or atrial myxoma.

Characteristic features in the history include:

- Sudden onset, with maximal severity at onset
- Onset usually during activity, in awake state; presentation on awakening is unusual
- Recurrent TIAs in different anatomical areas.

Typical clinical presentation of various arterial territories:

Infarcts of the middle cerebral artery (MCA) territory

- Contralateral motor and/or sensory deficit of face and arm more than leg
- Higher cerebral dysfunction (aphasia, apraxia)
- Conjugated ipsilateral eye deviation in large infarcts
- Homonymous visual field defects, alone or in combination with above.

Infarcts of the anterior cerebral artery territory

- Contralateral hemiparesis with emphasis on the lower limb

Posterior (vertebral, basilar and posterior) circulation infarcts (usually embolic)

- Ipsilateral cranial nerve palsy with contralateral motor and/or sensory deficit
- Bilateral motor and/or sensory deficit
- Disorder of conjugate eye movement (vertical=midbrain, horizontal=pons)
- Cerebellar dysfunction without ipsilateral long-tract deficit
- Altered consciousness
- Dysarthrophonia, dysphagia
- Horner syndrome (also in carotid artery dissection)
- Isolated homonymous visual field defect.

Large artery thrombosis

Large vessel disease may cause stroke by post-stenotic perfusion deficit, sudden atherothrombotic occlusion, or arterio-arterial embolism. The clinical picture may not differ significantly from that in systemic embolism.

However, the clinical history may reveal:

- Typical atherogenic risk factors
- Frequent TIAs, e.g. amaurosis fugax (internal carotid artery stenosis), in the *same* arterial territory
- Onset often during sleep or atherothrombotic stroke during activity, a gradual progression or stepwise course over minutes to hours is characteristic (attributable to gradual accumulation of thrombus or to lowering of blood pressure, e.g. following antihypertensive therapy).

Dissection of cervical arteries

Apart from cardiac embolism, consider dissection of cervical arteries. The (typically younger) patient's history may reveal risk factors such as:

- Recent trauma
- Previous infection

- Signs of connective tissue abnormalities (hyperextensible joints, Marfan syndrome, known mitral valve prolapse).

The characteristic clinical presentation is a focal neurological syndrome in combination with unilateral headache or neck pain, pulsatile tinnitus, and an ipsilateral Horner syndrome in the case of internal carotid artery dissection.

NOTE

Stroke also occurs in **young persons, including children.**

There are many other mechanisms of stroke and stroke-like episodes. You can find further information in the following references.



Caplan LR. Uncommon Causes of Stroke. 2nd ed. Cambridge: Cambridge University Press; 2008. ISBN: 978-0-5218-7437-3

Caplan LR. Caplan's Stroke: A Clinical Approach. 4th ed. Philadelphia: Saunders Elsevier; 2009. ISBN: 978-1-4160-4721-6

3. DIAGNOSTIC PROCEDURES

This task allows us to assess the value of investigative procedures and how far they influence management decisions, for example, in relation to treatment and transfer.

Technical diagnostic tests are performed for the following purposes:

- The main 'switch point' in the direction of your acute treatment and secondary prophylaxis is the early differentiation of ischaemic stroke from intracerebral haemorrhage or subarachnoid haemorrhage (SAH). This is crucial for the early management of stroke.
- Based on the physical and neurological evaluation and skilled use and interpretation of emergency diagnostic tests, different causes of ischaemic stroke can be identified. These may indicate the need for specific therapeutic procedures and influence the choice of a secondary prophylaxis.

The first step can be achieved by performing a non-contrast cranial computed tomography (cranial CT) scan.

NOTE **If there is delay in performing cranial CT**, you may wish to consider other emergency tests, e.g. carotid Doppler. However, all efforts should be directed at avoiding such a delay. The same holds true for MRI.

Cerebral computed tomography (CCT) and its interpretation

See also PACT module on Traumatic brain injury

According to their density the various structures of the head absorb radiation to a different degree. The higher the density i.e. their absorption of radiation, the more opaque is their appearance on the scan: bone, intraparenchymal calcification > blood > thrombosed vessel > grey matter (e.g. thalamus, basal ganglia, cortex), white matter > oedematous brain tissue.

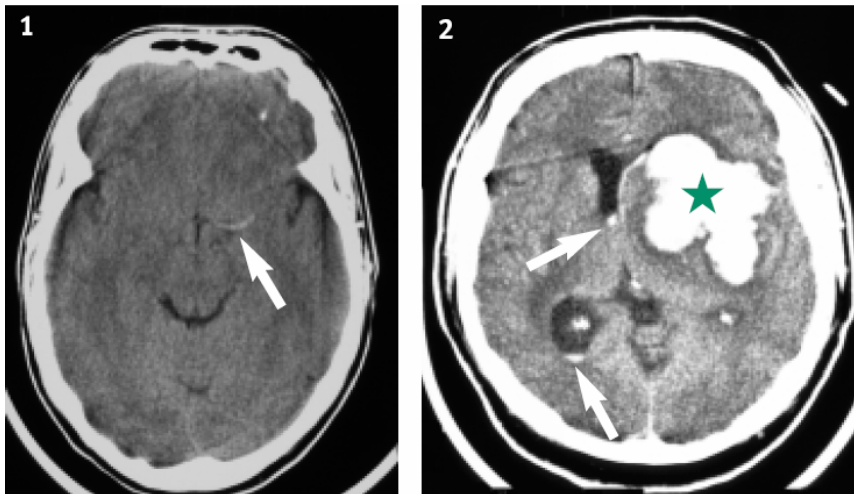
Addition of CT angiography (CTA) and CT perfusion will not only help to make the diagnosis of stroke but these techniques will provide the physician with information on location of vessel occlusion, presence and quality of collateral blood flow, cerebral blood flow, cerebral abscesses and cerebral blood volume. These will allow the use of the so-called ASPECTS score, which has some prognostic properties in terms of reperfusion and clinical outcome.



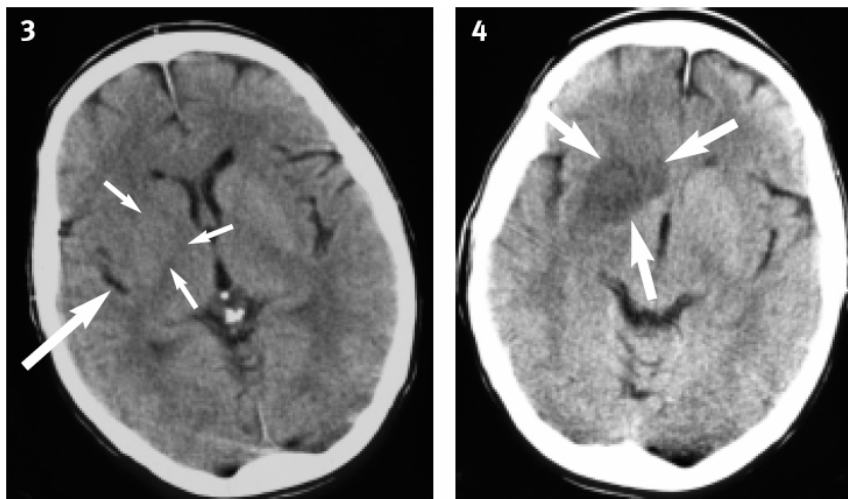
Parsons MW, Pepper EM, Chan V, Siddique S, Rajaratnam S, Bateman GA, et al.
Perfusion computed tomography: prediction of final infarct extent and stroke outcome. *Ann Neurol* 2005; 58(5): 672–679. PMID 16240339

Dzialowski I, Hill MD, Coutts SB, Demchuk AM, Kent DM, Wunderlich O, et al.
Extent of early ischemic changes on computed tomography (CT) before thrombolysis: prognostic value of the Alberta Stroke Program Early CT Score in ECASS II. *Stroke* 2006; 37(4): 973–978. PMID 16497977

NOTE Before examining any CT scan always check the patient's details, the date and time, and the anatomical orientation (i.e. right is left and left is right). The patients in images 1 and 2 presented with severe right-sided hemiparesis and aphasia. The onset of symptoms in both cases was two hours before the scan was taken.



The two patients in images 3 and 4 awoke with left-sided hemiparesis.



THINK in which cases is thrombolytic treatment contraindicated (see Task 4).

Interpretation

Image 3 shows only early signs (see later) which are no longer considered a contraindication to thrombolysis (as long as these signs do not exceed 1/3 of the MCA territory). However, the decision to administer thrombolysis must not be based on imaging alone, and has to include the clinical circumstances, especially the time window. Stroke MRI can be performed in patients with a later or unclear time window as a basis for treatment decisions. That, however, might mean an individual, off-label therapy with recombinant tissue plasminogen activator (rtPA), for which consent should be obtained.

NOTE **This is one important difference between** the European Cooperative Acute Stroke Study (ECASS) and the National Institute of Neurological Disorders and Stroke (NINDS) trial. The US trial included several patients with early signs of infarction (documented to be less than six hours, and occasionally less than three hours, from stroke onset). For further information see the following references.



Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, Larrue V, Lees KR, Medeghri Z, Machnig T, Schneider D, von Kummer R, Wahlgren N, Toni D; ECASS Investigators. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med* 2008; 359(13): 1317–1329. PMID 18815396

[No authors listed] Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. *N Engl J Med* 1995; 333(24): 1581-1587 PMID 7477192

Fisher M, editor. *Stroke Therapy*. 2nd ed. Boston: Butterworth Heinemann; 2001. ISBN: 0750672366. p. 261

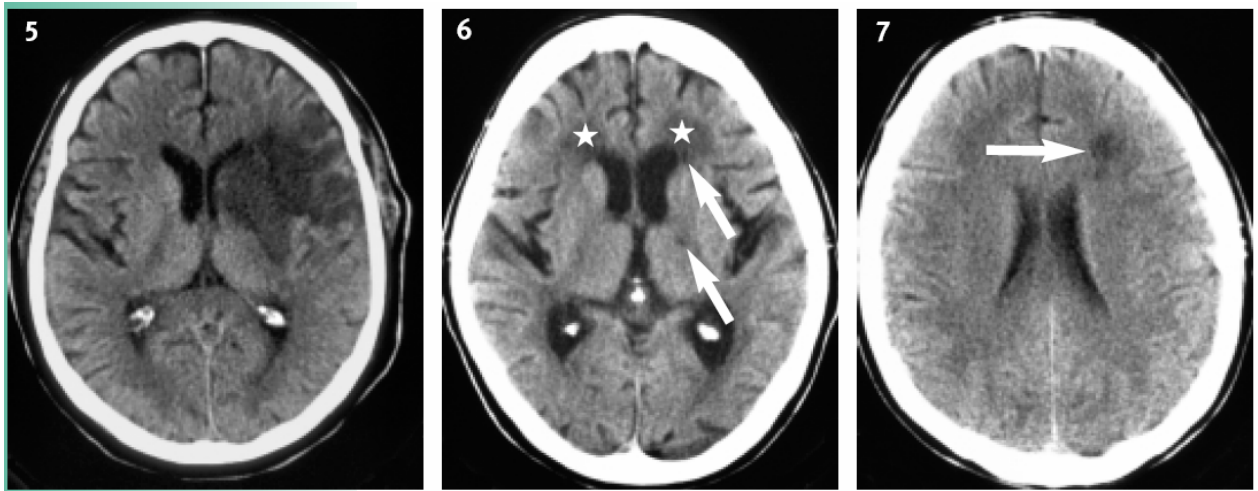
The first and the third cranial CT (images 1 and 3) seem to be normal on initial viewing, but if you look carefully, you may see the so-called ‘early cranial CT signs of infarction’.

The density will further decrease during subsequent days, indicating a progressive liquefaction of the infarcted tissue. After several weeks, resorption of a haemorrhage will also lead to a hypodense lesion, often considerably smaller than the primary hyperdense lesion.

Having differentiated an ischaemic from a haemorrhagic stroke and said something about the age of the stroke, what further information can you extract from the CT scan?

Examine the following CT scans from three stroke patients.

Cranial CT is also a valuable tool for assessing the cause of stroke



Q. Image 5 shows a so-called territory infarction due to embolic occlusion of a left MCA branch. What do you think would be the mechanism of the stroke illustrated by images 6 and 7? What would be your approach to the emergency management of these patients?

A. Image 6 shows small lacunar lesions (arrows) and a hypodensity of the white matter with emphasis on periventricular regions (stars), indicating arteriosclerotic leukencephalopathy, without early signs of a territory infarction. You would suppose a microangiopathic stroke and very cautiously consider thrombolysis or full anticoagulation because this type of stroke might be associated with an increased bleeding risk. Image 7 shows an older lesion in the border zone between the left MCA and ACA territory (arrow). You therefore suspect a haemodynamic stroke due to left carotid artery stenosis or occlusion.

If the cranial CT has just been performed and the patient is still within the therapeutic window, do not waste time with ultrasound evaluation; consider CT angiography for quick and safe assessment of the patency or occlusion of large intracranial vessels. Ensure that this procedure does not delay treatment.

Q. From this information, what is the consequence if you consider initiation of thrombolysis?

A. You may see a basilar occlusion for which intra-arterial thrombolysis may be indicated; furthermore you would transfer a patient with basilar occlusion directly to the ICU for further treatment.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) has become increasingly established as an investigative tool for the diagnosis of acute stroke in many hospitals. The equipment is not, however, available in all hospitals admitting and treating stroke patients. In the future we might more and more see telemedical networks that will accelerate patient treatment. For your information:

MRI diffusion- (DW) and perfusion (PW)-weighted imaging, is helpful in

quantifying both the size of the infarcted area and the tissue at risk, even for smaller brainstem infarctions. MRI angiography (MRA) can visualise large vessel occlusion or stenosis. In sinus venous thrombosis, both the occlusion and the resultant parenchymal blood flow impairment may be clearly visualised. MRI with fat suppression technique, may confirm a suspected dissection and demonstrate the mural haematoma. Stroke MRI, including MRA/DWI/PWI, can be helpful in wake-up strokes or those who present later in the time window for assessing the potential of thrombolysis. Sometimes, intravenous thrombolysis can be initiated, and stroke MRI then be performed without time loss with the purpose of gaining more information and further guiding reperfusion therapy (bridging concept). In the case of haemorrhagic stroke, MRI might immediately provide information on the underlying cause such as arteriovenous malformations.



Köhrmann M, Schellinger PD. Stroke-MRI: extending the time-window: recent trials and clinical practice. *Int J Stroke* 2007; 2(1): 53–54 Review. PMID 18705990

Electrocardiogram

An electrocardiogram (ECG) is indispensable because of the high incidence of heart disease in stroke patients. Atrial fibrillation or recent myocardial infarction may be responsible for emboli.

Ultrasound studies

Continuous wave (cw)-Doppler of extracranial arteries and pulsed wave (pw)-Doppler of intracranial arteries facilitates identification of an occluded or stenotic vessel, evaluation of the quality of collaterals, and confirmation of reperfusion. Duplex sonography allows visualisation of the extracranial vessels with good quality visualisation of intracranial vessels in patients with sufficient temporal bone windows. Today, vascular pathology, i.e. stenoses/dissections/thrombi/atherosclerosis, can be detected over a wide range of cerebral vessels. The method has the advantages of being non-invasive and repeatable, and is therefore excellent for dynamic assessments over time. It is, however, quite investigator-dependent. It is very important to keep in mind that ultrasound must not delay radiographic cerebral imaging!

Q. What is the impact of the result of an ultrasound study during the acute phase?

A.

If you find an occlusion or high-grade stenosis

- You will even more carefully control arterial pressure, attempt to maintain blood pressure in the higher range and observe the relationship between clinical symptoms and the pressure levels.
- For secondary prophylaxis you might prefer platelet inhibitors to anticoagulants. You will consider carotid revascularisation e.g. by referral to the vascular surgeons with a view to a carotid endarterectomy (CEA).

- You might omit further unnecessary diagnostic tests such as transoesophageal echocardiography (TEE).

Other ultrasound studies include transthoracic and transoesophageal echocardiography to screen for cardioembolic conditions. They are not usually performed acutely but may be useful within the first 24 hours after stroke onset.

Laboratory tests

The following tests are important in the management of stroke patients. They have been sub-divided into urgent (U) and subsequent (S) tests.

Category	Type of test	Importance
U	Electrolytes	For hypo- or hypernatraemia. Important for cerebral oedema, seizures and arrhythmias
U	Glucose	Hypoglycaemia may mimic stroke and has to be treated immediately. Hyperglycaemia may increase infarction size and impair late functional outcome
U	Haemoglobin/Haematocrit/RBC/WBC	Anaemia may aggravate brain ischaemia. Haemoconcentration may impair oxygen supply to the penumbra
U	Blood urea, Creatinine	Elevated serum urea may increase the risk of bleeding and fluid overload in the brain
U	CK, CKMB, Troponin I	Important to detect associated myocardial infarction
U	Transaminases	To eliminate chronic or acute liver disease
U	Coagulation– Fibrinogen, APTT, INR	To check potential contraindication for anticoagulation
S	Specific coagulation tests – Protein C, S, At III	As part of aetiologies for stroke
S	Sedimentation rate, CRP	To assess inflammatory context
S	Cholesterol, Triglycerides	As a stroke risk factor

NOTE Tests may be different in your institution.

In younger patients where there is no clear cause of their stroke, the following special laboratory tests are used:

- Protein C, S, aPC-resistance
- Cardiolipin-AB
- Homocysteine
- Vasculitis-screening

- CSF (in case of suspected SAH, meningitis or vasculitis)
- Urine toxicology screening.

Q. Why is an initial laboratory assessment so important in the acute setting? Which variables may influence your diagnostic and therapeutic options?

A.

Coagulation tests: These results have to be known e.g. INR, thrombocytopenia, and sometimes adjusted before starting a thrombolytic therapy or invasive procedures.

Link to **ESICM Flash Conference:** Claude Hemphill. Warfarin reversal in trauma and stroke: is time brain? Summer conference, Dublin 2010

Blood glucose: Exclusion of hypoglycaemia is crucial since hypoglycaemia can mimic an acute ischaemic infarction. Diagnosis and treatment of hypoglycaemia may thus prevent misdiagnosis with possibly dangerous diagnostic and therapeutic consequences. Furthermore, hypoglycaemia worsens functional outcome and increases infarct size in stroke patients. At the same time, significant hyperglycaemia is associated with a worse stroke outcome, and thus should be treated.

Link to **ESICM Flash Conference:** Nino Stocchetti, Milan, Italy. Tight glucose control: what's so special about the brain? Summer conference, Dublin 2010

Blood urea nitrogen and creatinine may influence your choice of diagnostic imaging procedure such as avoidance of IV contrast agents.

Acute phase/infection parameters: these might explain fever, which is detrimental in stroke and may suggest the need to identify a source of infection and start antibiotic treatment.

4. GENERAL CRITICAL CARE AND STROKE TREATMENT

Intensive care management is indicated for a number of stroke patients. Appropriate triage and the decision to admit a patient to the ICU can best be achieved through the collaboration of neurologists and intensivists.

Which stroke patients are transferred to the ICU?

- Any stroke patient with severe impairment of vital functions such as respiratory dysfunction, severe bradycardia, tachycardia and arrhythmias, severe hypo- or hypertension.
- Patients treated by thrombolysis measures who need to be monitored if no bed is available on a stroke unit.
- Stroke patients with high risk lesions:
 - Basilar occlusion/brainstem infarction
 - Large hemispheric infarction, especially in younger patients
 - Large territorial cerebellar infarction prone to swelling.

Managing the critically ill stroke patient

Once the patient has been transferred to the ICU, monitoring (e.g. ECG or blood pressure, pulse oximetry, or where available, other methods such as transcranial Doppler and end-tidal CO₂) and global treatment (such as insertion of cannulae and intubation, if necessary) should be initiated according to the protocols in your ICU.

Some routine techniques in intensive care must be applied with caution in stroke patients, especially if elevated ICP is present or suspected. However, optimal oxygenation and blood flow are paramount:

Stroke patients have special requirements in intensive care

- Central venous lines in presence of elevated ICP: catheters located in the internal jugular vein and the catheter itself may impede cerebral venous drainage and further increase ICP. If required, consider femoral or subclavian catheters.
- Laryngoscopy and intubation: consider the risk of further haemodynamic impairment, especially in those with carotid artery stenosis, keep blood pressure stable during these procedures.
- For intubation, short acting anaesthetic agents are recommended. Consider propofol (2–4 mg/kg) or etomidate (0.15–0.3 mg/kg) in conjunction with a non-depolarising neuromuscular blocking agent such as rocuronium (1.0 mg/kg given in a rapid sequence) if indicated.



Only undertaken by those with expertise in the use of these drugs and the associated airway and circulatory management.

- Further analgosedation regimens depend on the brain lesion, expected clinical time course and non-cerebral conditions of the patient. Agents often involved in neurocritical analgosedation are sedatives such as midazolam or propofol, with possible adjuncts such as clonidine or dexmedetomidine, in combination with opioids (morphine, fentanyl, remifentanyl, sufentanyl) for analgesia. Use of these drugs requires systemic and cerebral monitoring and is a matter of individual approach to the patient. Sedation scales are recommended and (if available) bispectral index (BIS) monitoring.

[Link to PACT module on Sedation and analgesia](#)

- Note that high PEEP levels may exacerbate intracranial hypertension, although this effect may be less significant than formerly thought (see references).
- Consider primary, elective tracheostomy in patients with a predicted long ICU stay or in patients with a normal level of consciousness but impaired airway and swallowing reflexes.



Pulmonary Aspects of Neurological Intensive Care. In: Ropper AH, Gress DR, Diringer MN, Green DM, Mayer SA, Bleck TP. Neurological and Neurosurgical Intensive Care. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2004. ISBN 0-7817-3196-8. p. 52

Georgiadis D, Schwarz S, Kollmar R, Baumgartner RW, Schwab S. Influence of inspiration:expiration ratio on intracranial and cerebral perfusion pressure in acute stroke patients. Intensive Care Med 2002; 28(8): 1089–1093. PMID 12185430

Georgiadis D, Schwarz S, Baumgartner RW, Veltkamp R, Schwab S. Influence of positive end-expiratory pressure on intracranial pressure and cerebral perfusion pressure in patients with acute stroke. Stroke 2001; 32(9): 2088–2092. PMID 11546901

NOTE

If the patient deteriorates further during the first hours or days of treatment, in addition to thinking about the complications related to the stroke, eliminate the usual complications in ICU patients, such as infection, cardiac dysfunction, pulmonary embolism, gastroparesis, paralytic ileus, malnutrition not specifically related to stroke.

Basic measures

- Keep the head in the midline and slightly elevated at approximately 20–30°. The midline position is of special importance since it influences venous drainage. Placement of a jugular vein catheter may be hazardous due to the need for neck rotation.

- Ensure adequate, deep sedation and analgesia (adjusted with BIS-monitoring, if available). Otherwise, stimuli may increase ICP by evoking motor responses such as coughing and Valsalva manoeuvres.
- Fever is detrimental in cerebral ischaemia (with or without oedema) and should be vigorously treated.
- Avoid and treat electrolyte abnormalities, especially hyponatraemia which can aggravate the cerebral oedema.
- Extreme arterial hypertension can increase brain oedema and should be prevented.



Intracranial Pressure Monitoring. In: Waldmann C, Soni N, Rhodes A, editors. Oxford Desk Reference: Critical Care. Oxford: Oxford University Press; 2008. ISBN 13: 978-0-199-22958-1. p. 130

Respiratory dysfunction

Respiratory dysfunction may result from:

- Upper airway obstruction due to oropharyngeal muscular dysfunction
- Neurogenic pulmonary oedema or neurogenic heart disease (particularly in patients with right hemispheric infarctions including the insula, however rare)
- Hypoventilation due to impaired central respiratory drive by brainstem lesions
- Deterioration of consciousness
- Nosocomial or aspiration pneumonia especially in dysphagic patients.

Further non specific causes may include:

- Atelectasis or pneumonia due to immobilisation
- Ventilator-associated pneumonia
- Hypoventilation due to critical illness polyneuromyopathy.

Circulatory dysfunction

Ascertain whether deterioration is likely to be attributable to abnormal blood pressure.

Hypotension

Check if brain circulation problems occurred in the context of large vessel occlusion or high-grade stenosis. This has to be diagnosed during the emergency tests such as Doppler evaluation or CT angiography (see Tasks 1 and 3); try to establish a normal or slightly increased blood pressure (with reference to pre-morbid values). Check the initial imaging strategy to determine if there was brainstem ischaemia that could explain abnormal blood pressure control.

Hypertension

Check if it is an adaptation to increased ICP elevation. If not, keep the pressure at an acceptable (for heart and brain) high level.

If an ICP probe is in place CPP guided therapy should be applied, aiming for a CPP above at least 60 mmHg.

Secondary infarction

Secondary deterioration should be evaluated by a new cranial CT to determine whether the secondary infarction is occurring as a natural complication of the initial stroke or whether it is as a result of the therapeutic strategy.

Secondary deterioration: exclude a haemodynamic problem, a secondary infarction, secondary haemorrhage, or an increase in ICP

Seizures

Occasionally, you will admit stroke patients to your ICU who would normally have been designated for treatment in a general ward but have developed seizures. Partial or secondary generalised epileptic seizures or even status epilepticus rarely occur in the acute phase of stroke (see reference below). For this reason there is no evidence to support the use of prophylactic anti-epileptic treatment but it is generally accepted that seizures should be treated and recurrences prevented. Appropriate anticonvulsants in the ICU are those that can be quickly administered intravenously, such as lorazepam, phenytoin, valproic acid, levetiracetam, or lacosamide. In generalised epileptic seizures, it is of utmost importance to disrupt seizure activity as quickly as possible. It thus might become necessary to administer sedative anti-epileptic drugs (benzodiazepines, barbiturates) and to intubate the patient. Continuous EEG monitoring is optimum.

Link to [ESICM Flash Conference](#): Tarek Sharshar, Paris, France. Seizures in the ICU: diagnosis and treatment. Summer conference, Dublin 2010

Q. Give reasons as to why pharmacological prevention of recurrent seizures is strongly recommended.

A. A seizure can lead to secondary damage of brain tissue due to increased metabolic demands, especially in the penumbra. Furthermore, it can worsen ischaemic oedema. There are some data indicating that recurrent seizures worsen the patient's functional outcome.

Intravenous lorazepam is used to abort the seizure, followed by oral or intravenous levetiracetam, phenytoin, or valproic acid. Dosages including the loading and maintenance dosage of phenytoin can be found in the first of the following references.



Hinds CJ, Watson JD. Intensive Care: A Concise Textbook. 3rd edition. Saunders Ltd; 2008. ISBN: 978-0-7020259-6-9. pp. 432–436. Status Epilepticus

Status epilepticus. In: Waldmann C, Soni N, Rhodes A, editors. Oxford Desk Reference: Critical Care. Oxford: Oxford University Press; 2008. ISBN: 978-0-199-22958-1. p.362.

Critical Care of Acute Stroke. In: Ropper AH, Gress DR, Diringer MN, Green DM, Mayer SA, Bleck TP. Neurological and Neurosurgical Intensive Care. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2004. ISBN 0-7817-3196-8. p 208

Intracerebral haemorrhage

Patients with ischaemic stroke may develop haemorrhagic transformation of the ischaemic area (40%), which may occur spontaneously and can be worsened or extended following thrombolytic or anticoagulant therapy. The risk of this complication is high for embolic and low for thrombotic stroke. Haemorrhagic transformation can be categorised as haemorrhagic infarction or parenchymal haematoma. The former refers to petechial or confluent petechial haemorrhage within the infarcted region and normally has few clinical consequences. In the latter, the region is filled with a mass of blood which may encroach on surrounding structures, resulting in midline shift and clinical deterioration. A clinically important, space-occupying intracranial haemorrhage (ICH) secondary to ischaemic stroke, is a different form of brain lesion in its own right, and the details of its management are beyond the scope of this module. Management may include a completely different approach to circulation and coagulation and procedures such as haematoma evacuation (rarely indicated), hemicraniectomy or the placement of extraventricular drains.

[Link to PACT module on Traumatic brain injury](#)

Intracranial hypertension

Is there an ICP increase?

Direct ICP measurement is critical when increased pressures are suspected. Cranial CT may be used to confirm the presence of a new mass lesion, evidence of shift, or other pathology. This is important because of the therapeutic implications: if the increase in ICP is due to bleeding in the infarcted area (e.g. due to thrombolysis, reperfusion damage, anticoagulation), you should withhold the full-dose treatment with heparin.

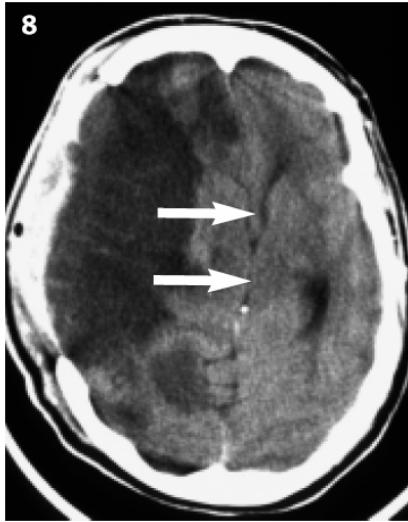


Detection of increased ICP is very important, since effective treatment exists to prevent or minimise secondary brain damage!

In most cases, the ICP increase is related to focal brain oedema which usually develops during the first 24-48 hours after ischaemic infarcts.

Image 8 shows the follow-up cranial CT scan of a patient who presented three days

previously with severe left-sided hemiparesis and hemianaesthesia together with a left-field hemianopsia. The initial cranial CT of this patient is shown in image 3 (see Task 3).



Further diagnostic tests in this patient demonstrated a distal carotid artery occlusion (at the so-called carotid T) of embolic origin. He was later found unconscious and with pronounced anisocoria, the right pupil dilated and unreactive, the left one hyporeactive.

On the follow-up cranial CT (previous above) you will now see a well-demarcated infarction of the whole MCA territory with additional lesion of the ACA territory on the right side. The right hemisphere swelling led to considerable midline shift (midline indicated by arrows). This mass effect explains the secondary clinical deterioration in this patient.

If you have looked carefully at the image, you may have noticed a discontinuity in the calvaria on the right side. The patient had already undergone hemicraniectomy which, in this case, did not lead directly to a normalisation of the midline position.

Q. Ischaemic stroke is associated with a greater or lesser degree of perifocal oedema. In which patients would you expect that oedema would cause a critical elevation in ICP requiring particular and frequent observation and therapy?

A. The risk for developing an increased ICP depends on the size and location of the brain infarction as well as the age of the patient and an individual predisposition for developing oedema. According to brain volume and compliance, the risk of ICP elevation is higher in younger patients. A supratentorial focal space occupying effect will often be compensated in older individuals because of the larger ventricles and subarachnoid space due to essential atrophy. Lacunar infarctions will not increase the ICP in contrast to large hemispheric infarctions (such as the malignant MCA infarction). Cerebellar infarctions may have more effects than a supratentorial infarction of the same size, since the posterior fossa allows minimal compensation; cerebellar swelling may lead to compression of the brainstem, impair the CSF circulation and also increase the supratentorial ICP due to internal hydrocephalus.



Even if you know the likely evolution, remember that in the individual patient, the clinical course cannot be predicted!

In the case, however, of a young patient with a large hemispheric infarction, you must consider transfer to a hospital with neurosurgical facilities, as is conventional practice in the case of patients with large cerebellar hemispheric infarctions. These patients are at high risk of ICP crises, refractory to conventional therapy, rendering them too unstable to be transferred later in the evolution of the stroke.

Diagnosing increased ICP

Clinically, the patient demonstrates decreased level of conscious, with vomiting and initially a unilateral loss of pupillary reflexes and anisocoria. On the follow-up cranial CT you will find a mass effect with a midline shift due to focal brain oedema (as shown in image 8 above). Such a mass effect could induce the following deleterious consequences:

- Herniation of the brain through the incisura, the foramen magnum or below the falx
- Distortion and further injury of vital brain structures
- Secondary ischaemic insults.

Increased intracranial pressure (ICP) should be confirmed by invasive techniques using special ICP monitoring transducers for intraventricular or ipsilateral intraparenchymal measurements. These techniques can also be useful in monitoring the effectiveness of treatment and determining cerebral perfusion pressure ($CPP = MAP - ICP$). ($MAP =$ mean arterial pressure).



Hinds CJ, Watson JD. *Intensive Care: A Concise Textbook*. 3rd edition. Saunders Ltd; 2008. ISBN: 978-0-7020259-6-9. pp. 409–410. Intracranial pressure monitoring

Intracranial Pressure Monitoring. In: Waldmann C, Soni N, Rhodes A, editors. *Oxford Desk Reference: Critical Care*. Oxford: Oxford University Press; 2008. ISBN: 9780199229581. p. 130

These procedures, however, need to be carried out by a neurosurgeon or in conjunction with a neurosurgical centre. Subsequent maintenance of the system and data interpretation requires an intensivist and intensive care nurses with specific experience. This combination of expertise is not available in most general hospital ICUs of urban hospitals. However, basic knowledge of general and pharmacological ICP treatment and practice is to be expected in every hospital.



Fisher M, editor. Stroke Therapy. 2nd ed. Boston: Butterworth Heinemann; 2001. ISBN 0750672366. p. 225

Management of Intracranial Hypertension and Mass Effect. In: Ropper AH, Gress DR, Diringer MN, Green DM, Mayer SA, Bleck TP. Neurological and Neurosurgical Intensive Care. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2004. ISBN 0-7817-3196-8. p 26

Although focused on traumatic brain injury, this Dublin 2010 flash conference lecture is recommended.

Link to [ESICM Flash Conference](#): Giuseppe Citerio, Monza, Italy. Intracranial pressure monitoring. Summer conference, Dublin 2010

Treatment of increased ICP

NOTE Remember that ICP elevation is a sensitive warning parameter which allows you to institute a strategy for CPP maintenance.

Link to [ESICM Flash Conference](#): Giuseppe Citerio, Monza, Italy. Medical strategies for controlling ICP. Summer conference, Dublin 2010

Maintaining an adequate CPP

This is one of the primary goals of treatment. It is of particular importance since cerebral autoregulation can be impaired in and around ischaemic lesions. Under these circumstances blood flow becomes linearly dependent on perfusion pressure. In addition, the lower limit of autoregulation may be shifted upwards in patients with chronic arterial hypertension. The question of the minimal CPP threshold that can be tolerated has not been answered yet, especially not in stroke patients. Some clinical studies suggest the lowest CPP tolerated is probably an individual value depending on the patient's autoregulatory capacity and course of the disease (so-called CPP-Opt concept). For patients with traumatic brain injury it is recommended to keep the CPP above 60 mmHg. For pragmatic reasons this threshold may serve as a guide in stroke patients.

Link to [ESICM Flash Conference](#): David Menon. CPP targeting and autoregulation evaluation in ICU. Summer conference, Dublin 2010

The following guidelines may help to maintain an adequate CPP (even when ICP is not measured):

- Lower the blood pressure only if marked hypertension is present (systolic BP >220 mmHg or diastolic BP >120 mmHg).
- **Avoid hypotension** or a sudden drop in blood pressure.

- All treatment modalities that lower ICP by reducing CBF must be considered as hazardous.
- Avoid hypovolaemia; give adequate volumes of crystalloid, colloid, and, if necessary, blood products.
- Patients with high cardiac output and decreased systemic vascular resistance (vasogenic hypotension, septic shock) may require vasopressors such as norepinephrine.
- In patients with low cardiac output (cardiogenic hypotension or cardiogenic shock) consider dobutamine or epinephrine.



Russell JA. Management of sepsis. N Engl J Med 2006; 355(16): 1699-1713 Review.
No abstract available Erratum in: N Engl J Med 2006; 355(21): 2267 PMID
17050894

Osmotherapy



Hinds CJ, Watson JD. Intensive Care: A Concise Textbook. 3rd edition. Saunders
Ltd; 2008. ISBN: 978-0-7020259-6-9. p. 417. Diuretics

Hypertonic crystalloid solutions such as mannitol, sorbitol, glycerol, or hypertonic saline are used to reduce the brain water content by creating an osmotic gradient between brain and plasma, drawing water into the plasma.

NOTE **There are practice differences between Europe and the US.** In the US hypertonic saline and glycerol are not used.

Which agent should you use and when?

Syphoning fluid saves cells

Acute effect: 200 ml of intravenous 15% mannitol or 100 ml of 7.5% hypertonic saline every 3-6 hours (short-term effects). There are a number of different preparations, concentrations and agents for osmotherapy. See references below for further details.

NOTE **In the US, mannitol is dosed by mass,** 0.25–0.5 g/kg administered over 20 minutes (can be repeated every 6 hours with maximum dose 2 g/kg), not by volume.



Dosage of mannitol is usually expressed in grams, not milligrams!

Subacute effect and more sustained action: up to 4 x 250 ml of 10% glycerol per day, each infusion over 2 hours (to avoid haemolysis).



García-Morales EJ, Cariappa R, Parvin CA, Scott MG, Diringner MN. Osmole gap in neurologic-neurosurgical intensive care unit: Its normal value, calculation, and relationship with mannitol serum concentrations. *Crit Care Med* 2004; 32(4): 986–991. PMID 15071390

Schwarz S, Schwab S, Bertram M, Aschoff A, Hacke W. Effects of hypertonic saline hydroxyethyl starch solution and mannitol in patients with increased intracranial pressure after stroke. *Stroke* 1998; 29(8): 1550-1555 PMID 9707191

Management of Intracranial Hypertension and Mass Effect. In: Ropper AH, Gress DR, Diringner MN, Green DM, Mayer SA, Bleck TP. *Neurological and Neurosurgical Intensive Care*. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2004. ISBN 0-7817-3196-8. p. 26



In the next five patients you treat for increased ICP, assess and discuss the effectiveness of the treatment manoeuvres with your colleagues. Review practice in your own institution. Establish a protocol for ICP assessment and management for your institution.

Consider possible negative longer-term side effects of repeated treatment with osmotic agents:

- Aggravation of cerebral oedema related to migration through a permeable blood-brain barrier, reversing the osmotic gradient and exacerbating swelling
- Dehydration and shrinkage of normal brain tissue, facilitating displacement of brain tissue thereby increasing the risk of herniation
- Electrolyte imbalances
- Raised serum osmolarity
- Hypervolaemia with cardiac failure
- Renal dysfunction.

Other medical therapy

The following alternative treatment procedures may be used when the clinical and cranial CT changes indicate a sustained elevation in ICP. However, many of these interventions should be considered, like hyperventilation, as a short-term, temporary measure of last resort, because side-effects and sometimes rebound effects are undesirable:

Hyperventilation



Hinds CJ, Watson JD. Intensive Care: A Concise Textbook. 3rd edition. Saunders Ltd; 2008. ISBN: 978-0-7020259-6-9. pp. 414–416. Mechanical ventilation

- Serum and CSF alkalosis induce cerebral vasoconstriction and reduce cerebral blood volume and ICP.
- Transient effect because of rapid compensation as CSF becomes alkalotic, with rebound vasodilatation.
- Risk of rebound increase in ICP if normoventilation is restored too rapidly.
- Severe hyperventilation may reduce cerebral blood flow, **leading to additional ischaemic damage**. Therefore, the arterial carbon dioxide tension (PaCO₂) levels should not fall **below 32 mmHg** (4.3 kPa).

Steroids

There is no indication for administration of steroids in severe post-ischaemic brain oedema or after intracerebral haemorrhage.

NOTE

The following second-line interventions are taken only when all the previous measurements fail to control the ICP.

Short-acting barbiturates

Of these thiopentone (thiopental) is commonly used and has the following features:

- Prompt and significant reduction in ICP.
- Only used to manage an acute crisis not controlled by mannitol.
- Due to cardiac depression and hypotension, the CPP might be lowered despite ICP reduction; therefore induced hypotension must be counteracted, e.g. using pressors such as norepinephrine.
- Consider various other side effects.
- No proven long-term beneficial effects of prolonged barbiturate coma in patients with elevated ICP. If using pentobarbital, the loading dose, 5 mg/kg of is given over 30 minutes; maintenance dose 3 to 5 mg/kg per hour is titrated to a burst suppression pattern. Burst suppression on EEG is usually seen at serum barbiturate levels of 30 to 40 mg/dl.



Hinds CJ, Watson JD. Intensive Care: A Concise Textbook. 3rd edition. Saunders Ltd; 2008. ISBN: 978-0-7020259-6-9. p.416. Sedation

Induced hypothermia in severe ischaemic stroke

Experimental studies have demonstrated a promising neuroprotective, ICP-lowering, and anti-oedematous effect. The optimal technical approach for applying hypothermia and its clinical effectiveness in stroke patients are still uncertain. This experimental treatment should therefore be used exclusively in centres with special expertise and neurocritical care facilities.



Steiner T, Friede T, Aschoff A, Schellinger PD, Schwab S, Hacke W. Effect and feasibility of controlled rewarming after moderate hypothermia in stroke patients with malignant infarction of the middle cerebral artery. *Stroke* 2001; 32(12): 2833–2835. PMID 11739982

van der Worp HB, Macleod MR, Kollmar R; European Stroke Research Network for Hypothermia (EuroHYP). Therapeutic hypothermia for acute ischemic stroke: ready to start large randomized trials? *J Cereb Blood Flow Metab* 2010; 30(6): 1079–1093. Review PMID 20354545

<http://www.eurotherm3235trial.eu/>

Link to **ESICM Flash Conference**: Peter Andrews, Edinburgh, UK. Resuscitating the brain from global ischemia: hypothermia and beyond. Summer conference, Dublin 2010

Neurosurgical treatment for increased ICP

What do you do when the symptoms of increased ICP do not improve and follow-up cranial CT shows increasing mass effects, in spite of optimised basic treatment and subsequent medical therapy? What would you do in cases, such as malignant infarction of the medial cerebral artery, where prognosis is known to be poor even if all medical measures of aggressive intensive care are undertaken?

In these cases, neurosurgical treatment is considered. An impasse occurs when no neurosurgical facilities are available in your hospital as these patients are usually too unstable for transportation. This re-emphasises the importance of identifying patients on admission who are likely to need future neurosurgical treatment.

Decompressive surgery

- Hemicraniectomy is an effective treatment strategy for otherwise uncontrollable increased ICP following severe hemispheric stroke.
- Hemicraniectomy prevents transtentorial herniation in patients with large MCA infarction. Controlled trials will be required to evaluate any outcome benefit.
- Surgical decompression of the posterior fossa may be life saving. It prevents brainstem compression with irreversible damage and occlusive hydrocephalus in space-occupying cerebellar infarctions. A significant

decrease in mortality and morbidity even in comatose patients, has been reported. You can find further details in the following reference.



Vahedi K, Hofmeijer J, Juettler E, Vicaut E, George B, Algra A, et al; DECIMAL, DESTINY, and HAMLET investigators. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. *Lancet Neurol* 2007; 6(3): 215–222. PMID 17303527

Jüttler E, Schellinger PD, Aschoff A, Zweckberger K, Unterberg A, Hacke W. Clinical review: Therapy for refractory intracranial hypertension in ischaemic stroke *Crit Care* 2007; 11(5): 231. Review PMID 18001491

Chen HJ, Lee TC, Wei CP. Treatment of cerebellar infarction by decompressive suboccipital craniectomy. *Stroke* 1992; 23(7): 957–961. PMID 1615544

NOTE

As the clinical course is highly predictable especially in young patients (<40 years) with severe MCA stroke, surgery within 24 to 48 hours may be considered when patients show the early neuroradiological criteria of complete MCA infarction together with further clinical deterioration.

Early selection of patients for decompressive surgery may reduce mortality from 70 % to less than 20%, with a trend to better functional performance and reduced disability. See references below. The duration of intensive care is significantly reduced in the group of patients treated early after severe stroke, thus further supporting earlier intervention.



Vahedi K, Hofmeijer J, Juettler E, Vicaut E, George B, Algra A, et al; DECIMAL, DESTINY, and HAMLET investigators. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. *Lancet Neurol* 2007; 6(3): 215–222. PMID 17303527

Unterberg A, Juettler E. The role of surgery in ischemic stroke: decompressive surgery. *Curr Opin Crit Care* 2007; 13(2): 175–179 Review PMID 17327739

When the ICP is elevated due to 'internal' hydrocephalus in a patient with cerebellar infarction, consider:

Drainage of CSF

Initially, an external intraventricular device for pressure monitoring and CSF drainage may be placed. However, decompressive surgery as initial treatment may be the first choice of action in situations where it might be considered.

NOTE

The management of these drainage devices needs special expertise, because it may lead to further brain shifts. Furthermore, consider the relatively high infection rate of 2-10%, which increases when drainage is maintained beyond ten days.



Fisher M, editor. Stroke Therapy. 2nd ed. Boston: Butterworth Heinemann; 2001. ISBN 0750672366. p. 225

Critical Care of Acute Stroke. In: Ropper AH, Gress DR, Diringer MN, Green DM, Mayer SA, Bleck TP. Neurological and Neurosurgical Intensive Care. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2004. ISBN 0-7817-3196-8. p 208

Stroke treatment – general and specific

General aspects

General critical care supportive management is applied to every stroke patient irrespective of the cause and has been detailed above and in the previous tasks. Optimal general treatment during the first two days after stroke onset reduces mortality and improves the functional outcome. Haemodynamic stability and adequate arterial oxygenation are essential for preserving the penumbra. Hyperglycaemia, hypoglycaemia and hyperthermia can increase the size of the infarction and worsen the functional outcome. All these factors can readily be monitored and treated during the hospital stay.

The immobilised and the comatose patient is at risk of deep vein thrombosis and subsequent pulmonary embolism. This can effectively be prevented by the subcutaneous administration of low-dose heparin, if the patient is not anticoagulated already. Physiotherapy helps to prevent thrombosis as well as contractions and decubitus ulcers.

Specific treatment

Specific treatment comprises:

- Recanalisation/Reperfusion therapy
- Secondary prophylaxis

Intravenous thrombolysis: inclusion and exclusion criteria according to the ECASS3 study are listed below.

Inclusion criteria

Ischaemic infarct with relevant neurologic deficit ($2 < \text{NIHSS} < 25$)

Symptoms not regressing spontaneously

Symptoms not minimal (however no NIHSS limit)

Exclusion criteria

(*criteria that the authors consider relative)

- *Time window >3h
- *Age >80 years
- *Very severe neurological deficit (i.e. hemiplegia, gaze deviation, coma)
- Suspicion of subarachnoid haemorrhage•
- Traumatic head and brain injury within last 3 months
- Myocardial infarct within last 3 months
- Gastrointestinal or urogenital bleeding within last 3 weeks
- Arterial puncture at an incompressible site within last week
- *Operation within last 2 weeks (NOTE: contact respective surgeons re risk of bleeding)
- *Seizures at symptom onset
- *History of intracerebral haemorrhage
- *Ischaemic stroke within last 3 months
- Blood pressure >185/100 mmHg despite antihypertensive therapy (In the US, a diastolic BP of >110 is used)
- Signs of acute bleeding or acute trauma
- Oral anticoagulant medication and INR >1.5 (in the US: INR ≥1.7)
- Heparin for last 48h with aPTT within normal range
- Platelets <100 000/μl
- *Diabetics with history of stroke
- *Large infarct in CT (early signs >1/3 of hemisphere)
- *Serum glucose < 50 mg/dl (2.7 mmol/l) or >400 mg/dl (22.2 mmol/l)
- Tumour with increased bleeding risk
- Acute pancreatitis
- Endocarditis

•Cerebral vasospasm-associated brain ischaemia which occurs in SAH is seen in the following references.



Hinds CJ, Watson JD. Intensive Care: A Concise Textbook. 3rd edition. Saunders Ltd; 2008. ISBN: 978-0-7020259-6-9. pp. 422–423. SAH-related vasospasm and ischaemia

Subarachnoid haemorrhage. In: Waldmann C, Soni N, Rhodes A, editors. Oxford Desk Reference: Critical Care. Oxford: Oxford University Press; 2008. ISBN: 978-0-199-22958-1. p. 368

These inclusion and exclusion criteria are derived from the results of the three randomised trials (NINDS, ECASS-1, -2) and experience that led to approval of recombinant tissue plasminogen activator (rtPA). The ECASS-3 showed significant benefit when IV-thrombolysis with rtPA was given within 4.5 hours. Though the European Stroke Organisation (ESO) recommends this time window, official approval has not been released yet. There are situations, in which over riding some of the ‘relative’ exclusion criteria may be beneficial for the patient. However, this means off-label use of rtPA and should ideally come with the patient’s consent, if obtainable.

Recanalisation therapy

Although recanalisation can be achieved with the use of thrombolytic agents or mechanical clot retrieving devices, the latter cannot yet be considered to be supported by sufficiently large trials. These techniques are currently a matter of individual application, and will therefore not be described in detail here. However if interested, see link to the following Dublin 2010 flash conference.

Link to **ESICM Flash Conference**: Paul Brennan. Forget t-PA, it's all about clot retrieval. Summer conference, Dublin 2010

Q. What is the purpose of recanalisation treatment in acute ischaemic stroke when brain tissue is known to be irreversibly damaged within 5-10 minutes of cessation of blood flow?

A. Administration of thrombolytic therapy in stroke is based on the concept that early restoration of circulation in the affected territory by recanalisation of an occluded intracranial artery preserves reversibly damaged neuronal tissue in the penumbra (see the answer to the question in the Physical Examination section) and thereby enhances recovery of neuronal function, reducing clinical neurological disability.

Two large controlled clinical studies have shown the benefit of early recanalisation, depending on the time window, infarction size, and general and specific contraindications. See references for details and websites for many more useful aspects of recanalisation.



Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, Larrue V, Lees KR, Medeghri Z, Machnig T, Schneider D, von Kummer R, Wahlgren N, Toni D; ECASS Investigators. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med* 2008; 359(13): 1317–1329. PMID 18815396

[No authors listed] Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. *N Engl J Med* 1995; 333(24): 1581-1587 PMID 7477192

European Stroke Organisation (ESO) Executive Committee; ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovasc Dis* 2008; 25(5): 457–507. PMID 18477843

Update January 2009. View PDFs, Slideshows and Teaching Tools on <http://www.eso-stroke.org>

<http://www.eusi-stroke.com>

Recanalising techniques include a) systemic and b) local intra-arterial thrombolysis. Systemic thrombolysis can, in principle, be performed in every hospital. The generally recommended thrombolytic agent is rtPA, whereas streptokinase is associated with an unacceptable risk of bleeding and cannot be

recommended for thrombolysis in acute stroke patients. Intra-arterial thrombolytic therapy should be performed in centres with special neurointerventional experience and neurological expertise.

Choosing the specific treatment depends on the time of onset.

Onset within 3 hours

These patients should be considered for thrombolysis, after cranial CT has excluded intracranial haemorrhage. The table above summarises the inclusion and exclusion criteria for thrombolysis. The potential risks and benefits of thrombolysis should be discussed with the patient and/or family.

After connecting the patient to a monitor, thrombolysis must be initiated immediately after CT is completed. Then, the patient should be transferred to a stroke or intensive care unit with therapy continuing. Monitoring should be continued, blood pressure controlled, and invasive procedures avoided. Thrombolysis must be stopped immediately and another emergent CT performed in case of sudden signs of cerebral or non-cerebral bleeding.

NOTE Ideally, the interventional radiologist, in discussion with the clinicians, will give the rtPA; alternatively a member of the clinical staff is present during performance of the cranial CT in order to prepare and give the rtPA solution, as soon as the diagnosis is confirmed.

Perform intravenous thrombolysis as follows:

- Check the indications and contraindications
- Ensure that there are two peripheral intravenous cannulae, do not attempt to insert an arterial or a central venous catheter
- Calculate the total dose of rtPA: 0.9 mg/kg; maximum of 90 mg
- Administer 10% of the total dose given as a bolus
- Give the remaining 90% over 60 minutes via an infusion pump.

Onset between 3–4.5 hours

NOTE In the US, it has been more common to date, to use intra-arterial thrombolysis for patients between 3 and 6h.

The ECASS3 trial in 2008, demonstrated that intravenous thrombolysis up to 4.5h is beneficial. The drug approval for this expanded time window is not obtained yet, though. This means that thrombolysis between 3 to 4.5h is currently an individual off-label treatment. It has to be understood that an expanded time window must not lead to delayed therapy! Thrombolysis is more effective the earlier it is applied.

Although it is now accepted that thrombolysis is effective and safe up to 4.5 h after stroke onset, this therapy is best started as soon as possible

Onset >6 hours

These patients should normally not be considered for intravenous thrombolysis because the bleeding risk considerably exceeds the possible benefit. You should therefore initiate secondary prophylaxis and perhaps, in specialist centres, consider other techniques (see Brennan flash conference lecture above).

NOTE In the case of basilar artery occlusion, in specialised centres, intra-arterial therapy using urokinase up to 1.5 million IU or rtPA up to 50 mg may be the treatment of choice. If cranial CT does not show any demarcated infarction, the time window for thrombolysis may be extended up to 12h.

Time of onset unclear

The patient may awake with the symptoms and signs, or be found aphasic, comatose or confused. The decision in this case must be individualised. Most practitioners believe that intravenous rtPA should not be administered when the time of onset of the stroke cannot be reliably ascertained. However, in individual cases, e.g. young patients, you may consider thrombolysis if cranial CT shows no demarcated infarctions or there are early cranial CT or clinical signs of an infarction of $\leq 1/3$ the MCA territory (see above), and there is no obvious contraindication to thrombolysis. Additionally, MRI can be used to estimate the age of infarction and diffusion/perfusion mismatch i.e. by depicting a penumbra that is worth saving. Recanalisation can then be individually decided on, and initiated intravenously, intra-arterially or by the use of mechanical devices. However, these are individual treatment trials best performed in specialised centres.

NOTE In the US there are differences in practice. In patients in whom the time of stroke onset cannot be determined (more precisely, the time at which the patient was last known to be well), thrombolysis would not be contemplated.

You may have heard about some further specific treatment strategies in acute ischaemic stroke such as neuroprotective agents and defibrinogenating enzymes. None of the many neuroprotective drugs that work in animal models of stroke have been convincingly shown to be helpful in humans.



European Stroke Organisation (ESO) Executive Committee; ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovasc Dis* 2008; 25(5): 457–507. PMID 18477843

Update January 2009. View PDFs, Slideshows and Teaching Tools on <http://www.eso-stroke.org>

<http://www.eusi-stroke.com>

Link to [ESICM Flash Conference](#): Paul Vespa. Applying evidence to acute ischemic stroke critical care: extended window IV t-PA and decompressive craniectomy. Summer conference, Dublin 2010



If the patient shows neurological deterioration following thrombolytic treatment, you should immediately initiate a follow-up cranial CT to exclude complications e.g. haemorrhage.

Secondary prophylaxis

Not all aspects described in the following are relevant to critical care of ischaemic stroke. However, the intensivist has to think ahead and take measures to facilitate safe and optimum discharge from critical care. Even if not all secondary prophylaxis is appropriate in the very acute phase of severe ischaemic stroke, it should generally be initiated as soon as possible.

An important component of acute stroke treatment is the prevention of further ischaemic events. This is the purpose of secondary prophylaxis. Finding the optimal secondary prophylaxis is as important in severe stroke as it is in transient ischaemic attacks with minor signs. Acetylsalicylic acid (ASA, aspirin) in a dose of 160-300 mg/day may be given before you decide on further definitive secondary prevention.

NOTE

In many hospitals, heparinisation is still used in acute ischaemic stroke. However as stated by the ESO guidelines, none of the recent randomised controlled trials have shown a net benefit from heparin treatment in any stroke subtype; a non-significant trend in special subgroups was observed. A meta-analysis, restricted to patients with acute cardio-embolic stroke, showed that anticoagulants given within 48 hours of clinical onset were associated with a non-significant reduction in recurrence of ischaemic stroke but with no substantial reduction in death or disability.

In deciding on the appropriate approach to secondary prevention for an individual patient, the cause of the stroke, as indicated by the clinical and supplementary examinations, is relevant (see Tasks 2 and 3). Despite the lack of evidence, some experts recommend full-dose heparin in selected patients, such as those with cardiac sources of embolism and high risk of re-embolism e.g. atrial fibrillation particularly if too early in the acute illness to start warfarin, arterial (carotid/vertebral) dissection, sinus vein thrombosis, fresh thrombus in carotid artery/heart or high-grade arterial stenosis prior to surgery.

Today, there are few indications for heparin treatment in stroke care; contraindications include large infarcts (e.g. more than 50% of middle cerebral artery territory), uncontrollable arterial hypertension and advanced microvascular changes in the brain.

Lacunar/microangiopathic stroke

While heparin or anticoagulants are not of proven benefit and may even increase morbidity and mortality by increasing the risk of intracranial haemorrhage, antithrombotic drugs have been shown to considerably reduce the risk of recurrence (25% risk reduction).

Although clopidogrel or the combination of dipyridamole and aspirin have been shown to be slightly more effective, we recommend the use of aspirin in the first instance; there is much experience with this drug and it is less expensive than other anticoagulants. In some countries triflusal is recommended for secondary prophylaxis, which has similar properties to aspirin but with less bleeding complications.



Costa J, Ferro JM, Matias-Guiu J, Alvarez-Sabin J, Torres F. Triflusal for preventing serious vascular events in people at high risk Cochrane Database Syst Rev 2005; (3): CD004296 Review. PMID 16034926

How to use aspirin: There is no proven advantage to prescribing low (<160 mg) rather than medium (160-325) or high (500-1500 mg) doses.

Q. What should you do if a patient presents with recurrent stroke but is already on daily aspirin? Or when the patient does not tolerate aspirin (e.g. because of gastrointestinal side effects). Or when the patient tolerates neither aspirin nor clopidogrel?

A.

In these cases you should change the medication to clopidogrel (1 x 75 mg daily) which seems to be more effective and is better tolerated. It is not widely used as the treatment of first choice due to cost. Patients who do not tolerate either ASA or clopidogrel may be treated with dipyridamole ret (2 x 200 mg daily).

A second crucial approach for secondary prevention of lacunar stroke is the treatment or the optimisation of treatment of the risk factors, especially arterial hypertension and diabetes mellitus.

Cardioembolic stroke

You assume cardioembolic stroke when you note a territory infarction on the cranial CT, while at the same time excluding, by ultrasound, significant atherosclerosis.

Significant thickening of the intima-media-complex of the common carotid artery is statistically correlated with aortic atherosclerosis, which may be an underestimated source for embolism and which has to be proven by transoesophageal echocardiography (TOE).

A specific source of cardioembolic stroke is bacterial endocarditis, frequently requiring critical care. This condition leads to septic embolic infarctions, which are very prone to secondary bleeding. Therefore, anticoagulation should NOT be administered in such cases.

If cardioembolic stroke is diagnosed or strongly suspected you should initiate intravenous heparinisation with a target aPTT 1.5-2-fold increase over baseline. When the patient is stable and you do not anticipate any surgical or other invasive procedures, you should start oral vitamin K antagonist anticoagulation e.g. warfarin or phenprocoumon.

Oral anticoagulation with an INR of 2-3 reduces the risk of recurrent stroke in patients with atrial fibrillation as well as other causes of embolism such as mechanical prosthetic valve replacement, rheumatic valvular heart disease, ventricular aneurysm, cardiomyopathy, or patent foramen ovale (PFO).

The optimum time to start oral anticoagulation is debated and consensus has not been achieved. After TIA or minor stroke, one could start immediately, but after major stroke with significant infarction on neuroimaging e.g. above a third of the MCA territory, one should wait for some weeks. Four weeks is suggested but this decision has to be individualised.

Macroangiopathic/haemodynamic and arterio-arterial embolic stroke

If high-grade stenoses or occlusions of the carotid arteries have caused stroke by arterio-arterial embolism or haemodynamic impairment, you should contact a vascular surgeon or a stroke centre to discuss the indication for carotid endarterectomy (CEA) or stenting. Early intervention (within the first days) after stroke can be highly effective in secondary prophylaxis. However, the controversy as to which procedure is the best is beyond the scope of this module and not entirely relevant to critical stroke care. The latter might be applicable to post-operative or post-interventional monitoring of these patients. The most important point to remember here is to limit hypertension, as this can lead to reperfusion injury. If a stent is placed, double antiplatelet therapy and temporary heparinisation are used. The intensivist needs to communicate closely with the surgeon or interventionalist. If you want to know more about the current evidence on this form of secondary prophylaxis, the following references will be of interest.



SPACE Collaborative Group, Ringleb PA, Alkenberg J, Brückmann H, Eckstein HH, Fraedrich G, Hartmann M, et al. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial. *Lancet* 2006; 368(9543): 1239–1247 Erratum in: *Lancet* 2006; 368(9543): 1238 PMID 17027729

Eckstein HH, Ringleb P, Alkenberg JR, Berger J, Fraedrich G, Hacke W, et al. Results of the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE)

study to treat symptomatic stenoses at 2 years: a multinational, prospective, randomised trial. *Lancet Neurol* 2008; 7(10): 893–902. PMID 18774746

International Carotid Stenting Study investigators, Ederle J, Dobson J, Featherstone RL, Bonati LH, van der Worp HB, de Borst GJ, et al. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial. *Lancet* 2010; 375(9719): 985–997. PMID 20189239

Sheffet AJ, Roubin G, Howard G, Howard V, Moore W, Meschia JF, Hobson RW 2nd, Brott TG. Design of the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST). *Int J Stroke* 2010; 5(1): 40-46 PMID 20088993

Rehabilitation

Rehabilitation of the stroke patient should be started as soon as possible. A multidisciplinary team approach is required. You can read about rehabilitation of stroke patients in the following references:



<http://www.eusi-stroke.com/>

Fisher M, editor. *Stroke Therapy*. 2nd ed. Boston: Butterworth Heinemann; 2001. ISBN 0750672366. p. 365

Neurorehabilitation. In: Waldmann C, Soni N, Rhodes A, editors. *Oxford Desk Reference: Critical Care*. Oxford: Oxford University Press; 2008. ISBN: 978-0-199-22958-1. p. 382

Q. In the ICU you will have patients with reduced level of consciousness. Should you order early rehabilitation for these patients; if so, why and what form should it take?

A.

Unconscious patients also need early rehabilitation to:

- Prevent contractures and joint pain
- Prevent distress for the patient when movement is restarted after immobilisation
- Minimise the risk of decubitus ulcers
- Minimise the risk of pneumonia
- Reduce the risk of deep vein thrombosis.

Rehabilitation in these patients is passive, using frequent passive limb and joint movements, chest vibration and positioning strategies. These interventions can be performed not only by the physiotherapist but also by the nurses and family members.

CONCLUSION

Stroke is a sudden or rapidly developing neurological deficit due to cerebrovascular pathology where timing is of vital importance. Crucial for the successful management of stroke is the early differentiation of ischaemic stroke from intracerebral haemorrhage, to determine whether to initiate the only acute therapy proven to be effective: (thrombolytic) recanalisation. General treatment includes control of blood pressure, temperature and blood glucose as well as ensuring adequate oxygenation. ICU transfer is required if stroke leads to coma, respiratory or cardiovascular instability. Stroke types frequently demanding neurointensive care are space-occupying hemispheric infarctions, space-occupying cerebellar infarctions, (some) haemodynamically unstable stenoses, and basilar thrombosis. Some routine techniques in intensive care must be applied with caution in stroke patients, especially if elevated ICP is present or suspected, but adequate oxygenation is always paramount.

A very important component of acute stroke treatment is the prevention of further ischaemic events. The present approach to secondary prophylaxis depends on the cause of the stroke as indicated by the clinical and technical examinations. Mobilisation and rehabilitation of the stroke patient should be started as early as possible.

SELF-ASSESSMENT QUESTIONS

EDIC-style Type K

1. Which of the following interventions have constantly shown to be effective in improving outcome after acute ischaemic stroke?

- A. Treatment in specialised stroke units
- B. Platelet inhibitors (as ASA) within 72 hours
- C. Recombinant factor 7a
- D. Intravenous thrombolysis within 4–5 hours

2. To distinguish between acute ischaemic stroke (AIS) and haemorrhagic stroke (HS) one may use the following findings from the clinical examination:

- A. Unilateral pupillary dilatation is more frequent with HS
- B. Hemiparesis is more often found in AIS
- C. Inverted plantar reflexes are more common with AIS
- D. No clinical signs may be used to distinguish between AIS and HS

3. Important clinical findings in favour of intracerebral haemorrhage and not ischaemic stroke is/are:

- A. Acute onset of headache
- B. Hypertensive crisis
- C. Rapid progression of symptoms (within minutes)
- D. Excessive vomiting

4. Horner syndrome may be found in the following:

- A. Carotid artery dissection
- B. Infarcts of the anterior cerebral artery
- C. Posterior circulation infarction
- D. Microangiopathic (lacunar) stroke

5. Relative or absolute contraindications to thrombolytic therapy in acute ischaemic stroke include:

- A. BP above 185/110 despite antihypertensive therapy
- B. Platelets <100 000
- C. Previous head injury one year ago
- D. Age >70 years

6. Contraindications to heparin in stroke management are

- A. Large infarcts e.g. greater than 50% of middle cerebral artery territory
- B. Uncontrollable arterial hypertension
- C. Advanced brain microvascular disease
- D. Small embolic event of cardiac origin e.g. in association with uncontrolled atrial fibrillation

7. Which of the following signs and symptoms are suggestive of an elevated ICP in stroke patients?

- A. Vomiting
- B. Secondary anisocoria
- C. Progressive reduction in state of consciousness
- D. Secondary disturbance in respiratory pattern

8. Which of the following are early cranial CT signs (within 6 hours after onset) of stroke?

- A. Hyperdense thrombus within the proximal MCA (so-called hyperdense MCA sign)
- B. Well-demarcated hyperdense lesion
- C. Loss of demarcation of the grey from the white matter
- D. Focal obliteration of sulci and cisterns

9. In the case of a stable stroke patient your decisions for acute therapy will be:

- A. Consider i.v. rtPA thrombolysis if the patient is within the 3 hour time window and ICH has been excluded by cranial CT
- B. Administration of full-dose heparin anticoagulation for every subtype of stroke and maintenance of dose for prophylaxis against recurrent stroke
- C. Organise acute carotid CEA in patients with large MCA infarction and 70% stenosis of the ipsilateral ICA
- D. Organise transfer of the acute stroke patient to a centre with neurosurgical and invasive neuroradiological expertise when your diagnostic efforts reveal acute basilar stroke or large cerebellar infarction

10. Measures to manage an elevated ICP in the ICU might include:

- A. Applying noxious stimuli to preserve an adequate level of wakefulness for further assessment
- B. Turning the head towards the contralesional side and elevating it by about 70–80°
- C. Monitored drainage of CSF from an intra-ventricular ICP measurement catheter
- D. Maintaining intravascular volume and blood pressure (but <220/120 mmHg) to maintain a sufficient Cerebral Perfusion Pressure

EDIC-style Type A

11. Which of the following investigations is the most important to perform immediately after hospital admission in a patient with clinical signs of stroke?

- A. Ultrasound of the carotid arteries
- B. Cerebral angiography
- C. Cerebral CT
- D. Electroencephalography
- E. End tidal CO₂ monitoring

12. Which of the following laboratory tests is NOT important to analyze at admission in a patient with acute stroke?

- A. Thrombocyte count
- B. Blood glucose
- C. Creatinine
- D. Albumin
- E. INR

13. Which of the following clinical presentations is most typical in ischaemic stroke in the region supplied by arteria cerebri media (middle cerebral artery):

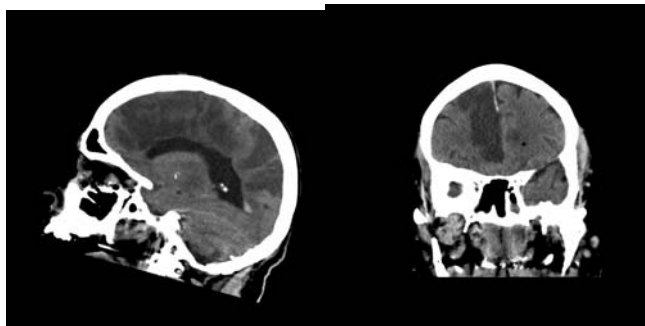
- A. Contralateral motor deficit of face and arm more than legs
- B. Ipsilateral sensory deficit of face and arm more than legs
- C. Contralateral motoric deficit of leg more than arm
- D. Bilateral sensory deficits in the face
- E. Ataxic hemiparesis

14. A 55-year-old male is admitted with acute ischaemic stroke. A CT reveals a large ischaemic lesion in the area of the middle cerebral artery. His GCS is 6, and he requires intubation and mechanical ventilation. There is CT indication of cerebral oedema. BP is 190/100 and his temperature is 39.2 °C. An ICP monitor is inserted and the initial reading shows 30 mmHg. What is the LEAST appropriate measure in the further treatment of his elevated ICP?

- A. Elevate the head 20-30°
- B. Reduce the temperature to 36–37 °C by active cooling
- C. Wake the patient intermittently to re-evaluate GCS
- D. Maintenance of the blood-pressure at current level
- E. Keep the patient normovolaemic by infusing normal saline (0.9%)

15. The CT scan (see figure) is typical for

- A. Posterior circulation infarction
- B. Infarct of the arteria cerebri media (middle cerebral artery).
- C. Infarct of the anterior cerebral artery
- D. Infarct of the cerebellum
- E. None of the above



Self-assessment answers**Type K**

Q1.	Q2.	Q3.	Q4.	Q5.
A. T	A. F	A. T	A. T	A. T
B. T	B. F	B. T	B. F	B. T
C. F	C. F	C. T	C. T	C. F
D. T	D. T	D. T	D. F	D. F

Q6.	Q7.	Q8.	Q9.	Q10.
A. T	A. T	A. T	A. T	A. F
B. T	B. T	B. F	B. F	B. F
C. T	C. T	C. T	C. F	C. T
D. F	D. T	D. T	D. T	D. T

Type A

11. Answer C is correct
12. Answer D is correct
13. Answer A is correct
14. Answer C is correct
15. Answer B is correct

PATIENT CHALLENGES

A 59-year-old man is found by his wife at about 11.00 hour lying in front of the couch, with scanty and mumbling verbal response and unable to stand up or move his left arm. Ten minutes before, he had appeared quite normal.

At 12.45, you are called to see the patient on admission to the emergency department. Blood has been taken for routine emergency tests via a peripheral intravenous cannula, inserted by the emergency physician. The patient's vital signs indicate an arterial blood pressure of 190/110 mmHg, an irregular pulse rate without detectable P waves on the ECG monitor, a mean pulse rate of 101 beats/min and a respiratory rate of 18 breaths/min. Oxygen saturation is 99% during administration of 2 l/min O₂ via a nasal cannula, applied by the nurse on the basis of an admission oxygen saturation of 92% breathing room air.

On neurological examination the patient shows conjugated eye deviation to the right, lower facial paresis, dysarthria, anosognosia, severe left sided hemiparesis (arm: 0/5, leg 2/5) and hemihyperalgesia; the right plantar reflexes are extensor.

Learning issues

Clinical diagnosis

Immediate tasks

Epidemiology of stroke

He is awake, responsive, oriented, and has no pupillary abnormalities. His wife tells you that he had a myocardial infarction three years before; his present medication consists of metoprolol and pravastatin. There are no further relevant diseases, in particular no hypertension or diabetes; he had stopped smoking after the myocardial infarction.

Q. What is your diagnosis? What are your next steps of acute management?

A. The most probable diagnosis is a large right hemispheric infarction due to cardio-embolic (note the finding of atrial fibrillation) occlusion of the M1 segment of the middle cerebral artery.

Q. What are your next steps of acute management?

A To exclude haemorrhage, a CT has to be performed. You try to minimise any delay because the patient still fits the time window for thrombolysis. In this case, even ultrasound neurovascular diagnostics should be omitted. You tolerate the elevated blood pressure.

Learning issues

Management of hypertension at the time of acute stroke

Refresh your CT interpretative skills

Diagnostic procedures, neuroimaging

The diagnosis is confirmed by the CT scan, which shows, besides normal parenchymal structures, a hyperdense middle cerebral artery (MCA) sign on the right side.

Thrombolysis was started immediately and the patient is transferred to the ICU at 13.20 hours. The patient's weight is assessed as 80 kg, and 75 mg of rtPA is prepared ($0.9 \times 80 \text{ kg} = 72 \text{ mg}$ rtPA). 7.5 mg (10%) are given as an intravenous bolus, followed by continuous infusion of the remaining dose over one hour.

In ICU, standard monitoring is applied and a second peripheral venous line is inserted. Neither the 12 channel ECG nor the subsequent laboratory results support the diagnosis of acute or subacute myocardial infarction. The patient is frequently observed clinically; the temperature, blood glucose, and the oxygen saturation are monitored closely and kept in normal range. Also the blood pressure is kept in the high normal range after starting the thrombolysis.

Learning issues

Specific therapy: Thrombolysis

Control of hypertension in stroke patients receiving thrombolysis

General treatment



European Stroke Organisation (ESO) Executive Committee; ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovasc Dis* 2008; 25(5): 457–507. PMID 18477843

Update January 2009. View PDFs, Slideshows and Teaching Tools on <http://www.eso-stroke.org>

Q. If the time of admission was 15.50, what decision would you have reached concerning recanalising measures?

A. There is evidence that patients treated within up to 4.5 h after onset may benefit from intravenous rtPA thrombolysis. However, beyond 4.5h up to 6h, if the infarcted area is more than 1/3 of the MCA territory as assessed by CT early signs or, if available, stroke MRI, the risk of bleeding in the infarcted area may exceed the expected benefit. In conclusion, our patient would not be assessed as suitable for thrombolysis if the admission was delayed until 15.50.

At 20.00 the transcranial Doppler still shows an M1 occlusion, while the patient's condition has not improved. The morning after, the patient is deeply unconscious and shows a slightly dilated right pupil with delayed reactivity.

Learning issues

ICU treatment of large MCA infarction

Q. What are your differential diagnoses and how do you proceed?

A. The most likely explanation is an early mass effect due to developing oedema or extended haemorrhage within the infarcted area. A cranial CT (CCT) has to be performed without delay to clarify the differential diagnosis and quantify the mass effect. Alternatively, a bedside transcranial B scan may reveal the diagnosis, if specialist expertise is available.

NOTE

Remember the risk of increased ICP in patients with large MCA infarction.

CCT now shows a space-occupying infarction of the whole right MCA territory with compression of the lateral ventricles and a midline shift of 4 mm.

Q. What are your treatment options?

A. If the necessary expertise is available in your hospital or within a reasonable distance, decompressive surgery should be considered. This intervention has been shown to reduce mortality, morbidity, and improve clinical outcome in patients with severe MCA infarction and significantly reduce the need for intensive care. If available, an intraparenchymal device for measuring ICP should be implanted to guide ICP management. Before hemicraniectomy can be performed or if surgical treatment is not available, elevated ICP has to be decreased primarily by administering hypertonic solutions. For a less acute effect with more sustained action consider using 3-4 x 250 ml of 10% glycerol (each application for at least 2 hour or longer). In the acutely deteriorating patient, an acute effect can be more reliably achieved using intravenous mannitol 25-50 g every 3-6h or 100 ml of intravenous 7% hypertonic saline with hydroxy ethyl starch. If ICP and CPP cannot be normalised by these measures consider additional treatment options, e.g. barbiturates, hypothermia.

Learning issues

Treatment of complications: ICP management



Critical Care of Acute Stroke. In: Ropper AH, Gress DR, Diringer MN, Green DM, Mayer SA, Bleck TP. Neurological and Neurosurgical Intensive Care. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2004. ISBN 0-7817-3196-8. p 208

Learning issues

Clinical assessment of mechanism and localisation of stroke
Treatment of increased ICP

Patient 2

A 68-year-old male, who awoke with weakness of the right arm and leg, is admitted to the emergency department. He also noted speech difficulties. He remembers that he had a transient blindness affecting the left eye three and eight days before. He is a heavy smoker and has a history of arterial hypertension treated with enalapril; arterial blood pressure measurements taken at home frequently revealed diastolic values of 100-110 mmHg. He also suffers from left-sided intermittent claudication (on walking more than 100 metres.) On examination you find a 4/5 hemiparesis on the right side and a mild aphasia. The blood pressure on admission is 205/105 mmHg.

Learning issues*Immediate tasks*

Q. Which stroke mechanism do you suspect?

A. The patient's history is highly suspicious of left internal carotid atherothrombosis with previous arterio-arterial embolic events (transient ipsilateral amaurosis). The actual neurological deficit may have developed following blood pressure decrease during sleep with hypoperfusion of the left hemisphere or the surrounding zones, respectively.

Q. What are your thoughts about further management?

A The acute management essentially does not differ from standard practice. Special emphasis however, has to be placed on maintaining a high to high-normal blood pressure.

Learning issues*Management and treatment of stroke**Blood pressure control*

CCT shows a hypodensity of the surrounding zone between the anterior cerebral artery (ACA) and the MCA territory on the left as well as some lacunar infarctions in the basal ganglia on both sides.

Extracranial Doppler examination reveals a 85-90% stenosis at the origin of the left internal carotid artery, stenoses of both external carotid arteries, and a collateralised occlusion of the right vertebral artery. B echographic mode shows extensive atherosclerosis with nonstenosing plaques also at the origin of the right internal carotid artery. In the transcranial Doppler the left proximal segment of the anterior cerebral artery is perfused retrogradely while the signal taken from left MCA reveals a lower flow velocity and a lower pulsatility compared to the right side.

Learning issues*Diagnostic procedures*

Q. How do you interpret these findings?

A. As above, a decrease in blood pressure during sleep may have led to a critical hypoperfusion of the surrounding zone between the ACA and MCA territory. Collateralisation of the high-grade stenosis of the left internal carotid artery via the Circle of Willis (here: the anterior communicating artery) does not lead to complete haemodynamic compensation.

Q. What are the guidelines for your further treatment?

A. Following the guidelines for general ischaemic stroke treatment, special effort has to be made to maintain an adequate arterial blood pressure. Thrombolysis is not appropriate because the time of infarct onset is unclear (during sleep) and there is already early demarcation of infarcts.

Learning issues

General treatment



European Stroke Organisation (ESO) Executive Committee; ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovasc Dis* 2008; 25(5): 457–507. PMID 18477843

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Learning issues

Specific therapy: Thrombolysis

The patient is transferred to the ICU for monitoring including continuous blood pressure measurements. Intravenous saline is running and as an embolic source is suspected 1000 units/h of heparin is being infused via a peripheral line. The aPTT 4 hours later is noted to be 56 sec. While initially the arterial blood pressure ranges between 205/110 and 160/90 mmHg, it falls to 120/60 mmHg at 3.00. The patient awakes and is only able to produce incomprehensible sounds and not able to move his right arm. You are called by the nurse and now find that his aphasia has worsened as well as his hemiparesis (1/5-2/5).

Learning issues

Use of heparin in stroke

Q. In the event that the patient does not improve within a few minutes of raising arterial blood pressure to 135/80 mmHg with 500 ml of intravenous fluid (crystalloid or colloid), how would you proceed?

A. If there is insufficient increase in blood pressure, consider low-dose pressors, e.g. 0.2 mg/h of norepinephrine. If the patient does not improve clinically in spite of effective blood pressure elevation (>160/90 mmHg), perform an emergency Doppler control. If you find the vessel occluded now, consider emergency carotid endarterectomy (CEA), if available in your hospital.

On reflection, the time delay is in itself a major influence on the therapeutic strategy for stroke. For this reason the time of onset of stroke is crucial. In addition, the context in which the stroke occurred is important, e.g. sleep-induced hypotension, emboli, thrombosis. Specific therapy is highly efficacious when indicated and supportive therapy is important, especially the maintenance of an adequate blood pressure, i.e. cerebral perfusion pressure (CPP).