## Clinical practice guidelines

# Early management of adult stroke patients - Medical aspects -

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Tel: +33 (0) 1 55 93 70 00; Fax: +33 (0) 1 55 93 74 00; www.anaes.fr, www.sante.fr
ANAES: French National Agency for Accreditation and Evaluation in Healthcare

2 avenue du Stade de France, 93218 Saint-Denis La Plaine Cedex, France

The French Agency for Accreditation and Evaluation in Health (ANAES) was asked to produce guidelines on *"Early management of adult stroke patients*" by the following learned societies:

- *Société française neuro-vasculaire*
- *Fédération de neurologie* (consisting of the *Collège des enseignants de neurologie*, the *Association des neurologues libéraux de langue française* and the *Collège des praticiens de neurologie des hôpitaux généraux*)
- *Association pour la promotion de l'expertise et de la recherche en soins infirmiers*
- *Association française pour la recherche et l'évaluation en kinésithérapie*
- *Association nationale des kinésithérapeutes salariés.*

The subject is vast and was divided into 4 subtopics, each managed by a different working group:

- Assessment of imaging during the acute phase of stroke to define diagnostic strategies;
- Guidelines for the early medical management of adult stroke patients (this report);
- The value of neurovascular units in the management of adult stroke patients;
- Guidelines for early management of adult stroke patients by nursing and other ancillary services.

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The work was coordinated by Dr. Nafissa Abdelmoumène, project manager, under the supervision of Dr. Patrice Dosquet, head of the Guidelines Department.

Documentary research was coordinated by Nathalie Dunia and Emmanuelle Blondet, with the help of Sylvie Lascols, under the supervision of Rabia Bazi.

Secretarial services were provided by Catherine Solomon-Alexander.

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# STEERING COMMITTEE

Professor Pierre Ambrosi, cardiologist, Marseille
Françoise Bizouard, physiotherapist, Paris
Anne-Marie Bonnery, nurse, Narbonne
Martine Cacheux, nurse, Maignelay-Montigny
Dr. Pascal Clerc, general practitioner, Issy-les-Moulineaux
Annie Compagnon, nurse, Créteil
Anne-Marie David, nurse, Paris
Dr. Philippe Decq, neurosurgeon, Créteil
Dr. Ghislaine Deklunder, cardiologist, Lille
Dr. Catherine Denis, French Health Products Safety Agency (AFSSAPS), Saint-Denis
Professor Didier Dormont, neuroradiologist, Paris
Professor Maurice Giroud, neurologist, Dijon
Françoise Gomez, physiotherapist, Bordeaux
Dr. Hubert Isnard, public health physician, InVS, Saint-Maurice
Alain Leroy, physiotherapist, Villejuif
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Franck Medina, speech therapist, Nîmes
Patrick Perignon, speech therapist, Châlons-en-Champagne
Dominique Piveteau, nurse, La Roche-sur-Yon
Dr. Jean Sengler, specialist in physical and rehabilitation medicine, Mulhouse
Dr. Denise Strubel, geriatrician, Nîmes
Dr. France Woimant, neurologist, Paris
Dr. Danielle Yatim, specialist in emergency medicine, Nantes

## WORKING GROUP

Professor Jean-Louis Mas, neurologist, Paris – Chairman
Dr. Guy Amah, cardiologist, Paris – Report author
Dr. Nafissa Abdelmoumène, ANAES, Paris - Project manager

Dr. Jean-François Albucher, neurologist, Toulouse
Dr. Caroline Auriche-Burstein, French Health Products Safety Agency (AFSSAPS), Saint-Denis
Professor Gilles Brassier, neurosurgeon, Rennes
Dr. Thomas Debroucker, neurologist, Saint-Denis
Professor Jean-Dominique de Korwin, specialist in internal medicine, Nancy
Professor Didier Dormont, neuroradiologist, Paris
Professor Robert Launois, economist, Paris
Professor Didier Leys, neurologist, Lille
Dr. Hervé Outin, medical intensivist/neurologist, Poissy-Saint-Germain-en-Laye
Dr. Suzel Ravaux, radiologist, Roanne
Dr. Gilles Rodier, neurologist, Mulhouse
Dr. Thierry Rusterholz, specialist in emergency medicine, Strasbourg
Dr. Rémy Sebbah, general practitioner, Marseille
Dr. Denise Strubel, geriatrician, Nîmes
Dr. Jean-Michel Verret, neurologist, Le Mans

## PEER REVIEWERS

Dr. Catherine Adnet-Bonte, neurologist, Roubaix
Professor Pierre Ambrosi, cardiologist, Marseille
Professor Benoit Bataille, neurosurgeon, Poitiers
Professor Joël Belmin, geriatrician, Ivry-sur-Seine
Dr. Maurice Benhamou, vascular surgeon, Neuilly-sur-Seine
Marie-Laure Berthaud, nurse, Limoges

Françoise Bizouard, physiotherapist, Paris
Dr. Marie-Ange Blanchon, geriatrician, Saint-Étienne
Jean-Pierre Bleton, physiotherapist, Paris
Professor Pierre-Édouard Bollaert, medical intensivist, Nancy
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Dr. Jacques Boulliat, neurologist, Bourg-en-Bresse
Dr. Philippe Bourrier, specialist in emergency medicine, Le Mans
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Professor Marie-Germaine Bousser, neurologist, Paris
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Professor Thierry Civit, neurosurgeon, Nancy
Dr. Jean-Noël Dautreppe, neurologist, Bainville-sur-Madon
Dr. Jean-Michel de Bray, neurologist, Angers
Dr. Philippe Decq, neurosurgeon, Créteil
Dr. Ghislaine Deklunder, cardiologist, Lille
Dr. Claude Depriester, neuroradiologist, Lille
Dr. Aude-Emmanuelle Develay, public health physician, Saint-Maurice – ANAES Scientific Council
Dr. Joëlle Dien, neurologist, Saint-Brieuc
Dr. Éric Drahi, general practitioner, Saint-Jean-de-Braye
Dr. Christian Dualé, anaesthesiologist, Clermont-Ferrand
Professor Pierre Dudognon, specialist in physical and rehabilitation medicine, Limoges
Dr. Nathalie Dumarcet, French Health Products Safety Agency (AFSSAPS), Saint-Denis
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Dr. Yves Lambert, anaesthesiologist, Versailles
Catherine Lamy, physiotherapist, Castres
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Professor Vincent Larrue, neurologist, Toulouse
Dr. Philippe Loirat, medical intensivist, Suresnes - ANAES Scientific Council
Dr. Christian Lucas, neurologist, Lille
Cédric Mabire, nurse, Toulouse
Dr. Guillaume Madinier, neurologist, Dijon
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Professor Claude Marsault, neuroradiologist, Paris Dr. Catherine Martin-Hunyadi, geriatrician, Strasbourg
Dr. Jean-Pierre Mattei, neurologist, Ajaccio
Dr. Claude Mekies, neurologist, Toulouse
Dr. Jean-Marc Minguet, specialist in emergency medicine, Draguignan
Nathalie Morin, speech therapist, Lay-Saint-Christophe
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Dr. François Mounier-Vehier, neurologist, Lens
Professor Jean-Philippe Neau, neurologist, Poitiers
Professor Jean-Marc Orgogozo, neurologist, Bordeaux
Patrick Perignon, speech therapist, Châlons-en-Champagne
Dr. Christian Peyroche, general practitioner, Lyon
Dr. Jean-Marc Philippe, specialist in emergency medicine, Aurillac
Dr. Jean-François Pinel, neurologist, Rennes
Dr. Alain Prigent, general practitioner, Évian
Professor Jean-Pierre Pruvo, neuroradiologist, Lille
Professor Muriel Rainfray, geriatrician, Pessac
Professor Gérald Rancurel, neurologist, Paris
Dr. Geneviève Reinhardt, radiologist, Haguenau
Dr. Frédérique Thiennot, specialist in emergency medicine, Saint-Jean-de-Verges
Professor Alain Tournade, neuroradiologist, Colmar
Professor Alain Vergnenègre, specialist in public health, Limoges – ANAES Scientific Council
Dr. Alain Viard, specialist in vascular medicine, Foix
Dr. France Woimant, neurologist, Paris

# I. INTRODUCTION

## I.1 Subject of these guidelines

These guidelines concern the management of stroke patients during the acute phase, i.e. during approximately the first fortnight. They do not cover meningeal haemorrhage. They are intended for all healthcare professionals involved in this phase of management.

## I.2 Level of evidence

Guidelines are graded A, B or C as follows:

- A grade A guideline is based on scientific evidence established by trials of a high level of evidence, e.g. randomised controlled trials of high power and free of major bias, and/or meta-analyses of randomised controlled trials or decision analyses based on properly conducted studies;
- A grade B guideline is based on presumption of a scientific foundation derived from studies of an intermediate level of evidence, e.g. randomised controlled trials of low power, well-conducted non-randomised controlled trials or cohort studies;
- A grade C guideline is based on studies of a lower level of evidence, e.g. case-control studies or case series.

In the absence of scientific evidence, the guidelines are based on agreement among professionals.

## I.3 Definitions and prevalence

There are several types of stroke:

- ischaemic stroke or cerebral infarction (85% of strokes);
- haemorrhagic stroke (15%) subdivided into cerebral haemorrhage (10 %) and meningeal haemorrhage (5%).

The term “cerebral ischaemic event” used in France covers both cerebral infarction and transient ischaemic attacks (TIA), which are episodes of reversible ischaemia where the symptoms resolve within 24 hours. TIAs are the most reliable precursor of cerebral infarction as they share the same causes and mechanisms. A TIA must be investigated rapidly to find the cause and give appropriate treatment.

In industrialised countries, stroke is the third most common cause of death after heart disease and cancer, and the main cause in adults of disability not caused by trauma. In France, the *PMSI* computerised medical information system recorded 169,843 cases of ischaemic and haemorrhagic stroke, including TIAs, in 1999.

## I.4 Diagnosis of stroke, type of stroke and territory involved

Sudden onset of focal neurological disorders or consciousness disorders points to stroke. This should be confirmed by brain imaging:

- immediate brain imaging (MRI, CT scan) is needed to confirm the diagnosis of stroke and to determine whether the stroke is ischaemic or haemorrhagic. Currently, the most powerful examination is MRI using echo-planar sequences (providing an image in an acquisition time of about 100 msec). It affords a very early diagnosis (within an hour) of ischaemia and intracerebral haemorrhage and assessment of whether the stroke is recent or old, its extent, and severity. It is also used to study the blood vessels;
- CT scan without injection of contrast medium will diagnose intracerebral haemorrhage in an emergency setting. The early signs of cerebral ischaemia vary and are difficult to interpret;

- MRI with venous MR-angiography sequences is the most powerful non-invasive examination for diagnosing cerebral venous thrombosis.

The aetiological diagnosis is a keyc step which governs both immediate management and secondary prevention.

# II. GUIDELINES FOR TREATMENT OF STROKE PATIENTS

Stroke is an emergency with regard to both diagnosis and treatment.

## II.1 Monitoring neurological status

Level of consciousness and neurological status should be recorded as soon as possible by the doctor in charge of the patient. Changes should be monitored until stabilisation, at intervals decided by the doctor (according to the patient's condition), and recorded in the patient's file. The following scales are recommended:

- *Scales for level of consciousness*: Use of a simple scale adapted from the Orgogozo scale (normal consciousness/spontaneous waking, drowsiness/clouding of consciousness, reaction (waking) to verbal commands, stupor/reaction to pain, coma/no appropriate reaction). The Glasgow score may also be used but is more suitable for coma induced by trauma than stroke;
- *Scales for neurological status*: Several scales are used in France: Orgogozo scale, Canadian scale, Scandinavian scale, and National Institutes of Health (NIH) scale. The NIH scale is the gold standard for fibrinolysis.

## II.2 Monitoring vital signs

- *Blood pressure (BP)* should be monitored at regular intervals decided by the doctor; the more recent the stroke, the more frequent the BP monitoring.
- An *ECG* should be performed at the start of treatment. Continuous monitoring by CardioScope for the first 48 hours after stroke will detect atrial fibrillation or other concomitant heart disease.
- *Respiratory function and body temperature* should be monitored at intervals decided by the doctor.

## II.3 Treatment of complications

- ***Blood pressure***

No attempt should be made to reduce BP during the acute phase of ischaemic stroke (grade C) or intracerebral haemorrhage, except in the following cases:

- *Ischaemic stroke*
  (i) If fibrinolytic therapy is to be given (BP must be lowered to <185/110 mmHg before treatment) (agreement among professionals based on inclusion criteria in pivotal studies);
  (ii) If fibrinolytic therapy is not likely to be given: if BP > 220/120 mmHg (agreement among professionals) or if there are complications of hypertension which are life-threatening in the short-term (e.g. aortic dissection, uncontrolled heart failure, hypertensive encephalopathy).

- *Intracerebral haemorrhage*
  Although some teams suggest that the treatment threshold should be reduced to 185/110 mmHg, there is no scientific evidence to support the use of different thresholds for intracerebral haemorrhage and ischaemic stroke.

If hypertension is to be treated:

- the method of choice is intravenous (IV) infusion to adjust for BP
- the intramuscular and sublingual routes should be avoided
- the best drugs are urapidil, labetalol and nicardipine; loading doses should be avoided (agreement among professionals)
- BP should be reduced gradually and maintained below 220/120 mmHg, with monitoring of neurological status to detect any deterioration. There is no evidence to support a specific target BP
- pre-existing antihypertensive therapy should be maintained. There is no evidence for a specific threshold below which pre-existing antihypertensive therapy should be discontinued.

• ***Respiratory problems***

The upper airway should be kept free. Bronchial congestion and aspiration pneumonia should be avoided. Routine oxygen therapy is not recommended (grade B).

• ***Pyrexia***

In the absence of any studies defining an intervention threshold, pyrexia (>37.5ºC) should be treated with an antipyretic such as paracetamol (agreement among professionals). Confirmed infection should be treated with appropriate antibiotics.

• ***Dysphagia and nutritional problems***

Dysphagia should always be excluded before food is given for the first time as it exposes the patient to the risk of aspiration pneumonia (grade B). If the patient has dysphagia:

- feeding by mouth should be discontinued and replaced by nutrition appropriate for the patient's nutritional status delivered via a nasogastric tube (gastrostomy feeding has not been assessed during the acute phase);
- an adequate calorie intake should be provided from 48 hours after the stroke (agreement among professionals).

• ***Water and electrolyte imbalance, hyperglycaemia***

- *Water and electrolyte balance and blood glucose* should be monitored and any abnormalities corrected. If IV infusion is required, physiological saline should be used rather than glucose solution.
- *Insulin therapy* should be started when the patient's blood glucose is ≥10 mmol/L although no study has yet defined an intervention threshold (agreement among professionals).

• ***Prevention of venous thrombosis***

Patients should be allowed to get out of bed at an early stage unless neurological symptoms worsen when they stand up.

- *Prevention of venous thrombosis by heparin in patients with acute ischaemic stroke:* When acute ischaemic stroke causes immobilisation or impaired circulation in the legs, low doses of low molecular weight heparin (LMWH) are recommended from the first 24 hours (agreement among professionals). However, the indication should be weighed up in relation to the risk of intra- or extracranial haemorrhage.
- *Use of compression stockings in ischaemic stroke:* There is insufficient evidence to recommend that patients with ischaemic stroke should routinely wear stockings to prevent venous thromboembolism, but they may be recommended when heparin is contraindicated.
- *Use of compression stockings in haemorrhagic stroke*: Immediate use of compression stockings is recommended as the safety of heparin has not been confirmed. Compression may be followed by preventive doses of heparin after 24-48 hours although this strategy is not based on proven evidence.

• ***Prevention of gastrointestinal haemorrhage***

As there are no specific studies concerning stroke, the use of antiulcer medication as a preventive measure is not recommended unless the patient has a history of ulcers.

- ***Anxiety and depression***

Their treatment has been insufficiently assessed during the acute phase of stroke.

- ***Other forms of treatment***

Guidelines for physiotherapy, speech therapy, nursing, prevention of bowel complications, management of incontinence and urinary retention, prevention of skin complications and management of anxiety and depression are dealt with *in "Early management of adult stroke patients – nursing and ancillary services*".

## II.4 Management of the neurological complications of stroke

- ***Cerebral oedema***

Accumulation of excess fluid should be avoided, particularly intracellular accumulation. If fluid restriction is indicated, it should be moderate, around 1,000 ml/day.

- *Hyperosmolar agents* (e.g. mannitol, glycerol) may be used for up to 5 days in patients whose clinical condition is deteriorating, notably if there are signs of cerebral involvement despite lack of scientific evidence for their efficacy.
- *Corticosteroids* should NOT be used (grade B) as they are not only ineffective but dangerous.
- *Decompressive surgery* and *external cooling therapy* are being assessed in the treatment of massive ischaemic stroke. Cooling therapy cannot be recommended as yet.
- The benefit of *intensive care techniques* (mechanical hyperventilation, thiopental) has not been demonstrated.

- ***Epilepsy***

Antiepileptic medication is not recommended as prevention against seizures but is recommended to prevent further seizures if the patient has already had a seizure during the acute phase. The drugs used have not been assessed for stroke, including in status epilepticus. Optimum duration of treatment has not been assessed; there is no evidence to support long-term therapy.

## II.5 Treatment of arterial ischaemic stroke

- ***Antithrombotic agents***

- *Aspririn* (160–300 mg/day) should be started as soon as possible after an ischaemic stroke (grade A), unless thrombolytic therapy is to be given.
- *Heparin****:*** Routine use of curative doses of heparin (unfractionated heparin, LMWH, or heparinoids) is not recommended during the acute phase of ischaemic stroke, including in non-valvular atrial fibrillation (grade A). Curative doses of heparin may be used selectively, when patients are assumed to be at high risk of recurrence or extension, such as heart disease with a high risk of embolism, severe arterial stenosis, presence of an intraluminal thrombus or extracranial arterial dissection (agreement among professionals). The potential benefit should be balanced against the risk of cerebral haemorrhage which is particularly high in the case of extensive cerebral infarct causing consciousness disorders, early signs of extensive ischaemia on imaging, or uncontrolled hypertension.

- ***Fibrinolysis***

- *Recombinant tissue plasminogen activator (rt-PA, alteplase):* Thrombolysis with IV rt-PA is recommended in patients with ischaemic stroke if the treatment can be started within 3 hours of onset of symptoms of stroke and there are no contraindications (grade A).
  - The recommended rt-PA dose is 0.9 mg/kg, maximum dose 90 mg, 10 % as a bolus and
    90 % infused over one hour (grade A).
  - During the 24 hours following rt-PA administration, antiplatelet and heparin therapy are contraindicated.
  - rt-PA may be used in patients taking aspirin at the time they had the stroke although the benefit/risk ratio is not known.
  - Before starting rt-PA treatment, blood pressure should be < 185/110 mmHg and maintained at this level throughout treatment and for the next 24 hours.
  - rt-PA treatment should be given only by doctors trained and experienced in neurology.
  - IV rt-PA should only be used in health care organisations specialising in stroke treatment (agreement among professionals). The clinical trials approving the efficacy of IV rt-PA were all carried out in specialist centres. Available data (case series) from non-specialist centres reveal higher mortality from cerebral haemorrhage, in particular because of lack of compliance with the indications.
- *Intravenous streptokinase* should not be used in fibrinolysis for ischaemic stroke (grade A).
- *Recombinant pro-urokinase plus heparin*: The only randomised trial on the benefit of intra-arterial fibrinolysis demonstrated the efficacy of this combination in patients with ischaemic stroke due to middle cerebral artery occlusion (angiographically documented), treated within 6 hours. No specific recommendations can be made.

- ***Other treatments***

- *Neuroprotective agents* are not recommended as their efficacy has not been proven (grade A). Their use during the 3 hours following a stroke should be assessed.
- *Haemodilution* is not recommended in the treatment of acute ischaemic stroke (grade B).

## II.6 Treatment of cerebral venous thrombosis

*Anticoagulation* at curative doses is recommended in all patients with confirmed cerebral venous thrombosis, including cases when imaging suggests haemorrhage (grade B).

## II.7 Indications for neurosurgery

- The indications for neurosurgery in cerebral haemorrhage and ischaemic stroke have not been sufficiently assessed.

- ***Cerebral haemorrhage***

The decision to operate is taken on the basis of:

- *clinical criteria:* patient's age; current therapy, particularly anticoagulation; level of consciousness (Glasgow School); pupil size; progression;
- *neuroradiological criteria*: size and location of haematoma; concomitant subarachnoid haemorrhage; mass effect; ventricle size. Their assessment requires expert knowledge and experience and preferably image transfer to a neurosurgery department.

- *Cerebellar haematoma*

  - Hydrocephalus caused by obstruction of the fourth ventricle is a reason for intervention (ventricular shunt or endoscopic ventriculocisternostomy) in patients whose clinical condition is worsening, conscious or with moderate consciousness disorders and in the absence of signs of brainstem compression (grade C).
  - Evacuation of haematoma may be undertaken in cases of haematoma >3 cm with hydrocephalus (grade C), coma (lasting for <2 hrs if the coma is deep) or progressive brainstem compression.
- *Lobar cerebral haemorrhage* with clinical aggravation in the absence of contraindications related to general condition (grade B). There is no indication for neurosurgery:
  - when the haematoma is small (<10 $cm^3$) or the neurological deficit minor (grade B);
  - in patients with a hemispheric haematoma and a Glasgow score $\leq 4$ (grade B).
- *Other cases of cerebral haemorrhage*: The best indications for neurosurgery have not yet been determined.

- ***Ischaemic stroke***
- *Temporary external lumbar drainage of cerebrospinal fluid (CSF)* is indicated in patients with a cerebellar infarction with acute hydrocephalus. Infarcted tissue should only very rarely be resected if symptomatic brainstem compression persists after shunting, if MRI does not show any extension of ischaemia to the brainstem itself.
- *Decompressive craniectomy* in malignant middle cerebral artery infarction is currently being assessed. Pending scientific evidence, this treatment may be given in young subjects with an extensive recent middle cerebral artery infarction with oedema (grade C).

### II.8 Indications for management in a medical intensive care unit

There are very few indications for management in an intensive care unit. These are:
- *curable serious concomitant disease* in patients with a good neurological prognosis, such as aspiration pneumonia or pulmonary embolism;
- *intracranial hypertension* if surgery is likely. If there is cerebral herniation, ventilation should be reserved for patients likely to undergo surgery in the near future;
- *unstable and reversible neurological conditions* such as cerebral venous thrombosis with consciousness disorders, status epilepticus, or eclampsia.

The decision whether or not to begin mechanical ventilation following acute stroke should as far as possible be taken jointly by intensivists, specialists in emergency medicine, neurologists and the patient's family. Absence of pupillary light reflex and corneal reflex is an indication of a strong likelihood of death and should be taken into account when deciding whether or not to begin mechanical ventilation.

## III. NEUROVASCULAR UNITS

Although there is no unequivocal definition of a neurovascular unit, the working group agreed with the internationally held view that the following are important:
- *global management of patients* during the acute phase, integrating diagnosis and treatment, treatment of complications, rehabilitation, and prevention of vascular events;
- *a co-ordinated multidisciplinary team* specialising in neurovascular disease, which receives regular training;
- *appropriate technical facilities* dedicated to the early treatment of stroke patients;
- *an upstream and downstream care network*;
- *consideration of the patient's goals, and involvement of their family in treatment.*

Whenever possible, suspected stroke patients should be admitted to a neurovascular unit (grade B), apart from patients who require immediate treatment in a medical or neurosurgical intensive care unit. The working group felt that it is a matter of urgency to be able to offer stroke

patients *structured care*, integrating both care during the acute phase and follow-up care and rehabilitation. *Improvement in prehospital treatment*, particularly in terms of speed of treatment and directing the patient to the right treatment centre, and a *downstream care network* are essential to ensure maximum efficacy of neurovascular units.

## IV. ORGANISATION OF THE CARE NETWORK – PREHOSPITAL MANAGEMENT

An information campaign is needed to raise awareness among the general public and teach them to recognise the warning signs of a TIA or stroke, and to treat these signs as an emergency (Box 1). All healthcare professionals should contribute to having stroke regarded as a medical emergency.

The patient should be transferred to hospital as rapidly as possible, ideally directly to a neurovascular unit or emergency department, as the results of treatment depend on this. In France, the medical emergency telephone centre should be called ("Centre 15").

**BOX 1.** Example of an information campaign for the general population

The 5 warning signs suggesting acute stroke (cerebral infarction or meningeal haemorrhage) are:

- sudden numbness or weakness of the face, arm or leg, especially on one side of the body
- sudden trouble seeing in one or both eyes
- sudden confusion, trouble speaking or understanding
- sudden, severe headache with no known cause
- sudden trouble walking, dizziness, loss of balance or coordination, particularly when combined with one of the above.

*Source: American Heart Association and the American Stroke Association*

- **What should and should not be done during the prehospital phase?**

- Check that there is no immediately life-threatening situation.
- Assess the level of consciousness, degree of deficit (presence or absence of stroke, ability to move upper and lower limbs against resistance or against gravity).
- Determine when the neurological disorders began (this can be done by the patient or by a witness), together with previous and current treatment, and send this information to the admission unit.
- Measure blood pressure while lying down.
- Arrange immediate transfer to a neurovascular unit.
- If the patient has a family, see that a family member accompanies them to hospital.
- Reduce any delay before treatment by neurologists in hospital.
- In the case of a TIA, arrange for an aetiological workup without delay.
- Do not give antihypertensive therapy, unless the patient has heart failure.
- Do not give corticosteroids.
- Do not give heparin.
- Do not give any intramuscular injections.