Clinical practice guidelines

Diagnosis and immediate management of transient ischaemic attacks (TIAs) in adults

May 2004
## Synopsis

<table>
<thead>
<tr>
<th>Title</th>
<th>Diagnosis and immediate management of transient ischaemic attacks (TIAs) in adults</th>
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<tbody>
<tr>
<td>Publication date</td>
<td>May 2004</td>
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<tr>
<td>Requested by</td>
<td>ANAES’ Scientific Council following a request by the French Neurovascular Society on related topics</td>
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<tr>
<td>Produced by</td>
<td>ANAES – French National Agency for Accreditation and Evaluation in Healthcare (Guidelines Department)</td>
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<tr>
<td>Intended for</td>
<td>Health professionals involved in managing adults who have had a TIA</td>
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</table>
| Objectives | - Update the definition of TIA  
- Specify clinical symptoms for a diagnosis  
- Address TIA prognosis  
- Describe tests for positive and aetiological diagnosis  
- Describe immediate treatment |
| Assessment method | - Systematic review of the literature (with evidence levels)  
- Discussion among members of a multidisciplinary working group  
- External validation by peer reviewers (see Anaes guide “Recommandations pour la pratique clinique – base méthodologique pour leur réalisation en France – 1999”) |
| Literature search | Jan 1993 – May 2003  
301 articles identified of which 128 analysed |
| ANAES project leader(s) | Dr. Philippe Martel (Department head: Dr. Patrice Dosquet)  
(Literature search: Marie George with the help of Sylvie Lascols (Department head: Rabia Bazi))  
Secretarial work: Elodie Sallez |
| Author of draft report | Dr Jean-François Albucher, neurologist, Toulouse |
| Collaborations and participants (annex 1) | - Learned societies  
- Steering committee  
- Working group (Chair: Professor Jean-Louis Mas, neurologist, Paris)  
- Peer reviewers |
| Internal validation | ANAES Scientific Council (Referees: Dr Bernard Ortolan, general practitioner, la Hay-lès-Roses; Professor Alain Vergnenègre, lung specialist, Limoges) |
| Other ANAES publications on the topic (in English) | Early management of adult stroke patients - Medical aspects (Sept. 2002) www.anaes.fr |
I. Introduction

I.1 Objective

The aim of these guidelines is to provide a strategy for the diagnosis and immediate treatment of transient ischaemic attacks (TIAs).

I.2 Scope of the guidelines

These guidelines provide and updated definition of TIA that takes account of current neuro-imaging data and management of neurovascular emergencies.

- specify the relevance of clinical signs suggesting a TIA and list differential diagnoses.
- assess the prognosis of TIA to determine time limits for diagnosis and initiation of treatment.
- describe the tests for a positive diagnosis and to find the cause.
- describe the immediate treatment to be given while awaiting results of tests to determine the cause.

These guidelines do not cover:

- a specific assessment of each test used to determine TIA cause.
- preventive measures to be implemented depending on the cause of the TIA; this will be the subject of future guidelines.
- TIA in children.

I.3 Context

These guidelines form part of a set of guidelines on stroke produced by ANAES at the request of the French Neurovascular Society. The other guidelines cover medical and paramedical aspects of the early management of adults who have had a stroke; imaging in stroke; the role of stroke units in the management of patients, and the return home of adults after a stroke.

II. Assessment method

The guidelines were produced using the method described in Annex 2:

- discussions within a multidisciplinary working group (3 meetings).
- comments by peer reviewers.

They were graded on the basis of the strength of the evidence of the supporting studies (Annex 2). If no grade is given, they are based on agreement among professionals.
within the working group after taking into account the comments of peer reviewers. Most of these guidelines are based on agreement among professionals. The data used in support are available in the full report (in French) on the ANAES website (www.anaes.fr).

III. Definition of TIA

III.1 Classic definition of TIA

The classic definition of TIA is a sudden neurologic or retinal deficit of ischaemic origin, confined to an area of the brain or eye supplied by one vascular system, the symptoms of which regress completely within 24 hours. This definition uses an arbitrary time interval of 24 hours which is simple to use, particularly for epidemiological purposes, but which has limitations:
- most TIA (approximately 2 out of 3) last less than an hour;
- the likelihood that symptoms lasting more than an hour will resolve within 24 hours is low (about 15%);
- some transient episodes are associated with ischaemic lesions on brain imaging; the longer symptoms last, the more common they are;
- the definition is not convenient as it may encourage waiting for a spontaneous resolution whereas such episodes should be managed as an emergency.

III.2 New definition of TIA

The TIA working group proposed a new definition: “A TIA is a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, and without evidence of acute infarction”.

The new definition is currently based on detection of acute infarction by imaging and gets rid of some of the limitations of the classic definition. Its main disadvantage is that it depends on the availability and quality of neuroimaging devices. In addition, the use of the adverb “typically” to qualify “lasting less than one hour” is ambiguous. Episodes lasting more than an hour with no proof of acute infarction will be classified as TIA in practice.

In the absence of a test that can discriminate satisfactorily between reversible and irreversible ischaemia, as in myocardial ischaemia, the working group considered that the new definition has more advantages than drawbacks, and proposed to adopt it.

III.3 In practice

The recommended medical approach in a patient with:
- a persistent neurological deficit, is to consider the situation as an acute stroke (i.e. an emergency), even if symptoms resolve quickly, and to put appropriate diagnostic and treatment measures into action,

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- a resolved neurological deficit, is to start the diagnostic and treatment measures described below without delay so that secondary prevention can begin as soon as possible. If brain imaging shows recent infarction in a territory compatible with clinical signs, the event is qualified as a regressive ischaemic stroke. If not, it is a TIA. Management is the same in both cases.

IV. Diagnosis of TIA

Diagnosis of TIA can prove difficult because of the wide range of symptoms, the number of differential diagnoses and because diagnosis is retrospective. Quality of diagnosis relies on careful questioning of patients and of witnesses to the attack. Equal attention should be paid to the symptoms themselves and to their timing and the circumstances in which they occurred.

Symptoms compatible with a diagnosis of TIA can be classified as either probable TIA or possible TIA (Table 1). TIA is probable if there is rapid onset, usually < 2 minutes, of one or more of the symptoms listed under “Probable TIA” (left-hand column). The symptoms in the right-hand column are compatible with a TIA but other diagnoses should be considered first, if one of these symptoms occurs in isolation. The diagnosis becomes probable TIA if these symptoms are combined, successively or concomitantly, with each other or with the symptoms given under “Probable TIA”.

Table 1. Symptoms of probable and possible TIA

<table>
<thead>
<tr>
<th>Probable TIA</th>
<th>Possible TIA</th>
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<tbody>
<tr>
<td><strong>Symptoms suggesting carotid TIA</strong></td>
<td>Vertigo</td>
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<tr>
<td>- Monocular blindness</td>
<td>Diplopia</td>
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<tr>
<td>- Speech deficit (aphasia)</td>
<td>Dysarthria</td>
</tr>
<tr>
<td>- Unilateral motor and/or sensory symptoms</td>
<td>Trouble swallowing</td>
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<tr>
<td>affecting the face and/or limbs; these symptoms</td>
<td>Loss of balance</td>
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<tr>
<td>usually indicate ischaemia in the carotid territory, but in the absence of other signs it is not possible to tell whether the attack is of carotid or vertebrobasilar origin.</td>
<td>Isolated sensory symptoms affecting only part of a limb or half the face</td>
</tr>
<tr>
<td><strong>Symptoms suggesting vertebrobasilar TIA</strong></td>
<td>Drop attack</td>
</tr>
<tr>
<td>- Motor and/or sensory symptoms affecting the face and/or limbs, bilateral or changing sides between attacks;</td>
<td></td>
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<tr>
<td>- Loss of vision in the right or left field of vision (homonymous hemianopsia) or in both fields of vision (cortical blindness); homonymous hemianopsia may also be seen in carotid TIAs.</td>
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</tbody>
</table>

The symptoms in Table 2 should not suggest TIA, except under exceptional circumstances.

Table 2. Symptoms that do not suggest TIA

| Impaired consciousness with no other sign of vertebrobasilar circulation disorder |
|----------------------------------|----------------------------------|
| Isolated confusion               | Isolated dizziness               |
| Isolated amnesia                 | General weakness                 |
| Fainting                         | Scintillating scotoma            |
| Isolated tinnitus                | Urinary and/or anal sphincter incontinence |
| Stepwise progression of symptoms (particularly sensory) involving several parts of the body | Acute behavioural problems |

IV.1 Differential diagnosis of TIA

Differential diagnoses are listed in Table 3.

Table 3. Differential diagnoses

<table>
<thead>
<tr>
<th>Neurological disorders</th>
<th>Non-neurological disorders</th>
<th>In case of transient monocular blindness</th>
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</thead>
<tbody>
<tr>
<td>Migraine with aura</td>
<td>Metabolic disorders (particularly hypoglycaemia)</td>
<td>Amaurosis related to malignant hypertension</td>
</tr>
<tr>
<td>Focal epileptic seizure</td>
<td>Vertigo of ENT origin (Ménière's disease, benign paroxysmal positional vertigo, vestibular neuritis)</td>
<td>Acute glaucoma</td>
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<tr>
<td>Other:</td>
<td>Syncpe</td>
<td>Intracranial hypertension</td>
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<tr>
<td>- Brain tumour</td>
<td>Orthostatic hypotension</td>
<td>Central retinal vein thrombosis</td>
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<tr>
<td>- Cerebrovascular malformation</td>
<td>Hyperventilation syndrome</td>
<td>Retrobulbar optic neuritis</td>
</tr>
<tr>
<td>- Subdural haematoma</td>
<td>Hysteria, simulation</td>
<td>Detached retina</td>
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<tr>
<td>- Brain haemorrhage</td>
<td></td>
<td></td>
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<tr>
<td>- Multiple sclerosis</td>
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<tr>
<td>- Transient global amnesia</td>
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<td></td>
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<tr>
<td>- Myasthenia</td>
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<tr>
<td>- periodic paralysis</td>
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V. Strategy for diagnosis and treatment

V.1 Time limits and management strategy

TIA should be considered as a diagnostic and treatment emergency because:
- the risk of ischaemic stroke after TIA is high, particularly near to the episode (2.5-5% at 48 hours, 5-10% at 1 month, 10-20% at 1 year); these data concern TIAs fulfilling the criteria of the classic definition;
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- effective treatments for secondary prevention are available (level of evidence 1). A workup is needed to find the cause of the TIA as this determines treatment. The workup and brain imaging should be performed promptly in all patients but the literature does not provide evidence on time limits. The more recent the attack, the more urgent they are. The working group proposed that they should be performed on an emergency basis in patients with recent TIA. Admission to a specialized unit is recommended:
  - if a work-up can be obtained sooner;
  - in the event of recurrent and recent TIAs, and of TIAs in patients receiving anti-platelet therapy;
  - if the patient’s circumstances warrant it (concomitant morbidity, age, social isolation).

### V.2 Brain imaging

If a TIA is suspected, brain imaging:
- helps to eliminate some differential diagnoses in an emergency situation, particularly intracranial bleeding which would contraindicate antithrombotic therapy;
- may help to confirm previous cerebral ischaemia and so confirm the presence of a vascular disorder;
- is necessary for a positive diagnosis of TIA under the new definition (“absence of acute infarction”);
- may demonstrate signs of recent ischaemia in the appropriate territory (ischaemic stroke under the new definition).

The recommended investigation is magnetic resonance imaging (MRI) with a diffusion-weighted sequence (Grade C). If MRI is not possible or is contraindicated, brain scan without injection of contrast medium should be used.

### V.3 Determining the cause

Investigation of the cause should be tailored to each individual, the circumstances, the clinical history and suspected cause. Tests should be in 2 steps.

**Initial tests** should be carried out as soon as possible:
- non-invasive investigation by Doppler ultrasound of the arteries supplying the brain (with transcranial Doppler if possible). Depending on the equipment available, the first-line investigations may be magnetic resonance angiography or spiral CT angiography when combined with brain imaging;
- electrocardiography (ECG);
- lab tests, including at least: complete blood count, erythrocyte sedimentation rate (ESR), C-Reactive Protein (CRP), blood electrolytes, blood glucose, blood creatinine, prothrombin time (PT), activated partial thromboplastin time (APTT).

**Subsequently**, other tests may be carried out for more thorough investigation or confirmation of the cause:
- transthoracic or transoesophageal echocardiography;
- further investigations of the cervical and cerebral arteries, including catheter angiography if necessary;
- further blood glucose tests and lipids;
- depending on the circumstances (list not exhaustive): antiphospholipid autoantibodies, 24-hour Holter monitoring, examination of the cerebrospinal fluid, etc.

In patients who have had a TIA and who have atherosclerotic lesions or risk factors for atherosclerosis, other asymptomatic locations of atherosclerosis, particularly coronary, are common. Further study is needed to determine whether they are worth routine investigation. In the absence of scientific evidence, the working group considered that investigation for possible asymptomatic coronary lesions should be decided on a case-by-case basis.

### V.4 Treatment

After a TIA, aspirin therapy should be started as soon as possible at a loading dose of 160-300 mg/day if there are no contraindications, while awaiting results of tests to find the cause. This recommendation is based on:
- the risk of occasionally rapid onset of stroke after a TIA (2.5-5% at 48 hours)
- the rapid action of aspirin
- its efficacy in secondary prevention after a TIA (level of evidence 1)
- its efficacy in preventing recurrence during the acute phase of ischaemic stroke (level of evidence 1).

To ensure that no intracranial bleeding contraindicates the use of anti-platelet drugs, an MRI or brain CT-scan should be performed urgently before starting aspirin therapy. If they are not immediately available, the working group and peer reviewers considered that anti-platelet treatment could nevertheless be offered because this strategy is likely to have a positive benefit/risk ratio.

Treatment should be reassessed when the results of aetiological tests of the TIA are available. These should be carried out as soon as possible as the risk of stroke after a TIA and the secondary prevention measures to be used (anti-platelet drugs, anticoagulants, carotid surgery, management of cardiovascular risk factors) depend largely on cause. These measures will be dealt with in future guidelines.
Annex 1 – Participants

Learned societies consulted

Collège national des généralistes enseignants
Société de formation thérapeutique du généraliste
Société française d’angiologie
Société française de cardiologie
Société française de chirurgie vasculaire
Société française d’hématologie
Société française de gériatrie
Société française de médecine générale
Société française de médecine vasculaire
Société française de neurologie
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Dr France Woimant, neurologist, Paris

ANAES / Guidelines Department / May 2004
Annex 2 – Assessment method

The ANAES method for producing these clinical practice guidelines\(^3\) comprised the following steps:

**Defining the scope of the guidelines (Steering committee).** ANAES invited representatives from learned societies concerned by the topic to take part in a steering committee whose job was to define the scope of the guidelines, to review previous work on the subject, and to define which professionals should take part in a working group or act as peer reviewers.

**Literature search (ANAES Documentation Department):** See below

**Drafting the guidelines (Working group).** The ANAES project manager formed a working group of 17 professionals from a number of disciplines, working in different types of practice, from all over the country. The chair of the working group coordinated the production of the guidelines with the help of the project manager whose job was to ensure conformity with the methodological principles of guideline production. One member of the working group identified, selected, and analysed relevant studies (from a literature search performed by the ANAES Documentation Department) and wrote a draft report. This draft report was discussed by the working group over 3 meetings and amended accordingly. Proposals for future studies and action were made.

**External validation (Peer reviewers).** Peer reviewers were appointed according to the same criteria as working group members. They were consulted by post after the second working group meeting, with regard to the readability, applicability and relevance of the guidelines (scores from 1 to 9). The ANAES project manager summarized their comments and submitted them to the working group prior to the third meeting. Peer reviewers were asked to sign the final document.

**Internal validation (Evaluation Section of the Anaes Scientific Council).** Two members of the Council acted as referees reporting to the Council. The working group finalized the guidelines with due regard to the Council's suggestions.

- **Literature search and analysis (general procedure)**

The scope of the literature search was defined by the steering committee and the project manager. The search was carried out by the ANAES Documentation Department and focused on searching:
- medical and scientific databases over an appropriate period, with special emphasis on retrieving clinical practice guidelines, consensus conferences, articles on medical decision-making, systematic reviews, meta-analyses and other assessments already published nationally or internationally (articles in French or English)
- specific and/or financial/economic databases, if necessary
- all relevant websites (government agencies, professional societies, etc.)

\(^3\) Full details are given in “Recommandations pour la pratique clinique – base méthodologique pour leur réalisation en France – 1999” (ANAES)
- the grey literature (documents not identified through the usual information distribution circuits)
- legislative and regulatory texts.

Further references were obtained from citations in the articles retrieved above and from working group members’ and peer reviewers’ own reference sources. The search was updated until the project was completed.

The articles selected were analysed according to the principles of a critical appraisal of the literature, using a checklist, to allocate a level of scientific evidence to each study. Whenever possible, the working group based their guidelines on this review of the literature. Guidelines were graded from A to C as shown in Table 1 depending on the level of the evidence of the supporting studies. If no grading is given, they are based on agreement among professionals.

Table 1. Grading of guidelines

<table>
<thead>
<tr>
<th>Level of published scientific evidence</th>
<th>Grade</th>
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<tbody>
<tr>
<td><strong>Level 1</strong></td>
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<tr>
<td>Randomised controlled trials of high power</td>
<td>A: Established scientific evidence</td>
</tr>
<tr>
<td>Meta-analyses of randomised controlled trials</td>
<td></td>
</tr>
<tr>
<td>Decision analyses based on properly conducted studies</td>
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<tr>
<td><strong>Level 2</strong></td>
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<tr>
<td>Randomised controlled trials of low power</td>
<td>B: Presumption of scientific foundation</td>
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<tr>
<td>Properly conducted non-randomised controlled trials</td>
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<tr>
<td>Cohort studies</td>
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<tr>
<td><strong>Level 3</strong></td>
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<tr>
<td>Case-control studies</td>
<td>C: Low level of evidence</td>
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<tr>
<td><strong>Level 4</strong></td>
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<tr>
<td>Comparative studies with major bias</td>
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<td>Retrospective studies</td>
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<td>Case series</td>
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