What is a Transient Ischemic Attack?

A transient ischemic attack (TIA) is a focal neurological deficit of sudden onset, which, by definition, lasts less than 24 hours. Most TIAs, however, last less than 20 minutes. They are usually diagnosed in retrospect by careful history-taking. The neurological examination should be nor-
TIAs are of concern to the clinician, as they portend an increase risk of stroke, (approximately 12% in the first year post-TIA). Approximately 40% of individuals with stroke have experienced at least one preceding TIA.1

TIAs may be classified according to the vascular territory in which they occur. TIAs may affect the retinal circulation, the anterior circulation (carotid artery territory TIA) or the posterior circulation (vertebrobasilar territory TIA). Of these, TIAs occurring in the retinal circulation and carotid artery territory are the most common.

Retinal territory TIAs are called transient monocular blindness (TMB), or amaurosis fugax. TMB is characterized by the sudden onset of painless, unilateral visual loss. Patients may sometimes describe a curtain descending in front of their eye. More commonly, patients simply are aware of a sudden loss of vision in the eye. Patients should be questioned as to whether they covered each eye.

Most TIA patients should undergo carotid ultrasonography to determine the presence and degree of carotid stenosis and cranial CT scanning in order to exclude intracranial lesions that may mimic TIAs.
alternately and confirmed the monocular nature of the symptom. Occasionally, attacks of TMB can be multiple over a short period of time (e.g., one or twice daily for a week). Although TIAs generally last minutes, TMB is probably the only type of TIA that can last seconds. Generally, the prognosis of TMB is more favorable than with other types of TIA.

Carotid artery territory TIAs are characterized by symptoms referable to one side of the body, as well as other hemispheric specific symptoms (e.g., dysphasia, visual field defect, etc.). Typical carotid territory TIA symptoms include transient hemiparesis (weakness of face, arm and leg on one side of the body), with or without speech disturbance or hemisensory impairment.

Vertebrobasilar territory TIAs are typified by their complex symptomatology, reflecting ischemia to one of several levels of the brainstem and cerebellum. Symptoms strongly suggesting a vertebrobasilar territory TIA include limb clumsiness, double vision, vertigo, bilateral motor and/or sensory symptoms or gait instability.

The Management of TIAs

TIAs must be differentiated from other disorders that may have a neurologic, cardiac or non-specific origin. Generalized fatigue or weakness, non-specific dizziness, isolated vertigo and episodic loss of consciousness are rarely due to transient ischemic attacks. These latter complaints have other systemic etiologies including anemia, depression or cardiac disease.

TIAs must also be differentiated from migraine, seizure activity and syncope. Headache may rarely accompany a true TIA, but is never a major symptom. Migrainous aura can usually be readily distinguished from a TIA. A migrainous aura is usually accompanied by positive symptoms, (e.g., flashing or colored lights, paresthesias, etc.), whereas as TIA symptoms usually include loss of function or negative symptoms (e.g., weakness, visual loss, sensory loss). Only very rarely are TIAs accompanied by uncontrolled motor activity. The latter is much more suggestive of seizure activity rather than a TIA. Syncope, usually produced by global cerebral hypoperfusion (e.g., fainting spell, cardiac dysrhythmia, etc.) is only very rarely associated with focal neurological symptoms.

Since TIAs usually have resolved by the time that the patient has sought a physician’s attention, office management is appropriate. Referral to an emergency room is usually not required, except under certain circumstances (see below). A thorough history of the event is mandatory. The patient’s cardiovascular-risk-factor profile should be established, (e.g., history of hypertension, diabetes, smoking, coronary artery disease, hypercholesterolemia). A complete neurological and cardiac examination is indicated, looking specifically for the presence of hypertension, a carotid bruit, atrial fibrillation or a new cardiac murmur. Most patients with a TIA should be prescribed an antiplatelet medication for prevention of future stroke and recurrent TIA (see article on “Prevention of Ischemic Stroke,” by Dr. Robert

**TIAs occurring in patients with a history of recent head trauma or in patients already taking oral anticoagulants may indicate intracerebral hemorrhage, and should be referred to hospital.**
Coté in this issue of *The Canadian Journal of CME*). Most TIA patients should undergo carotid ultrasonography to determine the presence and degree of carotid stenosis and cranial CT scanning in order to exclude intracranial lesions that may mimic TIAs.

Although most TIAs can be managed in the office, certain TIAs would be considered quite worrisome and for these, urgent emergency room referral is indicated. Any patient experiencing multiple TIAs over a short period of time (“crescendo TIAs”) should be referred to hospital. Such TIAs often occur in the context of high-grade carotid artery stenosis and are associated with a high risk of stroke. TIAs occurring in patients with a history of recent head trauma or in patients already taking oral anticoagulants (e.g., warfarin) may indicate intracerebral hemorrhage, and should be referred to hospital. In addition, patients experiencing TIAs in different vascular territories or in the context of severe headache or neck pain should be referred to hospital.

Patients experiencing a TIA in the setting of atrial fibrillation should have prompt referral (usually on an outpatient basis) to a neurologist and cardiologist. Cranial computed tomography (CT) scanning is considered more urgent in these individuals, as they will likely be prescribed oral anticoagulants. Those TIA patients noted to have a carotid bruit appropriate to the side of a recent carotid territory event should have urgent outpatient referral to a neurologist. Such patients may require carotid endarterectomy.

**What is a Stroke?**

A stroke refers to a focal neurological deficit of sudden onset, presumed vascular in origin, accompanied by abnormal neurological signs persisting beyond 24 hours. A stroke is a clinical syndrome that is usually accompanied by a vascular lesion seen on cranial CT scanning or magnetic resonance imaging (MRI). Vascular lesions seen on CT or MRI, without clinical accompaniment, should be referred to as infarctions or silent strokes.

**Stroke Subtypes**

Strokes may be either ischemic or hemorrhagic. Approximately 85% of strokes are ischemic and the remainder hemorrhagic. Of the ischemic strokes, fully 50% are secondary to either large vessel atherosclerotic disease (e.g., carotid artery stenosis) or intracranial small vessel disease, (as is frequently seen in hypertensive or diabetic patients). About 20% of ischemic strokes are cardioembolic in origin, occurring in the context of atrial fibrillation, valvular heart disease or ventricular dysfunction (usually secondary to coronary artery disease). In about 20% to 30% of individuals with ischemic stroke, no specific origin or etiology can be established. Five per cent of all ischemic strokes are due to unusual etiologies such as hypercoagulable (or prothrombotic) state.

**Epidemiology of Stroke in Canada**

The incidence of stroke in Canada is approxi-
mately 138 cases per 100,000 population.\(^2\) Approximately 40,000 to 50,000 strokes occur annually in Canada. Of these, over 16,000 individuals are expected to die from stroke annually, making stroke the third leading cause of death in Canada. It is estimated that there are about 200,000 to 300,000 stroke survivors living in Canada. About 25% of stroke survivors will have made a complete recovery, whereas the majority (about 60%) will have residual functional disabilities. Stroke recurrence rates range from 5% to 12% per year, depending upon stroke subtype (see above) and the patient’s particular cardiovascular-risk-factor profile.

The Financial Cost of Stroke

The cost of stroke in Canada is estimated to be about $2.5 billion.\(^3\) The average cost to the health-care system for an acute stroke is about $27,500 per patient. A severe stroke may cost up to $80,000 per patient. The average cost for inpatient stroke rehabilitation is about $32,000 per patient.

The Management of Acute Ischemic Stroke

Patients experiencing an acute stroke should usually be referred to a local emergency room with experience in the management of acute stroke. Emergency room referral is indicated because:

- Stroke symptoms, at their onset, cannot be distinguished from a TIA;
- A hemorrhagic stroke cannot reliably be distinguished from an ischemic stroke on clinical grounds without a cranial CT scan; and
- Specific treatments for acute stroke exist and these can only be administered within a hospital setting.

Patients with stable stroke symptoms of several days duration need not necessarily be referred to the emergency room. Hospital referral may, however, be required for such patients if there is a significant functional deficit (e.g., weakness, speech impairment, swallowing difficulties, etc.).

Specific Treatment Options

**Thrombolysis for Acute Stroke.** Intravenous recombinant tissue plasminogen activator (rt-PA) has been approved in Canada, since February 1999, for the treatment of acute ischemic stroke within three hours of symptom onset. This approval had been granted based on the positive results of a single, two-part trial carried out by the National Institute of Neurologic Diseases and Stroke (NINDS) in 1995.\(^4\) The NINDS trial reported an 11% to 15% absolute benefit of rt-PA over placebo. Those treated with rt-PA were one-third more likely to have a very

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**Table 1**

**Factors That Can Exacerbate Stroke**

- Hypertension
- Hyperglycemia
- Hypoxia
- Fever

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favorable outcome compared with those who had received placebo. This benefit was noted at three months after stroke, as measured by performance on several standardized, validated neurological and functional scales. The benefit of rt-PA extended to a variety of stroke subtypes, including small-vessel occlusive stroke (lacunar infarctions), large-vessel occlusive stroke and cardioembolic stroke. Overall mortality rates did not differ between the rt-PA group and the placebo group. From a safety point of view, however, symptomatic intracranial hemorrhages were more common in the rt-PA-treated group. The symptomatic intracranial hemorrhage rate in the rt-PA group was approximately one in 15, and almost half of these hemorrhages were fatal.

The overall beneficial results of the NINDS trial were not seen in a European trial carried out around the same time, and trials designed to increase the time to treatment with rt-PA, (e.g., three to six hours) provided either neutral results or indicated harm from treatment.5-7

All patients presenting to hospital within three hours of stroke-symptom onset should be considered potential candidates for intravenous rt-PA, providing that no contraindications exist (see below) and that treatment is begun within three hours of symptom onset. For a patient who has awakened with a stroke, the time of onset of symptoms is assumed to be when the patient was last known to be well—usually the time the patient went to bed. Therefore, most patients who awaken with stroke (a quite common occurrence) are not candidates for rt-PA.

Contraindications to the Use of rt-PA

Guidelines for the use of rt-PA, including inclusion and exclusion criteria have been previously published.8 Any sign of intracranial hemorrhage on the initial cranial CT is an absolute contraindication for the use of rt-PA. Those with a previous history of intracranial hemorrhage (recent or remote) should not receive rt-PA. The presence of any form of coagulopathy (e.g., concurrent use of warfarin with an INR ≥ 5.5, use of heparin within the previous 48 hours, thrombocytopenia with a platelet count <100,000/mm³) is a contraindication for the use of rt-PA. Recent acetylsalicylic acid (ASA) use is not a contraindication. Those with a history of recent transmural (Q wave) myocardial infarction, major head injury, gastrointestinal or genitourinary bleeding or recent (< 21 days) major surgery are not candidates for rt-PA. Inability to maintain blood pressure less than 180/100 mmHg, despite simple, non-aggressive measures (e.g., topical nitroglycerin) is also a contraindication to the use of rt-PA.

All potential rt-PA candidates must undergo cranial CT scanning to exclude an intracranial hemorrhage. The initial CT scan, ideally, should be free of any signs of recent cerebral infarction. Presumably there would be no benefit to re-perfuse tissue destined for infarction, and, moreover, re-establishing blood flow to infarcted blood vessels and brain tissue could lead to hemorrhagic transformation of the infarction. In most instances, however, the initial cranial CT scan will show early and subtle signs of infarction. For the most part, such signs would not represent contraindications to the use of rt-PA. Major signs of infarction (e.g., hypodensity greater than one-third of the territory of the middle cerebral artery, shift of midline structures, or ventricular compression) usually predict poor outcome and may increase the risk of rt-PA associated intracerebral hemorrhages. Patients presenting with such signs on their initial cranial CT should not receive rt-PA.

Only personnel who are experienced in the diag-
nosis and management of acute ischemic stroke should administer rt-PA. CT scanning and interpretation must be available 24 hours per day. Treatment with rt-PA is generally given in the emergency department and post-treatment monitoring of vital signs (particularly blood pressure) should be done in either a dedicated stroke unit, intermediate medical care unit, or, if these are unavailable, an intensive care unit. Hematological and neurosurgical consultants should be available in case treatment-related complications develop. Patients should undergo routine cranial CT scanning 24 hours after treatment regardless of status. Cranial CT scan should be performed on an urgent basis if there is deterioration in the patient’s neurological status. Most intracerebral hemorrhages related to rt-PA treatment occur within the first 24 hours after treatment.

**Stroke Patients Ineligible For rt-PA**

Unfortunately, most stroke patients will be ineligible for rt-PA. The most frequent reason for exclusion is failure to present to hospital early enough to initiate treatment within three hours of symptom onset.

Although both heparin (intravenous or subcutaneous) and ASA are frequently used in the context of acute ischemic stroke, their precise role has only recently been clarified. The results of two acute stroke “mega-trials” indicate that ASA, when given early after ischemic stroke, can prevent about nine deaths or recurrent non-fatal strokes per 1,000 patients in the first few weeks. Early ASA treatment is also associated with 13 fewer dead or dependent per 1,000 patients several weeks or months following acute ischemic stroke. Heparin, on the other hand, had no net benefit in the setting of acute ischemic stroke and may even be harmful. Neither ASA nor heparin, however, re-establish blood flow to ischemic tissue.

Most, if not all, patients with acute stroke who are ineligible for rt-PA should be prescribed ASA. Doses can range between 160 mg to 325 mg once daily for a period of two to four weeks. ASA could be withheld in patients with significant swallowing difficulties until the latter resolves. Low-dose subcutaneous heparin (e.g., 5,000 units twice per day) should be prescribed to those at high risk for the development of a deep venous thrombosis (e.g., the densely hemiplegic patient). Intravenous heparin may still be considered an option for those patients with progressing stroke (see below) or fluctuating stroke, particularly in the vertebrobasilar territory.

**Acute Cardioembolic Stroke**

Cardioembolic stroke often occurs in the setting of underlying non-valvular atrial fibrillation. Because of the low risk of recurrent stroke within the first two weeks and the risk of hemorrhagic
transformation (see below), it is generally recom-
manded to avoid the use of heparin acutely in
patients with presumed cardioembolic stroke.
Depending on the clinical evolution, such patients
may simply be started on warfarin three to 14 days
after the initial stroke, providing that there is no
hemorrhage seen on a repeat cranial CT scan.

**Other Specific Treatments For Stroke**

Intra-arterial rt-PA has been shown to be effective in
certain individuals with large ischemic hemispheric
strokes. This treatment, however, can only be
offered in a small number of specialized centers,
thus limiting its large-scale applicability.

Trials conducted on other specific stroke treat-
ments, including low-molecular-weight heparins,
heparinoids, defibrinogenating agents and a variety
of neuroprotectant agents have failed to demon-
strate efficacy.

**Factors That Can Exacerbate Acute Stroke**

There are several factors that can exacerbate stroke
and adversely affect outcome (Table 1).

**Hypertension** is seen commonly in the context of
acute stroke, particularly when the stroke is large.
In most cases, the hypertensive response is appro-
priate in that a higher mean arterial blood pressure
is required to overcome raised intracranial pressure
and maintain adequate cerebral perfusion. In most
instances, blood pressure will return to pre-stroke
values after several days. It is generally recom-
mended to avoid antihypertensive treatments in the
early phases of acute stroke. The American Stroke
Association recommends treating blood pressure, in
the context of acute stroke, only if values exceed
230 mmHg systolic or 130 mmHg diastolic. For
those stroke patients who are candidates for intra-
venous rt-PA, however, blood pressure must be
maintained at or below 180/100 mmHg.

**Hyperglycemia** may be seen in the context of
acute stroke, either secondary to underlying dia-
abetes mellitus or secondary to a stress response.
Hyperglycemia has been shown to increase the size
of experimental infarction and is associated with
worsened prognosis from stroke. The goal should
be to maintain euglycemia, usually with an insulin
sliding scale or continuous infusion.

**Hypoxia** can occur in the setting of vertebrobas-
ilar territory stroke or large hemispheric stroke.
Underlying chronic obstructive pulmonary disease
and aspiration may further exacerbate hypoxia.
Although the routine use of supplemental oxygen is
not recommended, oxygen may be prescribed when
arterial blood gas measurements reveal hypoxemia.

**Fever**, in the setting of acute stroke, is usually
secondary to an underlying infection such as aspi-
ration pneumonia or urosepsis. Fever is associated
with worsened neurological outcome from stroke.
The source of the fever should be identified and
treated and the fever should be controlled with the
use of acetaminophen.

**Medical Complications of Stroke**
Aspiration pneumonia occurs in about 10% to 15% of stroke patients, and usually occurs in the setting of significant swallowing difficulties (dysphagia) (Table 2). The prognosis for dysphagia is quite favorable, as most patients recover in one to two weeks. Stroke patients should not be permitted oral intake initially to lessen the risk of aspiration. Swallow testing can be done with sips of sterile water or with barium fluoroscopy. Many patients will require thickened liquids and pureed foods for some period of time after stroke. Deep venous thrombosis. Stroke patients are considered to be at moderate risk for the development of deep venous thrombosis (DVT). Patients should be mobilized as soon as possible after stroke. A patient with a dense hemiplegia should receive subcutaneous heparin (5,000 units twice per day) if no contraindications exist, and should also wear anti-embolic stockings. Urinary incontinence and urinary tract infection. Up to 50% of stroke patients will suffer initially from urinary incontinence after stroke. For most, this problem is self-limited. For those with ongoing incontinence (usually overflow incontinence), either a condom catheter (for males) or intermittent catheterization is suggested. Indwelling urinary catheters should be avoided, if possible, as they cause limited mobilization after stroke and may increase the risk of urinary tract infection. Neurological Complications of Stroke Stroke progression is defined as increasing neurological deficit observed since a patient’s admission to hospital (Table 2). This is said to occur in approximately 20% to 40% of patients. Many factors may be responsible for stroke progression, including propagation of thrombus, hemorrhagic transformation, edema and local metabolic derangements. In most instances, a repeat cranial CT scan is required to exclude cerebral hemorrhage. In the face of progressing stroke with an absence of hemorrhage on cranial CT scan, intravenous heparin is sometimes prescribed. Cerebral edema. Most moderate to large cerebral infarctions will be accompanied by edema. This type of edema is referred to as cytotoxic edema and does not respond to measures that improve other types of cerebral edema (e.g., vasogenic edema seen in the presence of a brain tumor). Cytotoxic edema is maximal between two and four days after stroke and, when severe, leads to cerebral herniation and death. Corticosteroids are of no use for cytotoxic edema. Some patients with severe cytotoxic edema may respond to intubation, hyperventilation and intravenous mannitol infusions. Hemicraniectomy, with or without hemispherectomy, may be life saving for younger stroke patients with large cerebral infarctions and “malignant edema.” Hemorrhagic transformation of an ischemic infarction usually occurs between six and 48 hours after the initial stroke. Using sequential CT scanning techniques, hemorrhagic transformation is seen in about 15% to 25% of cases. Large strokes and cardioembolic strokes are said to be at the greatest risk for hemorrhagic transformation. Hemorrhagic transformation may be asymptomatic or symptomatic. Cessation of antithrombotic medication is required, and rarely, surgical evacuation is necessary. Stroke Recurrence Recurrence of ischemic stroke within the first two weeks is uncommon. For patients in normal sinus rhythm, recurrence rates are about 4% for the first two weeks, whereas for those with non-valvular
atrial fibrillation, recurrence rates are only about 5% during this same time period.9

Stroke Units and Stroke Teams

A stroke unit refers to a geographic area within a hospital that is dedicated nearly entirely to stroke care. Stroke team members include physicians, nurses, occupational, physical and speech therapists, social workers and pharmacists. Stroke units that combine acute management with early post-stroke rehabilitation have been shown to reduce overall mortality and disability from stroke.13

Conclusion

Stroke is the third leading cause of death and the number one cause of long-term disability in Canada. Proven and effective therapies for acute stroke are now available, including intravenous thrombolysis with tissue plasminogen activator. Through the delivery of such treatments, as well as the recognition and treatment of factors that can exacerbate stroke, it is hoped that the burden of stroke will be diminished.

References