Eighty percent of strokes are ischemic. Twenty percent of ischemic events involve tissue supplied by the posterior (vertebrobasilar) circulation (Fig. 1). The paralysis of vertebrobasilar stroke can be devastating, and some forms have high rates of death. Many cases of vertebrobasilar disease remain undiagnosed or are incorrectly diagnosed. Some common symptoms, such as dizziness or transient loss of consciousness, are misattributed to posterior-circulation ischemia. Formerly, clinicians used the catchall term “vertebrobasilar insufficiency” to indicate a hemodynamic cause of all cases of posterior-circulation ischemia. During the past 15 years, information provided by detailed clinical studies and brain imaging has revolutionized our understanding of the clinical aspects, causes, mechanisms, treatments, and prognosis of posterior-circulation ischemia.

The most common causes of vertebrobasilar ischemia are embolism, large-artery atherosclerosis, penetrating small-artery disease, and arterial dissection. Migraine, fibromuscular dysplasia, coagulopathies, and drug abuse are much less frequent causes. Emboli arise from the heart, aorta, and proximal vertebral and basilar arteries. The distribution of large-artery atherosclerosis differs according to race and sex. White men often have atherosclerosis at the origin of the vertebral arteries from the subclavian arteries. Patients with atherosclerosis at this site often have carotid, coronary, and peripheral vascular disease. Intracranial large-artery atherosclerosis is most common among blacks, Asians, and women.

The small arteries that supply the brain stem and thalamus arise from the intracranial vertebral, basilar, and posterior cerebral arteries (Fig. 1). Hypertension increases the likelihood of lipohyalinotic thickening of these arteries, which, in turn, causes small infarcts. Atherosclerosis of parent arteries can block or extend into the origins of these penetrating arteries or form microatheromas within these branches, leading to blockage (intracranial atheromatous branch disease).

Dissections occur in the portions of the extracranial vertebral arteries that are most freely movable. These are the third portion of the vertebral artery that extends around the upper cervical vertebrae and the first portion of the vertebral artery between its origin and its entrance into the intervertebral foramina.

Dizziness, vertigo, headache, vomiting, double vision, loss of vision, ataxia, numbness, and weakness involving structures on both sides of the body are frequent symptoms in patients with vertebrobasilar-artery occlusive disease. The most common signs are limb weakness, gait and limb ataxia, oculomotor palsies, and oropharyngeal dysfunction. Posterior-circulation ischemia rarely causes only one symptom but rather produces a...
collection of symptoms and signs depending on which area is ischemic. Fewer than 1 percent of patients with vertebrobasilar ischemia in the New England Medical Center Posterior Circulation Registry (NEMC-PCR) had only a single presenting symptom or sign.\textsuperscript{1,3,5}

**EMBOLISM**

The most frequent arterial sites of emboli are the intracranial vertebral arteries, which usually lead to cerebellar infarction, and the distal basilar artery, which leads to infarcts in the upper cerebellum, midbrain, thalamus, and territories of the posterior cerebral artery — so-called top-of-the-basilar infarcts.\textsuperscript{1,3,5,19-22} Patients with cerebellar infarcts often report dizziness, occasionally in conjunction with frank vertigo, blurred vision, difficulty walking, and vomiting. They often veer to one side and cannot sit upright or maintain an erect posture without support. Patients may have hypotonia of the arm on the side of the infarct, a sign best elicited by having them hold their arms straight ahead and then rapidly lower them, quickly braking the movement. The hypotonic arm overshoots on both descent and rapid ascent. Nystagmus is common. Patients with pure cerebellar infarcts do not have hemiparesis or hemisensory loss.

Embolic infarcts can involve one posterior cerebral artery, which most often leads to a hemianopia of the contralateral visual field,\textsuperscript{1,3,20,23} as in the patient described in Figure 2. The patient described in Figure 2 had occlusion of a vertebral artery causing transient ischemic attacks (TIAs) related to the lower brain stem and followed by an intraarterial embolus to the right posterior cerebral artery, causing an occipital-lobe infarct and a left hemianopia. Sometimes, hemisensory symptoms are present on the same side of the body and face as the hemianopia. Difficulty reading and naming colors often accompanies large infarcts of the left posterior cerebral artery, whereas neglect of the left visual field and disorientation to place may accompany infarcts of the right posterior cerebral artery. Bilateral infarcts of the posterior cerebral arteries cause bilateral visual-field defects and, sometimes, cortical blindness. Inability to make new memories as well as an agitated state can also occur.\textsuperscript{1,3,21,22} Embolic infarction of the rostral midbrain and thalamus leads to a top-of-the-basilar syndrome characterized by somnolence and sometimes, stupor; inability to make new memories; small, poorly reactive pupils; and defective vertical gaze.\textsuperscript{1,3,21,22}

A group of patients with vertebrobasilar ischemia may present with vertigo, blurred vision, and dizziness, occasionally in conjunction with frank vertigo, blurred vision, difficulty walking, and vomiting. They often veer to one side and cannot sit upright or maintain an erect posture without support. Patients may have hypotonia of the arm on the side of the infarct, a sign best elicited by having them hold their arms straight ahead and then rapidly lower them, quickly braking the movement. The hypotonic arm overshoots on both descent and rapid ascent. Nystagmus is common. Patients with pure cerebellar infarcts do not have hemiparesis or hemisensory loss.

**ATHEROSCLEROTIC STENOSIS AND OCCLUSION**

Atherostenosis at or near the origin of a vertebral artery in the neck is often manifested as brief TIAs, consisting of dizziness, difficulty focusing visually, and loss of balance.\textsuperscript{13} Attacks occur after a patient has been standing or in situations that reduce blood pressure or blood flow. These symptoms are related to ischemia of vestibulocerebellar structures in the medulla and cerebellum.\textsuperscript{13} In some patients, posterior cerebral, cerebellar, or top-of-the-basilar symptoms and signs occur suddenly, owing to embolism from the vertebral-artery occlusive lesion. Atherostenosis or occlusion of an intracranial vertebral artery most often causes symptoms and
signs related to ischemia in the lateral medullary tegmentum, which are referred to as the Wallenberg, or lateral medullary, syndrome (Table 1 and Fig. 3A). Occlusion of an intracranial vertebral artery can also then become a source of emboli to the rostral basilar artery and its branches. When both intracranial vertebral arteries are compromised, the most frequent clinical pattern is spells of decreased vision and ataxia, often precipitated by standing or a reduction in blood pressure. In the NEMC-PCR, 13 of 407 patients had hemodynamically sensitive ischemia, most commonly caused by bilateral intracranial vertebral-artery occlusive disease, and they had multiple brief episodes of dizziness, veering, perioral paresthesias, and diplopia.5,24

Atherostenosis and occlusion of the basilar artery usually cause bilateral symptoms and signs or crossed findings (involving one side of the face and the contralateral side of the trunk and limbs).1,3,25,26 Motor and oculomotor signs and symptoms predominate (Table 2) and, when severe, can cause the locked-in syndrome (Fig. 3B).

**Penetrating Artery Disease**

Infarcts in the paramedian pons cause pure motor strokes characterized by weakness of the face, arm, and leg or arm and leg on one side without visual, sensory, cognitive, or behavioral abnormalities. At times, the weak limbs also show a cerebellar type of incoordination— an ataxic hemiparesis.1,3,14-16 Thalamic lacunes present as pure sensory strokes with numbness or paresthesias involving the face, arm, and leg on one side without motor, visual, cognitive, or behavioral abnormalities.1,3,14,16

**Arterial Dissection**

The cardinal symptom in patients with vertebral dissections is pain, most often in the posterior part of the neck or occiput, spreading into the shoulder.1,17,18 Diffuse, mostly occipital, headache also occurs. Dizziness, diplopia, and signs of lateral medullary or cerebellar infarction can ensue from embolism or extension of the dissection to the intracranial vertebral artery. Intracranial vertebral-
artery dissections cause medullary, cerebellar, and pontine ischemia and can cause subarachnoid hemorrhage.27

**Symptoms Not Usually Caused by Posterior-Circulation Disease**

Symptoms referable to systemic, circulatory, vestibular, and aural origins are often falsely attributed to posterior-circulation ischemia.

**Isolated Attacks of Dizziness, Light-headedness, or Vertigo**

“Dizziness” may be used to refer to light-headedness, a lack of mental clarity, or frank vertigo. Vertigo indicates dysfunction of the peripheral vestibular or central vestibulocerebellar system. Vertigo in patients with peripheral vestibulopathies is often triggered by sudden movements and positional changes and is commonly associated with aural symptoms. Vertebral-artery disease can cause transient attacks of vertigo that are usually accompanied by other brain-stem or cerebellar symptoms. In our experience, isolated episodes of vertigo continuing for more than three weeks are almost never caused by vertebrobasilar disease. Rarely, and almost exclusively in patients with diabetes, occlusion of the branch of the anterior inferior cerebellar artery of the basilar artery supplying the inner ear can cause vertigo, unilateral hearing loss, or both before causing brain-stem infarction.28

Light-headedness usually reflects presyncope related to circulatory, systemic, or cardiac disease. In the absence of neurologic symptoms or signs, light-headedness is rarely a manifestation of vertebrobasilar disease. The diagnostic yield of neurovascular testing (neuroimaging and ultrasonography) in patients with isolated syncope is very low.29 Isolated syncope poses no increased risk of stroke.30

**Transient Decrease in Consciousness**

Seizures and syncope are much more common causes of temporary loss of consciousness than is cerebrovascular disease. The reticular activating system, which promotes wakefulness, is located in the paramedian tegmentum of the upper brain stem. Basilar-artery occlusions can interrupt the function of these fibers and impair consciousness. Coma may occur. However, basilar occlusive disease always causes other accompanying findings, such as oculomotor and motor signs.

**Drop Attacks**

A drop attack is defined as a sudden loss of postural tone and falling without warning. Associated loss of consciousness implicates syncope or seizures as the cause. Drop attacks have inappropriately been attributed to transient ischemia of the posterior circulation. Brain-stem ischemia can affect corticospinal tracts subserving motor control of the limbs, but when it does so, it usually causes persistent weakness. Not a single patient in the NEMC-PCR had a drop attack as the only symptom.1,3,5 In the absence of symptoms or findings that suggest brain-stem or cerebellar dysfunction, posterior-circulation ischemia is rarely the cause of drop attacks.

**Evaluation of Patients with Suspected Posterior-Circulation Ischemia**

Thorough evaluation of a patient’s history and findings on physical and neurologic examinations should provide guidance regarding which investigations to perform. All patients in whom vertebral-artery-territory strokes or TIAs are suspected should undergo neuroimaging, preferably magnetic resonance imaging (MRI), because computed tomography (CT) provides less complete visualization of the brain stem, owing to artifacts related to the skull. MRI with diffusion-weighted imaging is the most sensitive test available to detect acute infarcts.

Most patients with posterior-circulation strokes and some patients with TIAs related to the posterior-

<table>
<thead>
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<th>Table 1. Signs and Symptoms of Lateral Medullary Infarct.</th>
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<td><strong>General Symptoms</strong></td>
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<tr>
<td>Dizziness, vertigo</td>
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<td>Facial pain</td>
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<tr>
<td>Difficulty sitting without support, veering to one side</td>
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<tr>
<td>Hoarseness</td>
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<td>Dysphagia</td>
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Patients with pacemakers or other circumstances that do not permit the use of MRI should undergo CT and CT angiography unless such approaches are contraindicated. High-quality CT angiography can be used to delineate the extracranial and intracranial posterior circulation and is very helpful for evaluating patients with suspected basilar-artery occlusion.\(^{36}\) Duplex ultrasonography can also be used to show the proximal vertebral arteries,\(^{37}\) and Doppler studies of the vertebral arteries in the neck can reveal whether blood flow is antegrade or reversed. Transcranial Doppler studies can be used to show occlusive lesions in the intracranial vertebral and proximal basilar arteries. Ultrasonography of the carotid arteries is seldom useful in the evaluation of patients with posterior-circulation ischemia. In rare cases of embolism, the posterior cerebral artery arises anomalously directly from the intracranial carotid artery.

Cardiac investigations including electrocardiography, echocardiography, and rhythm monitoring are important parts of the evaluation to search for cardiac and aortic sources of the embolism, especially in patients with no cervicocranial occlusive lesions that explain the symptoms and signs and in patients with multiple brain infarcts in different vascular territories.

Screening blood and coagulation tests should include a complete blood count and coagulation studies. Other tests for genetic and acquired coagulopathies and measurement of antiphospholipid antibodies may be appropriate in patients who have a history suggesting prior venous or arterial occlusions or in those in whom no cardiac, aortic, or cervicocranial lesions are found.

Accurate diagnosis of the specific type of stroke and vascular and brain lesions requires the following: a demographic assessment (age, race, and sex) and an evaluation of risk factors for stroke; knowledge of the course of symptoms (for example, whether the stroke was preceded by a single or multiple varied or stereotypical TIAs, whether the onset was sudden and not preceded by TIAs, and whether the ischemia is progressive); matching of the patient’s symptoms and signs to known pattern of ischemia; and brain and vascular imaging.

**PROGNOSIS**

The outcome of vertebrobasilar stroke depends on the severity of the neurologic signs, the presence or absence of arterial lesions, the location and extent
of infarction, and the mechanism of ischemia.\textsuperscript{1,38} The rate of death immediately after posterior-circulation stroke is approximately 3 to 4 percent.\textsuperscript{38,39} In the NEMC-PCR, 3.6 percent of patients died, and 18 percent of patients had a major disability.\textsuperscript{38}

Cardiac embolism, basilar-artery involvement, and the involvement of multiple intracranial territories increase the risk of a poor outcome irrespective of the patient’s age and underlying risk factors.\textsuperscript{38} Basilar-artery occlusive disease carries a high risk of disability and death, and efforts should be directed at identifying this lesion as quickly as possible.\textsuperscript{1,26,38}

**Immediate and Preventive Therapy**

Various medical, interventional, and surgical approaches are available to treat ischemia of the posterior circulation of the brain, but none have been thoroughly tested in randomized trials. The potential treatments are the same as those used for ischemia of the anterior circulation of the brain. However, few trials have classified patients with ischemic stroke according to whether they have anterior-circulation or posterior-circulation disease. Among the trials that have done so, only a handful have evaluated and reported the cardiac, arterial, and hematologic causes of the strokes.

**Short-Term Medical Management**

The National Institute of Neurological Disorders and Stroke (NINDS) trial showed that intravenous administration of tissue plasminogen activator (t-PA) enhances neurologic recovery from ischemic stroke when administered within three hours after the onset of stroke, after brain hemorrhage has been excluded on the basis of CT.\textsuperscript{40} Three studies of the intravenous administration of thrombolytic agents for vertebrobasilar disease reported mixed results.\textsuperscript{41-43} Following the NINDS guidelines, Grond et al. treated 12 patients with t-PA within three hours after the onset of stroke. Ten of the 12 patients had favorable outcomes, 1 had a poor outcome, and 1 died.\textsuperscript{41} In another study of five patients who received t-PA within six hours after the onset of symptoms,\textsuperscript{42} two patients had minor partial reperfusion and one had complete reperfusion. Three of the patients died, and one remained “locked-in.” Montavont et al. treated 18 patients within seven hours after the onset of stroke.\textsuperscript{43} Three months after treatment, 10 of the 18 patients were independent (i.e., they were able to look after themselves with no or only slight disability), but 2 had died and the condition of 6 was poor.\textsuperscript{43}

Thrombolytic agents are also administered intra-arterially through a catheter directed to the thrombus. In a retrospective study of 65 patients with vertebrobasilar occlusions, the 43 patients given urokinase or streptokinase — two thirds of whom were treated within 24 hours after the onset of stroke — had better survival rates and more favorable outcomes than the 22 patients who were treated with antithrombotic agents. Among the patients who were given thrombolytic agents, only those in whom the occlusive artery recanalized survived.\textsuperscript{44} In nine additional reports, among 285 patients who were mostly given t-PA more than eight hours after the onset of stroke,\textsuperscript{45} 62 percent had good recanalization and 28 percent of the overall population subsequently did well. Brandt et al. found that among 51 patients who underwent thrombolysis for acute vertebrobasilar lesions, those with embolic occlusions that were short and involved the proximal basilar artery with good collateral arteries were most likely to have recanalization and a good outcome. Patients who were comatose or tetraplegic or who had chronic white-matter abnormalities had poor outcomes.\textsuperscript{46}

Clinicians have insufficient data to guide the choice between intravenous and intraarterial thrombolytic therapy for vertebrobasilar ischemia. If patients present within three hours after the onset of symptoms, some neurologists follow NINDS guidelines and administer t-PA intravenously after CT has excluded hemorrhage. We favor brain and vascular imaging (CT with CT angiography or diffusion-
weighted MRI with magnetic resonance angiography) before deciding whether to use thrombolysis, especially if more than three hours has passed since the onset of symptoms or the diagnosis is uncertain. If a vertebral-artery occlusion is found, we give intravenous t-PA. When imaging studies suggest basilar-artery occlusion, we recommend cerebral angiography and intraarterial thrombolysis, because basilar-artery occlusions carry an increased risk of death and disability and there is extensive experience with intraarterial thrombolysis, even if it is given 12 to 24 hours after the onset of stroke in this condition.\textsuperscript{44,45}

Some patients with intracranial vertebrobasilar occlusive disease are very sensitive to changes in brain perfusion from decreases in blood pressure or blood volume, and even from sitting up or standing.\textsuperscript{44,47} In these patients, maximizing blood flow and blood volume by using fluids and pressors is important.

\textbf{Prevention}

Strong evidence from randomized, controlled trials provides support for the efficacy of anticoagulation with warfarin to prevent subsequent cerebrovascular events in patients with embolic stroke of cardiac origin. In a retrospective comparison of the effectiveness of warfarin and aspirin among 68 patients with symptomatic intracranial-artery stenosis that was arteriographically documented, warfarin was superior in patients with vertebrobasilar occlusive disease.\textsuperscript{48} However, a prospective, double-blind study involving patients with symptomatic intracranial stenosis of 50 to 99 percent, which was prematurely terminated after the randomization of 569 patients to warfarin or aspirin (1300 mg), showed that both agents were equally effective but that warfarin caused significantly more serious hemorrhages.\textsuperscript{49} The Warfarin–Aspirin Recurrent Stroke Study of secondary prevention also showed that aspirin and warfarin were equally efficacious in patients with noncardioembolic stroke.\textsuperscript{50}

The results of prospective trials showed that antiplatelet agents (aspirin, ticlopidine, clopidogrel, dipyridamole, and the combination of aspirin and dipyridamole) were beneficial in series of patients with TIAs and strokes. However, only two studies analyzed the findings in relationship to arterial territories, and none reported the nature of the vascular occlusive lesions. Ticlopidine was superior to aspirin for secondary cerebrovascular protection, especially in patients with symptomatic posterior-circulation disease.\textsuperscript{51} In the European Stroke Prevention Study, among patients with clinically documented vertebrobasilar-territory TIAs or strokes, strokes occurred in 5.7 percent of 255 patients treated with the combination of aspirin and modified-release dipyridamole, as compared with 10.8 percent of patients who received placebo (P=0.005).\textsuperscript{52}

We treat patients with large-artery stenosis and small-artery disease with antiplatelet agents. For patients with severe, large-artery, flow-limiting stenosis and vertebral-artery dissection,\textsuperscript{18} we consider treatment with anticoagulants in order to prevent distal embolization and progression of infarcts. When imaging shows atherosclerotic plaques, we also prescribe statins unless the patient has a low-density lipoprotein cholesterol level of less than 70 mg per deciliter (1.8 mmol per liter).\textsuperscript{53} Patients with large-artery atherostenosis who continue to have ischemic events while receiving medical therapy are referred for surgery, angioplasty, or stenting, depending on the nature and location of the arterial lesions (see below). Randomized trials should be designed to address which therapeutic options are most appropriate for specific stroke mechanisms and arterial occlusive lesions.

\textbf{Future Directions}

\textbf{Endovascular Procedures}

Evidence provided by scattered case series suggests that vertebrobasilar angioplasty and stenting may become important therapeutic strategies for large-artery vertebrobasilar disease. Preliminary results of angioplasty or stenting of occlusive vertebral-artery lesions in the neck show that restenosis is more common than with carotid-artery stenting.\textsuperscript{54} The small diameter and angulation of the vertebral-artery origin complicate endovascular treatment. Intracranial vertebral- and basilar-artery angioplasty and stenting have produced mixed results, with a relatively high rate of complications.\textsuperscript{55} Although the results are preliminary, mechanical removal of thromboemboli may become potentially useful in patients who cannot receive thrombolytic drugs and as an adjunct to thrombolysis.\textsuperscript{56} We await large, controlled trials comparing endovascular revascularization with various medical therapies.

\textbf{Surgery}

Endarterectomy for severe extracranial vertebral-artery disease has low rates of complications and mortality when performed by surgeons with ex-
tensive experience. The indications for vertebral-artery surgery are still uncertain. Before the advent of intracranial angioplasty, bypass shunts were surgically created between extracranial arteries and the intracranial posterior circulation, with some success, but no trials were undertaken to prove their effectiveness. Supported by a grant (0475008R) from the American Heart Association (to Dr. Savitz). Dr. Caplan reports having served on advisory boards of GlaxoSmithKline, Wyeth, Boehringer Ingelheim, and AstraZeneca.

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