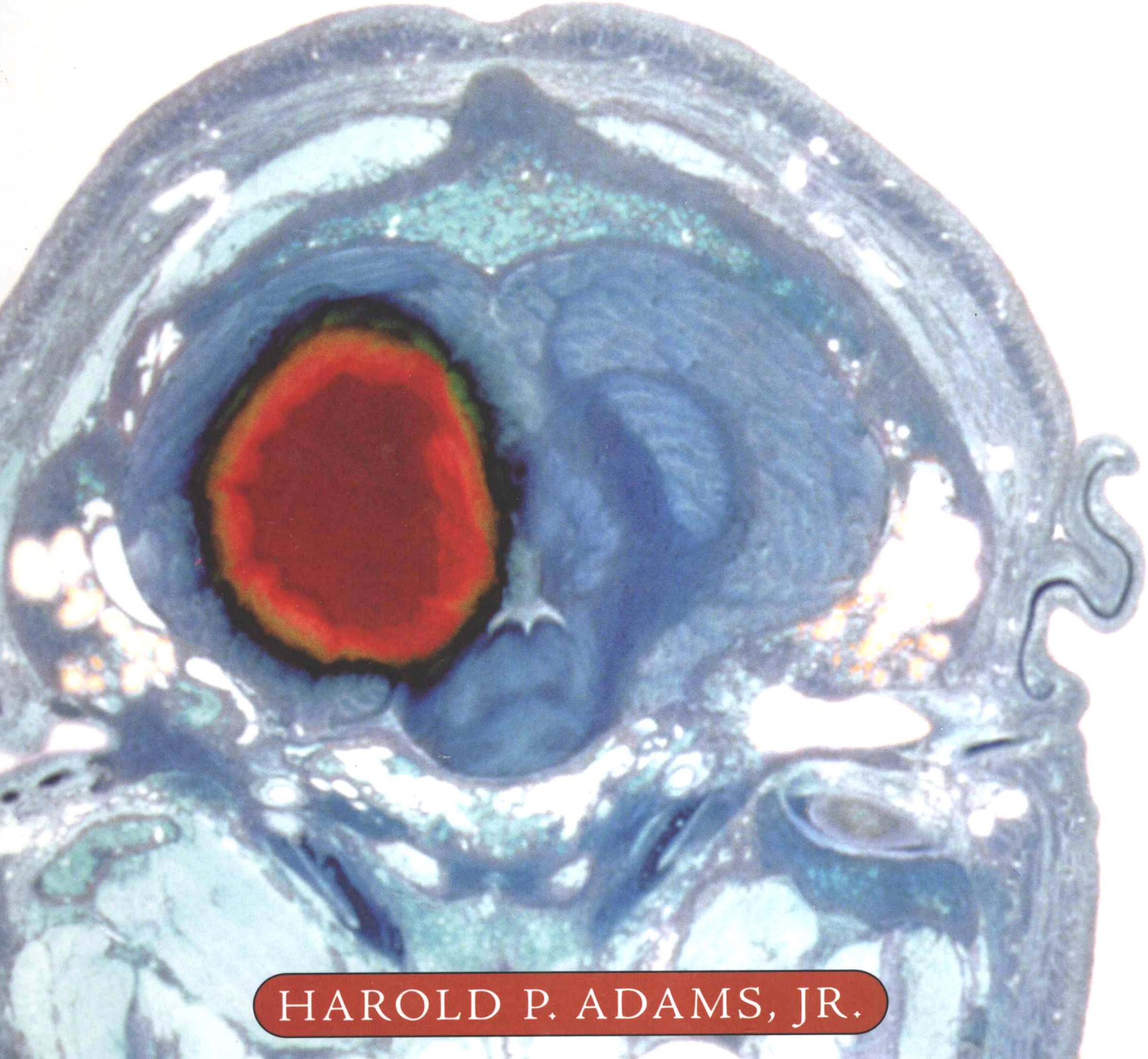
PRINCIPLES OF

# CEREBROVASCULAR DISEASE



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# PRINCIPLES OF CEREBROVASCULAR DISEASE

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# Principles of Cerebrovascular Disease



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# PREFACE

Cerebrovascular disease is a leading cause of death and human suffering around the world. Despite advances in prevention and treatment, far too many people suffer severe neurological injuries that result in changes to their lives and to those of their loved ones. The effects of stroke on patients' families and to society are huge. The economic consequences of stroke in both health care–related costs and lost productivity are massive. Thus, actions to forestall stroke or limit the subsequent neurological damage following stroke must be expanded. These efforts include continued advances in the knowledge of the basic science underpinnings for the diagnosis and treatment of stroke. These efforts also include translational and clinical research, which already is resulting in dramatic changes in patient care. These advances need to be complemented by increased public and professional understanding about stroke. This book is aimed at providing information about clinical findings, diagnostic studies, and treatment of persons with cerebrovascular disease, including therapies to prevent or treat stroke. While some information about the anatomy and pathophysiology of stroke is included, this is not a neuroscience text. Rather, the book is oriented toward providing clinical insights that might be useful to practicing physicians, residents, and students.

This book is organized to run parallel with the course of evaluation and treatment of a hypothetical patient with cerebrovascular disease. It includes chapters about both ischemic stroke and hemorrhagic stroke that are intermixed throughout the volume. Whenever possible, I included figures and tables to convey information.

The first chapters generally relate to the epidemiology of stroke, identification of persons who are highest risk for stroke, and the risk factors for stroke that can be modified or treated. The third chapter describes the organization of stroke treatment resources (public education, emergency medical services, hospitals, and physicians) that could improve patient care, especially in an acute setting. Chapters describing transient ischemic attacks, ocular manifestations of cerebrovascular disease, ischemic stroke, and hemorrhagic stroke follow. Chapter 8 reviews the usually ordered diagnostic studies including brain, vascular, and cardiac imaging and other tests performed in the evaluation of a patient with stroke. Chapters 9 through 16 then describe the gamut of diseases that may produce either ischemic or hemorrhagic stroke. Also included are chapters describing the causes of stroke in children and young adults and venous thrombosis, pituitary apoplexy, and spinal cord vascular disease. The subsequent chapters describe interventions to prevent and treat ischemic and hemorrhagic stroke. The evidence for the safety and utility of specific medical and surgical therapies is described. In the case of medications, I included some information about the pharmacology of the agents. Complications of stroke and their prevention and treatment are included in this section. The book closes with a review of rehabilitation after stroke and measures to help an individual to return to society.

This is a single-author text and, thus, my perceptions about the utility of specific interventions are expressed. However, I tried to be dispassionate in approach to my evaluation of the data and provide any recommendations about treatment using the rules of evidence. Thus, both therapies that have been shown to be effective and those that are not established as useful are discussed. Some therapies that hold promise but for which there are limited data also are reviewed. The limitations of current knowledge about management and areas where continued research is needed also are discussed. Because new information about stroke is appearing rapidly, I tried to make this book as up-to-date as possible. While I recognize that a book that has a strong emphasis on management may become dated, I hope that this book will provide a foundation for the interpretation of the results of future clinical trials.

# ACKNOWLEDGMENTS

The task of writing a book is a considerable undertaking and I have a large number of people to thank. Their contributions to this book are huge and I would not have been able to complete this book without their help.

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# CHAPTER 1

# *Classification of Stroke, Commonly Used Terms in Cerebrovascular Disease, and the Pathophysiology of Stroke*

*All physicians, regardless of their practice, encounter patients with cerebrovascular disease. Because strokes are common, serious neurological diseases, physicians are faced with decisions about emergency treatment of these conditions. Because of the widespread prevalence of cerebrovascular disease, physicians are required to make recommendations for the prevention of stroke. And because cerebrovascular diseases are a leading cause of long-term disability, physicians are responsible for organizing care of chronically ill patients who have had strokes. In order to provide an update on the management of these patients, this book focuses on the principles for the diagnosis and treatment of vascular diseases of the central nervous system.*

## ► CEREBROVASCULAR ACCIDENT

Many physicians and other health care providers use the term *cerebrovascular accident* (CVA) to denote stroke. This usage is inappropriate because there is nothing accidental about stroke. The term CVA also implies that nothing can be done to prevent stroke or to limit its neurological consequences, which in turn can lead to a sense of nihilism in stroke care. However, strokes can be prevented. Strokes are due to vascular diseases of the brain, which can be treated. Acute strokes can be treated and patients' neurological outcomes can be improved. The term CVA should be abandoned.

## ► CLASSIFICATION OF STROKE

In this book, the terms *cerebrovascular disease* and *stroke* include hemorrhagic and ischemic vascular diseases that affect any location of the central nervous system. Several different systems are used to classify these strokes. Cerebrovascular disease is most commonly separated into events that are secondary to bleeding or ischemia, the location of the brain or spinal cord that is affected, the involved vascular territory, the presumed cause, the clinical course, or the time course (Table 1-1). In addition, cerebrovascular disease also includes vascular events that affect eyes or ears. Most strokes are due to occlusion or rupture of an artery or arteriole. Less commonly, stroke can be secondary to venous disease.

### Ischemic Stroke

*Ischemic stroke* secondary to arterial occlusion accounts for approximately 80 percent of all cerebrovascular events. Most cases of arterial occlusion are secondary to *thromboembolism*. The term *cerebral thrombosis* encom-

**▶ TABLE 1-1.** CLASSIFICATION OF CEREBROVASCULAR DISEASES

| |
|---|
| General classification |
| Ischemic cerebrovascular disease |
| Ischemic stroke (arterial thromboembolic stroke) |
| Cerebral infarction |
| Cerebral thrombosis |
| Cerebral embolism |
| Hemorrhagic cerebrovascular disease |
| Hemorrhagic stroke |
| Traumatic intracranial hemorrhage |
| Spontaneous intracranial hemorrhage |
| Venous thrombosis |
| Spinal cord hemorrhage or infarction |
| Pituitary apoplexy |

passes those cases of occlusion that are secondary to de novo formation of a clot in an artery. In *cerebral embolism*, the thrombus develops in the heart or a proximal extracranial or intracranial artery and subsequently migrates to a distal artery resulting in an occlusion. Occasionally, embolism can be secondary to nonthrombotic material, such as fat or atherosclerotic debris.

### Hemorrhagic Stroke

Bleeding in the brain, spinal cord, or adjacent structures accounts for the cases of *hemorrhagic stroke*.

## ▶ VASCULAR CLASSIFICATION

Knowledge of the vascular anatomy of the central nervous system is crucial for understanding the myriad variations of cerebrovascular disease and for making educated decisions about evaluation and treatment of affected patients. Categorization of vascular events often is based on the involved vascular territory—*carotid* or *vertebrobasilar* circulation. This differentiation is particularly important when deciding about local interventions (surgery or endovascular procedure). The location of an ischemic stroke often is denoted by the name of the occluded artery, for example, the middle cerebral artery (Table 1-2). In addition, recognition of the involved vessel is crucial for the diagnosis and management of patients with hemorrhagic stroke. For example, the location of an aneurysm influences decisions about surgical treatment.

### Aorta

Thromboembolic events to the brain can arise from the left atrium, the left ventricle, the ascending aorta, or the *arch of the aorta* (Fig. 1-1). Atherosclerotic disease of the aorta is an increasingly recognized cause of embolic events to the brain. The descending aorta gives rise to intercostal branches that serve as the parents of radicular arteries, which in turn send branches to the *anterior* and *posterior spinal arteries* that perfuse the spinal cord. The largest of these collateral vessels, named the *artery of Adamkiewicz*, usually arises from the lower segment of the thoracic aorta. In addition, the cervical portion of

**▶ TABLE 1-2.** ARTERIAL VASCULAR ANATOMY OF THE BRAIN

| |
|---|
| Arch of the aorta |
| Brachiocephalic (innominate) artery |
| Right common carotid artery |
| Right internal carotid artery |
| Right external carotid artery |
| Right subclavian artery |
| Right vertebral artery |
| Left common carotid artery |
| Left internal carotid artery |
| Left external carotid artery |
| Left subclavian artery |
| Left vertebral artery |
| Carotid (anterior) circulation - internal carotid artery |
| Ophthalmic artery |
| Anterior choroidal artery |
| Posterior communicating (posterior cerebral) artery |
| Anterior cerebral artery |
| Recurrent artery of Huebner |
| Anterior communicating artery |
| Orbito-frontal artery |
| Fronto-polar artery |
| Calloso-marginal artery |
| Pericallosal artery |
| Middle cerebral artery |
| Lenticulostriate arteries |
| Anterior, middle, and posterior temporal arteries |
| Prefrontal artery |
| Precentral artery |
| Central artery |
| Superior and inferior parietal arteries |
| Angular artery |
| Vertebrobasilar (posterior) circulation |
| Vertebral artery |
| Posterior inferior cerebellar artery |
| Anterior spinal artery |
| Basilar artery |
| Anterior inferior cerebellar artery |
| Internal auditory (labyrinthine) artery |
| Penetrating (pontine) arteries |
| Superior cerebellar artery |
| Posterior cerebral artery |
| Interpeduncular-thalamic artery |
| Posterior choroidal artery |
| Thalamo-perforating artery |
| Thalamo-geniculate artery |
| Anterior and posterior temporal arteries |
| Parieto-occipital artery |
| Calcarine artery |

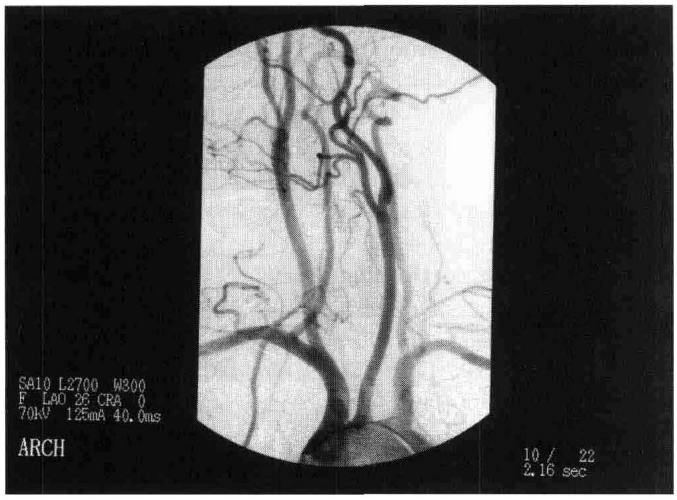


**Figure 1-1.** Anteroposterior view of a normal arch aortogram demonstrates the major branches of the aorta including the brachiocephalic, left common carotid, and left subclavian arteries. Both vertebral arteries and the bifurcations of the carotid arteries are also shown.

the spinal cord receives collateral branches from the vertebral arteries and the anterior spinal artery receives blood supply from the distal portions of the vertebral arteries. At this location, the anterior spinal artery can perfuse the medial portion of the caudal medulla and its occlusion can lead to bilateral pyramidal infarctions. The venous drainage of the spinal cord is largely via a dorsal plexus of vessels. Vascular malformations, most commonly located dorsal to the cord, can be a cause of hemorrhagic or ischemic lesions of the spinal cord.

## Vertebrobasilar Circulation

The *vertebral* and *basilar arteries* supply the brain stem, cerebellum, and the posterior portions of the cerebral hemispheres. The two vertebral arteries arise from the subclavian arteries. In most persons, the *left subclavian artery* is a branch of the arch of the aorta and the *right subclavian artery* is a branch of the *brachiocephalic (innominate) artery*. Occlusive disease of the subclavian artery proximal to the origin of the vertebral artery can give rise to the *subclavian steal syndrome*, in which blood ascends via one vertebral artery and then diverts down the other vessel to perfuse the arm—a circumstance that results in blood being shunted from the cerebral circulation. The vertebral arteries ascend to the head through the transverse foramina located in the lateral processes of the sixth through the second cervical vertebrae. The arteries then perforate the dura to enter the cranial vault via the foramen magnum. The two vertebral arteries unite to form the basilar artery at approximately the pontomedullary junction. The major branches of the vertebral arteries are the anterior spinal artery, short penetrating arteries that perfuse the dorsolateral medulla, and the *posterior inferior cerebellar artery* (PICA). This vessel sends penetrating branches to the dorsolateral medulla and provides blood to the inferior and lateral aspects of the cerebellum. Branches of the vertebral artery can be involved in vascular malformations located in the posterior fossa and the origin of PICA can be the site of a saccular aneurysm.

The basilar artery sits in the pre-pontine and interpeduncular cisterns in front of the brain stem. The artery divides into its terminal branches, the *posterior cerebral arteries*, at the mesencephalic-diencephalic junction (Fig. 1-2). Several short penetrating arteries rising from the basilar artery enter the anterior and medial portions of the pons and midbrain. Besides the posterior cerebral arteries, the other major branches include the *anterior inferior cerebellar arteries* (AICA) and the *superior cerebellar arteries*. The superior cerebellar artery perfuses rostral cerebellum and the dorsolateral aspects of the midbrain. The dorsolateral pons and the medial and anterior aspects of the cerebellum receive blood via AICA. The *internal auditory artery (labyrinthine artery)* provides blood to the inner ear. This vessel can arise either directly from the basilar artery or as a branch of the AICA. The perfusion beds of the cerebellum can vary considerably between individuals. In some circumstances, one or more of the cerebellar arteries can be hypoplastic or absent and the vascular beds can differ between the left and right cerebellar hemispheres. Venous drainage from the brain stem and cerebellum is

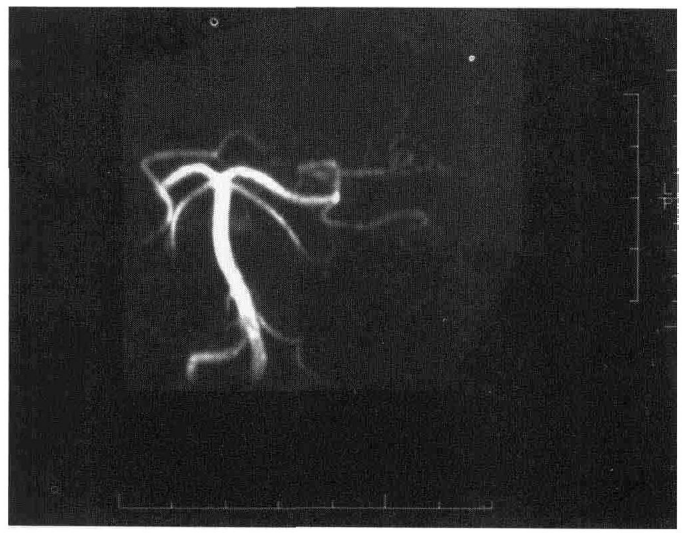

**Figure 1-2.** Anteroposterior view of a magnetic resonance angiogram of the posterior circulation shows the distal segments of the vertebral arteries, the origin of the posterior inferior cerebellar arteries, the superior cerebellar arteries, and the posterior cerebral arteries.

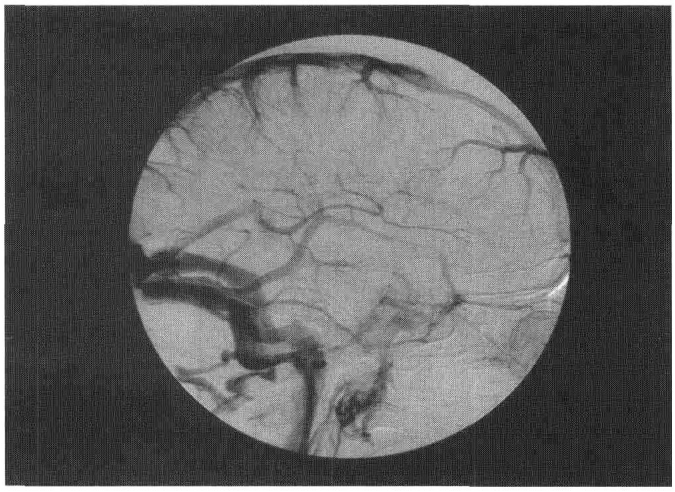

**Figure 1-3.** Lateral view of the venous phase of the right carotid arteriogram shows both the deep and superficial venous systems draining the cerebral hemisphere.

via small vessels that empty into the *basal vein of Rosenthal*, the *great vein of Galen*, or the *transverse* or *sigmoid sinuses* (Fig. 1-3, Table 1-3).

The diencephalon receives blood from multiple small penetrating arteries that arise from the basilar artery, the proximal portion of the posterior cerebral arteries, or the *posterior communicating artery*. Anatomists have given several names to these arteries, and the resultant confusion has complicated our understanding of these vessels and their vascular territories. In this book, *interpeduncular-thalamic artery*, *posterior choroidal artery*, *thalamoperforating artery*, and *thalamogeniculate artery* are used when describing the small arteries that perfuse the thalamus and adjacent diencephalic structures. The posterior cerebral artery also can receive blood from the internal carotid artery via the posterior communicating artery. In approximately 20 percent of persons, one posterior cerebral artery is a direct branch of the internal carotid artery and the proximal portion of the artery corresponds to the posterior communicating artery. This variation is sometimes described as an embryonic origin of the posterior cerebral artery. The basilar bifurcation and the origin of the posterior communicating artery from the internal carotid artery are frequent sites for saccular aneurysms. The cortical branches of the posterior cerebral artery perfuse the occipital lobe, the medial and inferior portions of the temporal lobe, and the superior and medial aspects of the parietal lobe. The *calcarine artery*, which supplies the primary visual cortex, is a branch of the posterior cerebral artery.

**▶ TABLE 1-3.** VENOUS DRAINAGE OF THE BRAIN

| |
|---|
| Cavernous sinus |
| Venous drainage of the cerebral cortex |
| Superior sagittal sinus |
| Cortical veins |
| Veins of Trolard and Labbé |
| Inferior sagittal sinus |
| Venous drainage of deep hemispheric structures |
| Internal cerebral vein |
| Basal vein of Rosenthal |
| Great vein of Galen |
| Straight sinus |
| Transverse sinus |
| Sigmoid sinus |
| Internal jugular vein |

## Carotid Circulation

In most persons, the *left common carotid artery* is a direct branch of the aorta, arising proximal to the left subclavian artery, and the *right common carotid artery* is a branch of the brachiocephalic artery (see Fig. 1-1). Both common carotid arteries ascend in the anterior aspect of the neck just lateral to the trachea and medial to the *internal jugular vein*. The common carotid artery bifurcates into *internal* and *external carotid arteries* at approximately the angle of the jaw (Fig. 1-4). The external carotid artery perfuses the soft tissues of the face, the scalp, and the meninges. The external carotid artery is an important collateral channel (usually via orbital and meningeal branches) for maintaining blood flow in a patient with an occlusion of the internal carotid artery.

The internal carotid artery supplies the ipsilateral eye and most of the ipsilateral cerebral hemisphere (Fig. 1-5(a) to 5(c)). Deep penetrating branches of the internal carotid artery provide blood to the basal ganglia, internal capsule, and deep hemispheric white matter. Cortical branches perfuse the insula, the frontal lobe, the superior aspect of the temporal lobe, and the anterior, lateral, and inferior portions of the parietal lobe. The extracranial (cervical) portion of the internal carotid artery ascends just lateral to the vertebral bodies. This portion of the artery is the most common site for atherosclerosis or arterial dissection. The internal carotid artery enters the cranial vault via the carotid canal (this segment is called the petrous portion). The artery then moves anteriorly and medially in an S-shaped curve to lie in the *cavernous sinus* (cavernous portion). Atherosclerotic disease can involve this portion of the artery. Injury to the cavernous portion of the carotid artery can lead to a carotid cavernous fistula. Aneurysms also can arise from the cavernous portion of the internal carotid artery. Branches to the pituitary gland arise from the internal carotid artery as it penetrates the dura to enter the subarachnoid space. The

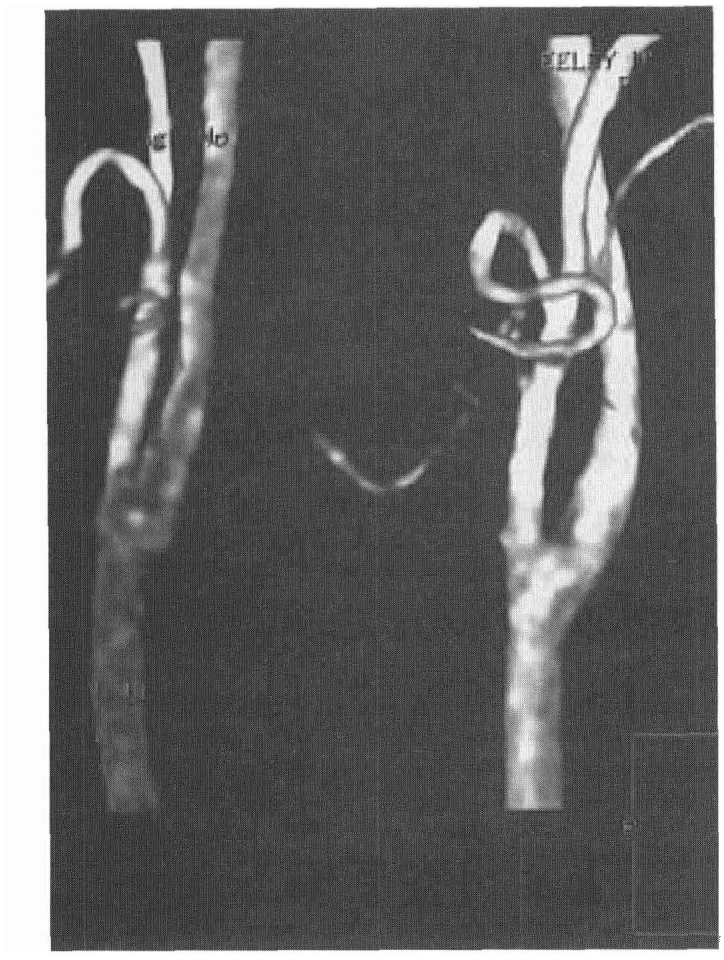

**Figure 1-4.** Magnetic resonance angiograms of both internal and external carotid arteries show the normal appearance of the bifurcations. The first branches of the external carotid arteries are seen.

*ophthalmic artery*, which supplies the eye, is the first major intracranial branch. Other important branches of the internal carotid artery are the posterior communicating artery, *anterior choroidal artery*, *anterior cerebral artery*, and *middle cerebral artery* (see Fig. 1-5(a) and 1-5(b)). The middle cerebral artery is the terminal branch. The anterior choroidal artery perfuses the optic tract, the posterior limb of the internal capsule, adjacent portions of the basal ganglia and thalamus, and the lobar white matter.

The anterior cerebral artery moves anteriorly and medially to a parasagittal location along the medial aspect of the frontal lobe (see Fig. 1-5(a) and 1-5(b)). A deep penetrating branch, the *recurrent artery of Huebner* perfuses the inferior and anterior portion of the head of the caudate nucleus. Cortical branches supply the medial and anterior aspects of the frontal lobe. The major cortical branches are named the *orbito-frontal*, *fronto-polar*, *calloso-marginal*, and *pericallosal* arteries. The proximal portions of both anterior cerebral arteries are connected via the *anterior communicating artery*. Approximately one-third of intracranial saccular aneurysms arise in the region of the anterior communicating artery.

The middle cerebral artery moves laterally from the internal carotid artery to enter the Sylvian cistern and Sylvian fissure. Thereafter it moves posteriorly and superiorly, giving rise to several cortical branches that supply the lateral and inferior portions of the frontal lobe, the insula, the inferior and anterior portions of the parietal lobe, and the superior portion of the temporal lobe (see Fig. 1-5(a) and Fig. 5(b)). These vessels, which are located along the pial surface of the hemisphere, are aligned from anterior to posterior to form a series of wedges that extend from the cortical surface to deep, adjacent portions of the lobar white matter. These branches are named *prefrontal*, *precentral*, *central*, *superior parietal*, *inferior parietal*, *angular*, and *anterior*, *middle*, and *posterior temporal* arteries. Aneurysms arising from the proximal portion of the middle cerebral artery are most commonly located in the Sylvian fissure. Several deep penetrating branches of the middle cerebral artery *(lenticulostriate arteries)* supply the putamen, the head of the caudate nucleus, and the anterior limb of the internal capsule.

## Venous Anatomy of the Hemispheres

The cavernous sinus consists of a plexus of smaller veins that drain blood from eyes, nose, and face (see Table 1-3). There are prominent collateral channels between the two cavernous sinuses. These collateral veins pass around the region of the pituitary. Venous drainage of the cerebral hemispheres is via cortical and deep channels. In general, flow is in an anterior to posterior direction. The cortical veins generally drain into the *superior sagittal sinus*, *inferior sagittal sinus*, and *transverse sinus*; the largest cortical veins are named the *vein of Labbe* and the *vein of Trolard* (see Fig. 1-3). The former vessel usually drains inferiorly, while the latter vein empties into the superior sagittal sinus. The deep hemispheric structures are drained via the *thalamostriate vein* and *septal vein*. At the foramen of Munro, these two veins merge to form the *internal cerebral vein*, which moves posterior along the medial aspect of the thalamus. The internal cerebral vein joins the basal vein of Rosenthal to form the great vein of Galen at the mesencephalic—diencephalic junction. The great vein of Galen and the inferior sagittal sinus unite to create the *straight sinus*. At the torcula, the straight sinus joins the superior sagittal sinus to form the transverse sinuses. The left and right transverse sinuses often are asymmetrical in caliber and the majority of venous blood may travel via one of the sinuses. The transverse sinuses move laterally and anteriorly along the tentorium and the petrous portion of the temporal bone. From this point

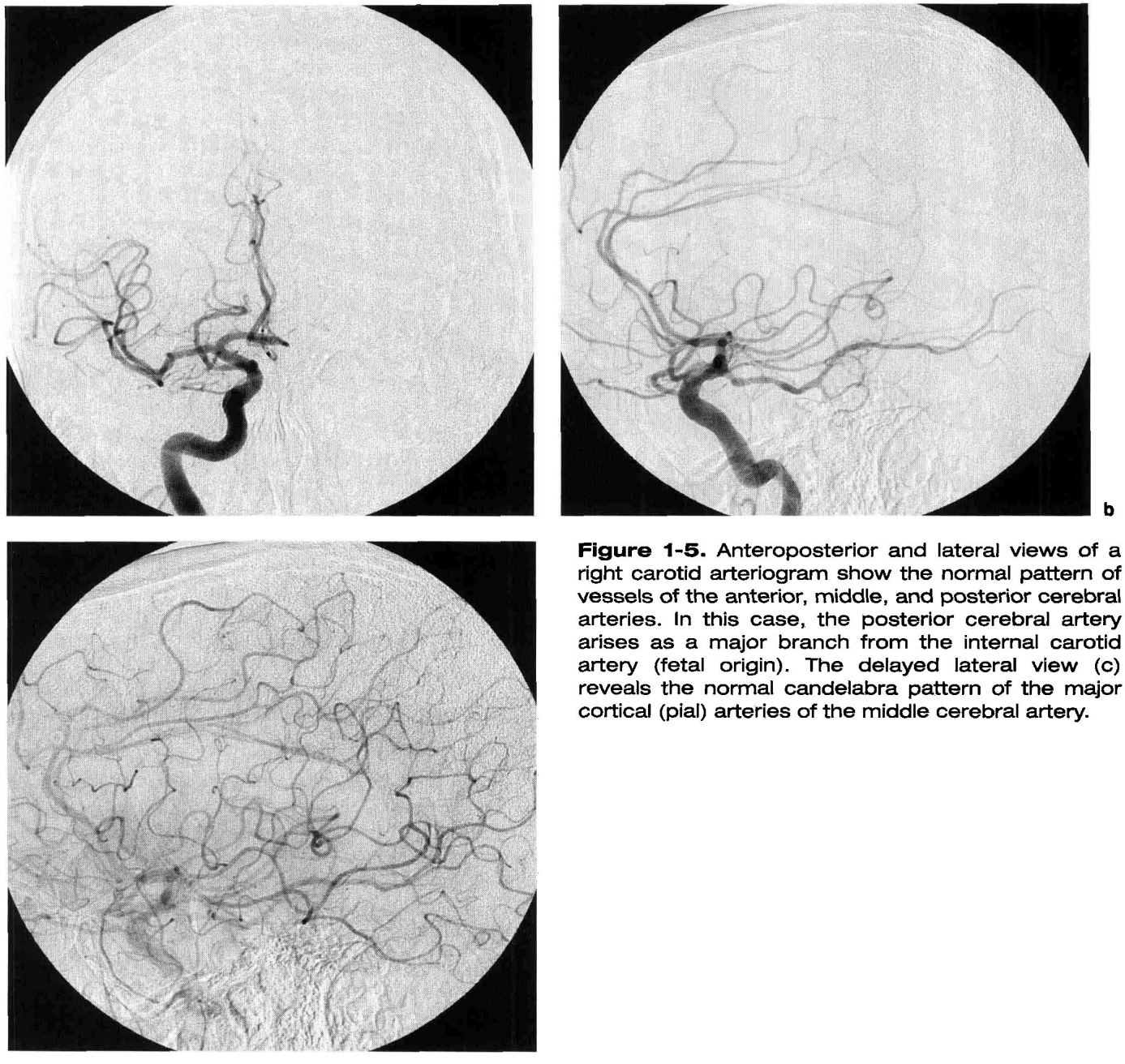


**Figure 1-5.** Anteroposterior and lateral views of a right carotid arteriogram show the normal pattern of vessels of the anterior, middle, and posterior cerebral arteries. In this case, the posterior cerebral artery arises as a major branch from the internal carotid artery (fetal origin). The delayed lateral view (c) reveals the normal candelabra pattern of the major cortical (pial) arteries of the middle cerebral artery.

onward, the sinus is known as the *sigmoid sinus*. The sigmoid sinus exits the skull via the jugular foramen; from this point onward, the vessel is known as the *internal jugular vein*.

## Penetrating Arteries

Several short penetrating arteries perfusing the brain stem and the deep structures of the cerebral hemispheres are end vessels (see Table 1-2). Occlusions of these vessels produce relatively small (<1.5-cm diameter) strokes (*lacunar infarction*) and fairly stereotyped neurological syndromes (*lacunar syndromes*). These short penetrating arteries are vulnerable to the effects of hypertension, and thus, *hypertensive hemorrhage* occurs primarily in the areas of the brain perfused by these vessels. Larger deep hemispheric infarctions are secondary to thromboembolic occlusion of larger cerebral arteries; the most common is occlusion of the middle cerebral artery that causes a stroke in the distribution of several lenticulostriate arteries (*striatocapsular infarction*).

## Collaterals

A broad spectrum of neurological impairments can occur with occlusion of major arteries. For example,

**▶ TABLE 1-4.** COLLATERAL CIRCULATIONS

| |
|---|
| External carotid artery/internal carotid artery |
| Circle of Willis |
| Pial collaterals—terminal branches of cerebral hemispheres |
| Middle cerebral artery |
| Anterior cerebral artery |
| Posterior cerebral artery |
| Pial collaterals—terminal branches of the cerebellum |
| Posterior inferior cerebellar artery |
| Anterior inferior cerebellar artery |
| Superior cerebellar artery |

one patient may die from a multilobar infarction secondary to an internal carotid artery occlusion while another person may be asymptomatic. The discrepancies partially result from the anatomic presence of collateral vessels of adequate caliber (Table 1-4). Three major systems of collaterals can protect the brain from an arterial occlusion: branches of the external carotid artery, the circle of Willis, and the pial arteries. First, anastomoses between branches of the external carotid artery and branches of the internal carotid artery can maintain adequate brain perfusion in a patient with an occlusion of the internal carotid artery (Fig. 1-6). Muscular branches in the neck can connect with vessels

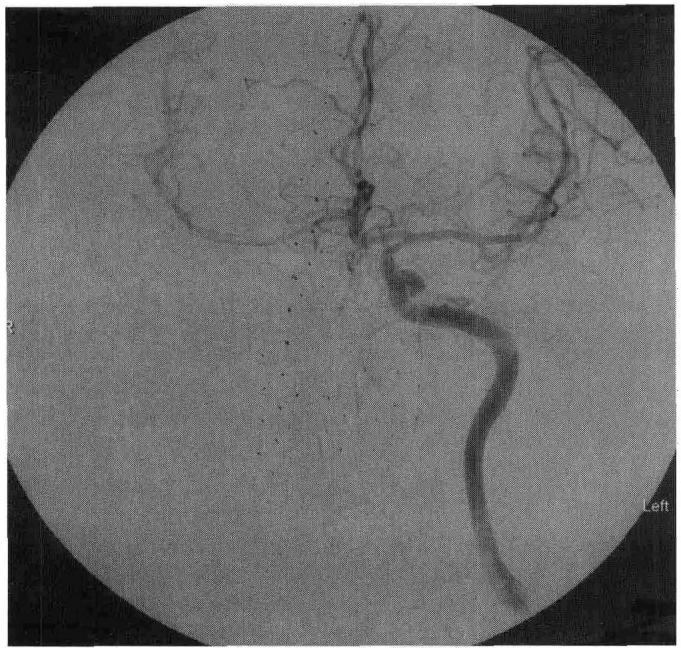


**Figure 1-6.** Anterior–posterior view of a left carotid arteriogram demonstrates flow in the right middle cerebral artery via collateral flow through the anterior communicating artery. The patient had an occlusion of the right internal carotid artery.

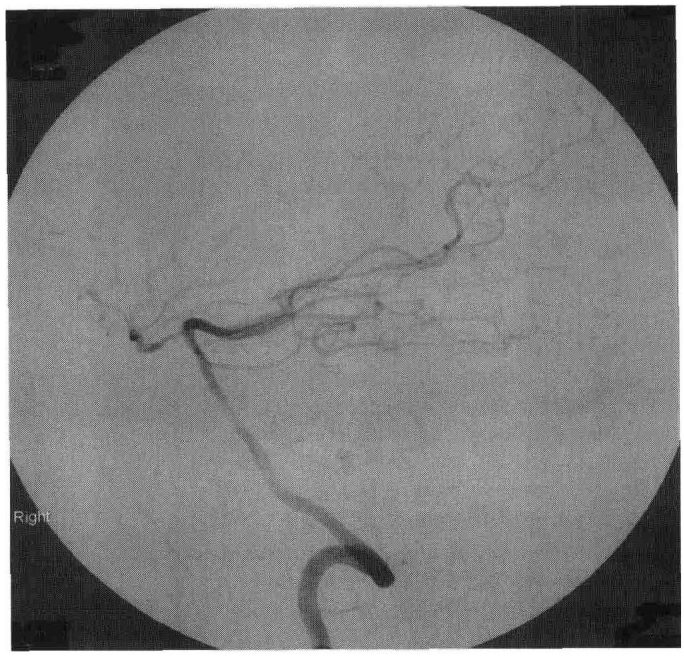


**Figure 1-7.** Lateral view of a vertebral arteriogram demonstrates flow in the middle cerebral artery via collateral flow through the posterior communicating artery.

in the posterior circulation. The *circle of Willis* constitutes the second major collateral system (Figs. 1-7 and 1-8). The integrity of the circle of Willis differs between persons; in particular, the anterior communicating artery or one or both of the posterior communicating arteries can be atretic. Depending upon the presence of these collateral arteries, the vascular bed of the internal carotid artery can be isolated. In these circumstances, an infarction also can affect the territories of both the anterior and middle cerebral arteries. In some patients, the proximal segment of the anterior cerebral artery may be hypoplastic and the distal anterior cerebral artery receives blood from the contralateral anterior cerebral artery via the anterior communicating artery. The third collateral circulation for the cerebral hemisphere is based on the pial cortical branches of the anterior, middle, and posterior cerebral arteries. A similar pial collateral circulation for the cerebellar hemisphere involves distal branches of the superior cerebellar artery, AICA, and PICA. Because the distal branches of the pial arteries interdigitate, it is possible for blood to be diverted from cortical branches of a patent artery distally to an occlusion of another pial artery. On the other hand, these cortical branches represent the distal arterial territories of the major intracranial vessels. Because perfusion pressure is lowest in these terminal regions, the areas of the brain supplied by these terminal vessels are affected with hypotensive ischemia, leading to *watershed (borderzone)* infarctions.

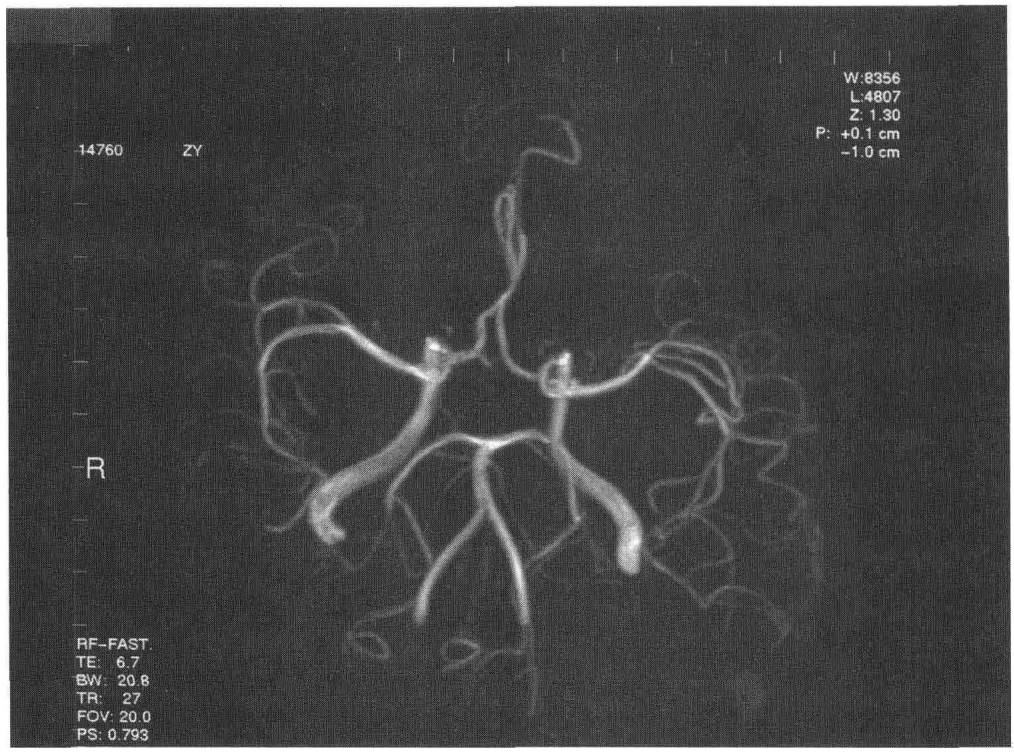


**Figure 1-8.** Submental vertex view of a magnetic resonance angiogram demonstrates the distal segments of the vertebral arteries, the basilar artery, and the posterior cerebral arteries. Also shown are the origins of the superior cerebellar arteries. In addition, the study visualizes both internal carotid arteries and the anterior and middle cerebral arteries. This view provides important information about the anatomy of the circle of the Willis.

## ▶ CLASSIFICATION BY THE TYPE AND DURATION OF SYMPTOMS

Ischemic cerebrovascular events are categorized by the presence and the duration of neurological symptoms. While the subcategories are sometimes considered as different diseases, in reality, these ischemic events should be considered as part of a continuum from asymptomatic disease to a fatal stroke (Table 1-5).

### Clinically Silent Stroke

In some cases, the neurological symptoms might be so subtle that neither the patient nor observers are aware that a stroke has occurred. Brain imaging subsequently leads to discovery of the vascular brain injury—a *clinically silent stroke*.[1,2] Most of these lesions, which often are discovered during the evaluation following another stroke or unrelated neurological complaints, are located in the deep structures of the cerebral hemispheres. Clinically silent infarctions are most common among patients with other evidence of vascular disease.[2] Similarly, asymptomatic arterial disease might be detected by physical examination or by vascular imaging. The most common situation is an *asymptomatic bruit* or *stenosis* of the internal carotid artery.

▶ **TABLE 1-5.** TIME-RELATED CLASSIFICATION OF ISCHEMIC CEREBROVASCULAR DISEASE

| |
|---|
| Asymptomatic arterial disease |
| Asymptomatic bruit |
| Asymptomatic stenosis |
| Clinically silent stroke |
| Transient ischemic attack |
| Amaurosis fugax |
| Cerebral infarction with transient symptoms |
| Minor stroke |
| Acute ischemic stroke |
| Hyperacute stroke (brain attack) |
| Stroke-in-evolution (progressing stroke) |
| Completed stroke |
| Vascular dementia (multi-infarction dementia) |

### Transient Ischemic Attack

A *transient ischemic attack* (TIA) is diagnosed when a patient has focal neurological symptoms that completely resolve and are ascribed to vascular disease.[3] A TIA should not be considered as different from ischemic stroke. Rather, it is the mildest form of ischemic cerebrovascular disease that forms a continuum to include life-threatening cerebral infarction.[4] A TIA represents a thromboembolic event that abates because of lysis of the clot or because collateral flow permits adequate reperfusion to the brain. While a TIA does not leave any neurological residuals, it is a warning that the patient's vascular disease has changed and that the risk of impending stroke is considerable.[3,5] For these reasons, a patient should be managed urgently, instituting effective stroke prophylaxis. Unfortunately, the diagnosis of TIA

is difficult and not all transient episodes of neurological dysfunction are due to ischemia. While the definition of TIA includes duration of up to 24 h, most events last only a few minutes.[6] Physicians should not wait 24 h to exclude the diagnosis of TIA so as to initiate treatment of patients with ischemic stroke. When a patient has neurological signs persisting for more than 1 h, the prudent course is to diagnose acute ischemic stroke rather than TIA. Most patients with neurological signs that resolve after 1 h will subsequently have a stroke detected by brain imaging.[7,8] In these cases, the term *cerebral infarction with transient symptoms* (CITS) is often used.

## Minor Ischemic Stroke

In the past, diagnoses such as *reversible ischemic neurological deficit* (RIND) or *partially reversible ischemic neurological deficit* (PRIND) were made when a patient's symptoms lasted for prolonged periods (even>24 h) or when a patient's impairments largely resolved. These terms probably are not very useful and their use has been abandoned in favor of the diagnosis of a *minor ischemic stroke* because in fact affected patients have had strokes that largely resolved.[9] More recently, the term *acute recovered cerebral ischemia* (ACRI) has been used to distinguish those patients whose strokes have largely resolved within a few hours and who appear to have a very high risk for another, more serious stroke.[10] The reason to substitute this term for minor ischemic stroke is not obvious. The diagnosis of minor ischemic stroke is important because it not only implies that the underlying vascular pathology is unstable but that the collateral circulation and other compensatory mechanisms may not be sufficient to completely ease the consequences of recurrent thromboembolism. There is evidence that the risk of a major stroke is higher among patients with a minor stroke than among persons with TIA. Because the ophthalmic artery is the first major branch of the internal carotid artery, ischemia of the eye also portends an increased risk of ischemic stroke in the ipsilateral cerebral hemisphere. A painless, brief episode of monocular visual loss *(amaurosis fugax)* is the result of transient thromboembolic occlusion of the ophthalmic artery or its retinal branches.

## Brain Attack

Advances in treatment are prompting a change in the approach to management of patients with acute ischemic or hemorrhagic cerebrovascular disease. Because of the time-linked changes in the brain and vasculature, the interval from onset of symptoms to treatment is crucial. During the first few hours following onset, the patient has the potential for either neurological improvement or worsening. In an effort to highlight the importance of urgent treatment, public-awareness programs are using the term *brain attack* to describe stroke.[11] The aim is to make the public respond to stroke with the same alacrity as for a heart attack.[12,13] Patients seen within the first few hours following an arterial occlusion can be diagnosed as having an *acute (hyperacute) ischemic stroke*.[14] In general, the time limit for acute ischemic stroke is 12–24 h, while the hyperacute designation would include a shorter time limit of 3–6 h. This is the time limit for treatment with interventions such as thrombolytic agents.

## Stroke-in-Evolution

Some patients have neurological worsening during the first hours following stroke. These patients are thought to have a *stroke-in-evolution (progressing stroke)* secondary to early recurrent embolization, progression of thrombosis, or perfusion failure secondary to inadequate collateral flow.[15,16] However, these patients must be differentiated from patients whose neurological status declines secondary to medical or neurological complications of the stroke or other medical illnesses. Patients with stroke-in-evolution represent a group that demands urgent care because their outcomes are poorer than those whose neurological status remains stable.

## Cerebral Infarction

Patients with mild-to-severe neurological impairments that persist for more than 24 h are considered to have had a *completed stroke (cerebral infarction)*. Strokes range in size from small lesions that produce mild, focal neurological impairments to multilobar infarctions that can cause severe neurological deficits or death (Table 1-6).[17] The priorities in therapy reflect the size and location of the brain lesion and the type and severity of neurological deficits. Still, patients who survive an ischemic stroke have a high risk of recurrent cerebrovascular events.

## Vascular Dementia

While a single stroke produces focal neurological deficits that correspond with the location of the brain injury, multiple recurrent strokes can lead to dysfunction causing cognitive decline *(vascular dementia)*.[18,19] Patients with a history of either ischemic or hemorrhagic cerebrovascular disease have an enhanced risk of dementia. Vascular disease is second to degenerative disease (Alzheimer disease) as a cause of dementia; it accounts for approximately one-third of the cases of dementia.[18] Approximately one-fourth of survivors of stroke will subsequently develop dementia.[20,21] In addition, stroke is recognized as a contributing factor in the development of symptomatic Alzheimer disease.[22]

**▶ TABLE 1.6.** OXFORDSHIRE CLASSIFICATION OF STROKE SYNDROMES

| |
|---|
| Lacunar infarction |
| Contralateral motor or sensory impairments |
| Alone or in combination |
| Usually affect face, upper extremity, and lower extremity |
| Dysarthria |
| Cognitive, behavioral, or visual impairments are mild or absent |
| Partial anterior cerebral infarction |
| Prominent cognitive or behavioral impairments |
| Differ in dominant or nondominant hemisphere |
| Contralateral motor and sensory impairments |
| Face, upper extremity, and lower extremity not equally affected |
| Contralateral visual field impairment |
| Total anterior cerebral infarction |
| Normal to slightly depressed consciousness |
| Prominent cognitive or behavioral impairments |
| Differ in dominant or nondominant hemisphere |
| Contralateral motor and sensory impairments |
| Usually affect face, upper extremity, and lower extremity |
| Contralateral visual field impairment |
| Ipsilateral conjugate eye deviation |
| Dysarthria |
| Posterior circulation infarction |
| Normal consciousness to coma |
| Unilateral (contralateral) or bilateral motor impairments |
| Contralateral sensory impairments (can be dissociated) |
| Disturbances in ocular motility |
| Ipsilateral cranial nerve palsies |
| Dysarthria |
| Ipsilateral cerebellar signs |

Adapted from Bamford et al.[17]

Differentiating vascular dementia from Alzheimer disease can be difficult. A number of clinical and imaging findings are used to help distinguish these causes of cognitive decline. A widely used clinical scale is that developed by Hachinski et al.,[23] which includes a number of historicaland physical findings. While cases of vascular dementia often are ascribed to multiple small infarctions deep in the cerebral hemisphere *(multi-infarction dementia)*, the development of new brain imaging technologies has allowed for the detection of extensive white matter changes in a sizable number of patients with cognitive impairments (Table 1-7). The imaging changes, which are primarily periventricular in location, are known as *leukoaraiosis* and often are ascribed to disease of small arterioles.[19] These white matter changes are associated with an increased probability of dementia.[24] Still, evidence correlating the imaging findings with other types vascular disease seems to be circumstantial. The cause-and-effect relationship between microvascular disease and leukoaraiosis has not been established. However, the imaging findings have prompted an increase in the diagnosis of *Binswanger disease* as a variety of vascular dementia.[25] This diagnosis remains difficult and controversial.

**▶ TABLE 1-7.** HACHINSKI SCALE TO DIFFERENTIATE VASCULAR (MULTI-INFARCTION) DEMENTIA FROM DEGENERATIVE (ALZHEIMER DISEASE) DEMENTIA

| | |
|---|---|
| Abrupt onset of neurological symptoms | 2 points |
| History of focal neurological symptoms | 2 points |
| History of focal neurological signs | 2 points |
| History of stroke | 2 points |
| Fluctuating course of symptoms | 2 points |
| Stepwise neurological deterioration | 1 point |
| Nocturnal confusion | 1 point |
| Relative preservation of personality | 1 point |
| Depression | 1 point |
| Prominent somatic complaints | 1 point |
| Pseudobulbar affect | 1 point |
| History of hypertension | 1 point |
| Evidence of atherosclerosis | 1 point |

7 or more points suggests vascular dementia and 4 or fewer points suggests degenerative dementia.
Adapted from Hachinski et al.[23]

## ▶ SPECTRUM OF CEREBROVASCULAR DISEASES (STROKE AS A SYMPTOM)

Besides having a variety of clinical findings based on the location and size of the ischemic stroke, the cause of an arterial occlusion (stroke subtype) also affects the patient's symptoms and signs.[26] It also influences decisions about management. The differential diagnosis for the cause of ischemic stroke is extensive and uncommon etiologies should be considered when a patient presents with atypical symptoms.

**▶ TABLE 1-8.** GENERAL CATEGORIES CAUSES OF ISCHEMIC STROKE

| |
|---|
| Hypotension and perfusion failure |
| Watershed (borderzone) infarction |
| Thromboembolism |
| Atherosclerosis |
| Extracranial large artery disease |
| Intracranial large artery disease |
| Small (penetrating artery) disease |
| Cardioembolism |
| Nonatherosclerotic vasculopathies |
| Infectious vasculitic |
| Noninfectious, inflammatory vasculitic |
| Noninflammatory vasculopathies |
| Hypercoagulable (prothrombotic) disorders |
| Other causes of embolism |

▶ **TABLE 1-9.** CATEGORIZATION OF SUBTYPES OF ISCHEMIC STROKE

| |
|---|
| Large artery atherosclerosis |
| Clinical findings of cortical or multilobar hemispheric infarction or findings of major brain stem or cerebellar infarction |
| Brain imaging findings compatible with cortical or multilobar hemispheric infarction or findings of major brain stem or cerebellar infarction |
| Demonstration of high-grade stenosis or occlusion of appropriate artery by vascular imaging |
| (Probable—absence of another equally plausible explanation for stroke) |
| Cardioembolism |
| Clinical findings of cortical or multilobar hemispheric infarction or findings of major brain stem or cerebellar infarction |
| Brain imaging findings compatible with cortical or multilobar hemispheric infarction or findings of major brain stem or cerebellar infarction |
| Demonstration of high-risk cardiac lesion by cardiac evaluation or demonstration of a lower (or undetermined) risk cardiac lesion during evaluation and absence of any other etiology |
| (Probable—absence of another equally plausible explanation for stroke) |
| Small artery occlusion |
| Clinical findings of a traditional lacunar syndrome |
| Brain imaging findings of small (<1.5-cm diameter) subcortical hemispheric or brain stem infarction |
| (Probable—absence of high-grade stenosis or occlusion of relevant major intracranial or extracranial artery and absence of high-risk cardiac lesion) |
| Stroke of other etiology |
| Broad spectrum of clinical findings |
| Brain imaging shows infarction |
| Evaluation demonstrates a nonatherosclerotic vasculopathy or prothrombotic state |
| (Probable—absence of other cause of stroke) |
| Stroke of undetermined etiology |
| Broad spectrum of clinical findings |
| Brain imaging shows infarction |
| Evaluation not performed |
| Evaluation negative for cause of stroke |
| Evaluation demonstrates two or more causes that are equally plausible |

## Large Artery Atherosclerosis

Atherosclerosis is the leading arterial disease that promotes thromboembolism (Tables 1-8 and 1-9). Thrombosis of a large extracranial or intracranial artery usually is secondary to an atherosclerotic plaque or stenosis *(large artery atherosclerosis)* (Fig. 1-9). The thrombosis can lead to occlusion or artery-to-artery embolism.

## Small Artery Occlusive Disease

Persons with risk factors for large artery atherosclerosis also have a high likelihood of developing occlusion of a small penetrating artery that leads to a lacunar infarction *(small artery disease.)*

## Hypoperfusion

Profound declines in blood pressure can aggravate the effects of impaired flow distal to a stenosis. Global *hypotension*, such as that which occurs during cardiovascular operations, also can lead to brain ischemia. The most vulnerable areas of the cerebral hemispheres for hypotensive injury are at the end of the perfusion beds of the major intracranial arteries. The resultant infarctions are often described as having a watershed pattern of ischemic stroke.

## Cardioembolic Stroke

Approximately one-fourth of ischemic strokes are secondary to emboli that arise in the heart *(cardioembolism)* (Fig. 1-10).

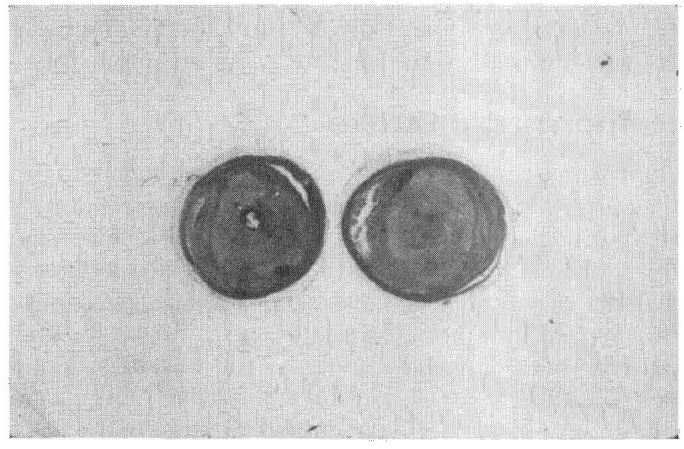

**Figure 1-9.** Cross section of a basilar artery demonstrates thrombotic occlusion of the artery superimposed on an atherosclerotic plaque. (*Courtesy of S.S. Schochet, M.D., Department of Pathology, University of West Virginia.*)