Overview of the evaluation of stroke

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INTRODUCTION

The symptoms of brain ischemia may be transient, lasting seconds to minutes, or may persist for longer periods of time. Symptoms and signs remain indefinitely if the brain becomes irreversibly damaged and infarction occurs. Unfortunately, neurologic symptoms do not accurately reflect the presence or absence of infarction, and the tempo of the symptoms does not indicate the cause of the ischemia [1,2]. This is a critical issue because treatment depends upon accurately identifying the cause of symptoms.

An overview of the evaluation of patients who present with neurologic symptoms that may be consistent with stroke is discussed here. This evaluation includes the following:

- Understanding the classification of stroke
- An initial quick evaluation to stabilize vital signs, determine if intracranial hemorrhage is present, and, in patients with ischemic stroke, decide if reperfusion therapy is warranted (see "Initial assessment and management of acute stroke")
- Forming a hypothesis of the stroke etiology based upon the history, physical examination, and initial brain imaging study (usually a noncontrast head CT scan)
- Confirming the precise pathophysiologic process with more directed diagnostic testing

The approach to patients with transient brain ischemia is reviewed separately. (See "Initial evaluation and management of transient ischemic attack and minor ischemic stroke".)

CLASSIFICATION

Cerebrovascular disease is caused by one of several pathophysiologic processes (table 1) involving the blood vessels of the brain:

- **Intrinsic vessel abnormality** – The process may be intrinsic to the vessel, as in atherosclerosis, lipohyalinosis, inflammation, amyloid deposition, arterial dissection, developmental malformation, aneurysmal dilation, or venous thrombosis.
- **Embolism** – The process may originate remotely, as occurs when an embolus from the heart or extracranial circulation lodges in an intracranial vessel.
- **Inadequate blood flow** – The process may result from inadequate cerebral blood flow due to decreased perfusion pressure or increased blood viscosity.
- **Vessel rupture** – The process may result from rupture of a vessel in the subarachnoid space or intracerebral tissue.

The first three processes can lead to transient brain ischemia (transient ischemic attack [TIA]) or permanent brain infarction (ischemic stroke), while the fourth results in either subarachnoid hemorrhage or an intracerebral hemorrhage (primary hemorrhagic stroke). Approximately 80 percent of strokes are due to ischemic cerebral infarction and 20 percent to brain hemorrhage.

Transient brain ischemia — TIA is now defined as a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction. This tissue-based definition of TIA relies on the absence of end-organ injury as assessed by imaging or other techniques. The proposed advantages of the tissue-based definition are that the defined end point is biological (tissue injury) rather than arbitrary (24 hours). (See "Definition, etiology, and clinical manifestations of transient ischemic attack", section on 'Definition of TIA'.)

The approach to patients with TIA is reviewed separately. (See "Initial evaluation and management of transient ischemic attack and minor ischemic stroke".)

Intracerebral hemorrhage — Bleeding in intracerebral hemorrhage (ICH) is usually derived from arterioles or small arteries. The bleeding is directly into the brain, forming a localized hematoma which spreads along white matter pathways. Accumulation of blood occurs over minutes or hours; the hematoma gradually enlarges by adding blood at its periphery like a

snowball rolling downhill. The most common causes of ICH are hypertension, trauma, bleeding diatheses, amyloid angiopathy, illicit drug use (mostly amphetamines and cocaine), and vascular malformations. Less frequent causes include bleeding into tumors, aneurysmal rupture, and vasculitis. Neurologic symptoms usually increase gradually over minutes or a few hours. (See "Spontaneous intracerebral hemorrhage: Pathogenesis, clinical features, and diagnosis" and "Clinical diagnosis of stroke subtypes".)

Subarachnoid hemorrhage — Rupture of arterial aneurysms is the major cause of subarachnoid hemorrhage (SAH). Aneurysm rupture releases blood directly into the cerebrospinal fluid (CSF) under arterial pressure. The blood spreads quickly within the CSF, rapidly increasing intracranial pressure. Death or deep coma ensues if the bleeding continues. The bleeding usually lasts only a few seconds but rebleeding is common. With causes of SAH other than aneurysm rupture (eg, vascular malformations, bleeding diatheses, trauma, amyloid angiopathy, and illicit drug use), the bleeding is less abrupt and may continue over a longer period of time.

Symptoms of SAH begin abruptly, occurring at night in 30 percent of cases. The primary symptom is a sudden, severe headache (97 percent of cases) classically described as the "worst headache of my life." The headache is lateralized in 30 percent of patients, predominantly to the side of the aneurysm. The onset of the headache may or may not be associated with a brief loss of consciousness, seizure, nausea, vomiting, focal neurologic deficit, or stiff neck (figure 1) [3]. There are usually no important focal neurologic signs at presentation unless bleeding occurs into the brain and CSF at the same time (meningocerebral hemorrhage). (See "Aneurysmal subarachnoid hemorrhage: Clinical manifestations and diagnosis".)

Ischemia — There are three main subtypes of brain ischemia:

- Thrombosis
- Embolism
- Systemic hypoperfusion

Thrombotic stroke — Thrombotic strokes are those in which the pathologic process giving rise to thrombus formation in an artery produces a stroke either by reduced blood flow distally (low flow) or by an embolic fragment that breaks off and travels to a more distant vessel (artery-to-artery embolism). All thrombotic strokes can be divided into either large or small vessel disease (table 2).

- Large vessel disease includes both the extracranial and intracranial arterial system; atherothrombosis is by far the most common pathologic process. (See "Intracranial large artery atherosclerosis: Epidemiology, clinical manifestations, and diagnosis".)

- Small vessel disease refers specifically to penetrating arteries that arise from the distal vertebral artery, the basilar artery, the middle cerebral artery stem, and the arteries of the circle of Willis. These arteries thrombose due to atheroma formation at their origin or in the parent large artery, or due to lipohyalinosis (a lipid hyaline build-up distally secondary to hypertension). Penetrating artery (small vessel) disease can result in small deep infarcts usually referred to as lacunes. (See "Lacunar infarcts".)

Embolic stroke — Embolism refers to particles of debris originating elsewhere that block arterial access to a particular brain region. Since the process is not local (as with thrombosis), local therapy only temporarily solves the problem; further events may occur if the source of embolism is not identified and treated.

Embolic strokes are divided into four categories (table 2). (See "Stroke: Etiology, classification, and epidemiology".)

- Those with a known source that is cardiac
- Those with a possible cardiac or aortic source based upon transthoracic and/or transesophageal echocardiographic findings
- Those with an arterial source
- Those with a truly unknown source in which these tests are negative or inconclusive

Systemic hypoperfusion — Systemic hypoperfusion is a more general circulatory problem, manifesting itself in the brain and perhaps other organs. Reduced perfusion can be due to cardiac pump failure caused by cardiac arrest or arrhythmia, or to reduced cardiac output related to acute myocardial ischemia, pulmonary embolism, pericardial effusion, or bleeding. Hypoxemia may further reduce the amount of oxygen carried to the brain. (See "Clinical diagnosis of stroke subtypes".)

INITIAL GENERAL ASSESSMENT

Sudden loss of focal brain function is the core feature of the onset of ischemic stroke. However, patients with conditions other than brain ischemia can present in a similar fashion (table 3). In addition, patients who have an ischemic stroke may present with other serious medical conditions. Thus, the initial evaluation requires a rapid but broad assessment. The goals in this initial phase include:

- Ensuring medical stability
- Quickly reversing any conditions that are contributing to the patient's problem

- Moving toward uncovering the pathophysiologic basis of the patient's neurologic symptoms

Diagnosing an intracerebral or subarachnoid hemorrhage as soon as possible can be lifesaving and prevent or minimize permanent neurologic damage. The history may provide clues to these diagnoses, but early triage of the patient to CT scan or MRI is critical. However, it is important to assess and optimize vital physiologic function **before** sending the patient for an imaging study. (See "Initial assessment and management of acute stroke".)

Vital signs — Parameters of particular concern in patients with stroke include blood pressure, breathing, and temperature.

Blood pressure — The mean arterial blood pressure (MAP) is usually elevated in patients with an acute stroke. This may be due to chronic hypertension, which is a major risk factor for ischemic stroke. However, an acute elevation in blood pressure often represents an appropriate response to maintain brain perfusion. The decision to treat requires a balance between the potential danger of severe increases in blood pressure, and a possible decline in neurologic functioning when blood pressure is lowered. (See "Initial assessment and management of acute stroke", section on 'Blood pressure management'.)

Breathing — Patients with increased intracranial pressure (ICP) due to hemorrhage, vertebrobasilar ischemia, or bihemispheric ischemia can present with a decreased respiratory drive or muscular airway obstruction. Hypoventilation, with a resulting increase in the partial pressure of carbon dioxide, may lead to cerebral vasodilation which further elevates ICP.

Intubation may be necessary to restore adequate ventilation and to protect the airway. This is especially important in the presence of vomiting, which occurs commonly with increased ICP, vertebrobasilar ischemia, and intracranial hemorrhage.

Fever — Fever may occur in patients with an acute stroke and can worsen brain ischemia [4]. Normothermia should be maintained for at least the first several days after an acute stroke. (See "Initial assessment and management of acute stroke", section on 'Fever'.)

History and physical examination — The history and physical examination should be used to distinguish between other disorders in the differential diagnosis of stroke (table 3). As examples, seizures, syncope, migraine, and hypoglycemia can mimic acute ischemia. The most difficult cases involve patients with focal signs and altered level of consciousness. It is important to ask the patient or a relative whether the patient takes insulin or oral hypoglycemic agents, has a history of a seizure disorder or drug overdose or abuse, medications on admission, recent trauma, or hysteria (see "Differential diagnosis of transient ischemic attack and acute stroke").

The history is also important in separating ischemia from hemorrhage and distinguishing between subtypes of ischemia and hemorrhage.

Ischemia versus hemorrhage — Noncontrast computed tomography (CT) is typically the first diagnostic study in patients with suspected stroke. The main advantages of CT are widespread access and speed of acquisition. CT is highly sensitive for the diagnosis of hemorrhage in the acute setting [5]. Intracerebral hemorrhages are evident almost instantly after onset as focal white hyperdense lesions within the brain parenchyma. (See "Spontaneous intracerebral hemorrhage: Pathogenesis, clinical features, and diagnosis", section on 'Head CT'.)

Intracerebral hemorrhages can also be defined by MRI; the use of susceptibility sequences improves the sensitivity of MRI for early detection of hemorrhage. Gradient-echo images can also show the presence of old hemorrhages since this technique is very sensitive to hemosiderin, which can remain in old hemorrhages indefinitely. (See "Spontaneous intracerebral hemorrhage: Pathogenesis, clinical features, and diagnosis", section on 'Brain MRI'.)

Small subarachnoid hemorrhages can be missed by either CT or MRI. Lumbar puncture may be needed to make the diagnosis in such patients. (See "Aneurysmal subarachnoid hemorrhage: Clinical manifestations and diagnosis", section on 'Lumbar puncture'.)

MRI is more sensitive than CT for the early diagnosis of brain infarction, although CT may identify subtle indicators of infarction within six hours of stroke onset in a significant number of patients (see "Neuroimaging of acute stroke", section on 'Assessment of early infarct signs'). Fluid-attenuated inversion recovery (FLAIR) MRI sequences and diffusion-weighted images (DWI-MRI) are especially useful in showing infarcts early after the onset of symptoms. In patients with ischemia who do not yet have brain infarction, both CT and MRI may be normal. (See "Neuroimaging of acute stroke", section on 'Assessment of early infarct signs'.)

Is the patient a candidate for reperfusion? — Timely restoration of blood flow is the most effective maneuver for salvaging ischemic brain tissue that is not already infarcted. Removal of occlusive intracranial thrombi must be accomplished quickly, since the benefit of reperfusion therapy for ischemic stroke decreases in a continuous fashion over time. An important aspect of the hyperacute phase of stroke assessment is to determine if the patient is eligible for intravenous thrombolysis and/or mechanical thrombectomy:

- Intravenous thrombolytic therapy with alteplase (recombinant tissue-type plasminogen activator or rt-PA) improves outcomes in patients with acute ischemic stroke who can be treated within 3 to 4.5 hours from stroke onset and meet additional eligibility criteria

(table 4). This issue is discussed in detail separately. (See "Approach to reperfusion therapy for acute ischemic stroke", section on 'Alteplase'.)

- Intra-arterial mechanical thrombectomy using a second-generation stent retriever device can improve outcomes for well-selected patients with ischemic stroke caused by a large artery occlusion in the proximal anterior circulation when started up to 24 hours from the time last seen. This therapy is reviewed in detail elsewhere. (See "Mechanical thrombectomy for acute ischemic stroke".)

DETERMINING A PRESUMPTIVE DIAGNOSIS OF STROKE SUBTYPE

After completing the initial assessment, the goal of the subsequent evaluation is to determine the underlying pathophysiology of the stroke in order to guide therapy (table 1). This part of the discussion assumes that patients with subarachnoid hemorrhage have already been identified by the initial history and physical examination and noncontrast head CT (with or without lumbar puncture). A review of the clinical features and diagnosis of subarachnoid hemorrhage is found separately. (See "Aneurysmal subarachnoid hemorrhage: Clinical manifestations and diagnosis".)

In addition, the presence of intracerebral hemorrhage should already be evident by this phase of the evaluation; the diagnostic evaluation in these patients is reviewed elsewhere. (See 'Evaluation of patients with intracerebral hemorrhage' below.)

In practice, then, this second stage of evaluation is focused upon distinguishing between embolic and thrombotic strokes; in patients with the latter, it is worth differentiating between large vessel and small vessel (penetrating artery or lacunar) infarcts since the causes, outcomes, and treatments are different. Some patients will have more than one potential etiology for stroke, although the majority will have only one predominant cause [6]. (See "Stroke: Etiology, classification, and epidemiology" and "Clinical diagnosis of stroke subtypes".)

A presumptive diagnosis of the stroke subtype can be made following a thorough history, physical examination, and imaging study such as CT or MRI. However, confirmation of the diagnosis requires more extensive testing.

A history of carotid stenosis is a significant risk factor for large artery thrombotic stroke, but these patients need to have other stroke subtypes considered in the differential diagnosis. In the North American Symptomatic Carotid Endarterectomy Trial (NASCET), of patients with 70 to 99 percent stenosis who subsequently had an ischemic stroke, 20 and 45 percent of strokes that

occurred in the territory of symptomatic and asymptomatic carotid arteries, respectively, were unrelated to carotid stenosis [7].

History — A number of features in the clinical history may be useful in determining the type of stroke:

- Clinical course
- Ecology
- Previous transient ischemic attack (TIA)
- Activity at the onset or just before the stroke
- Associated symptoms

Clinical course — The most important historical item for differentiating stroke subtypes is the pace and course of the symptoms and signs and their clearing [8]. Each subtype has a characteristic course.

- Embolic strokes most often occur suddenly (figure 2). The deficits indicate focal loss of brain function that is usually maximal at onset. Rapid recovery also favors embolism.
- Thrombosis-related symptoms often fluctuate, varying between normal and abnormal or progressing in a stepwise or stuttering fashion with some periods of improvement (figure 3).
- Penetrating artery occlusions usually cause symptoms that develop during a period of hours or at most a few days (figure 4), compared with large artery-related brain ischemia, which can evolve over a longer period.
- Intracerebral hemorrhage (ICH) does not improve during the early period; it progresses gradually during minutes or a few hours (figure 5).
- Aneurysmal subarachnoid hemorrhage (SAH) develops in an instant. Focal brain dysfunction is less common.

Patients often do not give a specific history regarding the course of neurologic symptoms. I may ask if the patient could walk, talk, use the phone, use the hand, etc, as the events developed after the first symptoms occurred [8].

Ecology — Ecology refers to known demographic and historical features that provide probabilities of the patient having one or more of the stroke subtypes. Age, sex, and race are important demographic variables generally known to the clinician before taking the history [9].

- Most thrombotic and embolic strokes related to atherosclerosis occur in older patients. Individuals under age 40 rarely have severe atherosclerosis unless they also have major risk factors such as diabetes, hypertension, hyperlipidemia, smoking, or a strong family history. By contrast, cardiac-origin embolism is common in young people who are known to have heart disease.

- Hypertensive ICH is more common among Black individuals and individuals of Asian descent (eg, Chinese and Japanese) compared with White individuals.

- Premenopausal women have a lower frequency of atherosclerosis than men of similar age unless they have major stroke risk factors. Even after adjusting for age, the incidence of atherosclerotic stroke is four times higher in men [10].

- Black and Asian individuals have a lower incidence of occlusive disease of the extracranial carotid and vertebral arteries than White men.

Hypertension is the most common and most important stroke risk factor, including isolated systolic hypertension (see "Overview of secondary prevention of ischemic stroke", section on 'Hypertension'). Epidemiologic studies show that there is a gradually increasing incidence of both coronary disease and stroke as the blood pressure rises above 110/75 mmHg (figure 6) [11,12]. However, these observations do not prove a causal relationship, since increasing blood pressure could be a marker for other risk factors such as increasing body weight, which is associated with dyslipidemia, glucose intolerance, and the metabolic syndrome. The best evidence for a causal role of increasing blood pressure in cardiovascular complications is an improvement in outcome with antihypertensive therapy. This evidence is reviewed elsewhere.

Chronic hypertension is a risk factor for both thrombotic extracranial and intracranial large artery disease and penetrating artery disease. Conversely, the absence of a history of hypertension or of present hypertension reduces the likelihood of penetrating artery disease.

Smoking increases the likelihood of extracranial occlusive vascular disease, more than doubling the risk of stroke [13]. The risk of ischemic stroke decreases over time after smoking cessation. In one series of middle-aged women, for example, the excess risk among former smokers largely disappeared two to four years after cessation [13]. (See "Cardiovascular risk of smoking and benefits of smoking cessation".)

Several other risk factors for stroke have been identified:

- Diabetes increases the likelihood of large and small artery occlusive disease.

- The use of amphetamines increases the likelihood of both ICH and SAH but not brain ischemia.
- Cocaine-related strokes are often hemorrhagic (ICH and SAH), due to aneurysms and vascular malformations [14]. Cocaine is also associated with brain ischemia, especially involving the posterior circulation intracranial arteries; this is probably due to vasoconstriction.
- Heart disease, including cardiac valvular disease, prior myocardial infarction, atrial fibrillation, and endocarditis, increases the probability of a stroke due to embolism.
- Stroke during the puerperium has an increased likelihood of being related to venous or arterial thrombosis.
- The presence of a known bleeding disorder or prescription of warfarin or other anticoagulants predisposes to hemorrhage, into either the brain or the cerebrospinal fluid (CSF).

The link between stroke and oral contraceptive use has been a controversial issue. Initial studies suggesting this association were performed with oral contraceptives containing higher doses of estrogen; the risk may not be as great with current low dose oral contraceptives. (See "Combined estrogen-progestin contraception: Side effects and health concerns", section on 'Cardiovascular effects'.)

The presence of these risk factors increases the odds that a stroke is due to a particular mechanism, but the clinician cannot make a firm diagnosis simply on the basis of probability. As examples: some conditions such as hypertension predispose to more than one subtype (thrombosis, intracranial hemorrhage); the presence of a prior myocardial infarction increases the likelihood of cardiac origin embolism, but also increases the likelihood of carotid and vertebral artery neck occlusive disease (thrombosis); and an older patient with severe atherosclerosis may also harbor an unexpected cerebral aneurysm.

Previous transient ischemic attack — A history of TIA (especially more than one) in the same territory as the stroke strongly favors the presence of a local vascular lesion (thrombosis). Attacks in more than one vascular territory suggest brain embolism from the heart or aorta. TIAs are not a feature of brain hemorrhage.

Patients often will not volunteer a prior history of symptoms consistent with a TIA. Many patients, for example, do not relate prior hand or eye problems to subsequent leg problems. Thus, the physician must ask directly about specific symptoms. "Did your arm, hand, or leg ever

transiently go numb?" "Did you ever have difficulty speaking?" "Did you ever lose vision? If so, in which part of your vision? Was it in one eye and, if so, which one?"

Activity at the onset or just before the stroke — Hemorrhages (ICH and SAH) can be precipitated by sex or other physical activity, while thrombotic strokes are unusual under these circumstances. Trauma before the stroke suggests traumatic dissection or occlusion of arteries or traumatic brain hemorrhage. Sudden coughing and sneezing sometimes precipitates brain embolism. Similarly, getting up during the night to urinate seems to promote brain embolism (a matutinal embolus).

Associated symptoms — The presence of certain associated symptoms is suggestive of specific stroke subtypes.

- Fever raises the suspicion of endocarditis and resulting embolic stroke.
- Infections activate acute phase blood reactants, thereby predisposing to thrombosis.
- Headache is typically a feature of hemorrhagic strokes, but some patients have headaches in the prodromal period before thrombotic strokes.
- Vomiting is common in patients with ICH, SAH, and posterior circulation large artery ischemia (figure 1).
- Seizures are most often seen in patients with lobar ICH or brain embolism; they are rare in patients with acute thrombosis [15].
- Reduced alertness favors the presence of hemorrhage. Accompanying neurologic signs are suggestive of ICH, while the absence of focal signs suggests SAH. Loss of consciousness is also common in patients with thrombotic and embolic strokes that are large or involve the posterior circulation large arteries.

Physical examination — Important clues in the general physical examination include the following:

- Absent pulses (inferior extremity, radial, or carotid) favors a diagnosis of atherosclerosis with thrombosis, although the sudden onset of a cold, blue limb favors embolism.
- The internal carotid arteries in the neck cannot be reliably palpated but, in some patients, occlusion of the common carotid artery in the neck can be diagnosed by the absence of a carotid pulse.

- The presence of a neck bruit suggests the presence of occlusive extracranial disease, especially if the bruit is long, focal, and high pitched.

- Palpating the facial pulses is helpful in diagnosing common carotid and internal carotid artery occlusions and temporal arteritis. The facial pulses on the side of the occlusion are often lost with common carotid artery occlusions. By contrast, some patients with internal carotid artery occlusion will have increased facial pulses on the side of the occlusion because collateral channels develop between the external carotid artery facial branches and the carotid arteries intracranially. In patients with temporal arteritis, the temporal arteries are often irregular and have sausage-shaped areas of dilatation, may be tender, and are often pulseless.

- Cardiac findings, especially atrial fibrillation, murmurs, and cardiac enlargement, favor cardiac-origin embolism. (See "Auscultation of cardiac murmurs in adults".)

- Careful examination of the optic fundus may reveal a cholesterol crystal, white platelet-fibrin, or red clot emboli. Subhyaloid hemorrhages in the eye suggest a suddenly developing brain or subarachnoid hemorrhage. When the carotid artery is occluded, the iris may appear speckled and the ipsilateral pupil can become dilated and poorly reactive. The retina in that circumstance may also show evidence of chronic ischemia (venous stasis retinopathy).

Neurologic examination — The patient's account of his or her neurologic symptoms and the neurologic signs found on examination tell more about the location of the process in the brain than the particular stroke subtype. The blood supply to various parts of the brain and associated neurologic findings are shown in the figures (figure 7A-G).

Nevertheless, some constellations of symptoms and signs occasionally suggest a specific process (table 5).

- Weakness of the face, arm, and leg on one side of the body unaccompanied by sensory, visual, or cognitive abnormalities (pure motor stroke) favors the presence of a thrombotic stroke involving penetrating arteries or a small ICH.

- Large focal neurologic deficits that begin abruptly or progress quickly are characteristic of embolism or ICH.

- Abnormalities of language suggest anterior circulation disease, as does the presence of motor and sensory signs on the same side of the body (figure 8).

- Vertigo, staggering, diplopia, deafness, crossed symptoms (one side of the face and other side of the body), bilateral motor and/or sensory signs, and hemianopia or bilateral visual field loss suggest involvement of the posterior circulation. (See "Posterior circulation cerebrovascular syndromes".)

- The sudden onset of impaired consciousness in the absence of focal neurologic signs is characteristic of SAH.

Imaging studies — Brain imaging and a comprehensive neurovascular evaluation should be obtained for most patients suspected of having acute ischemic stroke or transient ischemic attack. Neurovascular imaging is important to determine the potential sources of embolism or low flow in ischemic stroke and to detect possible aneurysms or vessel malformations in hemorrhagic stroke. (See "Neuroimaging of acute stroke".)

The location and size of a brain infarct on CT or MRI may further aid in distinguishing between stroke subtypes.

- Small subcortical (deep) infarcts are most commonly located in the basal ganglia, internal capsule, thalamus, and pons. They are potentially within the blood supply of a single penetrating artery. The most common cause of a small deep infarct is lacunar infarction due to degenerative changes in the penetrating arteries.

- Rostral brainstem (midbrain and thalamus), occipital lobe, and cerebellar infarcts are most commonly caused by brain embolism. (See "Posterior circulation cerebrovascular syndromes".)

On the other hand, large subcortical infarcts, infarcts that are limited to the cerebral cortex, and infarcts that are both cortical and subcortical are commonly caused by thrombosis or embolism.

CONFIRMING THE DIAGNOSIS

The previous assessment should allow the formation of a presumptive diagnosis of the underlying stroke pathophysiology. The next phase of the evaluation is to confirm this hypothesis with diagnostic tests.

Embolic stroke — Embolism is especially likely in the following circumstances:

- The onset is sudden and the neurologic deficit is maximal from the beginning
- The infarct and deficit are large
- There is a known cardiac or large artery lesion present

- The infarct is or becomes hemorrhagic on CT or MRI
- There are multiple cortical or cortical/subcortical infarcts in different vascular territories
- Clinical findings improve quickly (so-called "spectacular shrinking deficit") [16]

In addition, embolic stroke is common in patients who have had a posterior circulation stroke; in a registry of 361 patients who had vertebrobasilar strokes or transient ischemic attacks (TIAs) and were admitted to a university hospital, 41 percent had an embolic event [17].

A possible cardiac source should be considered in all patients with suspected embolic stroke, particularly in patients under age 45, whether or not they have clinical evidence of heart disease. This issue is discussed below. (See 'Cardiac evaluation' below.)

Vascular studies — The extracranial and intracranial arteries are also common sources of brain embolism and should be studied. (See "Stroke: Etiology, classification, and epidemiology".)

- If the infarct and brain symptoms are within the anterior circulation (carotid artery supply), then the extracranial and intracranial carotid arteries, and the middle and anterior cerebral artery branches should be the focus of the examinations.

- When the infarct is within the posterior circulation (vertebrobasilar system), the extracranial and intracranial vertebral arteries, the basilar artery, and the posterior cerebral arteries should be the focus of the vascular investigations.

The anterior circulation can be studied using duplex ultrasound of the neck and transcranial Doppler (TCD) of the intracranial arteries [18,19]. B-mode images of the carotid artery also demonstrate the degree of stenosis and irregularities or ulcerations within plaques.

Alternatively, CT angiography (CTA) or MR angiography (MRA) of the neck and head arteries may be sufficient. Conventional angiography is performed when the screening tests do not fully define the lesion and more characterization is warranted, and when surgery or interventional treatment through an arterial catheter (angioplasty or intra-arterial thrombolysis) may be indicated.

Within the posterior circulation, duplex and color-flow Doppler investigation of the origins of the vertebral arteries [20] and ultrasound of the subclavian arteries (especially when the radial pulse or blood pressure on one side is lower than the other) can detect lesions of the proximal portion of the vertebral arteries. Atherosclerosis most often affects this proximal region. The ultrasonographer can then insonate over the rest of the vertebral artery in the neck using a continuous-wave Doppler to detect the direction of flow within the artery (craniad as would be normal, or reversed or to-and-fro flow suggesting proximal obstruction).

CTA and MRA of the neck vertebral arteries are also helpful, but these tests may not adequately show the origins of the vertebral arteries [21]. The clinician must be certain that the films are adequate to see the complete extracranial and intracranial vertebrobasilar system.

An important advance in the detection of brain embolism is monitoring by TCD [22]. Emboli that pass under ultrasound probes make a high-pitched chirp and are recorded as high-intensity transient signals (HITS). The location and pattern of these emboli can help define the presence of embolism and give clues as to the source. TCD monitoring can also help to assess the effectiveness of treatment.

Artery-to-artery versus cardiac sources of embolism — The distinction between artery-to-artery and non-artery-to-artery sources of embolism can be difficult. Suspicion of the former typically arises once vascular pathology in a large vessel has been identified (eg, with noninvasive testing). Repetitive spells within a single vascular territory are also suggestive of an artery-to-artery source, as is a normal echocardiogram. However, caution must be used in interpreting the results of a transthoracic echocardiogram. As previously mentioned, this study can exclude a cardiomyopathy and most atrial and mitral valve pathology, but may miss other potential embolic sources such as clot in the atrial appendage, a patent foramen ovale, mitral valve lesions, and aortic atherosclerosis. Transesophageal echocardiography (TEE) is better for identifying these lesions. However, transthoracic echocardiography (TTE) is generally superior to TEE for identifying left ventricular apical thrombus. (See 'Echocardiography' below.)

Small vessel (lacunar) stroke — Most patients with lacunar infarcts have risk factors for penetrating artery disease (eg, hypertension, diabetes mellitus, or polycythemia). The clinical findings typically conform to one of the well-recognized lacunar syndromes: pure motor hemiparesis, pure sensory stroke, dysarthria-clumsy hand, or ataxic hemiparesis. (See "Lacunar infarcts".)

Further testing is of low yield in patients suspected of having a lacunar infarction who have the typical risk factors, clinical neurologic findings, and characteristic brain imaging (eg, small subcortical infarct). On the other hand, some patients seen within the first few hours after symptom onset with clinical findings suggestive of lacunar infarction are found to have large artery disease; this has been particularly true for patients of Asian descent. (See "Intracranial large artery atherosclerosis: Epidemiology, clinical manifestations, and diagnosis", section on 'Racial and ethnic differences'.)

Vascular imaging (CTA or MRA) can be performed at the same time as brain imaging (CT or MRI) to exclude occlusion of the parent feeding artery, a condition that can mimic a lacunar infarct. (See "Lacunar infarcts", section on 'Evaluation and diagnosis'.)

It is particularly important to perform intracranial vascular imaging in Black patients and patients of Asian descent, since intracranial large artery occlusive disease is common in these patients. An alternative diagnostic test to exclude intracranial occlusive disease is TCD, a technique that measures the blood flow velocities in the large intracranial arteries using an ultrasound probe placed over the orbit, temporal bone, and foramen magnum [18]. (See "Neuroimaging of acute stroke", section on 'Ultrasound methods'.)

Large vessel atherothrombotic stroke — Large vessel atherothrombotic strokes are often preceded by TIAs, and the onset may or may not be abrupt. The course of neurologic symptoms and signs fluctuates or is progressive in development. Infarcts that are large and subcortical are usually caused by occlusion of intracranial arteries.

Patients with suspected large vessel atherothrombotic strokes need to have both intracranial and extracranial vascular testing. Extracranial vascular testing can be performed with MRA, CTA, or duplex carotid ultrasound. All are reliable and specific for detecting important severe occlusive lesions in the extracranial carotid arteries. Ultrasound devices such as color-flow Doppler imaging and power Doppler improve the resolution and quantification of carotid artery lesions. (See "Evaluation of carotid artery stenosis".)

One approach to patients with suspected carotid artery stenosis is to first perform carotid duplex ultrasound. Patients with stenoses less than 50 percent are followed with serial examinations, usually on an annual basis to determine if there is progression. Transcranial Doppler and either MRA or CTA should be performed if the carotid stenosis is greater than 50 percent on the duplex ultrasound. Both MRA and CTA accurately define abnormalities within the carotid and vertebral arteries in the neck and their intracranial branches. MRI can be performed at the same time as MRA; the presence or absence of a brain infarct can help determine treatment. (See "Evaluation of carotid artery stenosis".)

Head CT and CTA are acceptable alternatives to MRI and MRA and may be more available than MR in some centers. Head CT and CTA should be done if MRI and MRA are contraindicated or impractical.

Conventional angiography is rarely performed; indications include patients who cannot tolerate an MRA or CTA, patients with discrepant CTA/MRA and ultrasound findings, and patients with suspected nonatherosclerotic disease (eg, dissection, fibromuscular dysplasia).

Patients with carotid artery stenosis who have had nondisabling strokes may be candidates for carotid endarterectomy or carotid artery stenting. (See "Management of symptomatic carotid atherosclerotic disease".)

CARDIAC EVALUATION

A cardiac evaluation is important in most patients with brain ischemia [23]. Not only are cardiac and aortic origin emboli common, but many patients with cerebrovascular occlusive disease have concurrent coronary heart disease that can lead to significant morbidity and mortality [24-27]. The basic evaluation includes a thorough history focusing on the presence of cardiac ischemia and arrhythmias, a careful cardiac examination, and an electrocardiogram.

Monitoring for subclinical atrial fibrillation — All patients with ischemic stroke should have cardiac monitoring for at least the first 24 hours after stroke onset to look for subclinical atrial fibrillation (AF) [28]. In addition, we suggest ambulatory cardiac monitoring for several weeks (eg, 30 days) for patients with a cryptogenic ischemic stroke or transient ischemic attack (TIA). These patients are characterized by brain ischemia not attributable to a definite source of cardioembolism, large artery atherosclerosis, or small artery disease despite extensive vascular and cardiac evaluation, including no evidence of AF on standard 12-lead electrocardiogram (ECG) and 24-hour cardiac monitoring (see "Cryptogenic stroke and embolic stroke of undetermined source (ESUS)").

Prolonged cardiac event monitoring increase the detection of subclinical AF in patients with TIA or acute ischemic stroke who present with sinus rhythm [29-34]. By contrast, subclinical AF, if transient, infrequent, and largely asymptomatic, may be undetected on standard cardiac monitoring such as continuous telemetry and 24- or 48-hour Holter monitors. This issue is illustrated by the following observations among trials of patients without an identified mechanism for stroke or TIA:

- In The CRYSTAL AF trial, 441 patients with cryptogenic stroke and no evidence of AF during at least 24 hours of ECG monitoring were randomly assigned to prolonged ambulatory cardiac monitoring with a subcutaneous insertable cardiac monitor (also sometimes referred to as implantable cardiac monitor or implantable loop recorder) recorder or to a control group with conventional follow-up [29]. At six months, AF detection was significantly higher in the monitored group (8.9 percent, versus 1.4 percent in the control group, hazard ratio [HR] 6.4, 95% CI 1.9-21.7).

- In the EMBRACE trial, 572 patients who had a cryptogenic stroke or TIA (with no AF after 24-hour cardiac monitoring) in the previous six months were randomly assigned to additional ambulatory monitoring with a 30-day external loop recorder (intervention group) or a 24-hour Holter monitor (control group) [30]. At study end, the rate of AF

detection was significantly greater in the intervention group (16.1 percent, versus 3.2 percent in the control group, 95% CI 8.0-17.6).

- The PER DIEM trial randomly assigned 300 patients within six months of ischemic stroke and no known AF (66 percent had a cryptogenic stroke) in a 1:1 ratio to monitoring with either an insertable cardiac monitor (placed for one year) or an external loop recorder (worn for four weeks) [33]. At 12 months, detection of new AF lasting more than two minutes was observed in a greater number of patients in the insertable cardiac monitor group compared with the external loop recorder group (15.3 versus 4.7 percent, absolute difference 10.7 percent, 95% CI 4.0-17.3 percent).

Long-term cardiac monitoring can detect subclinical AF even among patients with a known mechanism for ischemic stroke. The STROKE-AF trial randomly assigned 492 patients with ischemic stroke attributed to large vessel or small vessel disease in a 1:1 ratio to monitoring with an insertable cardiac monitor or to site-specific usual care (external cardiac monitoring with ECG, Holter, telemetry, or event recorders) [34]. At 12 months, detection of AF lasting more than 30 seconds was higher in the insertable cardiac monitor group compared with the usual care group (12.1 versus 1.8 percent, absolute difference approximately 10.3 percent, HR 7.4, 95% CI 2.6-21.3).

These results parallel other data showing that prolonged cardiac event monitoring increases the detection of subclinical AF [31,35-39]. Such monitoring may then reduce the risk of recurrent ischemic stroke by prompting the appropriate use of long-term anticoagulation [40]. However, rigorous evidence is lacking that anticoagulation of subclinical AF improves outcomes for patients initially diagnosed with cryptogenic stroke [41]. The approach to treatment of subclinical AF detected on monitoring is reviewed separately. (See "Cryptogenic stroke and embolic stroke of undetermined source (ESUS)", section on 'Occult or subclinical atrial fibrillation on monitoring'.)

In addition, the minimum duration of time (in minutes) of the episodes of AF that increases the risk of thrombus formation in the atria and thereby increases the risk of cardioembolic stroke has not been firmly established. (See "Stroke in patients with atrial fibrillation", section on 'Long-term anticoagulation'.)

The optimal cardiac monitoring method (ie, continuous telemetry, ambulatory electrocardiography, serial electrocardiography, transtelephonic ECG monitoring, or insertable cardiac monitor) is uncertain. (See "Ambulatory ECG monitoring".)

Other potential indicators that may predict which patients have or are likely to develop atrial fibrillation include determination of the left atrial appendage ejection fraction by

transesophageal echocardiography [42] and demonstration of an atrial fibrillation phenotype on left atrial appendage pulse wave Doppler even when the surface ECG shows normal sinus rhythm [43]. In addition, measurements of B-type (brain) natriuretic protein (BNP) and the N-terminal fragment of BNP indicate that these values are elevated in patients with atrial fibrillation who have cardiogenic embolism, even in those with normal ventricular function, when compared with patients who have noncardiogenic stroke (see "Blood biomarkers for stroke", section on 'Cardioembolic stroke'). These measurements in patients with normal cardiac ventricular function might identify those who have intermittent atrial fibrillation or are prone to develop it. Further research is needed to confirm whether these indicators are clinically useful.

Atrial cardiopathy characterized by a large left atrium and abnormal function and morphology of the left atrium and left atrial appendage can predispose to thrombus formation even without atrial fibrillation. (See "Cryptogenic stroke and embolic stroke of undetermined source (ESUS)", section on 'Atrial cardiopathies'.)

Echocardiography — All patients with suspected embolic stroke should have an echocardiogram. The choice between transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) as the initial imaging test to identify a source of embolism should be individualized on a case-by-case basis. (See "Echocardiography in detection of cardiac and aortic sources of systemic embolism".)

TTE is the preferred initial test for the majority of patients with a suspected cardiac or aortic source of emboli, including:

- Patients ≥45 years with a neurologic event and no identified disease on neurovascular imaging studies
- Patients with a high suspicion of left ventricular thrombus
- Patients in whom TEE is contraindicated (eg, esophageal stricture, unstable hemodynamic status) or who refuse TEE

TEE is the preferred initial test to localize the source of embolism in the following circumstances:

- Patients <45 years without known cardiovascular disease (ie, absence of myocardial infarction or valvular disease history)
- Patients with a high pretest probability of a cardiac embolic source in whom a negative TTE would be likely to be falsely negative
- Patients with atrial fibrillation (a situation where left atrial or left atrial appendage thrombus is a likely cause of ischemic stroke), but only if the TEE would impact

management

- Patients with a mechanical or bioprosthetic heart valve; although the long-term risk of thrombus is higher with mechanical valve than with bioprosthetic valve, both can develop thrombus
- Patients with suspected aortic pathology

Transesophageal versus transthoracic echo — While TTE and TEE have advantages and disadvantages, both are effective diagnostic tests with a role in the evaluation of suspected cardioaortic source of embolism. In most patients, TEE yields higher quality images and has a greater sensitivity and specificity than TTE, but a few conditions (eg, left ventricular thrombus) are better seen on TTE. However, TEE is an uncomfortable invasive procedure that may not be tolerated by very ill patients. Because it is less invasive and readily available in most institutions, TTE is often reasonable as the initial test of choice.

A TEE is often performed to examine the atria, atrial septal region, and the aorta if the TTE and preliminary cardiac and vascular imaging tests do not clarify the cause of brain ischemia [44,45]. (See "Initial evaluation and management of transient ischemic attack and minor ischemic stroke".)

A TEE is the best test to exclude significant ascending aortic atheromatous disease. It is also the best test to look for evidence of patent foramen ovale (PFO), atrial septal aneurysm, or atrial septal defect, conditions that can cause otherwise cryptogenic stroke. (See "Thromboembolism from aortic plaque" and "Embolism from atherosclerotic plaque: Atheroembolism (cholesterol crystal embolism)" and "Atrial septal abnormalities (PFO, ASD, and ASA) and risk of cerebral emboli in adults".)

TEE is also the best way to identify clot in the left atrial appendage. These emboli are 3 mm or less in diameter and are usually beyond the resolution of the transthoracic echocardiographic ultrasound probe. By contrast, left ventricular thrombi in patients with heart failure or a previous myocardial infarction are best seen with TTE since the true left ventricular apex is not well seen on TEE. (See "Echocardiography in detection of cardiac and aortic sources of systemic embolism".)

BLOOD TESTS

A number of blood tests may be indicated in select patients with brain ischemia or hemorrhage, including [28,46]:

- Blood glucose

- Complete blood count, including hemoglobin, hematocrit, white blood cell count, and platelet count
- Prothrombin time, international normalized ratio (INR), and activated partial thromboplastin time
- Thrombin time and/or ecarin clotting time if patient is known or suspected to be taking a direct thrombin inhibitor or a direct factor Xa inhibitor
- Blood lipids, including total, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) cholesterol, and triglycerides

D-dimer and fibrinogen levels may be helpful in detecting patients whose brain ischemia can be related to cancer or inflammatory disease. (See "Blood biomarkers for stroke".)

Hypercoagulable studies — While hypercoagulable states are sometimes found in patients who have had an ischemic stroke, widespread testing for these disorders is limited by a number of factors including a relatively low prevalence of thrombophilias and alteration of the sensitivity and specificity of the tests involved in the setting of an acute ischemic event and in patients taking heparin or warfarin [47]. Furthermore, it remains unclear if the inherited thrombophilias directly predispose to stroke as they do to venous thrombosis.

A case-control study found that one in seven patients with a first ever acute ischemic stroke tested positive for one of the inherited thrombophilias, but that the relationship was likely to be coincidental rather than causal in almost all cases [48]. In a systematic review, the prevalence of inherited deficiencies of protein C, protein S, antithrombin III, or plasminogen was low in unselected patients with ischemic stroke [49]. The pretest probabilities of other coagulation defects in these patients were as follows:

- Lupus anticoagulant 3 percent (8 percent in patients ≤50 years)
- Anticardiolipin antibodies 17 percent (21 percent in patients ≤50 years)
- Activated protein C resistance/factor V Leiden mutation 7 percent (11 percent in patients ≤50 years)
- Prothrombin mutation 5 percent (6 percent in patients ≤50 years)

The posttest probabilities of these abnormalities increased with increasing pretest probability and features of the patients' history and clinical presentation suggestive of coagulopathy (eg, cerebral or venous thrombosis without precipitating factors).

In the absence of definitive data, it is my practice to obtain testing for hypercoagulable conditions in patients who have:

- A personal or family history of systemic thromboses

- No clear etiology for ischemic stroke or transient ischemic attack (TIA), despite cardiac and vascular imaging, especially when involving young patients
- Clinical findings that suggest systemic lupus erythematosus or the antiphospholipid antibody syndrome

Antiphospholipid antibodies — The role of antiphospholipid antibodies (aPL) in the pathogenesis of ischemic stroke remains unclear. Transient elevations of aPL or lupus anticoagulants can be seen in the setting of acute stroke. Thus, elevated levels may simply be a sequel to stroke and not related to its cause. On the other hand, aPL may be associated with thrombosis or a cardiac valve abnormality that is the cause of stroke.

The evidence is conflicting as to how to interpret positive aPL assays among the full complement of ischemic stroke patients, as illustrated by the following reports [50,51]:

- A large, prospective, cohort study (APASS) of 1770 patients with ischemic stroke found that the presence of aPL, either LA or aCL, did not predict increased risk for subsequent vascular ischemic events, including ischemic stroke; did not confer increased risk for subgroups of patients younger than 55 years or those with cryptogenic stroke; and did not predict a differential response to aspirin or warfarin therapy [50]. A small subgroup (120) positive for both LA and ACL had a tendency toward higher risk of vascular occlusive events at two years than those without aPL (31.7 versus 24 percent). (See "Clinical manifestations of antiphospholipid syndrome", section on 'Neurologic involvement'.)
- In patients with systemic lupus erythematosus, one study found that the levels of both aCL binding to beta 2 glycoprotein I, and anti-phosphatidylserine antibodies binding to prothrombin were significantly higher in patients with a history of cerebral infarction compared with those who had no history of cerebral infarction [52]. Furthermore, lupus patients who were positive for both of these antibodies had a 77 percent prevalence of cerebral infarction (odds ratio 30.0, 95% CI 11-86). The presence of either antibody alone was not associated with a significantly increased stroke risk.
- In 2712 women and 2262 men in the Framingham Heart Study cohort who were free of stroke or TIA at the time of their baseline examination and were followed for 11 years, elevated serum concentrations of ACL independently and significantly predicted the risk of first ischemic stroke or TIA in women but not men [51].

In the absence of definitive data, we recommend obtaining antiphospholipid antibody testing in patients who have:

- A history of lupus or symptoms compatible with lupus
- Features that suggest the antiphospholipid syndrome such as miscarriages, venous thrombosis, or migraine headaches
- Cryptogenic stroke or TIA at a young age

Others — Plasma fibrinogen levels are risk factors for coronary heart disease and stroke [53,54]. However, the routine use of fibrinogen as a cardiovascular risk marker is limited by measurement variability. (See "Blood biomarkers for stroke" and "Overview of possible risk factors for cardiovascular disease".)

Other studies may include hemoglobin electrophoresis in patients suspected of having a hemoglobinopathy, and an erythrocyte sedimentation rate, tests for Lyme disease, syphilis, and HIV infection in selected patients.

EVALUATION OF PATIENTS WITH INTRACEREBRAL HEMORRHAGE

CT scans usually define the size and location of intracerebral hemorrhage (ICH) and the presence of intraventricular blood [55]. Mass effect caused by the intracerebral mass, shift of midline structures, herniation of brain contents from one compartment to another, and the presence of hydrocephalus are also easily seen on CT. MRI with echo-planar T2*-weighted (susceptibility) images can also show hemorrhages soon after the onset of symptoms. Microbleeds (tiny older hemorrhages) are shown using this technique and can be clues to the presence of cerebral amyloid angiopathy. It is not necessary to perform both CT and MRI to exclude hemorrhage if echo-planar MRI scanning is available. A detailed description of the MRI characteristics of hyperacute ICH is found separately. (See "Spontaneous intracerebral hemorrhage: Pathogenesis, clinical features, and diagnosis", section on 'Brain MRI'.)

Vascular malformations and brain tumor are better visualized on MRI. Echo-planar MRI can also show old hemorrhages not visible on CT scans. The location and appearance of the lesion as well as the history of the patient (eg, race, blood pressure, presence of known bleeding disorder, use of drugs) help determine the choice of additional diagnostic studies.

- **Hypertensive ICH** – No further diagnostic tests are necessary in the severely hypertensive patient with a well circumscribed and homogeneous hematoma that is located in a typical location for hypertensive ICH (eg, putamen/internal capsule, caudate nucleus, thalamus, pons, or cerebellum); the clinician can be confident that the patient has a hypertensive hemorrhage in this circumstance (see "Spontaneous intracerebral hemorrhage: Pathogenesis, clinical features, and diagnosis"). Similarly, a traumatic etiology can be

diagnosed with confidence in the patient who has had recent trauma and lesions in the appropriate location and with the appearance of contusion and traumatic hemorrhages (eg, anterior and/or orbital frontal lobes and anterior-medial temporal lobes).

- **Bleeding disorder** – Evaluation for a bleeding disorder (platelet count, prothrombin time, international normalized ratio (INR), activated partial thromboplastin time for all patients, and thrombin time and/or ecarin clotting time if the patient is known or suspected to be taking a direct thrombin inhibitor or a direct factor Xa inhibitor) should be performed in every patient with an intracranial hemorrhage, especially if the cause is not immediately clear. A bleeding tendency can cause or contribute to bleeding initiated by other etiologies. (See "Approach to the adult with a suspected bleeding disorder".)

  Iatrogenic prescription of anticoagulants is the most common bleeding disorder contributing to brain hemorrhages. Oral anticoagulant-related intracerebral hemorrhage is often lobar [56]. Compared with spontaneous intracerebral hemorrhages, anticoagulant-related hemorrhages are larger and associated with greater hematoma expansion and mortality [56,57]. (See "Risks and prevention of bleeding with oral anticoagulants".)

- **Lobar or atypical hemorrhage** – Amyloid angiopathy, bleeding into a tumor, and vascular malformations are likely etiologies of hemorrhages that are lobar or atypical in appearance.

  - **Cerebral amyloid angiopathy** – Hemorrhages related to amyloid angiopathy are usually lobar and have a predilection to cluster in posterior brain regions, including the parietal and occipital lobes. The hemorrhages are usually multiple. T2* weighted (susceptibility) MRI images may show the presence of old small hemorrhages ("microbleeds"). Patients with amyloid angiopathy are typically over the age of 60 years. (See "Cerebral amyloid angiopathy".)

  - **Vascular malformation or brain tumor** – Other bleeding lesions should be excluded in patients under the age of 60 if the blood pressure is not sufficiently elevated to make a firm diagnosis of hypertensive lobar hemorrhage. A repeat MRI after the blood has been reabsorbed (four to eight weeks) may show residual vascular malformations or a brain tumor. Vascular imaging using CT angiography (CTA) or MR angiography (MRA) of the intracranial circulation is useful as a screening test for vascular malformations and aneurysms. Contrast angiography by arterial catheterization may be necessary in patients with a CTA or MRA suggestive of vascular malformation. (See "Vascular

malformations of the central nervous system" and "Brain arteriovenous malformations".)

- **Cocaine use** – Patients with intracerebral hemorrhage after cocaine use (but not amphetamines) have a relatively high incidence of underlying aneurysms and vascular malformations. They require vascular imaging tests (eg, CTA, MRA, and/or conventional angiography).

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Stroke in adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Intracerebral hemorrhage (The Basics)" and "Patient education: Stroke (The Basics)")
- Beyond the Basics topics (see "Patient education: Stroke symptoms and diagnosis (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Classification** – Cerebrovascular disease is caused by one of several pathophysiologic processes (table 1 and table 2) involving the blood vessels of the brain. (See

'Classification' above.)

- **Initial evaluation** – Sudden loss of focal brain function is the core feature of the onset of ischemic stroke. However, patients with conditions other than stroke can present in a similar fashion (table 3). The initial evaluation requires a rapid but broad assessment to stabilize vital signs, determine if intracranial hemorrhage is present, and decide if reperfusion therapy with intravenous thrombolysis (table 4) or mechanical thrombectomy is warranted for patients with ischemic stroke. (See 'Initial general assessment' above and 'Is the patient a candidate for reperfusion?' above.)

- **Determining the type of stroke** – After completing the initial assessment, the goal of the subsequent evaluation is to determine the underlying pathophysiology of the stroke based upon the history, physical examination, and initial neuroimaging findings (table 1). Certain constellations of symptoms and signs can suggest a specific ischemic process (table 5). (See 'Determining a presumptive diagnosis of stroke subtype' above.)

- **Confirming the diagnosis** – Confirming the precise pathophysiologic process is aided by more directed diagnostic testing, including cardiac studies and neurovascular imaging. (See 'Confirming the diagnosis' above.)

- **Cardiac monitoring** – Cardiac monitoring for at least the first 24 hours after the onset of ischemic stroke is useful to look for arrhythmias. For patients with a cryptogenic ischemic stroke or transient ischemic attack (TIA) and no evidence of atrial fibrillation on electrocardiogram (ECG) and 24-hour cardiac monitoring, we suggest ambulatory cardiac monitoring for several weeks. All patients with suspected embolic stroke should have an echocardiogram. (See 'Cardiac evaluation' above and 'Echocardiography' above.)

- **Blood tests** – A number of blood tests are indicated in patients with brain ischemia, including a complete blood count, platelet count, prothrombin time and partial thromboplastin time, and serum lipids. However, indications to test for hypercoagulable disorders are limited. Furthermore, it remains unclear if the inherited thrombophilias directly predispose to arterial stroke as they do to venous thrombosis. (See 'Blood tests' above.)

- **Evaluation for a bleeding disorder in patients with hemorrhagic stroke** – In this setting, all patients require platelet count, prothrombin time, activated partial thromboplastin time, and thrombin time and/or ecarin clotting time if the patient is known or suspected to be taking a direct thrombin inhibitor or a direct factor Xa inhibitor. (See 'Evaluation of patients with intracerebral hemorrhage' above.)

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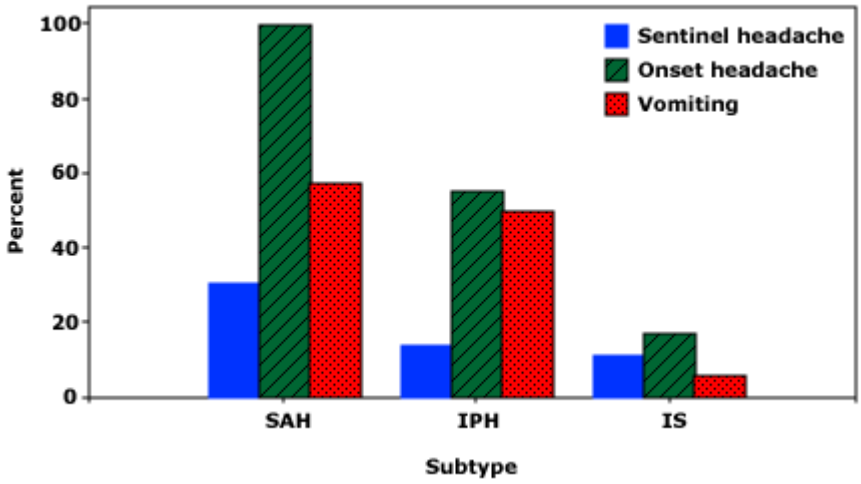
GRAPHICS

Characteristics of stroke subtypes

Stroke type	Clinical course	Risk factors	Other clues
Intracerebral hemorrhage	Gradual onset and progression during minutes or hours in most patients, but may present abruptly with maximal deficit at onset.	Hypertension, trauma, bleeding diatheses, illicit drugs (eg, amphetamines, cocaine), vascular malformations. More common in Black people and Asian people than in White people.	May be precipitated by sex or other physical activity. Patient may have reduced alertness
Subarachnoid hemorrhage	Abrupt onset of sudden, severe headache. Focal brain dysfunction less common than with other types.	Smoking, hypertension, moderate to heavy alcohol use, genetic susceptibility (eg, polycystic kidney disease, family history of subarachnoid hemorrhage) and sympathomimetic drugs (eg, cocaine)	May be precipitated by sex or other physical activity. Patient may have reduced alertness
Ischemic (thrombotic)	Stuttering progression with periods of improvement. Lacunes develop over hours or at most a few days; large artery ischemia may evolve over longer periods.	Atherosclerotic risk factors (age, smoking, diabetes mellitus, etc). Males affected more commonly than females. May have history of TIA.	May have neck bruit.
Ischemic (embolic)	Sudden onset with deficit maximal at onset. Clinical findings may improve quickly.	Atherosclerotic risk factors as listed above. Males affected more commonly than females. History of heart disease (valvular, atrial fibrillation, endocarditis).	Can be precipitated by getting up at night to urinate o sudden coughing or sneezing.

Graphic 69907 Version 5.0

Headache and vomiting in stroke subtypes



The frequency of sentinel headache, onset headache, and vomiting in three subtypes of stroke: subarachnoid hemorrhage, intraparenchymal (intracerebral) hemorrhage, and ischemic stroke. Onset headache was present in virtually all patients with SAH and about one-half of those with IPH; all of these symptoms were infrequent in patients with IS.

SAH: subarachnoid hemorrhage; IPH: intraparenchymal (intracerebral) hemorrhage; IS: ischemic stroke.

Data from: Gorelick PB, Hier DB, Caplan LR, Langenberg P. Headache in acute cerebrovascular disease. Neurology 1986; 36:1445.

Graphic 60831 Version 4.0

Pathophysiologic ischemic stroke classification

Large vessel atherothrombotic stroke
More common
Bifurcation of the common carotid artery
Siphon portion of the common carotid artery
Middle cerebral artery stem
Intracranial vertebral arteries proximal to middle basilar artery
Origin of the vertebral arteries
Less common
Origin of the common carotid artery
Posterior cerebral artery stem
Origin of the major branches of the basilar-vertebral arteries
Origin of the branches of the anterior, middle, and posterior cerebral arteries
Small vessel (lacunar) stroke
Mechanism
Lipohyalinotic occlusion
Less frequently proximal atherothrombotic occlusion
Least likely embolic occlusion
Most common locations
Penetrating branches of the anterior, middle, and posterior cerebral and basilar arteries
Cardioaortic embolic stroke
Cardiac sources definite - antithrombotic therapy generally used
Left atrial thrombus
Left ventricular thrombus
Atrial fibrillation and paroxysmal atrial fibrillation
Sustained atrial flutter
Recent myocardial infarction (within one month)
Rheumatic mitral or aortic valve disease
Bioprosthetic and mechanical heart valve
Chronic myocardial infarction with ejection fraction <28 percent

Symptomatic heart failure with ejection fraction <30 percent
Dilated cardiomyopathy
Cardiac sources definite - anticoagulation hazardous
Bacterial endocarditis (exception nonbacterial)
Atrial myxoma
Cardiac sources possible
Mitral annular calcification
Patent foramen ovale
Atrial septal aneurysm
Atrial septal aneurysm with patent foramen ovale
Left ventricular aneurysm without thrombus
Isolated left atrial spontaneous echo contrast ("smoke") without mitral stenosis or atrial fibrillation
Mitral valve strands
Ascending aortic atheromatous disease (>4 mm)
True unknown source embolic stroke
Other
Dissection
Moyamoya
Binswanger's disease
Primary thrombosis
Cerebral mass

Graphic 55099 Version 4.0

Acute stroke differential diagnosis

Migraine aura
Seizure with postictal paresis (Todd paralysis), aphasia, or neglect
Central nervous system tumor or abscess
Cerebral venous thrombosis
Functional deficit (conversion reaction)
Hypertensive encephalopathy
Head trauma
Mitochondrial disorder (eg, mitochondrial encephalopathy with lactic acidosis and stroke-like episodes or MELAS)
Multiple sclerosis
Posterior reversible encephalopathy syndrome (PRES)
Reversible cerebral vasoconstriction syndromes (RCVS)
Spinal cord disorder (eg, compressive myelopathy, spinal dural arteriovenous fistula)
Subdural hematoma
Syncope
Systemic infection
Toxic-metabolic disturbance (eg, hypoglycemia, exogenous drug intoxication)
Transient global amnesia
Viral encephalitis (eg, herpes simplex encephalitis)
Wernicke encephalopathy

Graphic 69869 Version 7.0

Eligibility criteria for the treatment of acute ischemic stroke with intravenous thrombolysis (recombinant tissue plasminogen activator or tPA)

Inclusion criteria

- Clinical diagnosis of ischemic stroke causing measurable neurologic deficit
- Onset of symptoms <4.5 hours before beginning treatment; if the exact time of stroke onset is not known, it is defined as the last time the patient was known to be normal or at neurologic baseline
- Age ≥18 years

Exclusion criteria

Patient history

- Ischemic stroke or severe head trauma in the previous three months
- Previous intracranial hemorrhage
- Intra-axial intracranial neoplasm
- Gastrointestinal malignancy
- Gastrointestinal hemorrhage in the previous 21 days
- Intracranial or intraspinal surgery within the prior three months

Clinical

- Symptoms suggestive of subarachnoid hemorrhage
- Persistent blood pressure elevation (systolic ≥185 mmHg or diastolic ≥110 mmHg)
- Active internal bleeding
- Presentation consistent with infective endocarditis
- Stroke known or suspected to be associated with aortic arch dissection
- Acute bleeding diathesis, including but not limited to conditions defined under 'Hematologic'

Hematologic

- Platelet count <100,000/mm^3*
- Current anticoagulant use with an INR >1.7 or PT >15 seconds or aPTT >40 seconds*
- Therapeutic doses of low molecular weight heparin received within 24 hours (eg, to treat VTE and ACS); this exclusion does not apply to prophylactic doses (eg, to prevent VTE)
- Current use (ie, last dose within 48 hours in a patient with normal renal function) of a direct thrombin inhibitor or direct factor Xa inhibitor with evidence of anticoagulant effect by laboratory tests such as aPTT, INR, ECT, TT, or appropriate factor Xa activity assays

Head CT

- Evidence of hemorrhage
- Extensive regions of obvious hypodensity consistent with irreversible injury

Warnings¶

- Only minor and isolated neurologic signs or rapidly improving symptoms$^{\Delta}$
- Serum glucose <50 mg/dL (<2.8 mmol/L)$^{\diamond}$

- Serious trauma in the previous 14 days[§]
- Major surgery in the previous 14 days[¥]
- History of gastrointestinal bleeding (remote) or genitourinary bleeding[‡]
- Seizure at the onset of stroke with postictal neurologic impairments[†]
- Pregnancy**
- Arterial puncture at a noncompressible site in the previous seven days[¶¶]
- Large (≥10 mm), untreated, unruptured intracranial aneurysm[¶¶]
- Untreated intracranial vascular malformation[¶¶]

Additional warnings for treatment from 3 to 4.5 hours from symptom onset[ΔΔ]

- Age >80 years
- Oral anticoagulant use regardless of INR
- Severe stroke (NIHSS score >25)
- Combination of both previous ischemic stroke and diabetes mellitus

ACS: acute coronary syndrome; aPTT: activated partial thromboplastin time; ECT: ecarin clotting time; INR: international normalized ratio; PT: prothrombin time; NIHSS: National Institutes of Health Stroke Scale; tPA: tissue plasminogen activator (alteplase or tenecteplase); TT: thrombin time; VTE: venous thromboembolism.

* Although it is desirable to know the results of these tests, thrombolytic therapy should not be delayed while results are pending unless (1) there is clinical suspicion of a bleeding abnormality or thrombocytopenia, (2) the patient is currently on or has recently received anticoagulants (eg, heparin, warfarin, a direct thrombin inhibitor, or a direct factor Xa inhibitor), or (3) use of anticoagulants is not known. Otherwise, treatment with intravenous tPA can be started before availability of coagulation test results but should be discontinued if the INR, PT, or aPTT exceed the limits stated in the table, or if platelet count is <100,000 mm^3.

¶ With careful consideration and weighting of risk-to-benefit, patients may receive intravenous thrombolysis despite one or more warnings.

Δ Patients who have a persistent neurologic deficit that is potentially disabling, despite improvement of any degree, should be treated with intravenous thrombolysis in the absence of other contraindications. Any of the following should be considered disabling deficits:

- Complete hemianopia: ≥2 on NIHSS question 3, or
- Severe aphasia: ≥2 on NIHSS question 9, or
- Visual or sensory extinction: ≥1 on NIHSS question 11, or
- Any weakness limiting sustained effort against gravity: ≥2 on NIHSS question 5 or 6, or
- Any deficits that lead to a total NIHSS >5, or
- Any remaining deficit considered potentially disabling in the view of the patient and the treating practitioner using clinical judgment

◇ Patients may be treated with intravenous thrombolysis if glucose level is subsequently normalized.

§ The potential risks of bleeding with tPA from injuries related to the trauma should be weighed against the anticipated benefits of reduced stroke-related neurologic deficits.

¥ The increased risk of surgical site bleeding with tPA should be weighed against the anticipated benefits of reduced stroke-related neurologic deficits.

‡ There is a low increased risk of new bleeding with tPA in the setting of past gastrointestinal or genitourinary bleeding. However, tPA administration within 21 days of gastrointestinal bleeding is not recommended.

† Intravenous thrombolysis is reasonable in patients with a seizure at stroke onset if evidence suggests that residual impairments are secondary to acute ischemic stroke and not to a postictal phenomenon.

** tPA can be given in pregnancy when the anticipated benefits of treating moderate or severe stroke outweigh the anticipated increased risks of uterine bleeding.

¶¶ The safety and efficacy of administering tPA is uncertain for these relative exclusions.

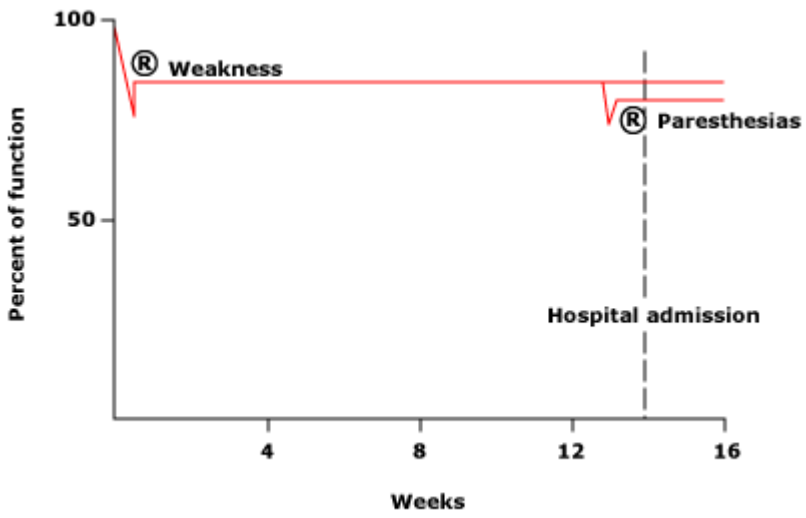
ΔΔ Although these were exclusions in the trial showing benefit in the 3 to 4.5 hour window, intravenous tPA appears to be safe and may be beneficial for patients with these criteria, including patients taking oral anticoagulants with an INR <1.7.

Adapted from:

1. *Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med 2008; 359:1317.*
2. *Del Zoppo GJ, Saver JL, Jauch EC, et al. Expansion of the time window for treatment of acute ischemic stroke with intravenous tissue plasminogen activator. A science advisory from the American Heart Association/American Stroke Association. Stroke 2009; 40:2945.*
3. *Re-examining Acute Eligibility for Thrombolysis (TREAT) Task Force:, Levine SR, Khatri P, et al. Review, historical context, and clarifications of the NINDS rt-PA stroke trials exclusion criteria: Part 1: rapidly improving stroke symptoms. Stroke 2013; 44:2500.*
4. *Demaerschalk BM, Kleindorfer DO, Adeoye OM, et al. Scientific rationale for the inclusion and exclusion criteria for intravenous alteplase in acute ischemic stroke: A statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2016; 47:581.*
5. *Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke 2019; 50:e344.*

Graphic 71462 Version 27.0

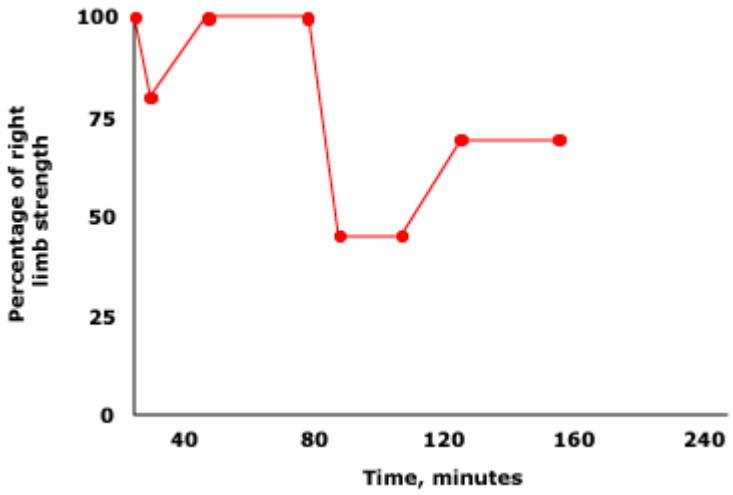
Time course of embolic stroke



Embolic stroke occurs suddenly, with symptoms maximal at onset. This patient had multiple embolic events with different clinical symptoms (initially weakness, followed by paresthesias).

Graphic 73261 Version 1.0

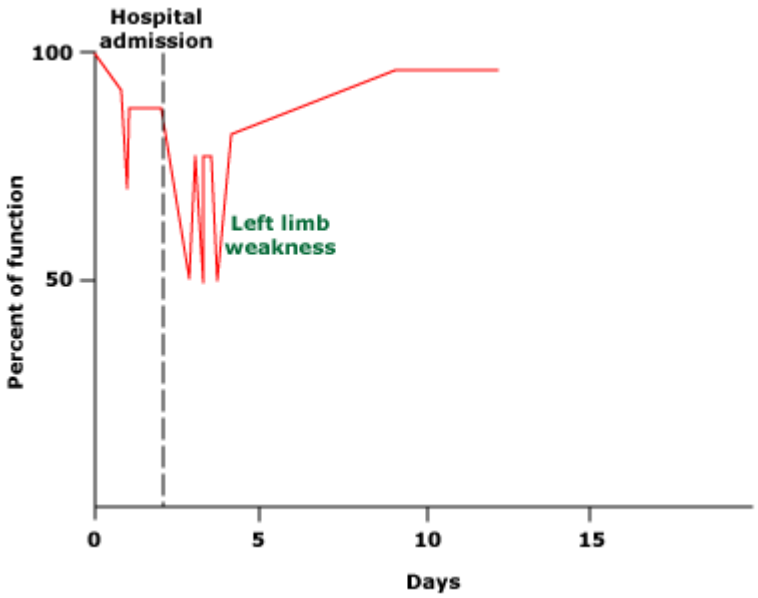
Stuttering time course of thrombotic stroke



The course of weakness of the right limb in a patient with a thrombotic stroke reveals fluctuating symptoms, varying between normal and abnormal, progressing in a stepwise or stuttering fashion with some periods of improvement.

Graphic 64107 Version 2.0

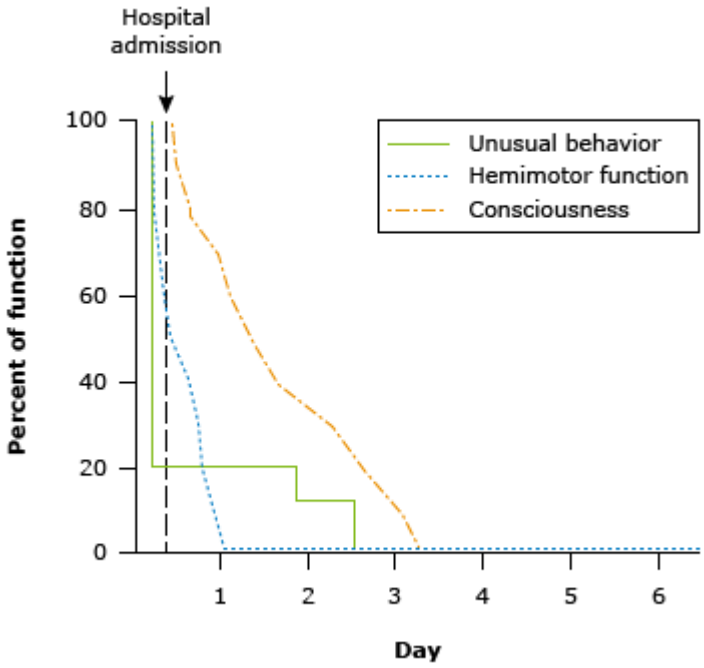
Time course of lacunar infarction



Penetrating artery occlusions usually cause symptoms that develop over a short period of time, hours or at most a few days, compared to large artery-related brain ischemia which can evolve over a longer period. A stuttering course may ensue, as with large artery thrombosis. This patient had a pure motor hemiparesis.

Graphic 52246 Version 1.0

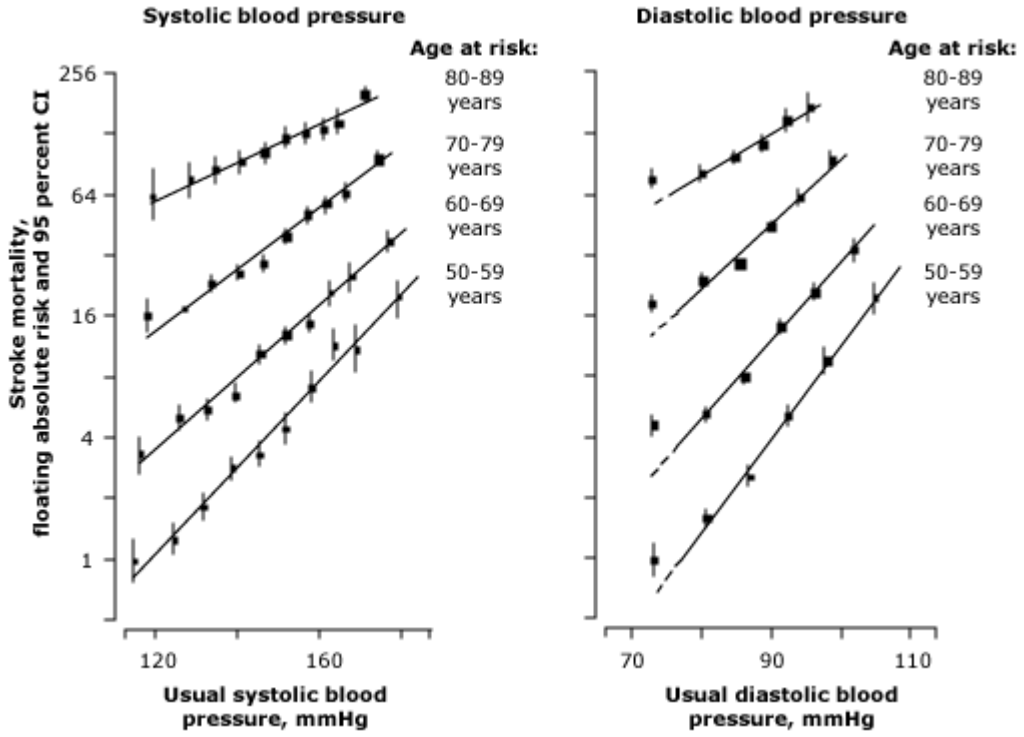
Time course of neurologic changes in intracerebral hemorrhage



Schematic representation of rapid downhill course in terms of unusual behavior (solid line), hemimotor function (dotted line), and consciousness (dash-dotted line) in a patient with intracerebral (intraparenchymal) hemorrhage.

Graphic 61491 Version 3.0

Stroke mortality related to blood pressure and age



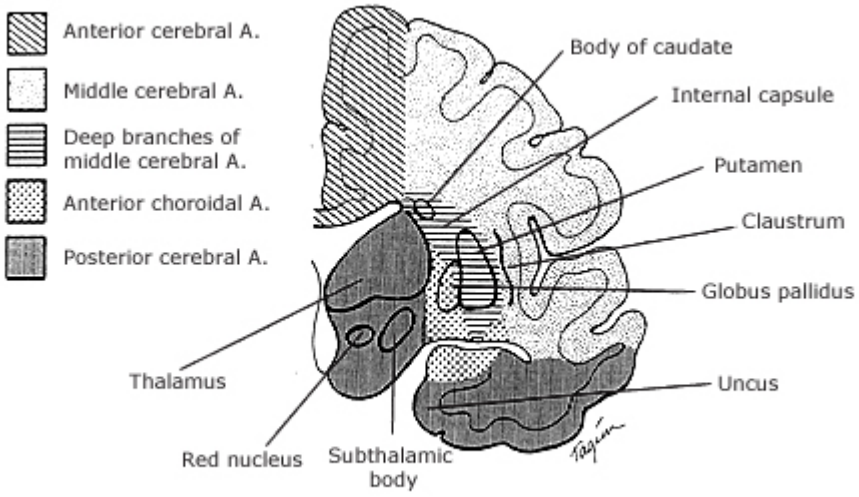
Stroke mortality rate, pictured on a log scale with 95% CI, in each decade of age in relation to the estimated usual systolic and diastolic blood pressure at the start of that decade. Stroke mortality increases with both higher pressures and older ages. For diastolic pressure, each age-specific regression line ignores the left-hand point (ie, at slightly less than 75 mmHg) for which the risk lies significantly above the fitted regression line (as indicated by the broken line below 75 mmHg).

CI: confidence interval.

Data from Prospective Studies Collaboration, Lancet 2002; 360:1903.

Graphic 66793 Version 5.0

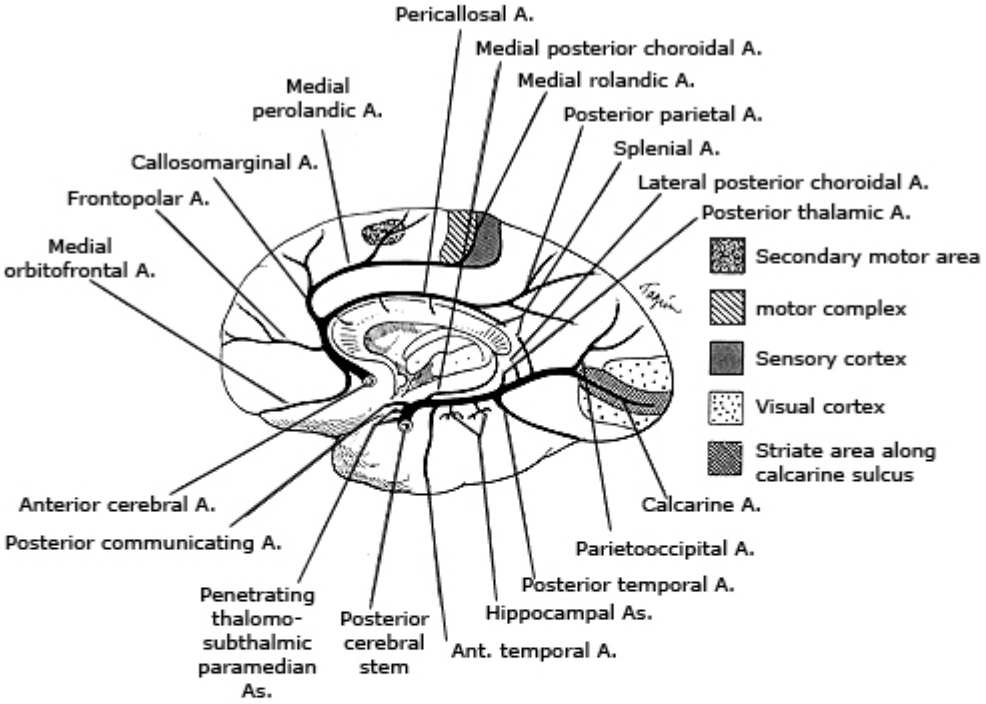
Major cerebral vascular territories



Representation of the territories of the major cerebral vessels shown in a coronal section of the brain.

Graphic 65199 Version 2.0

Anterior cerebral artery distribution and signs and symptoms of occlusion



Signs and symptoms of occlusion	Structures involved
Paralysis of opposite foot and leg	Motor leg area
A lesser degree of opposite arm paresis	Involvement of arm cortex or fibers descending to corona radiata
Cortical sensory loss over toes, foot, and leg	Sensory area for foot and leg
Urinary incontinence	Sensorimotor area in paracentral lobule
Contralateral grasp reflex, sucking reflex, gegenhalten (paratonic rigidity)	Medial surface of the posterior frontal lobe ?Supplemental motor area
Abulia (akinetic mutism), slowness, delay, intermittent interruption, lack of spontaneity, whispering, reflex distraction to sights and sounds	Uncertain localization - probably cingulate gyrus and medial inferior portion of frontal, parietal, and temporal lobes
Impairment of gait and stance (gait apraxia)	Frontal cortex near leg motor area
Dyspraxia of left limbs, tactile aphasia in left limbs	Corpus collusum

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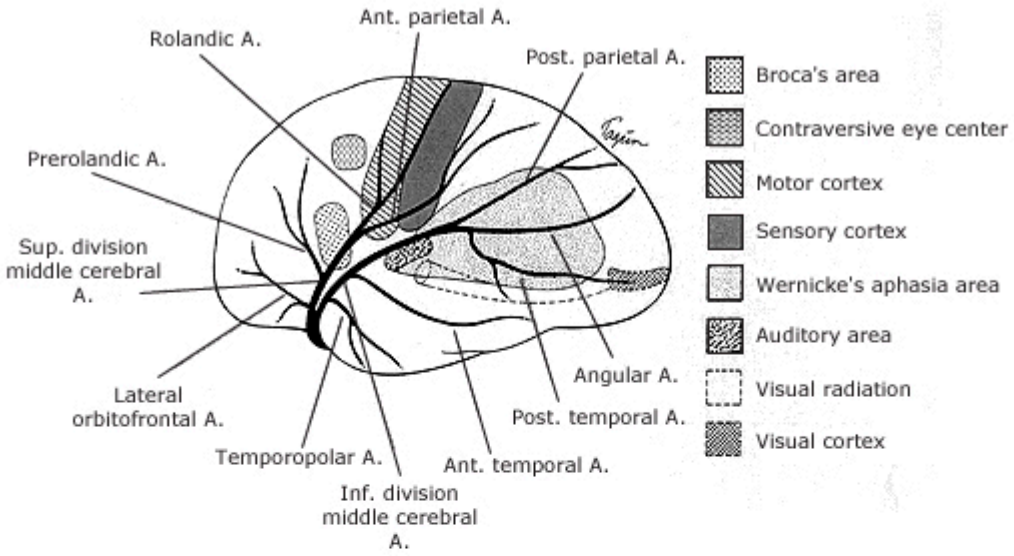
Graphic 60945 Version 3.0

Middle cerebral artery distribution and signs and symptoms of occlusion



Signs and symptoms of occlusion	Structures involved
Paralysis of contralateral face, arm, and leg; sensory impairment over the same area (pinprick, cotton touch, vibration, position, two-point discrimination, stereognosis, tactile localization, barognosis, cutaneographia	Somatic motor area for face and arm and the fibers descending from the leg area to enter the corona radiata and corresponding somatic sensory system
Motor aphasia	Motor speech area of the dominant hemisphere
Central aphasia, word deafness, anomia, jargon speech, sensory agraphia, acalculia, alexia, finger agnosia, right-left confusion	Central, suprasylvian speech area and parieto-occipital cortex of the dominant hemisphere
Apractognosia of the minor hemisphere (amorphosynthesis), anosognosia, hemisomatognosia, unilateral neglect, agnosia for the left half of external space, dressing "apraxia," contstructional "apraxia," distortion of visual coordinates, innacurate localization in the half field, impaired ability to judge distance, upside-down reading, visual illusions	Nondominant parietal lobe (area corresponding to speech area in dominant hemisphere); loss of topographic memory is usually due to a nondominant lesion, occasionally to a dominant one
Homonymous hemianopsia (often homonymous inferior quadrantonopsia	Optic radiation deep to second temporal convolution
Paralysis of conjugate gaze to the opposite side	Frontal contraversive field or fibers projecting therefrom

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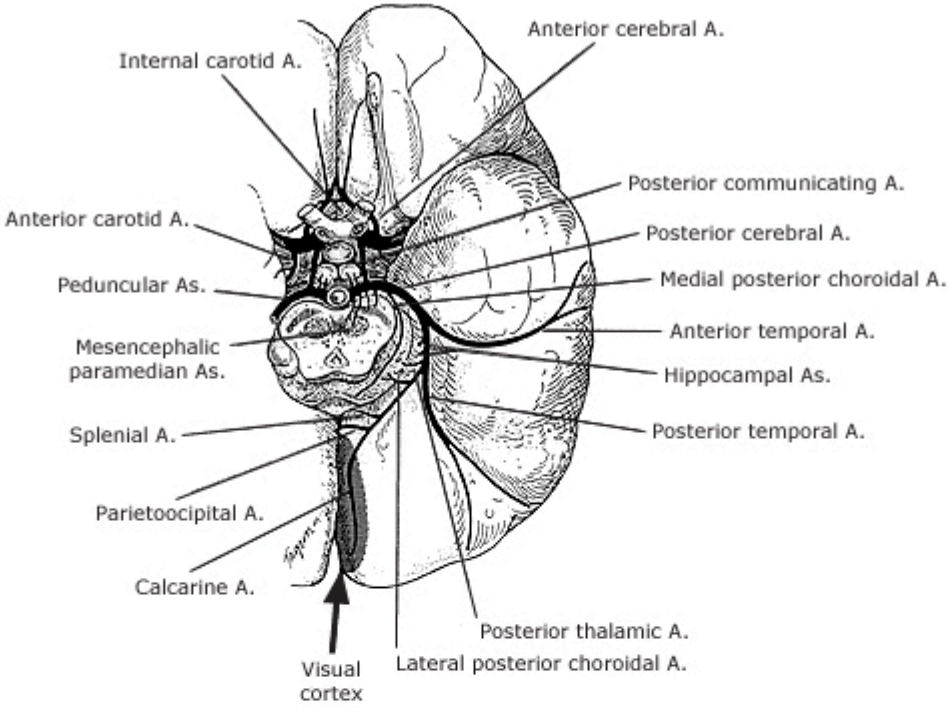
Graphic 81813 Version 2.0

Posterior cerebral artery distribution and signs and symptoms of occlusion



Signs and symptoms of occlusion	Structures involved
Peripheral territory	
Homonymous hemianopsia (often upper quadrantic)	Calcarine cortex or optic radiation nearby
Bilateral homonymous hemianopsia, cortical blindness, awareness or denial of blindness, tactile naming, achromatopsia (color blindness), failure to see to and fro movements, inability to perceive objects not centrally located, apraxia of ocular movements, inabiity to count or enumerate objects	Bilateral occipital lobe with possibly parietal lobe
Verbal dyslexia without agraphia, color anomia	Dominant calcarine lesion, posterior corpus callosum
Memory defect	Hippocampal lesion bilaterally or dominant side only
Topographic disorientation and prosopagnosia	Usually nondominant calcarine and lingual gyrus
Simultagnosia, hemivisual neglect	Dominant visual cortex, contralateral hemisphere
Unformed visual hallucinations, peduncular hallucinosis, metamorphopsia, teleopsia, illusory visual spread, distortion of outlines, central photophobia	Calcarine cortex
Complex hallucinations	Usually nondominant hemisphere
Central territory	
Thalamic syndrome: sensory loss (all modalities), spontaneous pain and dysesthesias, choreoathetosis, intention tremor, hand spasm, mild hemiparesis	Posteroventral nucleus of thalamus, involvement of adjacent subthalamus body or its afferent tracts
Thalamoperforate syndrome: crossed cerebellar ataxia with ipsilateral third nerve palsy	Dentatothalamic tract and issuing third nerve
Third nerve palsy and contralateral hemiplegia	Third nerve and cerebral peduncle

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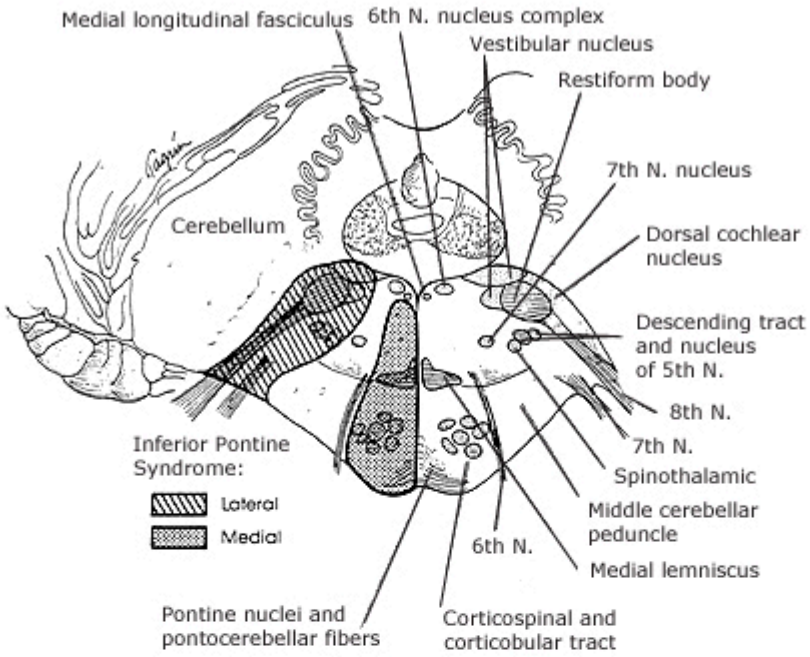
Graphic 60416 Version 2.0

Inferior pontine syndrome



Signs and symptoms	Structures involved
Medial inferior pontine syndrome (occlusion of paramedian branch of basilar artery)	
On side of lesion:	
Paralysis of conjugate gaze to side of lesion (preservation of convergence)	"Center" for conjugate lateral gaze
Nystagmus	Vestibular nucleus
Ataxia of limbs and gait	?Middle cerebellar peduncle
Diplopia on lateral gaze	Abducens nerve
On side opposite lesion:	
Paralysis of face, arm, leg	Corticobulbar and corticospinal tract in lower pons
Impaired tactile and proprioceptive sense over half of body	Medial lemniscus
Lateral inferior pontine syndrome (occlusion of anterior inferior cerebellar artery)	
On side of lesion:	
Horizontal and vertical nystagmus, vertigo, nausea, vomiting, oscillopsia	Vestibular nerve on nucleus
Facial paralysis	Seventh nerve
Paralysis of conjugate gaze to side of lesion	"Center" for conjugate lateral gaze
Deafness, tinnitus	Auditory nerve or cochlear nucleus
Ataxia	Middle cerebellar peduncle and cerebellar hemisphere
Impaired sensation over face	Descending tract and nucleus fifth nerve
On side opposite lesion:	
Impaired pain and thermal sense over half the body (may include face)	Spinothalamic tract

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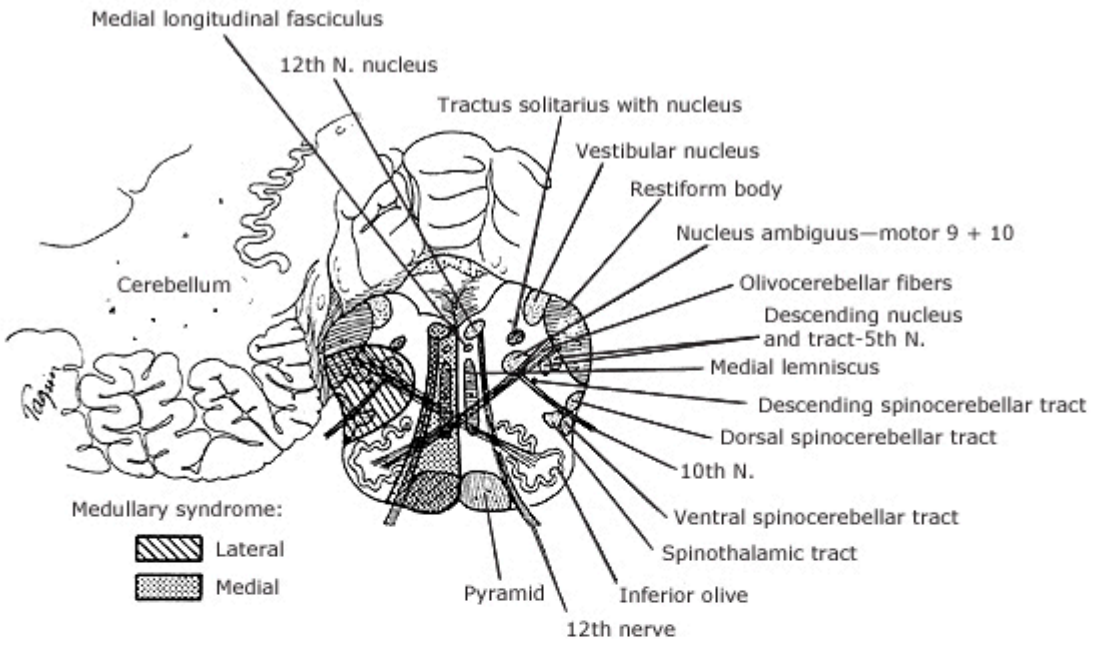
Graphic 71587 Version 1.0

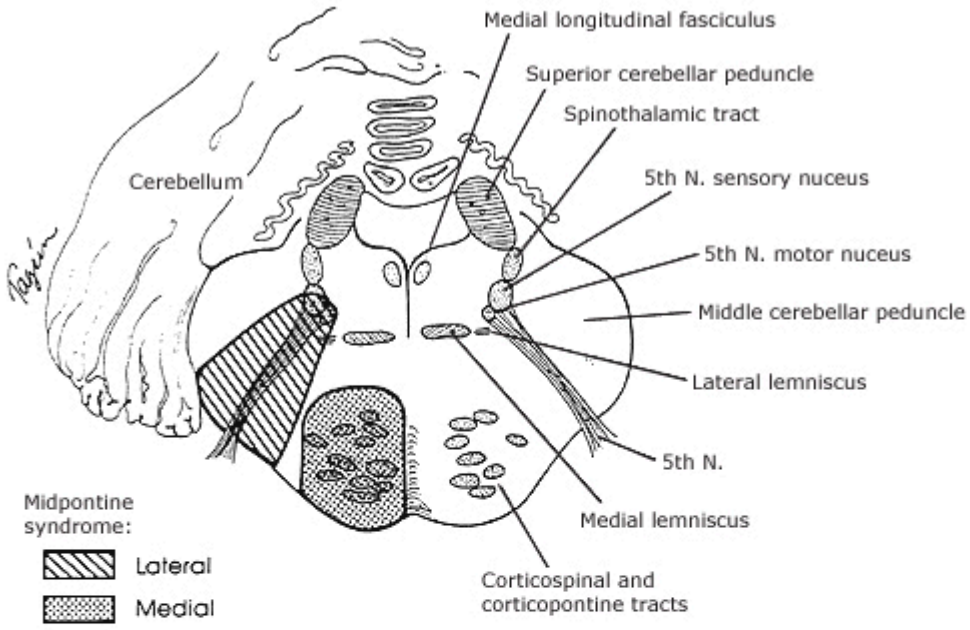
Medullary syndrome



Signs and symptoms	Structures involved
Medial medullary syndrome (occlusion of vertebral or branch of vertebral or lower basilar)	
On side of lesion:	
Paralysis with atrophy of half the tongue	Ipsilateral twelfth nerve
On side opposite lesion:	
Paralysis of arm and leg sparing face, impaired tactile and proprioceptive sense overy half body	Contralateral pyramidal tract and medial lemniscus
Lateral medullary syndrome (occlusion of either vertebral, PICA, or superior, middle, or inferior lateral medullary arteries)	
On side of lesion:	
Pain, numbness, impaired sensation over half face	Descending tract and nucleus fifth nerve
Ataxia of limbs, falling to side of lesion	Uncertain
Nystagmus, diplopia, oscillopsia, vertigo, nausea, vomiting	Vestibular nucleus
Horner's syndrome (miosis, ptosis, decreased sweat)	Descending sympathetic tract
Dysphagia hoarseness, paralysis of palate and vocal cord, diminished gag	Issuing fibers ninth and tenth nerve
Loss of taste Nucleus and tractus solitarius	Nucleus and tractus solitarius
Numbness of ipsilateral arm, trun, or leg	Cuneate and gracile nuclei
On side opposite lesion:	
Impaired pain and thermal sense over half body, sometimes face	Spinothalamic tract
Total unilateral medullary syndrome (occlusion of vertebral artery)	
Combination of medial and lateral syndromes	
Lateral pontomedullary syndrome (occlusion of vertebral artery)	
Combination of lateral medullary and lateral inferior pontine syndromes	

Graphic 73073 Version 1.0

Midpontine syndrome



Signs and symptoms	Structures involved
Medial pontine syndrome (paramedian branch of midbasilar artery)	
On side of lesion:	
Ataxia of limbs and gait (more prominent in bilateral involvement)	Pontine nuclei
On side opposite lesion:	
Paralysis of face, arm, and leg	Coricobulbar and corticospinal tract
Variable impaired touch and proprioception when lesion extends posteriorly	Medial lemniscus
Lateral midpontine syndrome (short circumferential artery)	
On side of lesion:	
Ataxia of limbs	Middle cerebellar peduncle
Paralysis of muscles of mastication	Motor fibers or nucleus of fifth nerve
Impaired sensation over side of face	Sensory fibers or nucleus of fifth nerve
On side opposite lesion:	
Impaired pain and thermal sense on limbs and trunk	Spinothalamic tract

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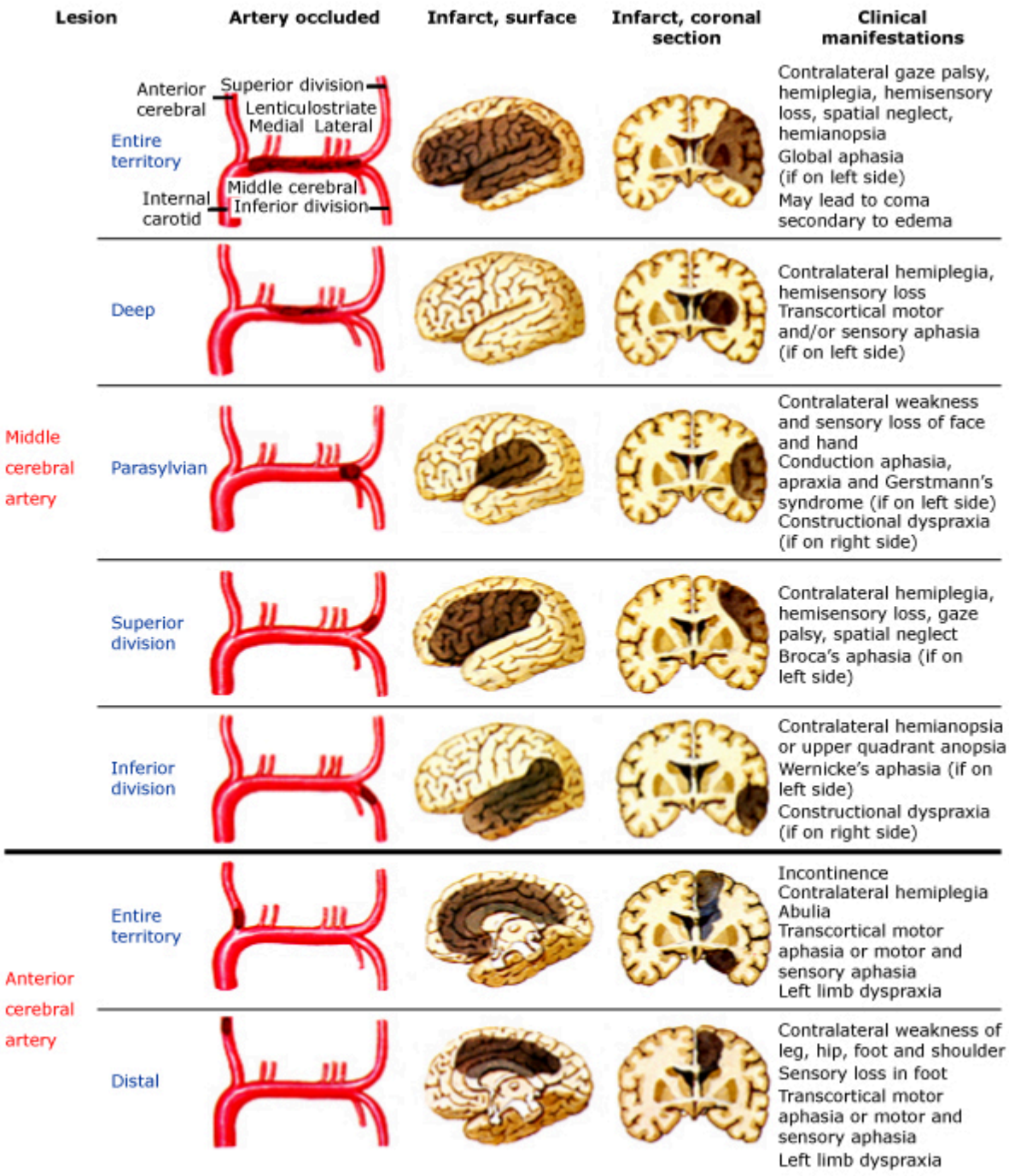
Graphic 68785 Version 1.0

Acute ischemic stroke syndromes according to vascular territory

Artery involved	Syndrome
Anterior cerebral artery	Motor and/or sensory deficit (leg > face, arm) Grasp, sucking reflexes Abulia, paratonic rigidity, gait apraxia
Middle cerebral artery	Dominant hemisphere: aphasia, motor and sensory deficit (face, arm > le > foot), may be complete hemiplegia if internal capsule involved, homonymous hemianopia Non-dominant hemisphere: neglect, anosognosia, motor and sensory deficit (face, arm > leg > foot), homonymous hemianopia
Posterior cerebral artery	Homonymous hemianopia; alexia without agraphia (dominant hemisphere); visual hallucinations, visual perseverations (calcarine cortex); sensory loss, choreoathetosis, spontaneous pain (thalamus); III nerve palsy, paresis of vertical eye movement, motor deficit (cerebral peduncle, midbrain)
Penetrating vessels	Pure motor hemiparesis (classic lacunar syndromes) Pure sensory deficit Pure sensory-motor deficit Hemiparesis, homolateral ataxia Dysarthria/clumsy hand
Vertebrobasilar	Cranial nerve palsies Crossed sensory deficits Diplopia, dizziness, nausea, vomiting, dysarthria, dysphagia, hiccup Limb and gait ataxia Motor deficit Coma Bilateral signs suggest basilar artery disease
Internal carotid artery	Progressive or stuttering onset of MCA syndrome, occasionally ACA syndrome as well if insufficient collateral flow

Graphic 75487 Version 7.0

Occlusion of middle and anterior cerebral arteries



Graphic 69630 Version 1.0