CHAPTER 10

EVALUATION OF COMMON NEUROLOGIC SIGNS AND SYMPTOMS

Common Neurologic Diseases

Scope of the Problem

Cerebrovascular disease (stroke) is a severe, common and expensive disorder. It is third most frequent cause of death and leading cause of adult disability. Of the 750,000 people who suffer stroke annually, 170,000 will die due to stroke. Fifty percent of hospitalized neurological patients suffer stroke. There are 3.5 million stroke survivors in this country. Many do not regain functional or vocational independence. The good news is that there has been a recent decline in stroke incidence mortality, probably due to improved risk factor control; for example, improved blood pressure control, better control of diabetes mellitus and dyslipidemia with newer medications, smoking cessation programs, better diet, more exercise and avoidance of bad habits e.g., illicit drugs, alcohol use (Box 10-1). As better control of hypertension occurs, the incidence of hypertensive cerebrovascular disease (e.g. hypertensive crisis, lacunar infarcts intracerebral hemorrhage) has decreased. On the other hand, with more frequent use of CT and MRI, the incidence of silent unrecognized stroke detected during life has increased; previously these vascular lesions would have been detected only at autopsy. Based upon CT and MRI criteria for stroke diagnosis, there are estimated 11 to 22 million unrecognized (silent) strokes. There is a 35% risk for stroke recurrence after initial symptomatic stroke and these patients may develop neurologic and mental disability (vascular cognitive impairment) from the cumulative effect of these strokes.

Classification

The term “stroke” is used to define symptomatic cerebrovascular disease. This is most commonly due to pathological changes in brain arterial and arteriolar circulation and less commonly due to hypercoagulability resulting in venous occlusive disease. Stroke is defined as sudden onset of focal neurological impairment (weakness, numbness, visual loss, imbalance, dysarthria, language dysfunction). Maximal neurological dysfunction is reached rapidly and subsequent delayed neurological deterioration is less common unless there is complicating pathophysiologic disturbance (e.g., cytotoxic edema, hemorrhage, stroke recurrence) or complicating medical condition. It is important to classify whether ischemic stroke is located in carotid or vertebrobasilar territories as the mechanisms and management options may differ. Also, it is important clinically to differentiate if the stroke is ischemic or hemorrhagic (intracerebral, subarachnoid). In ischemic stroke, there may be preceding transient ischemic attack (TIA). In intracerebral hemorrhage, there are usually preceeding symptoms of headache, nausea, vomiting, seizure or altered consciousness accompanying the sudden onset of focal neurological impairment and there is usually no preceding TIA. In subarachnoid hemorrhage,
there in sudden severe (thunderclap) headaches followed by development of stiff neck and the patient feels “ill.” Focal deficit does not usually accompany SAH unless ruptured aneurysm compresses neural structures or subarachnoid blood dissects into brain parenchyma.

The precise diagnosis of these cerebrovascular conditions is established by CT, MRI, and CSF findings and the causal vascular lesion is identified by vascular imaging (e.g., MRA, conventional catheter contrast angiography) procedures. In assessing potential stroke mechanisms, it is imperative to define the brain parenchymal pathological abnormality (ischemia, infarction, hemorrhage), the underlying vascular abnormality and any underlying coagulation disturbance (hypo- or hypercoagulable states) (Box 10-2).

**Vascular Anatomy**

The brain is supplied by carotid (anterior) and vertebral-basilar (posterior) arteries, which originate from the aorta and extend through neck and skull base to intracranial spaces. Right common carotid originates from right innominate artery; left common carotid originates from aortic arch. The common carotid artery branches into external (supplies face and scalp) and internal carotid arteries (ICA - supplies orbit and brain). The ICA branches into anterior (ACA) and middle cerebral arteries (MCA). The first branch of ICA is ophthalmic artery, which supplies retina and optic nerve. ACA supplies medial cerebral hemisphere; MCA supplies lateral hemisphere convexity. MCA originates as largest direct branch of ICA and then gives rise to 10 to 12 branches which can be seen in the Sylvian fissure. There is MCA trifurcation which divides into three major trunks (upper, lower, middle). There are superficial cortical divisions and deeper branches of MCA (medial and lateral lenticulostriate) which supply internal capsule and basal ganglia. ACA supplies medial and orbital surface of frontal lobes.

Vertebral arteries (VA) originate from subclavian artery. These paired VA travel upwards thru vertebral bodies to form the basilar artery (BA). The VA gives rise to anterior and posterior spinal arteries and posterior inferior cerebellar arteries, which supply inferior cerebellum and lateral medulla. The BA originates from VA merger which occurs at ponto-medullary junction. The anterior inferior cerebellar artery originates at lower pons and supplies middle portion of cerebellum and lateral pons. The superior cerebellar artery supplies midbrain and upper cerebellum and terminates as paired posterior cerebral arteries which supply occipital cortex, inferior temporal lobe and thalamus. It is through a series of thalamo-perforators and thalamo-geniculate arteries, that the midbrain, geniculate bodies and thalamus are perfused. The anterior communicating artery joins the two hemispheric circulations and posterior communicating artery connects carotid and vertebro-basilar arterial systems, thus uniting the anterior and posterior circulations. This comprises the circle of Willis. Adequate collateral flow provides alternative flow pathways when there is blood flow blockage. These collaterals include: (1) intracranial connections through circles of Willis; (2) connections between external carotids and intracranial circulations; (3) dural meningeal anastomoses.
PATHOPHYSIOLOGY OF CEREBRAL ISCHEMIA

When a cerebral vessel is occluded this brain region receives reduced blood flow and tissue becomes ischemic. The cerebral blood flow (CBF) is 50 to 60 ml/100 gm tissue per minute. When focal CBF is reduced to 25 ml, there is loss of electrical activity, but tissue remains metabolically active. Central core of ischemia receives inadequate perfusion (less than 25 ml) to maintain aerobic energy metabolism. If perfusion is not rapidly restored, within several hours, irreversible tissue damage (infarction) occurs. Surrounding the central core of ischemia is the penumbra; in the penumbra, cerebral perfusion is reduced such that neuronal dysfunction occurs but membrane pumps and ionic gradients continue to function. The tissue within the penumbra is “stunned” and dysfunctional but not dead or infarcted. The compensatory mechanism in occlusive cerebral ischemic states is for cerebral arterial vasodilation to occur (increased cerebral blood volume) and for oxygen extraction fraction to increase; this maintains normal tissue oxygen and glucose concentration. When cerebral blood flow falls below the level to which increased oxygen extraction can compensate, tissue oxygen levels fall and anaerobic metabolism begins; this inefficient anaerobic metabolism causes lactic acid formation which is toxic to the brain. Tissue infarction subsequently occurs in the penumbra if adequate CBF is not rapidly restored. In cerebral ischemia, protein, nucleic acid, and glucose metabolism derangements are the initial metabolic abnormalities to occur. Potential pathophysiological changes of ischemia include: (1) glutamate release resulting in excitotoxic cell injury; (2) glutamate binding to its receptor causes membrane depolarization and increased intracellular calcium levels which activates protease, lipase, endonuclease and cytokine activity; (3) ischemic depolarization, spreading depression and intracellular calcium increase; glutamate binds to N-methyl-D-aspartate receptor to enhance sodium cell entry; (4) anaerobic glucose metabolism causes acidosis to result in tissue necrosis; (5) activation of inflammatory mechanisms including leukocytes, cell surface adhesion molecules; (6) free radical activation; (7) cytotoxic and vasogenic edema. Unless perfusion is restored by pharmacological (thrombolysis) or mechanical techniques (endarterectomy, angioplasty) or techniques for neuro-protection are developed (to prevent ischemic cascade), irreversible cell death in the poorly perfused region occurs. At present, there are agents which may re-establish perfusion but no clinically approved neuroprotective agents. Specialized MRI imaging techniques such as 1) perfusion weighted imaging (PWI) with injection of gadolinium to image cerebral perfusion, and 2) diffusion weight imaging (DWI) to demonstrate early ischemic injury are available. If PWI area is large and DWI area is small or absent indicating ischemic cascade has not been activated, this demonstrates large ischemic tissue in which reperfusion enhancing strategy would be most likely to help salvage the tissue area. If PWI shows large areas of reduced perfusion and DWI shows large areas of ischemic brain injury, reperfusion (e.g. thrombolysis) has potential to be effective; however, since tissue already shows ischemic change, the potential risk of hemorrhage due to thrombolysis is high. If PWI shows no abnormality, then it is unlikely that vascular perfusion strategies can be effective as flow has been re-established either by break-up of the thrombus or adequate collateral flow or the vascular damage is arteriolar in origin and not be visualized by perfusion imagine. However, utilization of thrombolytic medication is effective in all types of stroke including arteriolar lacunar disease and MRI findings are not utilized in decision to utilize tPA.
PATHOGENESIS OF STROKE

Ischemic Stroke

Atherosclerosis

Atherosclerotic disease is due to plaque formation within the arterial wall. This is a disorder of the arterial wall that acts to narrow the vessel lumen (stenosis, occlusion) and reduces CBF (hypo-perfusion) or causes artery-to-artery embolism to occur. The plaque consists of lipid core and surrounding fibrous rim; the rim may be thick or thin. If the rim is thin, it may rupture or ulcerate. The irregular surface attracts platelet which become activated to form white clot which may occlude the vessel lumen and block arterial flow. It is important to visualize the geometry of the lesion-smooth tapering lesion which has lower thrombogenic potential than irregular sharp cut-off stenotic lesion which has higher thrombogenic risk. A plaque which has undergone ulceration, thrombus formation or hemorrhage is irregular in shape and contains soft plaque; this is more likely to cause distal embolization than smooth fibrotic tapering plaque which is less thrombogenic. The ruptured plaque can disrupt intimal surface causing intraplaque hemorrhage, thrombosis or ulceration; formation of these complicated plaques can suddenly occlude arterial lumen to result in clinical stroke.

The earliest atherosclerotic lesion is a fatty streak; this is visualized as yellowish area on the intimal arterial surface. This lesion consists of lipid-swollen macrophages (foam cells). It appears that low-density lipoprotein cholesterol is taken up by macrophages and smooth muscle cells. Atherosclerosis is a multifocal - and not diffuse - vascular process also involving coronary and peripheral vascular beds. Certain focal regions of intra- and extracranial branches of anterior (carotid) and posterior (vertebrobasilar) arteries have the predilection to develop arteriosclerotic changes. For example, the initial extracranial portion of internal carotid is most commonly narrowed by plaque. This is important because it is surgically accessible for carotid endarterectomy. Atherosclerotic plaque can narrow vessel lumen to reduce the blood flow (perfusion flow failure) or cause irregularity in vessel walls on which platelet-fibrin material adheres and embolizes distally to intracranial vessels. The process by which thrombotic material embolizes from one artery to another is referred to as artery-to-artery embolism. Embolization is more important in clinical ischemic stroke than is hypoperfusion. It is important to know plaque morphology – atheroma which is concentric, is nonthrombogenic but if eccentric, this is thrombogenic. Platelet-fibrin rich clot which forms on irregular shaped ulcerated plaque is best treated with antiplatelet medication. Thrombin rich (red clot) which occurs with slow flowing blood such as occurs in atrial appendage of atrial fibrillation or hypokinetic region or ventricle following myocardial infarction or cardiomyopathy is best treated with anticoagulation to achieve stroke prophylaxis.

Although the cause of atherosclerosis is still debated, important risk factors predispose or accelerate this process; these include genetic composition, high levels of low or very low density lipoproteins (LDL, VLDL) and low levels of high density lipoproteins (HDL), excessive saturated fats in diet, inactivity, diabetes with insulin resistance, and most importantly, hypertension. Thus, the profile of the person at highest risk for cerebral infarction emerges as a
middle-aged, overweight, sedentary, hypertensive, diabetic, heavy smoker who has family and personal history of cardiovascular and cerebrovascular disease. When used in moderation, alcohol reduces the incidence of stroke and CAD; however, alcohol abuse can contribute to stroke risk by induction of hypertension and cardiac arrhythmias, enhancement of platelet aggregation, and reduction of cerebral blood flow or induction of hypocoagulability to cause hemorrhage. Hypertension is the most deleterious factor contributing to stroke because it not only accelerates atherosclerosis but also is the underlying cause of small intracranial arteriolar changes (lipohyalinosis, fibrinoid degeneration) leading to intracerebral hemorrhage, lacunar infarcts, acute hypertensive crisis, and subcortical hypertensive leukoencephalopathy. Risk factors for stroke and CAD are quite similar; however, the mechanism of vascular injury is more heterogeneous in stroke patients. Remember TIA is not “cerebral angina” and stroke is not “heart attack of the brain.”

**CARDIAC EMBOLISM**

When there is cardiac dysfunction (Box 10-3), the pump does not function well and blood flow slows down and stagnates. When this occurs, thrombin rich red clots form. The thrombus fragments and is carried in the systemic arterial circulation. Since brain receives 20% of cardiac output, clot frequently embolizes to an intracranial artery which is occluded by the clot. The territory distal to the occluded vessel undergoes infarction if clot does not fragment and disperse. The forces of clot dispersal cause embolus to disperse usually within 24 hours; however, tissue infarction frequently has occurred before clot fragments. When flow is restored to infarcted tissue due to clot dispersal, pale infarct may undergo hemorrhagic transformation and clinical deterioration may occur due to tissue damage resulting from the hemorrhagic transformation. Since embolism lodges in major intracranial artery (e.g., major branch of MCA, top of the basilar artery), posterior cerebral artery, neurological deficit is frequently severe. CT shows multiple infarcts in different vascular territories usually with hemorrhage portions. Cardiogenic cerebral infarcts usually occurs in superficial territories or causes large deep infarcts. Because the embolus breaks up quickly, angiography only shows intracranial branch occlusion if done early. Cardiac evaluation (EKG, transthoracic and transesophageal echocardiography) are necessary if cardiogenic cerebral embolism is suspected.

In CCE, clinical features help establish this diagnosis: presence of a high-risk source of cardiac disease (see Box 10-4), evidence of systemic embolism, infarcts (visualized by CT/MRI) in more than one vascular territory, clinical pattern of superficial cortical ischemic pattern of superficial cortical ischemic pattern (isolated Wernicke’s aphasia, homonymous hemianopia, isolated facial or arm motor deficit) or top of basilar syndrome, minimal evidence of carotid atherosclerotic or small vessel arteriolar disease, CT evidence of hemorrhagic infarct, abrupt onset of neurologic deficit without progression, and no prior TIA. The initial CT can be normal or show nonhemorrhagic infarct in CCE patients; however, as embolus is lysed (within 48 to 72 hours), the infarct can undergo hemorrhagic transformation as a result of reperfusion of an infarcted region that has lost its ability to autoregulate its blood flow. In CCE patients, risk of embolization recurrence can be as high as 1% per day in the initial two weeks after a clinical stroke; however, the risk potential depends on underlying cardiac disease. Embolization
recurrence can be prevented by anticoagulation; however, this initiation of anticoagulation must be weighed against risk of hemorrhagic transformation.

The presence of valvular heart disease associated with 17-fold increased stroke risk and in patients with nonvalvular atrial fibrillation, stroke risk is 4.5% per year in atrial fibrillation patients. Certain clinical features (e.g., advanced age, congestive heart failure, TIA, coronary artery disease, hypertension and echocardiographic abnormalities may increase stroke risk to 12% per year. Stroke prevention is achieved by anticoagulation in patients with cardiogenic cerebral embolism, achieving an INR of 2.0 to 2.5. If patient has mechanical heart valve, an INR of 3.5 to 4.5 may be needed. The treatment of patent foramen ovale and inter-atrial aneurysm with anticoagulation is controversial.

Small vessel (arteriolar) lacunar infarction

Pathologically, there is arteriolar disease in the vessels supplying the internal capsule, basal ganglia thalamus, corona radiata and paramedian brainstem. There is lipohyalinosis and fibrinoid degeneration or microatheroma. Major risk factors for lacunar stroke include hypertension and diabetes mellitus. Lacunar infarcts are due to arteriolar disease and cause small and deeply placed infarcts.

Lacunar infarcts cause characteristic clinical syndrome including pure motor hemiparesis, pure sensory stroke, sensori-motor stroke, dysarthria-clumsy hand syndrome, and ataxic hemiparesis. CT may show small deeply situated hypodense lesions. MRI is more sensitive than CT in detecting ischemic disease and visualizing lacunar infarcts. Because vascular arteriolar lesions involved are below the resolving capacity of angiography, the arteriolar lesion cannot be visualized. Stroke prevention is achieved with control of hypertension and diabetes and use of antiplatelet medication which has lowest hemorrhage risk. Remember that the same arteriolar lesions (lipohyalinosis, fibrinoid degeneration) that cause lacunar infarcts also may result in intracerebral hemorrhage, under different clinical circumstances.

Intracranial Hemorrhage

Intracerebral hemorrhage (ICH)

This is bleeding into the brain parenchyma usually originating from small penetrating arteriole. Hypertension is major causal factor in microaneurysm (arteriolar) formation (Charcot-Bouchard). This arteriolar microaneurysm can not be visualized by angiography. When ICH occurs, patients usually have other end-organ dysfunction signs (retinopathy, cardiomegaly, proteinuria). This causes bleeding in characteristic locations-basal ganglia (putamen) thalamus, pons, and cerebellum. In nonhypertensive patients with ICH, bleeding may occur in lobar distribution (frontal, temporal, parietal, occipital) and may be due to vascular malformation (aneurysm angioma) or hypocoagulable state. In elderly patients, consider amyloid angiopathy as the cause of ICH.
SUBARACHINOID HEMORRHAGE (SAH)

SAH of nontraumatic origin usually results from vascular malformation or aneurysm. Aneurysms are due to congenital (absence of medial of arterial wall) and acquired (hypertension, smoking) factors which lead to breakdown of arterial wall. With sudden surge of arterial blood pressure, one of the multiple bleeding points on the aneurysm ruptures and this releases blood into subarachnoid spaces. Aneurysms are located at branch points along the circle of Willis. When SAH occurs, LP with CSF analysis shows blood and CT may show blood in subarachnoid spaces. Angiography can detect aneurysm or vascular malformation, which caused the SAH, and frequently there are multiple vascular anomalies.

ASYMPTOMATIC CAROTID ARTERY STENOSIS

Arterial bruits indicate that blood flow is no longer laminar but is turbulent. Not all “noises” in neck are due to carotid disease. If noise gets louder as stethoscope is moved towards the chest, consider cardiac murmurs and if noise disappears when patient is recumbent, consider jugular “venous hum.” Bruits develop because of hemodynamic conditions (anemia, thyrotoxicosis, obesity) which may not be associated with arterial stenosis; however, carotid bruits usually indicate arterial stenosis. Bruits occur in 3 to 4% of population older than age 45 and in 8% older than age 75. Bruits can be first sign of carotid stenosis: they occur when arterial cross section lumen is reduced by 50%. Bruits become louder as stenosis increases but can disappear when carotid artery is occluded. In patients with bruits it is possible to have high-grade stenosis without neurologic symptoms. Annual stroke risk for patients with asymptomatic carotid bruits is 1%; however, for patients with carotid bruits who have greater than 75% carotid stenosis (as measured by Doppler duplex imaging), annual stroke risk may be higher. Asymptomatic carotid bruit patients with Doppler evidence of high-grade carotid stenosis have 30% incidence for CT/MRI evidence of silent (asymptomatic) cerebral infarction; therefore, this indicates that carotid stenosis causes brain dysfunction, which maybe clinically recognized or silent. Patients with asymptomatic carotid stenosis have increased cardiac risk (myocardial infarction, congestive heart failure, atrial fibrillation, ruptured aortic aneurysm). This indicates that bruit is a marker of multifocal systemic arteriosclerotic disease. Severity and rate of progression of carotid stenosis (as measured by non-invasive vascular imaging studies) are best markers of risk for developing symptomatic cerebrovascular disease. Currently, patients with asymptomatic carotid stenosis of more than 60% should undergo carotid endarterectomy (CEA) because this intervention reduces 5-year risk for ipsilateral stroke compared with those patients treated with best medical management; however, recent utilization of angiotensin converting enzyme inhibitors, anti-platelet medication, statins, homocysteine-lowering agents, beta-adrenergic blocking agents, and other antihypertensive medications may lower stroke risk more effectively than carotid surgery. If progression of carotid disease went from asymptomatic states to transient deficit (TIA) to mild non-disabling stroke and then to major disabling stroke, treatment decisions would be easier; however, this graded progression does not always occur.
TRANSIENT FOCAL DEFICIT

When patients develop single or multiple transient episodes of sudden focal neurologic dysfunction, it is presumed that the mechanism is vascular (TIA) or electric disturbance (seizure, migraine). In focal seizures, there is rapid spread (usually occurring within several minutes) over involved body region (Jacksonian march), and clinical symptoms are characterized by positive (clonic motor jerks, sensory tingling, or paresthesias) symptoms. These represent cortical excitatory electrical activity. If focal seizure is suspected, EEG can detect focal spike discharges. If onset and spread occurs over a longer interval (10 to 20 minutes), includes prominent positive visual disturbances (fortification spectrum, scintillating scotoma), and is followed by contralateral headache, consider migraine. In migraine, the mechanism is believed to be spreading cortical electrical depressive (inhibitory) activity rather than vasospasm causing ischemia. The oligemia (reduced blood flow) seen in migraine is due to reduced cortical metabolism. Headache, spread of neurologic deficit, and positive types of visual disturbances are uncommon in TIAS. TIA episodes can result from embolism, hypoperfusion, hemodynamic crisis, vasospasm, or vascular thrombosis caused by hematologic or hemorheologic factors (Box 10-5).

TRANSIENT ISCHEMIC ATTACK (TIA)

TIAs are episodes of focal neurologic dysfunction of sudden onset and transient duration occurring in specific arterial distribution attributed to focal cerebral or retinal ischemia. By definition, episode lasts less than 24 hours; however, it is more common for TIA to last 24 minutes than 24 hours. These attacks can be single or recurrent. TIA patients should be evaluated for underlying vascular disturbance because therapy needs to be initiated to prevent stroke, which occurs in 30% to 35% of untreated TIA patients. The occurrence of TIA represents a neurological emergency as 11% of TIA patients have stroke within 90 days and half occur within first 2 days. Remember in TIA, the neurological deficit resolves; however, the risk of subsequent permanent disabling stroke is increased in these patients and does not disappear. TIA should be approached as a medical emergency. The occurrence of TIA should be approached with the same urgency as patient who presents with acute new onset chest pain.

Clinical Features

The physician must rely on patient history in arriving at TIA diagnosis because most episodes have resolved by the time patient is seen by the physician. Associated symptoms are important clues to TIA etiology. For example, cardiac symptoms, including angina pectoris or palpitations preceding TIA suggest cardiac embolus; neck movements precipitating V-B TIA suggest vertebral artery occlusive disease, possibly resulting from degenerative cervical spine disease; brain stem or cerebellar ischemia precipitated by arm exercise in patients with marked differences in blood pressure findings in the arms suggests subclavian steal syndrome; ipsilateral blindness and contra-lateral motor and sensory deficit suggest carotid disease.

TIA symptoms depend on whether carotid or V-B vessels are involved. With extracranial ICA occlusive disease, two patterns occur: one, cerebral (cortical) hemispheric symptoms including
contralateral hemiparesis or monoparesis, contralateral hemisensory deficit of cortical type, aphasia if dominant hemisphere is involved; and two, ocular, monocular visual blurring or blindness (amaurosis fugax) due to retinal ischemia. If patient has isolated motor hemiparesis or hemisensory deficit, this suggests subcortical TIA. The mechanisms of “cortical TIA” should prompt a search for ICA disease or cardiac embolism, whereas the mechanism of “subcortical TIA” usually suggests small-vessel arteriolar disease such as diabetes or hypertension. V-B TIA symptoms include vertigo usually associated with ataxia, diplopia, dysarthria, drop attacks, and dysphagia. Visual disturbances caused by posterior circulation TIA affect both eyes and consist of visual dimming or graying out of vision, scotomas, and visual field defects. Isolated vertigo is rarely a manifestation of TIA but is usually caused by vestibular dysfunction. V-B TIAs can be precipitated by changes in head or neck positions, considering cranial cervical junction abnormalities. If precipitated by rapid change in position or exercise, consider postural hypotension or hemodynamic factors such as low cardiac output or cardiac arrhythmias.

**Clinical Evaluation**

Clinical evaluation should delineate TIA mechanism. Routine blood chemistries and cardiac studies should be initially performed (Box 10-6) and more complex evaluation in selected patients (Box 10-7). In TIA patients, it is important to determine whether attacks involve carotid or V-B arteries. With carotid TIA, initially screen with Doppler duplex study. All TIA patients should have CT to exclude brain hemorrhage or nonvascular lesions (subdural hematoma, neoplasm). CT can show ischemic lesions, but MRI is more sensitive for early ischemic lesions especially those involving posterior fossa (cerebellum, brain stem). Angiography (MRA and conventional catheter angiography) is indicated to demonstrate extra- and intracranial carotid and V-B circulation but does not detect small vessel abnormalities (arterioles). If TIA involves V-B circulation, transcranial Doppler and angiography are indicated to delineate stenosis, occlusion, or blood vessel wall abnormality (dissection, fibromuscular dysplasia). In patients with TIA, lumbar puncture is not usually warranted unless headache is prominent, suggesting intracranial hemorrhage.

**REVERSIBLE ISCHEMIC NEUROLOGICAL DEFICIT (RIND) AND CEREBRAL INFARCTION WITH TRANSIENT SIGNS (CITS)**

It is irrational to classify cerebral ischemia by its temporal pattern alone. It is important to classify these events by 1) vascular mechanism-arterial wall abnormality, cardiac dysfunction (Box 10-4), coagulation disturbance and 2) neural changes in brain parenchyma. Disabling stroke development is the major subsequent risk of any type of transient ischemic event regardless of its nomenclature that said the varied patterns would be identified.

RIND is focal neurologic deficit of vascular origin lasting more than 24 hours but less than 3 days or, by some definitions, 3 weeks. Evaluation and treatment should be identical to that for TIA patients. Complete neuroimaging and vascular imaging should be performed to delineate causal vascular lesions. CITS is diagnosed when TIA symptoms rapidly resolve within 24 hours but CT/MRI shows causal ischemic lesion. CT may show ischemic lesion; however, MRI is
more sensitive and diffusion weighted MRI is most sensitive and most likely to show the lesion within several hours of clinical onset. It is more likely that long-duration ischemic events will show abnormal CT/MRI, whereas it is less likely that CT/MRI will show ischemic lesions with short-duration ischemics events. It is not known if risk of clinical stroke occurrence is greater if CT/MRI shows ischemic lesion than if these show no causal lesion. If TIA deficit does not resolve within 1 hour, there is an 80% probability that neurologic deficit will not resolve within 24 hours. As more sensitive imaging studies develop (CT, MRI, MRI with FLAIR and DWI sequences), more ischemic lesions are visualized. The term “minor stroke” has been used to describe stroke patients in whom minimal neurologic deficit remains after several weeks. All ischemic stroke patients (TIA, RIND, CITS, minor stroke) have a 30% to 35% risk of subsequently developing major disabling stroke. It is more important to determine underlying vascular mechanism than to classify these patients correctly on basis of temporal pattern of neurological deficit as treatment strategies is dependent upon the stroke mechanisms.

**MANAGEMENT OF REVERSIBLE ISCHEMIC VASCULAR EPISODES**

**Specific therapy is warranted in these conditions:**

1. If TIA occurs in carotid distribution, vascular imaging is mandatory. Carotid duplex ultrasound and MRA have 90% to 95% sensitivity for detecting angiographically proven 50% or greater stenosis; however, it is my opinion that all carotid territory TIA patients should have conventional catheter angiography rather than carotid ultrasound and MRA only. This allows complete assessment of extra-and intracranial circulation. If patient has symptomatic extracranial ICA stenosis plus an asymptomatic intracranial ICA aneurysm which would only be detected by conventional constrast angiography, this modifies therapy, as increasing flow by CEA would cause greater risk of aneurysm rupture. Therefore, in this situation, attention to the aneurysm would precede CEA. Based upon results of the North American Carotid Endarterectomy Study, CEA is beneficial for symptomatic patients with angiographically documented cervical carotid stenosis of at least 50%.

2. For TIA patients with a cardiogenic cerebral embolic source, anticoagulation is indicated. In recently completed studies of patients with nonvalvular arterial fibrillation (NVAF) with or without neurologic symptoms, warfarin (Coumadin) significantly reduced stroke occurrence by more than 70%. If there are contraindications to warfarin, antiplatelet medication can be used, but is less effective.

3. If TIA patients with angiographic evidence of greater than 50% stenosis involving intracranial artery (carotid, middle cerebral, vertebral, basilar), the risk of stroke is quite high. In this circumstance neurologists frequently initiate anticoagulation. This reduces stroke risk; however, it is associated with high risk of bleeding and does not protect against coronary artery disease; therefore, antiplatelet and statins medication are now preferred therapy.

4. If surgery and anticoagulation are not indicated in TIA patients, antiplatelet medication should be considered. There are several available drugs including aspirin, ticlopidine, clopidogrel and dipyridamole and combination therapy. Aspirin is effective in reducing
cardiovascular and cerebrovascular events. It is associated with relative risk reduction of 30% for stroke, 22% for stroke death, and 15% for cardiovascular and cerebrovascular mortality. Multiple studies have demonstrated that doses of 50 to 325 mg of aspirin are effective in stroke prevention. Aspirin inhibits cyclooxygenase to prevent thromboxane A2 formation (this substance has a proaggregatory and vasoconstrictive effects); and at high dosage, aspirin inhibits prostacyclin (this substance has vasodilation effect and inhibits platelet aggregation). The theoretical advantage for low-dose aspirin is that prostacyclin inhibition is avoided at low doses; the enhanced effectiveness of low-dose aspirin has been demonstrated in clinical trials. Ticlid (ticlopidine) is another antiplatelet drug used for stroke prevention. Ticlopidine acts to reduce platelet-fibrinogen binding within plaque and reduces “white” (platelet-fibrin) clot size. Unlike aspirin, ticlopidine is not a cyclooxygenase inhibitor; therefore it does not reduce stomach prostaglandins. These substances protect gastric mucosa; therefore ticlopidine causes less gastric irritation than aspirin. The most effective dosage of ticlopidine is 250 mg twice daily. Potential side effects of ticlopidine include diarrhea, dyspepsia, hepatic dysfunction, irreversible neutropenia and thrombocytopenia. Because of these side effects, ticlopidine is rarely utilized. Clopidogrel is similar in structure to ticlopidine and has similar antiplatelet effect but is associated with less adverse effects. In patients with cerebrovascular, coronary and peripheral vascular disease, clopidogrel is slightly more effective than aspirin in stroke prevention. The combination of extended release dipyridamole and aspirin (200 mgm dipyridamole and 25 mgm aspirin administered twice daily) is more effective than aspirin alone in stroke prevention. Extended release dipyridamole avoids the potential side effects of headache, dizziness and chest pain (related to cardiac steal phenomena). Remember dipyridamole has been used in patients with CAD as a “stress test.” In the dose used for stroke prevention, there is no evidence of increased cardiac morbidity. Dipyridamole has antiplatelet effects and stabilizes endothelial wall function. Warfarin has been utilized for stroke prevention in those patients who fail antiplatelet medications; however, there is no evidence for efficacy of this strategy. It is most likely that aspirin combined with clopidogrel or dipyridamole is most effective for stroke prevention. Anticoagulation should only be used for stroke prevention if there is cardiogenic source or vascular dissection.

**PROGRESSING OR DETERIORATING STROKE (STROKE IN EVOLUTION)**

Progressing stroke (stroke in evolution) is a common circumstance when the patient’s neurological deficit worsens after initial abrupt onset. Most stroke syndromes reach maximal deficit within minutes to hours; however, in some cases there is delayed neurologic deterioration. Potential mechanisms for progression of neurologic deficit within the first week include: 1) hemorrhage within ischemic lesion, suggestive of embolic infarction; 2) expansion of ischemic lesion caused by continued cerebral perfusion deficit; 3) distal clot propagation, or recurrent embolization; 4) edema of vasogenic (caused by impaired blood-brain barrier) or cytotoxic (because of impaired cerebral perfusion inadequate to maintain cellular metabolism) type; 5) seizure with prolonged postictal state; 6) systemic, hemodynamic, cardiac, or respiratory disturbances. Strokes most commonly associated with neurologic progression include large vessel (carotid, vertebrobasilar) disease with artery-to-artery embolism or distal clot propagation,
cardiogenic cerebral embolism, lacunar infarct, and watershed territory infarction with reduced perfusion of arterial border zones especially if the patient develops systemic hypotension. When the stroke is due to intracerebral hemorrhage, progression is unlikely; however, this rare occurrence can be due to increased hematoma size resulting from continued blood extravasation from the ruptured arteriole (Charcot-Bouchard aneurysm), vasogenic edema, herniation, or hydrocephalus.

Using serial CT/MRI studies it should be possible to delineate the mechanism of neurologic deterioration in progressing strokes of ischemic or hemorrhage type. With carotid and MCA occlusion, malignant cerebral edema may occur. Clinical features of this condition include persistent headaches and progressive decreased consciousness and worsening focal neurological deficit. CT/MRI show increased mass effect and enlarged infarcted-edematous region. This usually occurs with 48 to 72 after initial clinical presentation. Medical complications with fluctuating neurological pattern including hyperthermia due to febrile illness and excess reduction of cerebral perfusion pressure due to excess antihypertensive medication effect may also cause neurological worsening. After vascular occlusion, worsening with initial 24 hours occurs most commonly occurs with lacunar infarction and large artery occlusive disease. In lacunar stroke, excess lowering of blood pressure in patient with chronic hypertensive disease - who have minimal collateral flow - may reduce perfusion potential. Hypoperfusion in large artery occlusion disease may lead to stagnant flow and is best treated with thrombolysis or possibly anticoagulant medication or by volume expansion.

CEREBRAL ARTERIAL SYNDROMES

Internal Carotid Artery (ICA) and Middle Cerebral Artery (MCA) Syndromes

Neurologic findings in ICA and MCA ischemic stroke are hemiplegia associated with visual field defects, partial or complete sensory deficit, speech difficulties such as aphasia or dysphasia if the dominant hemisphere is involved, and anosognosia if nondominant hemisphere is infarcted. All symptoms depend on size of cerebral territory involved (Figure 10-2). With ICA occlusion motor deficit usually involves face and arm (MCA territory) as well as leg (ACA territory), whereas with MCA occlusive syndrome, leg is spared or less severely involved than face and arm. There can be incomplete syndromes as result of branch occlusions of distal branches of MCA, for example, Wernicke’s aphasia caused by occlusion of the inferior branch of MCA or Broca’s aphasia without hemiparesis due to superior branch of MCA. Other hemispheric MCA clinical features include anosognosia (denial of hemiplegia), unilateral spatial neglect, or inattention to left side of body such that patient does not dress left side nor is not even aware of left side. Ipsilateral blindness (caused by ophthalmic or central retinal artery occlusion) with contralateral motor or sensory deficit is characteristic of extracranial ICA bifurcation disease.

The initial portion of extracranial portion of ICA is most common site for atherosclerotic (Figure 10-2) plaque formation. This can cause stenosis of ICA and lead to TIA or completed stroke as result of hemodynamic factors and reduced tissue perfusion or artery-to-artery embolus. Platelet-fibrin clot or atherosclerotic plaque can dislodge from stenotic artery to embolize distally to cause TIA or stroke (artery-to-artery embolus). Occlusion of MCA most commonly results
from embolism originating from heart, aortic arch, or ICA (artery-to-artery embolus); however, less commonly thrombosis in-situ can involve proximal (origin) portion of MCA.

**ANTERIOR CEREBRAL ARTERY (ACA) SYNDROME**

Symptoms of ACA ischemic stroke syndrome vary depending on lesion size and whether there is uni- or bilateral frontal ischemia. Weakness and sensory impairment in lower extremity with mild or no involvement in upper extremity or face (leg monoparesis) suggests ACA territory ischemic lesion. Mental changes, apraxia, impairment of executive function, alterations in grasping and sucking reflexes, and problems with bowel and bladder incontinence can be due to ACA infarction especially if both frontal regions are supplied by one ACA through anterior communicating artery.

**Posterior Cerebral Artery (PCA) Syndromes**

+ Visual symptoms including poor vision, bumping into objects, and visual recognition difficulties of one side of objects or words in only one-half of the field of vision (indicating hemianopsia) are frequent complaints. The characteristic finding is the result of PCA occlusion with occipital lobe ischemia; this is homonymous hemianopsia. Other findings may include hemianesthesia; hemiplegia is an unexpected findings. Impaired memory and confusion are reported in patients with hippocampal (temporal lobe) lesions. Reading disorders (alexia) and visual distortions of objects (metamorphopsia) can be found in patients with dominant occipital hemispheric lesions.

**Vertebrobasilar Syndromes**

The basilar artery originates from paired vertebral arteries and is located on ventral surface of pons and midbrain. It terminates at upper midbrain to bifurcate into paired posterior cerebral arteries that supply occipital lobes, medial temporal cortex, and medial thalamus. If there is atherosclerotic disease of proximal subclavian artery before vertebral artery origin, exercise of arm can lead to vertigo and other manifestations of brain stem and cerebellar ischemia as blood is diverted from brain stem and cerebellum in retrograde pattern to the arms (subclavian steal syndrome). Although vertebral arteries are paired, one side is usually dominant and carries majority of blood flow; therefore, if dominant vertebral artery is occluded, there is high likelihood of brain stem and cerebellar ischemia. Thrombosis of basilar artery usually involves proximal portion supplying pons; whereas with embolism there is occlusion at the top of the basilar artery, where it bifurcates into paired PCA arteries to cause ischemia involving midbrain, thalamus, occipital, and medial temporal cortex. The vertebral artery can be injured by neck manipulation or rotation, as well as rapid head movements. This can cause intimal tears and dissection of vertebral arteries and can lead to thrombus formation and vertebral artery occlusion.
The most characteristic and well-recognized V-B stroke syndrome is lateral medullary infarction (Wallenberg syndrome) caused by occlusion of vertebral or posterior inferior cerebellar arteries (Box 10-8). Clinical features include sudden onset of vertigo and imbalance, ipsilateral cerebellar limb and gait ataxia, ipsilateral facial hypalgesia and contralateral hypalgesia of trunk and extremities, ipsilateral Horner syndrome, horizontal nystagmus, dysarthria, dysphonia, and dysphagia. With large cerebellar infarcts, CT/MRI can show cerebellar infarction with marked mass effect; there can be compression of the fourth ventricle and brain stem with resultant hydrocephalus. Removal of infarcted swollen cerebellar hemisphere may be necessary to decompress posterior fossa and prevent death. With top of basilar artery occlusion, pontine, midbrain, thalamic, and cortical (occipital, medial temporal) infarction can occur. These patients can have impaired consciousness, abnormal eye movements, miotic reactive pupils, and quadriplegia. This can simulate brain stem hemorrhage; however, hemorrhage is excluded by negative CT. In some cases there is thrombus propagation intracranially, and neurologic deficit can progress over 24 to 72 hours. This clot propagation can be prevented with intravenous anticoagulation and thrombolysis with tPA; this may disperse the clot and re-establish perfusion. There are more than 30 syndromes with eponyms for infarction of different level of brain stem. Box 10-8 lists the more common syndromes. MRI is a more reliable procedure than CT to detect brain stem ischemic lesion (Figure 10-1).

LESS CHARACTERISTIC (NONHEMIPLEGIC) STROKE SYNDROMES

Not all stroke patients are hemiplegic. It is important to be aware that focal neurologic deficit that results from stroke syndromes is not limited to classic hemiplegia or hemiparesis that most physicians equate with stroke. Sudden onset of many varied patterns of focal neurologic deficit are due to stroke. Examples of stroke syndromes without motor deficits are shown in Box 10-9.

EVALUATION AND MANAGEMENT OF ACUTE CEREBRAL ISCHEMIA

The first step is to regulate cerebral blood flow by correcting cardiorespiratory (hypoxia, hypercarbia, arrhythmias, congestive heart failure), systemic (hyperthermia), vascular and metabolic (hyperglycemia, acidosis) abnormalities. Assess cardiac status to ensure optimal cardiac output. Vital signs and neurologic condition should be monitored carefully on a one to two hour basis for the initial 72 hours to be certain that severe hypertension or hypotension does not occur and that subsequent neurologic deterioration does not occur. Rapid mobilization should be attempted to avoid decubitus, pneumonia, pulmonary embolism, and deep vein thrombosis as long as patient’s neurologic condition does not worsen with attempted postural change. Avoid oral intake until adequacy of swallowing mechanism is determined. Left-ventricular hypertrophy as detected on chest roentgenograms echocardiogram or ECG or arteriolar changes as seen on funduscopy indicate that hypertensive cardiovascular disease preceded and probably caused the stroke rather than being manifestation of reactive hypertension, which could be the consequence of the stroke. This reactive hypertension may occur as a result of transient catecholamine release or intracranial hypertension. The exact level
to which blood pressure should be lowered is not known; however, with chronic hypertensive vascular changes the elevated blood pressure (BP) may represent an effort to perfuse the ischemic brain and lowering BP may extend the penumbra to cause further neurological deterioration. Extension of ischemic infarcts can be induced iatrogenically by lowering blood pressure too rapidly or to levels below that necessary for adequate brain perfusion. If tPA is a therapeutic option, BP must be less than 185/110 mmHg prior to beginning the infusion. Cardiac arrhythmias, coronary artery disease symptoms, or cardiac valvular disease suggest potential cardiac embolism and potential need for anticoagulation. Monitor ECG and cardiac enzymes. Coagulation studies should be obtained in selected stroke patients, especially young patients and those in whom usual risk factors are not present.

CT should be initial study in all suspected acute stroke patients because this discloses unsuspected hemorrhages or nonvascular lesions that mimic ischemic lesion. CT is less sensitive than MRI for detecting ischemic lesion. MRI can show ischemic lesions within 3 hours and diffusion weighted MRI even earlier than one hour, whereas CT may not show ischemic lesions until 96 hours. CT can fail to show lacunar infarcts or brain stem infarcts, whereas these can be detected with MRI. Utilization of special MRI sequences and DWI, it is possible to detect ischemic lesion within 1 to 3 hours of onset and can determine the symptomatic lesion if there are multiple ischemic lesions detected. Lumbar puncture in acute stroke is not necessary except if vasculitis is suspected (syphilis or other inflammatory process) or if SAH is a possibility. Vascular imaging procedures are necessary to detect underlying vascular lesion.

**REPERFUSION**

Therapeutic strategies for patients with acute cerebral ischemia include those to reperfuse the brain and salvage the “ischemic penumbra” and to neuroprotect the portion of the brain at risk for further ischemic damage. **Reperfusion** ischemic stroke is caused by reduction of CBF through occlusion of arteries and arterioles. Utilization of thrombolysis and anticoagulation may “bust” the clot and re-establish flow. The goal of thrombolysis is to fragment the thrombus and restore blood flow. The potential risk of thrombolysis is that this treatment may precipitate brain hemorrhage in 6% of treated patients. The standard of care is to administer intravenous tPA (0.9 mgm/kgm with 10% as bolus and remainder infused over one hour) in patients who present within 3 hours of stroke onset and have no contra-indications (current use of oral anticoagulation with INR greater than 1.7, use of heparin within 48 hours, platelet count of less than 100,000 or other bleeding diathesis, prior stroke or serious head injury within last 3 months, major surgery within 14 days, seizure at onset, low blood sugar, GI or GU bleeding within last 21 days, recent myocardial infarction). Blood pressure must be lowered to level less than 185/110 mmHg). The earlier tPA is given, the better the outcome. Time is brain tissue and as each minute passes, more tissue is damaged and potential for neurological salvage is reduced. CT must show no evidence of hemorrhage; MRI is not necessary prior to infusion. High-risk patients for neurological deterioration and hemorrhagic transformation are those with CT evidence of hypodensity (representing infarction or edema) in greater than one-third of MCA territory. It is possible that intra-arterial thrombolysis or combination of intravenous and intra-arterial will be superior to IV alone; however, the time window will need to be expanded, as angiography is required for intra-arterial infusion. Utilization of anticoagulation to prevent distal clot
propagation has limited benefit. Heparin is now limited to patients with cardiac source stroke and arterial (carotid, vertebral) dissection. Antiplatelet medication should be started immediately after ischemic stroke onset to prevent ischemic stroke prevention.

It is important to maximize collateral flow to the ischemic region and prevent reduction of residual CSF in an effort to stop the surrounding ischemic penumbra from being converted into infarcted tissue. Avoid hypotension (usually iatrogenic as physician utilizes excessive anti-hypertensive medication) and dehydration -- utilize normal saline to maintain adequate volume status. Position patient head at less than 30 degree angle to maximize CBF. There is some evidence that induced hypertension, hypervolemia and hemodilution (avoidance of hemoconcentration) increases collateral flow and acts to reperfuse the brain; however there are no studies to demonstrate benefit.

**Neuroprotection**

Immediately following vascular occlusion, the “ischemic core” develops; this is a region of irreversibly damaged infarcted tissue. However, there is surrounding “ischemic penumbra” which is electrically dysfunctional (“stunned” but, functioning) region; this is poorly perfused, but has potential for salvage. Ideally, there would be medications to halt the ischemic cascade pathological changes but none have been shown to be of benefit in clinical studies; however, specific treatments may be initiated to minimize ischemic brain injury. These include the following:

1. **Glucose control.** Maintain normoglycemia. If there is hyperglycemic, there is anaerobic metabolism, lactic acid formation and accelerated cell death (cytotoxic edema). Utilize insulin to maintain normoglycemia.

2. **Temperature control.** Treat hyperthermia aggressively with antipyretic medication or cooling blanket to minimize ischemic injury.

3. **Blood gases.** Avoid hypoxia by utilizing supplemental oxygen; however, benefit of hyperbaric oxygen therapy has not been demonstrated. Avoid hypercarbia as this causes vasodilation and has two deleterious effects – increasing intracranial pressure and occurrence of “reverse CBF steal” as blood is taken from maximally dilated ischemic vessels to normal vessels which respond to normal autoregulatory stimulus.

4. **Cerebral edema.** In ischemic stroke there is cytotoxic (due to energy failure) and vasogenic (impaired blood brain barrier) edema. These may cause neurological deterioration in the initial 72 hours post-stroke. Traditional techniques (hyperventilation, mannitol, corticosteroids) are not effective in reducing cytotoxic edema; this is the major abnormality in ischemic stroke. In patients with large carotid and MCA occlusion, craniotomy with removal of infarcted tissue may reduce stroke mortality in those patients with malignant cytotoxic edema.
5. Avoid medical complications. These include deep vein thrombosis, aspiration pneumonia, urinary tract complications, bone breakdown due to immobility, cardiac disturbances (e.g., arrhythmias, myocardial infarction, congestive heart failure).

Prevention of Stroke Recurrence

It is clear that patients who have had ischemic stroke are at risk for vascular recurrence (stroke myocardial infarction); however, stroke patients are more likely to have recurrent stroke than to suffer heart attack.

1. Antihypertensive medication
   There is clear, direct, and continuous relation (including isolated systolic) hypertension between hypertension and all types of cerebrovascular disease. A 6mmHg blood pressure reduction results in 42% stroke reduction. In the nonacute setting, there is no evidence of minimum blood pressure below which the risk of stroke increases. All types of antihypertensive medication have been demonstrated to reduce stroke risk; however angiotensin converting enzyme inhibitors and angiotensin receptor blockers appear to have an enhanced effect in stroke prevention beyond that due to blood pressure lowering alone. This indicates vascular protective effect of these drugs.

2. Lipid lowering strategies
   In patients with coronary artery disease there is direct relationship of abnormal cholesterol metabolism with coronary artery disease. Stroke is a more heterogeneous disease and to analyze role of dyslipidemia and stroke, it is important to look at specific stroke subgroups. For ICH, there appears to be inverse relation as stroke risk increases with lower cholesterol levels. For cardiogenic cerebral embolism and lacunar stroke, the relationship between cholesterol and stroke has not been shown to be significant. For large and small vessel extra- and intracranial atherothrombotic strokes, the relation between stroke and dyslipidemia is directly similar to that of CAD. Utilization of “statins” (HMG-CoA reductase inhibitors) has 25% to 30% effect in lowering stroke incidence. At present, it is not established if TIA or stroke patients without coronary or peripheral vascular disease benefits from statin therapy in reducing stroke. The mechanism of “statin” effect in stroke prevention goes beyond lipid lowering; other protective effects include inducing plaque stabilization, improved endothelial wall function, reduced hypercoagulability, anti-platelet effect, reduced free radical formation and anti-inflammatory effect. Statins appear effective in stroke prophylaxis even if lipid profile is normal.

3. Homocysteine lowering
   Elevated homocysteine levels are associated with increased stroke incidence due to carotid artery intima-media thickening. Supplementation with folic acid, B$_{12}$, and B$_6$ (pyridoxine) will lower these levels and lower stroke risk.
4. Cigarette smoking cessation

Cigarette smoking is a major risk factor for ischemic stroke and brain hemorrhage (ICH, SAH). Smoking cessation lowers this risk by 50% within one year and by 5 years after cessation, the risk returns to that of the general population.

5. Diabetes Control

Insulin resistance has effects on intracranial blood vessels and this puts patients at increased risk of both macro- and microvascular disease. With tight blood pressure reduction and maintenance of normoglycemia control, hypertensive diabetics have 44% stroke risk reduction.

ANTIPLATELET MEDICATION – (see page____)

ANTICOAGULATION – (see page_____)

NONATHEROSCLEROTIC ISCHEMIC STROKE

When the physician is confronted with young, nonhypertensive, nondiabetic patient, nonatherosclerotic causes should be considered, including arteritis (collagen vascular disease, syphilis), spontaneous dissection of carotid arteries, fibromuscular hyperplasia, embolic lesions from atrial myxoma, patent foramen ovale or congenital heart disease, hematologic disorders such as sickle cell disease or other hemoglobinopathies, thrombotic thrombocytopenic purpura and mitochondrial disorders. In young females oral contraceptives or aortic arch syndrome (Takayasu’s disease) can be considered. Also, in young patients with history of migraine, this can leave permanent deficits (migraine stroke). Recurrent unilateral headache associated with neurologic symptoms can incorrectly be diagnosed as migraine but can be a manifestation of aneurysm or vascular malformation. Antiphospholipid antibodies (lupus anticoagulant, anticardiolipins) are acquired circulating globulins (IgG, IgM) that have been found associated with cerebral or ocular ischemic symptoms. Those occur predominantly in young females. In young patients with stroke syndrome, thorough evaluation for common and uncommon potential cardiac sources (patent foramen ovale, intraatrial aneurysm, atrial myxoma) must be undertaken (see Box 10-7). Also, blood and urine toxicology should be undertaken as illicit drugs are becoming increasingly common cause of strokes. Giant cell arteritis (temporal arteritis) usually involves branches of the external carotid artery and manifest as localized headaches, scalp tenderness, and monocular blindness. The disease is extremely rare before age 60, and the erythrocyte sedimentation rate is constantly elevated.

Hypertensive Encephalopathy (HE)

HE is reported in patients with recent-onset or longstanding hypertension and causes lethargy, weakness, headache, and vomiting, concomitant with a sudden rise in blood pressure (systolic, 240; diastolic 140) and followed by coma and seizures. Transient focal neurological findings are rare and CSF pressure is usually elevated with otherwise normal CSF findings. CT/MRI shows reversible posterior leukoencephalopathy and excludes SAH, ICH and cerebral infarction. There
is loss of cerebral autoregulation at the upper level of blood pressure. Treatment should focus on rapid but careful blood pressure lowering to reduce BP to the most recent level. Utilization of intravenous labetalol, angiotension converting enzyme inhibitors, hydralazine, calcium channel blocker or nitroprusside are effective. The latter is more difficult to monitor and may cause vasodilation which has potential to cause temporary intracranial hypertension. Cerebral infarction can result from too-rapid, aggressive lowering of blood pressure below cerebral perfusion pressure, which is higher in hypertensives than normotensives. The longer the blood pressure remains elevated, the greater the potential risk of intracranial hemorrhage.

**LACUNAR INFARCTS-LACUNAR STATE**

**Lacunar**

Lacunar infarcts are small (less than 15 mm) deep infarcts seen in the putamen, pons, thalamus, internal capsule, and caudate nucleus. They are caused by occlusive arteriolar disease resulting from hypertension. Pathologically there is evidence of lipohyalinosis and fibrinoid degeneration, but lacunar infarcts can also be caused by microatheroma, microembolism, or rarely arteritis. Because of their location and size of vessels involved; arterioles are below angiographic resolution; angiogram does not disclose arteriolar vascular lesions, but CT/MRI can demonstrate lacunar infarct. Lacunar syndromes include those in Box 10-10.

**Lacunar State**

Lacunar state is the end stage of severe and longstanding hypertensive brain arteriolar disease and consists of multiple and bilateral lacunes occurring in the basal ganglia or pons (Box 10-10). Clinical features include bilateral hemiparesis, imbalance, incontinence, short-step shuffling gait, and pseudobulbar signs. Patients have difficulty in swallowing, talking, controlling salivation, and moving their tongues. Patients have emotional incontinence with frequent uncontrolled and unprovoked outbursts of laughing or crying (pseudobulbar affect). Neurologic deficit is due to the cumulative effect or multiple lacunar infarcts. Because lacunes are subcortical, dementia might be expected to be uncommon even in the presence of multiple lacunes; however, there is some evidence that the cumulative effect of multiple lacunar infarcts is dementia. Because the cause of lacunar infarcts is hypertension, this should be aggressively controlled to prevent development of hypertensive arteriolar disease.

**BINSWANGER’S DISEASE**

Binswanger’s disease is one form of vascular dementia that most commonly occurs in elderly hypertensive patients. Clinical features include disorders of cognition, memory, mood (depression), with apathy, impaired attention, and concentration also being prominent. Bilateral corticospinal and corticobulbar signs are usually present. Clinical findings that are due to subcortical white matter demyelination are caused by ischemia secondary to occlusion of white
matter medullary penetrating arteries. The prominent demyelination is not due to multiple infarcts, and exact pathophysiology of white matter demyelination is not established. The disease is frequently progressive and is often interrupted by apoplectic episodes. CT/MRI demonstrates white matter abnormalities (hypodense periventricular lesions on CT and high signal intensity lesions on MRI) in cerebral hemispheres. These white matter changes are referred to as leuko-araiosis, but is not specific for Bingswanger’s disease as this CT/MRI pattern can be seen in other dementias and also in elderly patients. Treatment is aggressive control of hypertension.

HEMORRHAGIC STROKES

Nontraumatic hemorrhage into brain parenchyma or subarachnoid space can occur from variety of causes including hypertension, ruptured saccular arterial aneurysm, and ruptured arteriovenous malformations and a group of miscellaneous causes including blood dyscrasias, anticoagulants, drug abuse (e.g., cocaine, sympathomimetic agents including decongestants and diet pills, bleeding into tumors, and angiopathies). Ictal episodes can vary from severe onset of headache with minimal altered consciousness as is characteristic of mild subarachnoid hemorrhage (SAH) caused by ruptured aneurysm to deep coma as found in large intracerebral or brain stem hematoma. In stroke patients with headaches, nausea, vomiting, altered consciousness, or seizures, hemorrhagic stroke is more likely than ischemic stroke; however, CT is required for a definitive diagnosis of intracerebral hemorrhage.

HYPERTENSIVE INTRACEREBRAL HEMORRHAGE

This is the most frequent nontraumatic cause of intracerebral hemorrhage. Hemorrhages can be large or small. If large, mass effect and herniation can occur; hemorrhage can extend into ventricular system or subarachnoid spaces. The hemorrhage can originate in striatum (putamen) (Figure 10-3), thalamus, pons, or cerebellum. Certain hypertensive hemorrhage can arise from cerebral subcortical white matter (lobar hemorrhage), but alternate causes must be carefully excluded (e.g., aneurysm, angioma, tumor). The exact mechanism of hypertensive hemorrhage is not known, but sclerotic and necrotizing changes in deeply located arterioles such as lenticulostrate arterioles precede formation of miliary (arteriolar) aneurysms (Charcot-Bouchard aneurysms). Rupture of miliary aneurysms is believed to be the source of hypertensive hemorrhage (Box 10-11). Multiple unruptured miliary arteriolar aneurysms can be found at autopsy in hypertensive patients and are rarely found in normotensives (Figure 10-3).

Clinical Presentation

Initial symptoms are headaches, nausea, vomiting, altered consciousness or seizures. Focal deficit develops suddenly and the neurological pattern depends upon ICH location (Box 10-11).
Hypertensive patients who develop ICH usually show longstanding hypertensive changes including retinal arteriolar changes, left ventricular hypertrophy and evidence of renal impairment (elevated creatinine and proteinuria). Putaminal hemorrhage causes hemiplegia; hemianesthesia, hemianopsia, and horizontal ocular deviation toward the side of the hemorrhage (away form hemiplegic side). In thalamic hemorrhages similar findings can occur, but the eyes are usually deviated downward with paralysis of upward gaze. In pontine hemorrhages findings include coma, quadriplegia, pinpoint size but reactive pupils, absent oculocephalic and caloric responses, and respiratory disturbances. In cerebellar hemorrhage, patients develop dizziness, vomiting, and gait ataxia; the hemorrhage can enlarge to cause secondary brain stem dysfunction to simulate pontine hemorrhage.

**Treatment**

Treatment should be supportive with blood pressure control and maintenance of respiratory and cardiac functions. Blood pressure reduction prevents further damage to the blood vessel wall which might cause ICH enlargement. Prompt surgical evacuation of cerebellar hematoma can prevent brain stem compression. Other than clear value of cerebellar hemorrhage evacuation, there is no conclusive evidence that hematoma evacuation improves the prognosis of other types of hypertensive hemorrhage. If the patient shows continued deterioration and is unresponsive to medical management of intracranial hypertension, hematoma evacuation is a reasonable management option, but the outcome is still usually poor. Monitoring of intracranial pressure with aggressive treatment (i.e., hyperventilation, mannitol, glycerol, corticosteroids) is warranted because elevated intracranial pressure indicates a poor prognosis. Corticosteroids reduce vasogenic edema, but their value is still controversial because there is not convincing evidence of improved outcome with their utilization. If headache is severe, use analgesics but avoid narcotic medications that depress respiration as resultant carbon dioxide retention worsens intracranial hypertension. Avoid aspirin-containing products for headache control as these exacerbate bleeding and hemorrhage expansion. If seizures occur, treat with intravenous phenytoin, but seizure prophylaxis is probably not warranted. The prognosis is poor in large pontine, putaminal, thalamic hemorrhages; however, in small hemorrhages that prognosis is good for recovery.

**CEREBRAL AMYLOID (CONGOPHILIC) ANGIOPATHY**

Primary cerebral amyloid angiopathy consists of infiltration of amyloid in cerebral blood vessels and is not associated with systemic amyloidosis. The diagnosis should be suspected in cases of single or multiple intracerebral hemorrhages found in nonhypertensive patients usually over 60 years of age but can occur in younger patients especially in familial cases of amyloid. Hemorrhages are predominantly found at the junction of cortex and white matter in frontal, parietal, and occipital lobes (“lobar hemorrhages”). In one third of patients there is history of previous intracerebral hemorrhage. Treatment consists of supportive medical management or surgical evacuation of the hemorrhage.
SUBARACHNOID HEMORRHAGE CAUSED BY SACULAR ARTERIAL ANEURYSM

The most frequent cause of primary nontraumatic subarachnoid hemorrhage (SAH) is rupture of arterial sacular aneurysm – the so-called berry, or congenital, type. Aneurysms are arterial dilatations found at bifurcations of large arteries at brain base usually in the anterior portion of the circle of Willis. They arise at sites where congenital medial arterial wall defects (absence of muscular layer) are frequent. There is evidence that degeneration of elastic layer occurs at the same places, so endothelium and fibrous tissue yield to intravascular pressure forming sacular dilatation. Aneurysm wall is composed only of very thin intima and adventitia. They are multilobulated with multiple bleeding points. They are rarely seen in infancy or childhood and are more frequently symptomatic in young and middle-aged patients. In approximately 20% of patients, aneurysms are multiple. Although hypertension is seen in 50% of patients in the acute symptomatic phase, this is not the cause of SAH. Asymptomatic aneurysms are found in approximately 5% of the general population, being detected at angiography (done for reasons other than bleeding episodes) or at autopsy. The clinical spectrum of aneurysms includes the following (Box 10-12):

- **No symptoms.** Aneurysms is found incidentally at autopsy or angiography. The most frequent site of unruptured aneurysms is MCA bifurcation.
- **Compression of adjacent structures.** The third nerve is most frequently compressed neural structure. Third nerve palsy as a result of aneurysmal compression usually begins in acute fashion with orbital pain, ptosis, eye deviation outward and downward, and dilated paralytic pupil. Aneurysms usually arises from ICA at its junction with posterior communicating artery. Multiple cranial nerves (third, fourth, fifth, and sixth) can be compressed by aneurysms arising in the cavernous sinus portion of ICA. Aneurysms can enlarge sells turcica to simulate juxtasellar pituitary mass. Giant sacular aneurysms (larger than 3 cm) can compress brain tissue, block CSF pathways, cause mass effect, or cause SAH. In giant aneurysms there is frequently evidence of partial or complete aneurysm thrombosis, but SAH can occur. Posterior fossa aneurysms can appear as expanding infratentorial mass lesions compressing the brain stem or cerebellum.
- **Rupture.** This is the most frequent complication of symptomatic aneurysms. The most frequent site of the ruptured aneurysm is the ICA junction with the posterior communicating artery, followed very closely by anterior cerebral-anterior communicating artery junction (Figure 10.4). Rupture of an aneurysm can produce pure SAH, SAH with intracerebral and/or intraventricular hematoma, SAH with subdural hematoma, SAH with infarction secondary to vasospasm, or microembolism from the aneurysmal sac.

Symptomatology of Ruptured Aneurysms

SAH causes severe headache (“worst headache I ever had”) that can be associated with transitory loss of consciousness or weakness of the legs. This is described as “first and worst headache.” It comes on as a “thunderclap” without warning and without the gradual build-up phase usually
seen in migraine. This latter feature is characteristic of migraine headache and serves as an important differentiating feature of migraine from SAH. A stiff neck is not usually found early in SAH, but photophobia and miosis can be initial manifestations. Because no focal motor deficit is usually found, the emergency department or physician’s office treats with a prescription for analgesics and the patient is told that this is benign “vascular” or “tension” headache. This is a catastrophic mistake to fail to recognize (Figure 10-4) warning features of “sentinel bleed” in SAH patients. The neurologically intact SAH patient is the patient in whom CT is frequently negative and lumbar puncture is mandatory to diagnose SAH; however, frequently the opportunity for early diagnosis of “sentinel” or “warning” leak caused by a ruptured aneurysm is missed because of failure to recognize the need for these diagnostic procedures, especially LP. Lumbar puncture is the most definitive study to diagnose recent SAH. If lumbar puncture is delayed for several days, red blood cells and xanthochromia can disappear from CSF, and diagnosis of SAH can be missed. This can be quite dangerous because mortality from initial aneurysmal hemorrhage is 10%; however, mortality from second hemorrhage is greater than 50%. CT is sensitive to detect subarachnoid blood if performed within 48 hours of bleed; however, CT sensitivity falls off significantly after this time. If CT establishes diagnosis of SAH, there is no need to perform LP. A second hemorrhage can occur, usually in the first week, and at that point, an intracerebral hematoma can develop from the rebleeding aneurysm with severe deterioration in neurologic condition. Grading of patients according to their neurologic function helps surgical management and prognosis. Box 10-12 outlines the five grades.

Potential complications resulting from ruptured aneurysm include sudden and massive intracranial hypertension, mass effect and cerebral edema, hydrocephalus from mass effect and cerebral edema or from blood in subarachnoid spaces or ventricular system, vasospasm and cerebral ischemia from subarachnoid blood, and rebleeding. Demonstration of aneurysm and associated vasospasm is established by angiography. CT/MRI can demonstrate an infarcted brain mass-effect or hydrocephalus. Transcranial Doppler is an effective technique to follow noninvasively the increase or reduction of vasospasm without repeat angiogram.

**Treatment**

Treatment of an aneurysm patient varies depending on the patient’s clinical grade. Medical management consists of carefully controlling systemic arterial hypertension. Blood pressure should be monitored and stabilized according to clinical response. Sustained hypertension can be necessary to perfuse brain and prevent vasospasm. Total bed rest, sedation, and laxatives are used to avoid a sudden rise of blood pressure and development of intracranial pressure; both factors can cause rebleeding. It is important to treat headache, nausea, and vomiting. If these are not controlled, the patient can become agitated. Use of sedative drugs (phenobarbital, diazepam) can calm patients and prevent rebleeding. Cardiac arrhythmias are frequently detected in SAH patients and can be life threatening, so cardiac monitoring is warranted. Careful control of sodium and fluid balance is performed because hyponatremia can cause seizures. In managing fluids and electrolytes, do not use severe fluid restriction because this can contract blood volume and increase hematocrit and blood viscosity. When these abnormalities occur, this can initiate vasospasm to cause cerebral ischemia. Administer 2 to 3 liters for crystalloid fluids to maintain adequate intravascular volume. Use the central venous line or pulmonary wedge pressure
monitoring to avoid fluid overload. Avoid intracranial hypertension, which can result in cerebral ischemia or herniation. If conventional treatment (hyperventilation, corticosteroids) is not effective, barbiturate coma, diversionary shunting, or surgical hematoma evacuation may be necessary to control intracranial pressure. Serial CT studies are necessary to determine if hydrocephalus is developing; if so, ventricular drainage or a diversionary shunt may be necessary. Recurrent bleeding and vasospasm are the most dreaded complications of ruptured aneurysms. Surgical aneurysm clipping is necessary to avoid rebleeding. Endovascular therapy with the packing of the aneurysm with coils leads to obliteration of narrow neck aneurysms; however, if there is wide neck this may be more difficult to obliterate the aneurysm. To prevent vasospasm, volume expansion (supplemented by drug-induced hypertension) and calcium channel blocking agents nimodipine (60mgm, p.o. q 4 hrs for 21 days) are effective. The role of surgical clipping of the aneurysm versus the role of endovascular coiling is controversial at this time.

**VASCULAR MALFORMATIONS**

Vascular malformations are congenital lesions originating early in fetal life and varying in degree from dilatations of capillaries (telangiectasia, usually small and frequently found as incidental lesions at autopsy) to large cavernous arterial or venous dilatations that consist of arteriovenous malformations (AVM) or fistulas and can communicate without the intervening capillary bed. When these lesions are familial, they can be associated with neurocutaneous syndromes (phakomatoses).

**Signs and Symptoms**

Subarachnoid or intracerebral hemorrhage in a young patient with history of seizures is highly suggestive of vascular malformation. Seizure disorder can precede the onset of brain hemorrhage. Deep cerebral hemispheric, brain stem, or cerebellum malformations usually are not preceded by seizure disorder, and can appear as intracranial hemorrhage. Once the hemorrhage has occurred, the probability of recurrent bleeding is high. Mortality from bleeding is less than that associated with ruptured aneurysms.

**Diagnostic Studies**

CT/MRI can demonstrate vascular malformation (Figure 10-5); prior episodes of hemorrhage are best demonstrated by MRI. Angiography is necessary to define supplying and draining vessels of the vascular malformation.


Treatment

Treatment varies according to the site and size of the lesion but is predominantly surgical if the lesion is in a resectable area. If AVM is large, Embolization using particulate material introduced at the time of angiography through an arterial catheter can occlude supplying vessels to reduce AVM size. Medical management during the acute stage is similar to that of SAH (Figure 10-5) caused by ruptured aneurysm. It is necessary to be able to surgically resect the vascular malformation because clipping supplying and draining vessels is not effective.

INTRACRANIAL HEMORRHAGE OTHER CAUSES

Other causes of intracerebral hemorrhage are uncommon, and there are usually clinical clues to the cause. Blood dyscrasias and anticoagulants can produce multiple intracranial hematomas. Multiple hemorrhagic lesions visualized by CT with a pulmonary lesion indicate metastasis; a history of drug abuse suggests vasculitis, or endocarditis. Anemia, visceromegaly, and retinal splinter hemorrhages suggest leukemia. Investigate carefully for history of substance abuse, for example, cocaine or amphetamines, as this can cause the hemorrhage. If the patient is systemically ill and febrile, consider mycotic aneurysm due to endocarditis.

DURAL AND CORTICAL VEIN THROMBOSIS

Dural and cortical vein thrombosis can be septic. These are usually associated with pyogenic or fungal infections. This can occur as a complication of meningitis. Noninfectious or marantic thrombosis can occur as a complication of malnutrition, congenital heart disease, polycythemia, dehydration, head injuries, or coagulation disorders. The most commonly involved regions are superior sagittal, lateral, cavernous, and straight sinuses. Sinuses have a prominent role in CSF circulation; therefore venous sinus thrombosis leads to intracranial hypertension and hydrocephalus. In young females dural venous thrombosis is sometimes associated with oral contraceptive use. It also occurs during postpartum period or pregnancy and can be related to hypercoagulability. Clinical features can be increased intracranial pressure (headache and vomiting), seizures, and focal motor deficit. Angiography is the most specific diagnostic test for showing whether blood has filled veins and sinuses. CT/MRI can show thrombosed veins as well as hemorrhagic venous infarct. Magnetic resonance venography is usually adequate to demonstrate the venous occlusion although venous angiography may be necessary. Treatment depends on the cause. Intracranial hypertension is frequently present and should be aggressively managed. For prevention of venous thrombotic process, anticoagulants have been used; however, they have potential to cause further bleeding if a hemorrhagic infarct is present. For septic venous thrombosis, antibiotics are necessary to treat underlying infections.
SUGGESTED READINGS

Risk Factors
Progress Collaborative Group: Randomized trial of a perindopril based BP lowering regimen on individuals with previous stroke or TIA. Lancet 358:1033, 2001.

Asymptomatic Carotid Stenosis

Transient Ischemic Attacks

Treatment of Acute Stroke

**Prevention of Stroke Recurrence**

**Nonatherosclerotic Causes of Stroke**
Petitti DB and Sideny S: Stroke and users of low dose oral contraceptive, NEJM 335:8, 1996.

**Intracerebral Hemorrhage**

**Stroke Prevention**

**Cardiogenic Cerebral Embolism**

**Lacunar Disease**

**Aneurysms**

**Stroke Effects**

**Vascular Malformations**
Venous Sinus Thrombosis
### Box 10-1. Potential Risk Factors for Cerebrovascular Disease

<table>
<thead>
<tr>
<th>Modifiable</th>
<th>Nonmodifiable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Gender (male)</td>
</tr>
<tr>
<td>systolic</td>
<td>Race (African-American, Asian, Hispanic)</td>
</tr>
<tr>
<td>diastolic</td>
<td>Age</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>Family history</td>
</tr>
<tr>
<td>Glucose intolerance</td>
<td></td>
</tr>
<tr>
<td>Insulin resistance</td>
<td></td>
</tr>
<tr>
<td>Lipid abnormalities</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
</tr>
<tr>
<td>Hypercoagulability</td>
<td></td>
</tr>
<tr>
<td>Bad Habits</td>
<td></td>
</tr>
<tr>
<td>Excessive alcohol consumption</td>
<td></td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
<td></td>
</tr>
<tr>
<td>Illicit drug use</td>
<td></td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td></td>
</tr>
</tbody>
</table>

### Box 10-2. Mechanisms of Stroke

**Hemorrhage**

- Intracerebral
  - hypertensive
  - non-hypertensive

**Subarachnoid**

**Ischemic**

- Cardiac cerebral embolic
  - Large vessel extracranial
  - Large vessel intracranial
  - Lacunar
  - Hypercoagulable states
  - Cryptogenic stroke
Box 10-3. Potential Cardiac Sources of Cerebral Embolism

Valvular heart disease
  with atrial fibrillation
  without atrial fibrillation
Atrial fibrillation
Myocardial infarction
Cardiomyopathy
Congestive Heart Failure
Patent Foramen Ovale
Interatrial septal defects
Infective Endocarditis
Non-infective Marantic Endocarditis

Box 10-4. Source of Cardiogenic Cerebral Embolism

High Risk
  Nonvalvular atrial fibrillation
  Rheumatic valvular disease
  Recent myocardial infarction
  Atrial or ventricular thrombus
  Atrial myxoma
  Endocarditis
  Mechanical prosthetic valve
  Sick sinus syndrome
  Dilated cardiomyopathy

Low Risk
  Mitral valve prolapse
  Mitral annulus calcification
  Patent foramen ovale
  Lone atrial fibrillation
  Old myocardial infarction
  Atrial septal aneurysm
**Box 10-5. TIA Differential Diagnosis**

- Migraine
- Focal seizures
- Syncope
- Hyperventilation
- Metabolic disorder
- Drug intoxication
- Vertigo
- Transient global amnesia
- Psychogenic conversion reaction

**Box 10-6. Laboratory Evaluation of TIA Patient**

1. Complete blood count including platelet count
2. Erythrocyte sedimentation rate
3. Activated partial thromboplastin time and prothrombin
4. Lipid profile
5. Lupus anticoagulant and anticardiolipin antibodies (antiphospholipid syndrome)
6. Urine and serum toxicology
7. Syphilis serology
8. Plasma fibrinogen
9. Hemoglobin electrophoresis
10. Serum glucose
11. Urinalysis (for hematuria to suggest renal embolism and proteinuria to suggest hypertensive vascular disease)
12. Renal and hepatic function
## Box 10-7. Laboratory Studies in Selected TIA Patients

1. Protein S and C, antithrombin III levels
2. Urine amino acid screen for homocystinuria
3. Immune complex screening studies including studies for systemic lupus erythematosus and rheumatoid arthritis
4. Serum and whole body viscosity
5. Platelet function studies
6. HIV, Lyme, and cysticercosis screening tests
7. Pregnancy test
8. Serum protein electrophoresis
9. Coagulation factor analysis
10. Chest radiogram for sarcoidosis
### Box 10-8. Major Vertebrobasilar Ischemic Syndromes

<table>
<thead>
<tr>
<th>Artery Occluded</th>
<th>Ischemic Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertebral artery</td>
<td>Lateral medullary syndrome (Wallenberg syndrome)</td>
</tr>
<tr>
<td>Posterior inferior cerebellar artery</td>
<td>Lateral caudal pons</td>
</tr>
<tr>
<td>Anterior inferior cerebellar artery</td>
<td>Inferior medial pons (Foville syndrome)</td>
</tr>
<tr>
<td>Basilar artery</td>
<td>Lateral rostral pons and pons-midbrain junction</td>
</tr>
<tr>
<td>Paramedian branch of basilar artery</td>
<td>Superior medial pons</td>
</tr>
<tr>
<td>Superior cerebellar artery</td>
<td>Pons, midbrain, thalamus, occipital cortex</td>
</tr>
<tr>
<td>Paramedian penetrating midbrain basilar artery</td>
<td>Medial midbrain (Weber syndrome)</td>
</tr>
</tbody>
</table>

Ipsilateral cerebellar ataxia; Horner’s syndrome; facial hemianesthesia; contralateral arm and leg hemianesthesia; vertigo; horizontal nystagmus; dysarthria; dysphagia; hiccups

Ipsilateral cerebellar ataxia; facial anesthesia; facial paresis; horizontal gaze palsy (towards side of lesion); deafness; contralateral body anesthesia

Horizontal gaze palsy towards side of lesions; ipsilateral abducens and facial paresis; contralateral weakness and hemianesthesia

Ipsilateral cerebellar ataxia; facial hemianesthesia, Horner’s syndrome; contralateral hemianesthesia; superior oblique paresis (skew ocular deviation)

Internuclear ophthalmoplegia; palatal myoclonus; ipsilateral ataxia; contralateral hemiparesis

Abducens nerve paresis; internuclear ophthalmoplegia; impaired horizontal eye movements; ocular bobbing; miotic but reactive pupils; quadriplegia; coma if tegmentum involved, “locked in” if basis pointis involved

Ipsilateral oculomotor palsy and contralateral hemiplegia
**Box 10-9. Nonhemiplegia Forms of Stroke**

1. Transient global amnesia (TGA) can be the result of an ischemic process in posterior cerebral artery territory. TGA is usually a benign syndrome characterized by the sudden onset of disorientation, inability to form new memories with preservation of consciousness and speech, and no other neurologic signs. This lasts from 15 minutes to 48 hours and is usually precipitated by exercise, sexual intercourse, or emotional stress. Recurrences are rare. In most patients with TGA, CT/MRI and vascular imaging procedures show no abnormality, but can sometimes show temporal ischemic lesions.

2. Temporal lobe dominant hemisphere vascular lesions can cause receptive (fluent) aphasia with minimal or no motor deficit. It is not uncommon to see patients with receptive fluent (Wemicke’s) aphasia initially diagnosed as having psychiatric illness because speech is nonsensical, but because patients lack motor weakness, neurologic disease is not initially considered. If a nondominant temporal lobe vascular lesion occurs, the patient can develop an acute confusional state.

3. Acute onset of confusional states is caused by ACA territory involvement. This occurs if there is bilateral ACA ischemia as a result of the ACA being supplied by one ICA with flow through anterior communicating artery. Acute confusion with motor or sensory deficit can occur with right (nondominant) MCA involvement caused by temporal-parietal territory infarction.

4. With a lateral medullary infarct, the patient can experience vertigo and have unsteady gait, but no limb weakness.

5. Visual blurring because of homonymous hemianopsia is caused by PCA ischemia.
Box 10-10. Lacunar Syndromes

1. Pure motor hemiplegia without sensory deficit, aphasia, or cortical sensory deficit. This is due to lacune in pons or internal capsule.

2. Pure sensory stroke is due to thalamic lesion

3. Brain stem syndromes:
   a. Dysarthria-clumsy hand syndrome manifested by slurred speech and clumsiness of the arm
   b. Ataxia and hemiparesis involving the arm and leg on same side of body

4. Sensorimotor stroke is due to posterior capsular lacunar infarct

5. Hamichorea-nemiballismus is due to basal ganglia lacunar infarct
### Box 10-11. Findings in Hypertensive ICH

<table>
<thead>
<tr>
<th>Cerebellar</th>
<th>Pontine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea, vomiting</td>
<td>Quadriplegia</td>
</tr>
<tr>
<td>Ataxia</td>
<td>Pinpoint pupils</td>
</tr>
<tr>
<td>Facial weakness, coma</td>
<td>Absent horizontal eye movement</td>
</tr>
<tr>
<td>Decerebrate posturing</td>
<td>Bobbing of eyes</td>
</tr>
<tr>
<td></td>
<td>Coma</td>
</tr>
<tr>
<td></td>
<td>Respiratory abnormalities</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Putaminal</th>
<th>Thalamic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemiparesis or hemiplegia</td>
<td>Hemiparesis or hemiplegia</td>
</tr>
<tr>
<td>Hemianopsia</td>
<td>Hemisensory loss</td>
</tr>
<tr>
<td>Eyes look at the lesion</td>
<td>Downward deviation of eyes</td>
</tr>
<tr>
<td></td>
<td>Paralysis of upward gaze</td>
</tr>
<tr>
<td></td>
<td>Small but reactive pupils</td>
</tr>
</tbody>
</table>
Box 10-12. SAH Grading Systems

Grade 1  Patients are asymptomatic or alert and oriented and have a mild headache and slight neck stiffness.

Grade 2  Patients have moderate to severe headache with major meningeal signs, mild alteration in sensorium, and no neurologic deficit other than cranial nerve palsy caused by direct aneurismal compression.

Grade 3  Patients are drowsy, confused, or have mild focal deficit.

Grade 4  Patients show stupor, moderate to severe hemiparesis, possible early decerebrate rigidity, and vegetative disturbances.

Grade 5  Patients are in deep coma, with decerebrate rigidity and moribund appearance.
Figure 10-1. T-2 weighted axial MRI shows a high signal intensity lesion in the posterior-lateral brain stem (arrow) representing infarction.

Figure 10-2. A. CT scan of brain showing an infarct (lucent area within arrows) in part of the left middle cerebral artery. B. Horizontal section of the brain showing an infarct in the posterior portion of the left middle cerebral artery distribution (upper and lower arrows).
FIGURE 10-3. CT scans of brain hemorrhage
A, Cerebellar hemorrhage
B, Brain stem hemorrhage extending upward into thalamus
and causing third ventricular hemorrhage

FIGURE 10-3, cont’d. C, Thalamic hemorrhage
D, Putaminal hemorrhage
E, Autopsy specimen of the brain showing massive left thalamic hemorrhage with intraventricular extension.
FIGURE 10.4. A. CT shows blood in the calval-septal region. B. Blood is seen in anterior interhemispheric fissure (single arrow) and extending into left middle cerebral artery eistern (horizontal arrows). This is characteristic pattern of ruptured anterior-cerebral-anterior communicating artery aneurysm that was subsequently demonstrated by angiogram.

FIGURE 10.5. A. Noncontrast CT shows hyperdense noncalcified globular serpiginous areas representing abnormal vessels. B. There is dense contrast enhancement consistent with large arteriovenous malformation, confirmed angiographically.