BRAIN STROKE

Strokes are a heterogeneous group of disorders involving sudden, focal interruption of cerebral blood flow that causes neurologic deficit. Strokes can be ischemic (80%), typically resulting from thrombosis or embolism, or hemorrhagic (20%), resulting from vascular rupture (eg, subarachnoid or intracerebral hemorrhage). Stroke symptoms lasting < 1 h are termed a transient ischemic attack (TIA). Strokes damage brain tissue; TIAs often do not, and when damage occurs, it is less extensive than that due to strokes. In Western countries, stroke is the 3rd most common cause of death and the most common cause of neurologic disability.

Strokes involve the arteries of the brain, either the anterior circulation (branches of the internal carotid artery) or the posterior circulation (branches of the vertebral and basilar arteries).

Symptoms and Signs

Initial symptoms occur suddenly. Generally, they include numbness, paresthesias, weakness, or paralysis of the contralateral limbs and the face; aphasia; confusion; visual disturbances in one or both eyes (eg, transient monocular blindness); dizziness or loss of balance and coordination; and headache.

Neurologic deficits reflect the area of brain involved. Anterior circulation stroke typically causes unilateral symptoms. Posterior circulation stroke can cause unilateral or bilateral deficits and is more likely to affect consciousness, especially when the basilar artery is involved.

Selected Stroke Syndromes

Symptoms and Signs	Syndrome
Contralateral hemiparesis (maximal in the leg), urinary incontinence, apathy, confusion, poor judgment, mutism, grasp reflex, gait apraxia	Anterior cerebral artery (uncommon)
Contralateral hemiparesis (worse in the arm and face than in the leg), dysarthria, hemianesthesia, contralateral homonymous hemianopia, aphasia (if the dominant hemisphere is affected) or apraxia and sensory neglect (if the nondominant hemisphere is affected)	Middle cerebral artery (common)
Contralateral homonymous hemianopia, unilateral cortical blindness, memory loss, unilateral 3rd cranial nerve palsy, hemiballismus	Posterior cerebral artery
Monocular loss of vision (amaurosis)	Ophthalmic artery (a branch of the middle cerebral artery)
Unilateral or bilateral cranial nerve deficits (eg, nystagmus, vertigo, dysphagia, dysarthria, diplopia, blindness), truncal or limb ataxia, spastic paresis, crossed sensory and motor deficits*, impaired consciousness, coma, death (if basilar artery occlusion is complete), tachycardia, labile BP	Vertebrobasilar system
Absence of cortical deficits plus one of the	Lacunar infarcts

following:

- Isolated unilateral ataxia,
- Isolated unilateral dystonia
- Isolated unilateral parkinsonian signs
- Isolated hemiparesis
- Isolated unilateral sensory deficits
- Isolated dysarthria
- Unilateral ataxia plus hemiparesis
- Dysarthria plus hemiparesis, particularly of the face, tongue, and hand

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*Ipsilateral facial sensory loss or motor weakness with contralateral body hemianesthesia or hemiparesis indicates a lesion at the pons or medulla.

Other manifestations, rather than neurologic deficits, often suggest the type of stroke. For example, sudden, severe headache suggests subarachnoid hemorrhage. Impaired consciousness or coma, often accompanied by headache, nausea, and vomiting, suggests increased intracranial pressure, which can occur 48 to 72 h after large ischemic strokes and earlier with many hemorrhagic strokes; fatal brain herniation may result.

Complications

Stroke complications can include sleep problems, confusion, depression, incontinence, atelectasis, pneumonia, and swallowing dysfunction, which can lead to aspiration, dehydration, or undernutrition. Immobility can lead to thromboembolic disease, deconditioning, sarcopenia, UTIs, pressure ulcers, and contractures. Daily functioning (including the ability to walk, see, feel, remember, think, and speak) may be decreased.

Evaluation

Evaluation aims to establish whether stroke has occurred, whether it is ischemic or hemorrhagic, and whether immediate treatment is required.

Stroke is suspected in patients with any of the following:

- Sudden neurologic deficits compatible with brain damage in an arterial territory
- A particularly sudden, severe headache
- Sudden, unexplained coma
- Sudden impairment of consciousness

If stroke is suspected, immediate neuroimaging is required to differentiate hemorrhagic from ischemic stroke and to detect signs of increased intracranial pressure. CT is sensitive for intracranial blood but may be normal or show only subtle changes during the first hours of symptoms after anterior circulation ischemic stroke. CT also misses some small posterior circulation strokes and up to 3% of subarachnoid hemorrhages. MRI is sensitive for intracranial blood and may detect signs of ischemic stroke missed by CT, but CT can usually be done more rapidly. If CT does not confirm clinically

suspected stroke, diffusion-weighted MRI can usually detect ischemic stroke. If consciousness is impaired and lateralizing signs are absent or equivocal, further tests to check for other causes are done.

After the stroke is identified as ischemic or hemorrhagic, tests are done to determine the cause. Patients are also evaluated for coexisting acute general disorders (eg, infection, dehydration, hypoxia, hyperglycemia, hypertension). Patients are asked about depression, which commonly occurs after stroke. A dysphagia team evaluates swallowing; sometimes a barium swallow study is necessary.

Strategies to Prevent and Treat Stroke Complications

Applying tight elastic or air-filled support stockings and providing frequent active and passive leg exercises

Turning bedridden patients frequently, with special attention to pressure sites

Passively moving limbs at risk of contractures and placing them in the appropriate resting positions, using splints if necessary

Ensuring adequate fluid intake and nutrition, including evaluating patients for swallowing difficulties and providing nutritional support as necessary

Giving small doses of heparin (5000 U) sc q 12 h or an equivalent amount of low mol wt heparin (LMWH) or heparinoid, when not contraindicated, to prevent deep venous thrombosis and pulmonary embolism

Encouraging early ambulation (as soon as vital signs are normal), with close monitoring

Maximizing lung function (eg, smoking cessation, deep breathing exercises, respiratory therapy, measures to prevent aspiration in patients with dysphagia)

Looking for and treating infections early, especially pneumonia, UTIs, and skin infections

Managing urinary bladder problems in bedridden patients, preferably without using an indwelling catheter

Promoting risk factor modification (eg, smoking cessation, weight loss, healthful diet)

Prescribing early rehabilitation (eg, active and passive exercises, range-of-motion exercises)

Compassionately discussing residual function, prognosis for recovery, and strategies to compensate for lost function with the patient

Encouraging maximum independence through rehabilitation

Encouraging the patient and family members to contact stroke support groups for social and psychologic support

Treatment

Stabilization may need to precede complete evaluation. Comatose or obtunded patients (eg, Glasgow Coma Score $\leq$ 8) may require airway support. If increased intracranial pressure is suspected, intracranial pressure monitoring and measures to reduce cerebral edema may be necessary. Specific acute treatments vary by type of stroke.

Providing supportive care, correcting coexisting abnormalities (eg, fever, hypoxia, dehydration, hyperglycemia, sometimes hypertension), and preventing and treating complications are vital during the acute phase and convalescence; these measures clearly improve clinical outcomes. During convalescence, measures to prevent aspiration, deep venous thrombosis, UTIs, pressure ulcers, and undernutrition may be necessary. Passive exercises, particularly of paralyzed limbs, and breathing exercises are started early to prevent contractures, atelectasis, and pneumonia. Most patients require occupational and physical therapy to maximize functional recovery. Some need additional therapies (eg, speech therapy, feeding restrictions). Depression after stroke may require antidepressants; many patients benefit from counseling. For rehabilitation, an interdisciplinary approach is best. Modifying

risk factors through lifestyle changes (eg, stopping cigarette smoking) and drug therapy (eg, for hypertension) can help delay or prevent subsequent strokes.

ISCHEMIC STROKE

Ischemic stroke is focal brain infarction that produces sudden neurologic deficits persisting > 1 h. Common causes are (from most to least common) nonthrombotic occlusion of small, deep cortical arteries (lacunar infarction); cardiogenic embolism; arterial thrombosis that decreases cerebral blood flow; and artery-to-artery embolism. Diagnosis is clinical, but CT or MRI is done to exclude hemorrhage and confirm the presence and extent of stroke. Thrombolytic therapy may be useful acutely in certain patients. Depending on the cause of stroke, carotid endarterectomy, antiplatelet drugs, or warfarin may help reduce risk of subsequent strokes.

Etiology

Ischemia usually results from thrombi or emboli. Even infarcts classified as lacunar based on clinical criteria (morphology, size, and location) often involve small thrombi or emboli.

Thrombosis

Atheromas, particularly if ulcerated, predispose to thrombi. Atheromas can occur in any major cerebral artery and are common at areas of turbulent flow, particularly at the carotid bifurcation. Partial or complete thrombotic occlusion occurs most often at the main trunk of the middle cerebral artery and its branches but is also common in the large arteries at the base of the brain, in deep perforating arteries, and in small cortical branches. The basilar artery and the segment of the internal carotid artery between the cavernous sinus and supraclinoid process are often occluded.

Less common causes of thrombosis include vascular inflammation secondary to disorders such as acute or chronic meningitis, vasculitic disorders, and syphilis; dissection of intracranial arteries or the aorta; hypercoagulability disorders (eg, antiphospholipid syndrome, hyperhomocysteinemia); hyperviscosity disorders (eg, polycythemia, thrombocytosis, hemoglobinopathies, plasma cell disorders); and rare disorders (eg, moyamoya disease, Binswanger's disease). Older oral contraceptive formulations increase risk of thrombosis.

Embolism

Emboli may lodge anywhere in the cerebral arterial tree. Emboli may originate as cardiac thrombi, especially in the following conditions:

- Atrial fibrillation
- Rheumatic heart disease (usually mitral stenosis)
- Post-MI
- Vegetations on heart valves in bacterial or marantic endocarditis
- Prosthetic heart valves

Other sources include clots that form after open-heart surgery and atheromas in neck arteries or in the aortic arch. Rarely, emboli consist of fat (from fractured long bones), air (in decompression sickness), or venous clots that pass from the right to the left side of the heart through a patent foramen ovale with

shunt (paradoxical emboli). Emboli may dislodge spontaneously or after invasive cardiovascular procedures (eg, catheterization). Rarely, thrombosis of the subclavian artery results in embolic stroke in the vertebral artery or its branches.

Lacunar infarcts

Ischemic stroke can also result from lacunar infarcts. These small (≤ 1.5 cm) infarcts result from nonatherothrombotic obstruction of small, perforating arteries that supply deep cortical structures; the usual cause is lipohyalinosis (degeneration of the media of small arteries and replacement by lipids and collagen). Whether emboli cause lacunar infarcts is controversial. Lacunar infarcts tend to occur in elderly patients with diabetes or poorly controlled hypertension.

Other causes

Less commonly, ischemic stroke results from vasospasm (eg, during migraine, after subarachnoid hemorrhage, after use of sympathomimetic drugs such as cocaine or amphetamines) or venous sinus thrombosis (eg, during intracranial infection, postoperatively, peripartum, secondary to a hypercoagulation disorder).

Pathophysiology

Inadequate blood flow in a single brain artery can often be compensated for by an efficient collateral system, particularly between the carotid and vertebral arteries via anastomoses at the circle of Willis and, to a lesser extent, between major arteries supplying the cerebral hemispheres. However, normal variations in the circle of Willis and in the caliber of various collateral vessels, atherosclerosis, and other acquired arterial lesions can interfere with collateral flow, increasing the chance that blockage of one artery will cause brain ischemia.

Some neurons die when perfusion is < 5% of normal for > 5 min; however, the extent of damage depends on the severity of ischemia. If it is mild, damage proceeds slowly; thus, even if perfusion is 40% of normal, 3 to 6 h may elapse before brain tissue is completely lost. However, if severe ischemia (ie, decrease in perfusion) persists > 15 to 30 min, all of the affected tissue dies (infarction). Damage occurs more rapidly during hyperthermia and more slowly during hypothermia. If tissues are ischemic but not yet irreversibly damaged, promptly restoring blood flow may reduce or reverse injury. For example, intervention may be able to salvage the moderately ischemic areas (penumbras) that often surround areas of severe ischemia (these areas exist because of collateral flow).

Mechanisms of ischemic injury include edema, microvascular thrombosis, programmed cell death (apoptosis), and infarction with cell necrosis. Inflammatory mediators (eg, IL-1B, tumor necrosis factor-α) contribute to edema and microvascular thrombosis. Edema, if severe or extensive, can increase intracranial pressure. Many factors may contribute to necrotic cell death; they include loss of ATP stores, loss of ionic homeostasis (including intracellular Ca accumulation), lipid peroxidative damage to cell membranes by free radicals (an iron-mediated process), excitatory neurotoxins (eg, glutamate), and intracellular acidosis due to accumulation of lactate.

Symptoms and Signs

Symptoms and signs depend on the part of brain affected. Patterns of neurologic deficits often suggest the affected artery, but correlation is often inexact.

Deficits may become maximal within several minutes of onset, typically in embolic stroke. Less often, deficits evolve slowly, usually over 24 to 48 h (called evolving stroke or stroke in evolution), typically

in thrombotic stroke. In most evolving strokes, unilateral neurologic dysfunction (often beginning in one arm, then spreading ipsilaterally) extends without causing headache, pain, or fever. Progression is usually stepwise, interrupted by periods of stability. A stroke is considered submaximal when, after it is complete, there is residual function in the affected area, suggesting viable tissue at risk of damage.

Embolic strokes often occur during the day; headache may precede neurologic deficits. Thrombi tend to occur during the night and thus are first noticed on awakening. Lacunar infarcts may produce one of the classic lacunar syndromes (eg, pure motor hemiparesis, pure sensory hemianesthesia, ataxic hemiparesis, dysarthria–clumsy hand syndrome); signs of cortical dysfunction (eg, aphasia) are absent. Multiple lacunar infarcts may result in multi-infarct dementia.

Deterioration during the first 48 to 72 h after onset of symptoms, particularly progressively impaired consciousness, results more often from cerebral edema than from extension of the infarct. Unless the infarct is large or extensive, function commonly improves within the first few days; further improvement occurs gradually for up to 1 yr.

Diagnosis

Diagnosis is suggested by sudden neurologic deficits referable to a specific arterial territory. Ischemic stroke must be distinguished from other causes of similar focal deficits (eg, hypoglycemia; postictal [Todd's] paralysis; hemorrhagic stroke; rarely, migraine). Headache, coma or stupor, and vomiting are more likely with hemorrhagic stroke.

Although diagnosis is clinical, neuroimaging and bedside glucose testing are mandatory. CT is done first to exclude intracerebral hemorrhage, subdural or epidural hematoma, and a rapidly growing, bleeding, or suddenly symptomatic tumor. CT evidence of even large anterior circulation ischemic stroke may be subtle during the first few hours; changes may include effacement of sulci or the insular cortical ribbon, loss of the gray-white junction between cortex and white matter, and a dense middle cerebral artery sign. After 24 h of ischemia, medium-sized to large infarcts are usually visible as hypodensities; small infarcts (eg, lacunar infarcts) may be visible only with MRI. Diffusion-weighted MRI (highly sensitive for early ischemia) can be done immediately after CT initial neuroimaging.

Distinction between lacunar, embolic, and thrombotic stroke based on history, examination, and neuroimaging is not always reliable, so tests to identify common or treatable causes and risk factors for all of these types of strokes are routinely done. These tests typically include carotid duplex ultrasonography, ECG, transesophageal echocardiography, and various blood tests (CBC, platelet count, PT/PTT, fasting blood glucose, lipid profile, homocysteine, ESR, and, for at-risk patients, syphilis serology). Troponin I level is measured to detect concomitant MI. Magnetic resonance or CT angiography is also often done. Other tests (eg, antiphospholipid antibodies) are done if certain disorders are suspected clinically.

About 50% of patients with moderate or severe hemiplegia and most with milder deficits have a clear sensorium and eventually can take care of their basic needs and walk adequately. Complete neurologic recovery occurs in about 10%. Use of the affected limb is usually limited, and most deficits that remain after 12 mo are permanent. Subsequent strokes often occur, and each tends to worsen neurologic function. About 20% of patients die in the hospital; mortality rate increases with aging.

TREATMENT

Acute

Guidelines for early management of stroke are available from the Stroke Council of the American Heart Association/American Stroke Association. Patients with acute ischemic strokes are usually hospitalized. Supportive measures may be needed during initial evaluation and stabilization.

Perfusion of an ischemic brain area may require a high BP because autoregulation is lost; thus, BP should not be decreased except in the following situations:

- BP is > 220 mm Hg systolic or > 120 mm Hg diastolic on 2 successive readings > 15 min apart.
- There are signs of other end-organ damage (eg, aortic dissection, acute MI, pulmonary edema, hypertensive encephalopathy, retinal hemorrhages, acute renal failure).
- Use of recombinant tissue plasminogen activator (tPA) is likely.

If indicated, nicardipine 2.5 mg/h IV is given initially; dose is increased by 2.5 mg/h q 5 min to a maximum of 15 mg/h as needed to decrease systolic BP by 10 to 15%. Alternatively, IV labetalol can be used.

Patients with presumed thrombi or emboli may be treated with tPA, thrombolysis-in-situ, antiplatelet drugs, and/or anticoagulants. Most patients are not candidates for thrombolytic therapy; they should be given an antiplatelet drug (usually aspirin 325 mg po) when they are admitted to the hospital. Contraindications to antiplatelet drugs include aspirin- or NSAID-induced asthma or urticaria, other hypersensitivity to aspirin or to tartrazine, acute GI bleeding, G6PD deficiency, and use of warfarin.

Recombinant tPA is used for patients with acute ischemic stroke of < 3 h duration and no contraindications to tPA. Although tPA can cause fatal or other symptomatic brain hemorrhage, patients treated with tPA strictly following protocol have a higher likelihood of functional neurologic recovery. Thus, only physicians experienced in stroke management should use tPA to treat patients with acute stroke; inexperienced physicians are more likely to violate protocols, resulting in more brain hemorrhages and deaths. tPA must be given within 3 h of symptom onset—a difficult requirement. Because the precise time of symptom onset may not be known, clinicians must start timing from the moment the patient was last observed to be well. Before treatment with tPA, brain hemorrhage must be excluded by CT, and systolic BP must be <185 mm Hg and diastolic BP <110 mm Hg; antihypertensive drugs may be given as above. Dose of tPA is 0.9 mg/kg IV (maximum dose 90 mg); 10% is given by rapid IV injection, and the remainder by constant infusion over 60 min. Vital signs are closely monitored for 24 h after treatment, and BP is maintained below the target levels listed above. Any bleeding complications are aggressively managed. Anticoagulants and antiplatelet drugs are not used within 24 h of treatment with tPA.

Thrombolysis-in-situ (angiographically directed intra-arterial thrombolysis) of a thrombus or embolus can sometimes be used for major strokes if symptoms have begun > 3 h but < 6 h ago, particularly for strokes due to large occlusions in the middle cerebral artery. Clots in the basilar artery may be intra-arterially lysed up to 12 h after stroke onset, sometimes even later depending on the clinical circumstances. This treatment, although standard of care in some large stroke centers, is often unavailable in other hospitals.

Anticoagulation with heparin or low mol wt heparin is used for stroke caused by cerebral venous thrombosis and is sometimes used for emboli due to atrial fibrillation and when stroke due to presumed

progressive thrombosis continues to evolve despite use of antiplatelet drugs and cannot be treated any other way (eg, with tPA or invasive methods). Warfarin is begun simultaneously with heparin. Before anticoagulation, hemorrhage must be excluded by CT. Constant weight-based heparin infusion is used to increase PTT to 1.5 to 2 times baseline values until warfarin has increased the INR to 2 to 3 (3 in hypercoagulable disorders). Because warfarin predisposes to bleeding and is continued after hospital discharge, its use should be restricted to patients likely to comply with dosage and monitoring requirements and not prone to falls.

Long term

Supportive care is continued during convalescence. Controlling general medical risk factors (especially hyperglycemia and fever) can limit brain damage after stroke, leading to better functional outcomes.

Carotid endarterectomy is indicated for patients with recent nondisabling, submaximal stroke attributed to an ipsilateral carotid obstruction of 70 to 99% of the arterial lumen or to an ulcerated plaque if life expectancy is at least 5 yr. In other symptomatic patients (eg, patients with TIAs), endarterectomy with antiplatelet therapy is indicated for carotid obstruction of ≥ 60% with or without ulceration if life expectancy is at least 5 yr. The procedure should be done by surgeons who have a morbidity and mortality rate of < 3% with the procedure in the hospital where it will be done.

Oral antiplatelet drugs are used to prevent subsequent strokes (secondary prevention). Aspirin 81 or 325 mg once/day, clopidogrel 75 mg once/day, or the combination product aspirin 25 mg/extended-release dipyridamole 200 mg bid may be used. In patients taking warfarin, antiplatelet drugs additively increase risk of bleeding and are thus usually avoided; however, aspirin is occasionally used simultaneously with warfarin in certain high-risk patients. The combination of clopidogrel and aspirin is avoided because it has no advantage over aspirin alone in secondary stroke prevention and results in more bleeding complications.

TRANSIENT ISCHEMIC ATTACK

A transient ischemic attack (TIA) is focal brain ischemia producing sudden neurologic deficits that last < 1 h. Diagnosis is clinical. Carotid endarterectomy, antiplatelet drugs, and warfarin decrease risk of stroke after certain types of TIA.

TIA is similar to ischemic stroke except that symptoms last < 1 h; most TIAs last < 5 min. Infarction is very unlikely if deficits resolve within 1 h. Deficits that resolve spontaneously within 1 to 24 h have been shown on diffusion-weighted MRI and other studies to often be accompanied by infarction and are thus no longer considered to be TIAs. TIAs are most common among the middle-aged and elderly. TIAs markedly increase risk of stroke, beginning in the first 24 h.

Etiology

Most TIAs are caused by emboli, usually from carotid or vertebral arteries, although most of the causes of ischemic stroke can also result in TIAs. Uncommonly, TIAs result from impaired perfusion due to severe hypoxemia, reduced O_2-carrying capacity of blood (eg, profound anemia, carbon monoxide poisoning), or increased blood viscosity (eg, severe polycythemia), particularly in brain arteries with preexisting stenosis. Systemic hypotension does not usually cause cerebral ischemia unless it is severe or arterial stenosis preexists because autoregulation maintains brain blood flow at near-normal levels over a wide range of systemic BPs.

In subclavian steal syndrome, a subclavian artery stenosed proximal to the origin of the vertebral artery "steals" blood from the vertebral artery (in which blood flow reverses) to supply the arm during exertion, causing signs of vertebrobasilar ischemia.

Occasionally, TIAs occur in children with a severe cardiovascular disorder that produces emboli or a very high Hct.

Symptoms and Signs

Neurologic deficits are similar to those of strokes. Transient monocular blindness (amaurosis fugax), which usually lasts < 5 min, may occur when the ophthalmic artery is affected. Symptoms begin suddenly, usually last 2 to 30 min, then resolve completely. Patients may have several TIAs daily or only 2 or 3 over several years. Symptoms are usually similar in successive carotid attacks but vary somewhat in successive vertebrobasilar attacks.

Diagnosis and Treatment

Diagnosis is made retrospectively when sudden neurologic deficits referable to ischemia in an arterial territory resolve within 1 h. Isolated peripheral facial nerve palsy, loss of consciousness, or impaired consciousness does not suggest TIA. TIAs must be distinguished from other causes of similar symptoms (eg, hypoglycemia, migraine aura, postictal [Todd's] paralysis). Because an infarct, a small hemorrhage, and even a mass lesion cannot be excluded clinically, neuroimaging is required. Usually, CT is the study most likely to be immediately available. However, CT may not identify infarcts for >24 h. MRI usually detects evolving infarction within hours. Diffusion-weighted MRI is the most accurate imaging test to rule out an infarct in patients with presumed TIA but is not always available.

The cause of a TIA is sought as for that of ischemic strokes, including tests for carotid stenosis, cardiac sources of emboli, atrial fibrillation, and hematologic abnormalities and screening for stroke risk factors. Because risk of subsequent ischemic stroke is high and immediate, evaluation proceeds rapidly, usually on an inpatient basis. It is not clear which patients, if any, can be safely discharged from the emergency department.

Treatment is aimed at preventing strokes; antiplatelet drugs are used. Carotid endarterectomy or arterial angioplasty plus stenting can be useful for some patients, particularly those who have no neurologic deficits but who are at high risk of stroke. Warfarin is indicated if cardiac sources of emboli are present. Modifying stroke risk factors, when possible, may prevent stroke.

INTRACEREBRAL HEMORRHAGE

Intracerebral hemorrhage is focal bleeding from a blood vessel in the brain parenchyma. The cause is usually hypertension. Typical symptoms include focal neurologic deficits, often with abrupt onset of headache, nausea, and impairment of consciousness. Diagnosis is by CT or MRI. Treatment includes BP control, supportive measures, and, for some patients, surgical evacuation.

Most intracerebral hemorrhages occur in the basal ganglia, cerebral lobes, cerebellum, or pons. Intracerebral hemorrhage may also occur in other parts of the brain stem or in the midbrain.

Etiology and Pathophysiology

Intracerebral hemorrhage usually results from rupture of an arteriosclerotic small artery that has been weakened, primarily by chronic arterial hypertension. Such hemorrhages are usually large, single, and catastrophic. Use of cocaine or, occasionally, other sympathomimetic drugs can cause transient severe hypertension leading to hemorrhage. Less often, intracerebral hemorrhage results from congenital

aneurysm, arteriovenous or other vascular malformation (see Sidebar 1: Stroke (CVA): Vascular Lesions in the Brain), trauma, mycotic aneurysm, brain infarct (hemorrhagic infarction), primary or metastatic brain tumor, excessive anticoagulation, blood dyscrasia, or a bleeding or vasculitic disorder

Lobar intracerebral hemorrhages (hematomas in the cerebral lobes, outside the basal ganglia) usually result from angiopathy due to amyloid deposition in cerebral arteries (cerebral amyloid angiopathy), which affects primarily the elderly. Lobar hemorrhages may be multiple and recurrent.

Blood from an intracerebral hemorrhage accumulates as a mass that can dissect through and compress adjacent brain tissues, causing neuronal dysfunction. Large hematomas increase intracranial pressure. Pressure from supratentorial hematomas and the accompanying edema may cause transtentorial brain herniation, compressing the brain stem and often causing secondary hemorrhages in the midbrain and pons (see Fig. 1: Stupor and Coma: Tentorial and subfalcine herniation.). If the hemorrhage ruptures into the ventricular system (intraventricular hemorrhage), blood may cause acute hydrocephalus. Cerebellar hematomas can expand to block the 4th ventricle, also causing acute hydrocephalus, or they can dissect into the brain stem. Cerebellar hematomas that are > 3 cm in diameter may cause midline shift or herniation. Herniation, midbrain or pontine hemorrhage, intraventricular hemorrhage, acute hydrocephalus, or dissection into the brain stem can impair consciousness and cause coma and death.

Symptoms and Signs

Symptoms typically begin with sudden headache, often during activity. However, headache may be mild or absent in the elderly. Loss of consciousness is common, often within seconds or a few minutes. Nausea, vomiting, delirium, and focal or generalized seizures are also common. Neurologic deficits are usually sudden and progressive. Large hemorrhages, when located in the hemispheres, cause hemiparesis; when located in the posterior fossa, they cause cerebellar or brain stem deficits (eg, conjugate eye deviation or ophthalmoplegia, stertorous breathing, pinpoint pupils, coma). Large hemorrhages are fatal within a few days in about ½ of patients. In survivors, consciousness returns and neurologic deficits gradually diminish to various degrees as the extravasated blood is resorbed. Some patients have surprisingly few neurologic deficits because hemorrhage is less destructive to brain tissue than infarction.

Small hemorrhages may cause focal deficits without impairment of consciousness and with minimal or no headache and nausea. Small hemorrhages may mimic ischemic stroke.

Diagnosis and Treatment

Diagnosis is suggested by sudden onset of headache, focal neurologic deficits, and impaired consciousness, particularly in patients with risk factors. Intracerebral hemorrhage must be distinguished from ischemic stroke, subarachnoid hemorrhage, and other causes of acute neurologic deficits (eg, seizure, hypoglycemia).

Immediate CT or MRI and bedside blood glucose measurement are necessary. Neuroimaging is usually diagnostic. If neuroimaging shows no hemorrhage but subarachnoid hemorrhage is suspected clinically, lumbar puncture is necessary.

Treatment includes supportive measures and control of general medical risk factors. Anticoagulants and antiplatelet drugs are contraindicated. If patients have used anticoagulants, the effects are reversed when possible by giving fresh frozen plasma, vitamin K, or platelet transfusions as indicated. Hypertension should be treated only if mean arterial pressure is > 130 mm Hg or systolic BP is > 185 mm Hg. Nicardipine 2.5 mg/h IV is given initially; dose is increased by 2.5 mg/h q 5 min to a maximum of 15 mg/h as needed to decrease systolic BP by 10 to 15%. Cerebellar hemisphere hematomas that are > 3 cm in diameter may cause midline shift or herniation, so surgical evacuation is often lifesaving. Early evacuation of large lobar cerebral hematomas may also be lifesaving, but

rebleeding occurs frequently, sometimes increasing neurologic deficits. Early evacuation of deep cerebral hematomas is seldom indicated because surgical mortality is high and neurologic deficits are usually severe.

VASCULAR LESIONS IN THE BRAIN

Common brain vascular lesions include arteriovenous malformations and aneurysms.

Arteriovenous malformations (AVMs): AVMs are tangled, dilated blood vessels in which arteries flow directly into veins. AVMs occur most often at the junction of cerebral arteries, usually within the parenchyma of the frontal-parietal region, frontal lobe, lateral cerebellum, or overlying occipital lobe. AVMs can bleed or directly compress brain tissue; seizures or ischemia may result.

Neuroimaging may detect them incidentally; contrast or noncontrast CT can usually detect AVMs > 1 cm, but the diagnosis is confirmed with MRI. Occasionally, a cranial bruit suggests an AVM. Conventional angiography is required for definitive diagnosis and determination of whether the lesion is operable.

Superficial AVMs > 3 cm in diameter are usually obliterated by a combination of microsurgery, radiosurgery, and endovascular surgery. AVMs that are deep or < 3 cm in diameter are treated with stereotactic radiosurgery, endovascular therapy (eg, preresection embolization or thrombosis via an intra-arterial catheter), or coagulation with focused proton beams. (See also Recommendations for the management of intracranial arteriovenous malformations from the Stroke Council, American Stroke Association.)

Aneurysms: Aneurysms are focal dilations in arteries. They occur in about 5% of people. Common contributing factors may include arteriosclerosis, hypertension, and hereditary connective tissue disorders (eg, Ehlers-Danlos syndrome, pseudoxanthoma elasticum, autosomal dominant polycystic kidney syndrome). Occasionally, septic emboli cause mycotic aneurysms. Brain aneurysms are most often < 2.5 cm in diameter and saccular (noncircumferential); sometimes they have one or more small, thin-walled, outpouchings (berry aneurysm). Most aneurysms occur along the middle or anterior cerebral arteries or the communicating branches of the circle of Willis, particularly at arterial bifurcations. Mycotic aneurysms usually develop distal to the first bifurcation of the arterial branches of the circle of Willis.

Many aneurysms are asymptomatic, but a few cause symptoms by compressing adjacent structures. Ocular palsies, diplopia, squint, or orbital pain may indicate pressure on the 3rd, 4th, 5th, or 6th cranial nerves. Visual loss and a bitemporal field defect may indicate pressure on the optic chiasm. Aneurysms may bleed into the subarachnoid space, causing subarachnoid hemorrhage. Aneurysms occasionally cause sentinel (warning) headaches before rupture; subarachnoid bleeding may accompany sentinel headaches. Rupture causes a sudden severe headache called a thunderclap headache.

Neuroimaging may detect aneurysms incidentally.

Diagnosis requires angiography, CT angiography, or magnetic resonance angiography.

If < 7 mm, asymptomatic aneurysms in the anterior circulation rarely rupture and do not warrant the risks of immediate treatment. They can be monitored with serial imaging. If aneurysms are larger, are in the posterior circulation, or cause symptoms due to bleeding or to compression of neural structures, endovascular therapy, if feasible, is required.

Subarachnoid Hemorrhage (SAH)

Subarachnoid hemorrhage is sudden bleeding into the subarachnoid space. The most common cause of spontaneous bleeding is a ruptured aneurysm. Symptoms include sudden, severe headache, usually with loss or impairment of consciousness. Secondary vasospasm (causing focal brain ischemia), meningismus, and hydrocephalus (causing persistent headache and obtundation) are common. Diagnosis is by CT or MRI; if neuroimaging is normal, diagnosis is by CSF analysis. Treatment is with supportive measures and neurosurgery or endovascular measures, preferably in a referral center.

Etiology and Pathophysiology

Subarachnoid hemorrhage is bleeding between the arachnoid and pia mater. In general, head trauma is the most common cause, but traumatic subarachnoid hemorrhage is usually considered a separate disorder (see Traumatic Brain Injury (TBI)). Spontaneous (primary) subarachnoid hemorrhage usually results from ruptured aneurysms. A congenital intracranial saccular or berry aneurysm is the cause in about 85% of patients. Bleeding may stop spontaneously. Aneurysmal hemorrhage may occur at any age but is most common from age 40 to 65. Less common causes are mycotic aneurysms, arteriovenous malformations, and bleeding disorders.

Blood in the subarachnoid space causes a chemical meningitis that commonly increases intracranial pressure for days or a few weeks. Secondary vasospasm may cause focal brain ischemia; about 25% of patients develop signs of a TIA or ischemic stroke. Brain edema is maximal and risk of vasospasm and subsequent infarction (called angry brain) is highest between 72 h and 10 days. Secondary acute hydrocephalus is also common. A 2nd rupture (rebleeding) sometimes occurs, most often within about 7 days.

Symptoms and Signs

Headache is usually severe, peaking within seconds. Loss of consciousness may follow, usually immediately but sometimes not for several hours. Severe neurologic deficits may develop and become irreversible within minutes or a few hours. Sensorium may be impaired, and patients may become restless. Seizures are possible. Usually, the neck is not stiff initially unless the cerebellar tonsils herniate. However, within 24 h, chemical meningitis causes moderate to marked meningismus, vomiting, and sometimes bilateral extensor plantar responses. Heart or respiratory rate is often abnormal. Fever, continued headaches, and confusion are common during the first 5 to 10 days. Secondary hydrocephalus may cause headache, obtundation, and motor deficits that persist for weeks. Rebleeding may cause recurrent or new symptoms.

Diagnosis

Diagnosis is suggested by characteristic symptoms. Testing should proceed as rapidly as possible, before damage becomes irreversible. Noncontrast CT is > 90% sensitive. MRI is comparably sensitive but less likely to be immediately available. False-negative results occur if volume of blood is small. If subarachnoid hemorrhage is suspected clinically but not identified on neuroimaging or if neuroimaging is not immediately available, lumbar puncture is done. Lumbar puncture is contraindicated if increased intracranial pressure is suspected because the sudden decrease in CSF pressure may lessen the tamponade of a clot on the ruptured aneurysm, causing further bleeding.

CSF findings suggesting subarachnoid hemorrhage include numerous RBCs, xanthochromia, and increased pressure. RBCs in CSF may also be caused by traumatic lumbar puncture. Traumatic lumbar puncture is suspected if the RBC count decreases in tubes of CSF drawn sequentially during the same lumbar puncture (see Approach to the Neurologic Patient: Lumbar puncture (spinal tap)). About 6 h or more after a subarachnoid hemorrhage, RBCs become crenated and lyse, resulting in a xanthochromic CSF supernatant and visible crenated RBCs (noted during microscopic CSF examination); these

findings usually indicate that subarachnoid hemorrhage preceded the lumbar puncture. If there is still doubt, hemorrhage should be assumed, or the lumbar puncture should be repeated in 8 to 12 h. In patients with subarachnoid hemorrhage, conventional cerebral angiography is done as soon as possible after the initial bleeding episode; alternatives include magnetic resonance angiography and CT angiography. All 4 arteries (2 carotid and 2 vertebral arteries) should be injected because up to 20% of patients (mostly women) have multiple aneurysms.

On ECG, subarachnoid hemorrhage may produce ST-segment elevation or depression. It can cause syncope, mimicking MI. Other possible ECG abnormalities include prolongation of the QRS or QT intervals and peaking or deep, symmetric inversion of T waves.

Prognosis and Treatment

About 35% of patients die after the first aneurysmal subarachnoid hemorrhage; another 15% die within a few weeks because of a subsequent rupture. After 6 mo, a 2nd rupture occurs at a rate of about 3%/yr. In general, prognosis is grave with an aneurysm, better with an arteriovenous malformation, and best when 4-vessel angiography does not detect a lesion, presumably because the bleeding source is small and has sealed itself. Among survivors, neurologic damage is common, even when treatment is optimal.

Patients with subarachnoid hemorrhage should be treated in referral centers whenever possible. Hypertension should be treated only if mean arterial pressure is > 130 mm Hg; euvolemia is maintained, and IV nicardipine is titrated as for intracerebral hemorrhage (see Stroke (CVA): Acute). Bed rest is mandatory. Restlessness and headache are treated symptomatically. Stool softeners are given to prevent constipation, which can lead to straining. Anticoagulants and antiplatelet drugs are contraindicated.

Nimodipine 60 mg po q 4 h is given for 21 days to prevent vasospasm, but BP needs to be maintained in the desirable range (usually considered to be a mean arterial pressure of 70 to 130 mm Hg and a systolic pressure of 120 to 185 mm Hg). If clinical signs of acute hydrocephalus occur, ventricular drainage should be considered.

Occlusion of the aneurysm reduces risk of rebleeding. Detachable endovascular coils can be inserted during angiography to occlude the aneurysm. Alternatively, if the aneurysm is accessible, surgery to clip the aneurysm or bypass its blood flow can be done, especially for patients with an evacuable hematoma or acute hydrocephalus. If patients are arousable, most vascular neurosurgeons operate within the first 24 h to minimize risk of rebleeding and risks due to angry brain. If > 24 h have elapsed, some neurosurgeons delay surgery until 10 days have passed; this approach decreases risks due to angry brain but increases risk of rebleeding and overall mortality.