

## 2 Stroke

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*Brenda S. Mallory*

### **Background**

Strokes (also called cerebrovascular accidents) occur suddenly and are clinically defined as a focal vascular lesion, which causes an abrupt onset of a neurological deficit that lasts longer than 24 hours. The deficit depends on the area of brain affected. In a transient ischemic attack (TIA), the neurological deficits last less than 24 hours but are usually 5 to 15 minutes.

### **Stroke Statistics**

Approximately 700,000 strokes occur annually in the United States (200,000 are recurrent strokes).

- Stroke is the third leading cause of death in the United States, behind heart disease and cancer.
- There are 4.7 million stroke survivors in the United States.
- The first-stroke incident rate (per 100,000) is 167 for white males and 323 for black males.
- Stroke is the leading cause of disability in the United States.
- Approximately 25% of stroke survivors die within 1 year, and about 50% die within 8 years.
- Approximately 50–70% of stroke survivors obtain functional independence.
- Approximately 15–30% of stroke survivors remain permanently disabled.
- About 20% of stroke survivors require institutional care.

## ***Etiology***

Strokes are caused by ischemic infarction or hemorrhagic disruption of the brain. Ischemic strokes are the result of decreased blood flow and are caused by thrombosis, embolism, or other disorders of the blood or blood vessel walls.

### ***Ischemic Stroke (88% of All Strokes)***

#### *Arterial Thrombosis (Atherosclerosis)*

- A thrombus is an aggregation of primarily platelets and fibrin (that may have other cellular elements) within a blood vessel.
- Platelets stick to an ulcerated atherosclerotic plaque, forming a white thrombus (thrombogenesis).
- A red thrombus of fibrin and red blood cells forms and propagates on top of the white thrombus, especially in areas of slow-moving blood flow.
- Primary atherosclerotic thrombus fills the arterial lumen, partially or completely occluding the lumen.
- Secondary thrombi propagate retrogradely and antegradely.
- A lacunar infarction results from thrombosis in small brain arteries (30–300  $\mu\text{m}$ ) and leaves a lacune of about 3 mm to 2 cm.
- Arterial thrombosis may also be caused by other disorders of the vessels or blood.

#### *Embolism*

- Emboli plug downstream arteries and consist of pieces of thrombus or other material that originate from proximal arteries, the heart, or are paradoxical via a patent foramen ovale.
- Atrial fibrillation is the most common cause of cerebral embolism.
- The average annual stroke risk in patients with atrial fibrillation ranges from 0.5 to 15%, depending on the number of risk factors (older age, hypertension, poor left ventricular function, prior cardioembolism, diabetes, and thyrotoxicosis)
- The most common cause of artery-to-artery cerebral embolism is carotid bifurcation atherosclerosis.

#### *Other*

- Collagen vascular diseases.
- Vasculitis.
- Hypercoagulable states.

- Fibromuscular dysplasia.
- Temporal arteritis.
- Granulomatous arteritis.
- Moyamoya disease.
- Venous thrombosis.
- Carotid and vertebral artery dissection.
- Cerebral autosomal-dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL).
- Mitochondrial encephalopathy, lactic acidosis, and stroke-like syndrome (MELAS).

### ***Hemorrhage (12% of All Strokes)***

#### *Intracerebral Hemorrhage (9% of All Strokes)*

- Has a mortality rate of 50%.
- Main causes are hypertension (HTN), trauma, and cerebral amyloid angiopathy.
- Also caused by drug abuse (amphetamines and cocaine), tumors, vascular malformations, coagulation disorders, use of anticoagulants and/or thrombolytic agents, and hemorrhage into a cerebral infarct.

#### *Subarachnoid Hemorrhage (3% of All Strokes)*

- Main causes are trauma and rupture of a saccular aneurysm.
- Other causes are vascular malformations and the extension of an intracerebral hemorrhage.
- About 30,000 aneurysms rupture annually in the United States.
- The re-bleeding rate of a ruptured aneurysm is 20% in the first 2 weeks, and 3% per year afterward.

## **Pathogenesis**

### ***Ischemic Stroke***

Following a critical loss of blood flow, brain cells are reversibly or irreversibly injured, depending on the severity and duration of ischemia. After a stroke, there is a core area of severe injury and cell death surrounded by an area of less severely damaged cells called the *ischemic penumbra*. Cells in the ischemic penumbra are electrically silent but are able to maintain their membrane potentials, and can recover if reperfused. If blood flow is restored promptly, no or few cells die, and the patient experiences a TIA.

The following three major mechanisms promote cell death after a stroke:

1. Excitotoxicity.
  - a. There is failure to generate adenosine triphosphate.
  - b. There is electrical failure.

- c. There is ionic pump failure with an inability to maintain ionic gradients.
  - d. There is a release of the excitatory amino acid glutamate.
  - e. There is failure of glutamate reuptake.
  - f. Glutamate binds to postsynaptic membranes causing excessive  $\text{Ca}^{++}$  entry into damaged brain cells.
  - g. Calcium-dependent synthases and proteases break down cytoskeletal and enzymatic proteins and generate nitric oxide-free radicals and peroxynitrite anion.
2. Oxidative stress.
- a. Mitochondrial functions, such as oxidative phosphorylation, fail, and reactive oxygen radicals are released that attack proteins, lipids, and nucleic acids.
3. Apoptosis.
- a. Molecules promote cell death by mechanisms resembling apoptosis (programmed cell death).

### ***Hypertensive Intracerebral Hemorrhage***

The rupture of a small penetrating artery, weakened by lipohyalinosis, deep in the brain results in hypertensive intracerebral hemorrhage. The areas most commonly involved are the putamen and internal capsule, caudate nucleus, thalamus, cerebral lobes, pons, and cerebellum.

### ***Cerebral Amyloid Angiopathy***

This results from the deposition of amyloid in the walls of cerebral arterioles, which causes the arterioles to degenerate. It is thought to be a common cause of lobar hemorrhage in the elderly and has no specific treatment.

### ***Saccular Aneurysms***

These occur at the bifurcation of large-to-medium-sized intracranial arteries, and rupture results from thinning of the arterial wall.

## **Risk Factors for Stroke**

Many risk factors can be modified by medical or surgical interventions or changes in lifestyle, but some are not modifiable. Primary and secondary prevention of stroke can be determined by the identification of modifiable risk factors.

The following risk factors for stroke can be treated:

1. HTN.
  - a. High blood pressure (140/90 mmHg or higher) is the most important risk factor for stroke.

- b. Persons with blood pressure lower than 120/80 mmHg have about half the lifetime risk of stroke compared with those who have HTN.
2. Atrial fibrillation.
  - a. The use of anticoagulation medications depends on risk factors, such as age, previous TIA or stroke, HTN, heart failure, diabetes, clinical coronary artery disease, mitral stenosis, prosthetic heart valves, or thyrotoxicosis.
3. Diabetes.
  - a. Treatment of diabetes can delay complications that increase the risk of stroke.
4. Cigarette smoking.
  - a. Risk returns to baseline risk 5 years after quitting.
5. High blood cholesterol.
  - a. High levels of low-density lipoprotein ( $>100$  mg/dL) and triglycerides ( $\geq 150$  mg/dL) increase the risk of stroke in people with previous coronary heart disease, ischemic stroke, or TIA. Low levels ( $<40$  mg/dL) of high-density lipoprotein also may increase stroke risk.
6. Carotid stenosis.
  - a. The risk of stroke in patients with asymptomatic carotid artery stenosis ( $\geq 60\%$ ) is approximately 2% per year, whereas symptomatic patients have a 13%-per-year risk of stroke.
7. Transient ischemic attacks.
  - a. Following a TIA, 10% of patients will develop a stroke in 90 days, and 5% in 2 days. Patients at risk for stroke should be counseled to call 911 if they experience symptoms of sudden hemiplegia or hemianesthesia, gait disturbance, visual changes, difficulty with speech, or severe headache.
  - b. One type of TIA, amaurosis fugax, is transient monocular blindness resulting from emboli to the central retinal artery.
8. Other heart disease.
  - a. People with coronary heart disease or heart failure have a higher risk of stroke than those with hearts that work normally. Dilated cardiomyopathy, heart valve disease, and some types of congenital heart defects also raise the risk of stroke.
9. Physical inactivity.
  - a. There is a lower relative risk of stroke (0.86 in men and up to 0.66 in women) associated with vigorous exercise.
10. Excessive alcohol.
  - a. Drinking an average of more than one alcoholic drink a day for women or more than two drinks a day for men can raise blood pressure, and may increase the risk for stroke.
11. Illegal drugs.
  - a. Intravenous drug abuse carries a high risk of stroke. Cocaine use has been linked to strokes and heart attacks.

The following risk factors for stroke that cannot be treated:

1. Increasing age.
2. Gender.
  - a. Stroke is more common in men than in women. Women who are pregnant have a higher risk of stroke, as do women taking birth control pills who also smoke or have high blood pressure or other risk factors.
3. Heredity and race.
  - a. Stroke risk is greater if a parent, grandparent, sister, or brother has had a stroke.
  - b. African Americans have a much higher risk of death from a stroke than Caucasians, partly because blacks are more at risk for high blood pressure, diabetes, and obesity.
4. Prior stroke or heart attack.

## History

Patients with an acute stroke need to be evaluated urgently to determine if the stroke is ischemic, and whether the patient can be treated with intravenous recombinant tissue plasminogen activator (rtPA).

### ***Ischemic Stroke***

- Most patients will have a history of a sudden onset of a focal neurological symptom.
- Some will have a step-wise, gradual worsening or waxing and waning of symptoms.
- Most are alert.
- Some are lethargic. Try to get history from friends, family, or bystanders.
- Approximately 25% will have headaches.
- Nausea and vomiting can occur in brain stem or cerebellar strokes.
- Neurological symptoms depend on the arterial territory involved (*see Table 1*).
- Ask patients about medications, especially anticoagulants and antiplatelet agents.
- Symptom onset from the time that the patient was last known to be symptom free is needed to guide thrombolytic therapy.
- A history of recent medical or neurological events should include the following:
  - Epilepsy.
  - Migraines.
  - Previous stroke or myocardial infarction.
  - Surgery.
  - Trauma.
  - Hemorrhage.

**Table 1**  
**Stroke Syndromes**

<i>Artery</i>	<i>Anatomy supplied</i>	<i>Stroke syndrome</i>
Common carotid	Forebrain except occipital lobe	Asymptomatic or MCA syndrome
Internal carotid	Forebrain except occipital lobe	Asymptomatic or MCA syndrome
Middle cerebral	<p>Surface cortical branches</p> <ul style="list-style-type: none"> <li>• Most of the convexity of the hemisphere including: <ul style="list-style-type: none"> <li>▪ Lateral orbital surface of frontal lobe</li> <li>▪ Insula</li> <li>▪ Middle and inferior frontal gyri</li> <li>▪ Precentral gyrus</li> <li>▪ Postcentral gyrus</li> <li>▪ Inferior parietal lobule</li> <li>▪ Superior parietal lobule (inferior part)</li> <li>▪ Lateral surface of temporal lobe</li> </ul> </li> </ul> <p>Deep branches</p> <ul style="list-style-type: none"> <li>• Internal capsule (superior half)</li> <li>• Basal ganglia</li> <li>• Optic radiation</li> </ul>	<p>Contralateral hemiplegia</p> <ul style="list-style-type: none"> <li>• Arm/face &gt; leg (surface branches)</li> <li>• Proportional (deep branches)</li> </ul> <p>Contralateral sensory loss</p> <ul style="list-style-type: none"> <li>• Arm/face &gt; leg</li> </ul> <p>Homonymous hemianopsia</p> <p>Homonymous quadrantanopia</p> <ul style="list-style-type: none"> <li>• Lower (parietal lobe)</li> <li>• Upper (temporal lobe)</li> </ul> <p>Dominant</p> <ul style="list-style-type: none"> <li>• Motor aphasia</li> <li>• Sensory aphasia</li> <li>• Global aphasia</li> <li>• Apraxia</li> <li>• Gerstmann's syndrome</li> </ul> <p>Nondominant</p> <ul style="list-style-type: none"> <li>• Anosognosia</li> <li>• Unilateral asomatognosia</li> </ul>

*Continued*

**Table 1 (Continued)**

<i>Artery</i>	<i>Anatomy supplied</i>	<i>Stroke syndrome</i>
Anterior cerebral	Surface cortical branches <ul style="list-style-type: none"> <li>• Frontal pole</li> <li>• Part of orbital surface of frontal lobe</li> <li>• Anterior medial surface of frontal and parietal lobes including:               <ul style="list-style-type: none"> <li>▪ Paracentral lobule</li> <li>▪ Cingulate gyrus</li> <li>▪ Medial frontal gyrus</li> <li>▪ Corpus callosum (except splenium)</li> </ul> </li> </ul> Heubner's artery (deep branch) <ul style="list-style-type: none"> <li>• Anterior putamen</li> <li>• Inferior head of the caudate nucleus</li> <li>• Anterior limb of the internal capsule (inferior half)</li> </ul>	Contralateral leg weakness Contralateral leg sensory loss Contralateral hemiplegia <ul style="list-style-type: none"> <li>• Leg &gt; arm/face</li> <li>• Arm/face &gt; leg (Heubner's artery)</li> </ul> Mutism Abulia (akinetic mutism) Urinary incontinence Head and eyes deviate to side of lesion Gegenhalten rigidity Forced grasping Ideomotor apraxia Alien arm or hand Acute confusion Dominant <ul style="list-style-type: none"> <li>• Transcortical motor aphasia</li> <li>• Transcortical mixed aphasia</li> </ul>
Posterior cerebral	Surface cortical branches <ul style="list-style-type: none"> <li>• Uncus</li> <li>• Parahippocampal gyrus</li> <li>• Medial and lateral occipitotemporal gyri</li> <li>• Cuneus</li> <li>• Lingual gyrus</li> <li>• Precuneus</li> <li>• Posterolateral occipital lobe</li> </ul>	Hemispheric territory <ul style="list-style-type: none"> <li>• Contralateral homonymous hemianopsia</li> <li>• Alexia without agraphia</li> <li>• Color anomia</li> <li>• Amnesia</li> <li>• Prosopagnosia</li> <li>• Visual object agnosia</li> </ul>

*Continued*



**Table 1 (Continued)**

<i>Artery</i>	<i>Anatomy supplied</i>	<i>Stroke syndrome</i>
Posterior cerebral (Continued)	<p>Interpeduncular branches</p> <ul style="list-style-type: none"> <li>• Midbrain</li> </ul> <p>Perforating branches</p> <ul style="list-style-type: none"> <li>• Hypothalamus</li> <li>• Pituitary</li> <li>• Anterior medial thalamus</li> <li>• Mammillary bodies</li> <li>• Subthalamus</li> <li>• Globus pallidus</li> <li>• Lateral geniculate body</li> </ul>	<p>Thalamic syndrome</p> <ul style="list-style-type: none"> <li>• Contralateral sensory loss</li> <li>• Choreoathetosis</li> <li>• Ataxia</li> <li>• Tremor</li> <li>• Dejerine-Roussy syndrome</li> </ul> <p>Weber syndrome</p> <ul style="list-style-type: none"> <li>• Contralateral hemiplegia</li> <li>• Third nerve palsy</li> </ul>
Basilar	<p>Brainstem</p> <p>Cerebellum</p>	<p>Locked-in syndrome (paramedian branch occlusion at level of ventral basal pons)</p> <ul style="list-style-type: none"> <li>• Quadriplegia</li> <li>• Bilateral cranial nerve palsy</li> <li>• Preservation of spinothalamic sensation and upgaze</li> </ul> <p>Lateral medullary syndrome (Wallenberg's syndrome; may be caused by other artery occlusion)</p> <ul style="list-style-type: none"> <li>• Dysarthria</li> <li>• Ipsilateral limb ataxia</li> <li>• Vertigo</li> <li>• Nystagmus</li> </ul>
Posterior inferior cerebellar	<p>Medulla oblongata</p> <p>Inferior surface of cerebellum</p> <p>Dentate nucleus</p>	

*Continued*

**Table 1 (Continued)**

<i>Artery</i>	<i>Anatomy supplied</i>	<i>Stroke syndrome</i>
Posterior inferior cerebellar (continued)		<ul style="list-style-type: none"> <li>• Ipsilateral Horner's syndrome</li> <li>• Ipsilateral sensory loss face</li> <li>• Contralateral sensory loss in limbs and trunk</li> <li>• Dysphagia</li> <li>• Vocal cord paralysis</li> <li>• Hiccup</li> </ul>
Lacunar syndromes	Posterior limb of the internal capsule or ventral pons Ventrolateral thalamus Ventral pons Ventral pons or genu of the internal capsule Genu and anterior limb of the internal capsule	Pure motor hemiparesis Pure sensory stroke Ataxic hemiparesis Dysarthria and clumsy hand or arm Pure motor hemiparesis with motor
Aphasia		

Stroke syndromes are variable due to arterial anatomic variation and collateral circulation.  
 MCA, middle cerebral artery.

- The presence of one of the following symptoms double the chance of an individual having an intracranial hemorrhage:
  - Coma on arrival.
  - Vomiting.
  - Severe headache.
  - Current warfarin therapy.
  - Systolic blood pressure higher than 220 mmHg.
  - Glucose level higher than 170 mg/dL in a nondiabetic patient.

### ***Intracerebral Hemorrhage***

- The usual presentation is sudden onset of a focal neurological deficit that progresses over minutes to hours.
- Many patients will have maximum symptoms at onset.
- Associated symptoms are elevated blood pressure, depressed level of consciousness, headache, nausea, and vomiting.
- Approximately 6% will have seizures.
- No set of clinical features can reliably distinguish hemorrhagic from ischemic stroke.

### ***Subarachnoid Hemorrhage***

- The usual presentation is the sudden onset of a severe headache.
- The headache is often called “the worst headache of my life.” It is also described as a “thunderclap” headache.
- Associated symptoms may be a brief loss of consciousness, nausea or vomiting, focal neurological deficits, or a stiff neck.
- It is a medical emergency.

### **Definitions**

*Abulia* is lacking will, initiative, or drive.

*Agnosia* is the inability to recognize a previously known stimulus via a sensory modality, and is variously defined to include disorders at both the discriminative sensory level and the associative sensory level, or at the associative sensory level alone.

*Anosognosia* is the unawareness of left hemiparesis following a nondominant parietal lesion.

*Aphasia* is the loss or impairment (dysphasia) of language owing to a cerebral lesion.

*Apraxia* is the inability to produce a purposeful movement in the absence of a severe disorder of sensation, strength, coordination, cognition, perception, or language.

- Asomatognosia* is the loss of awareness of one's body schema and its relation to extrapersonal space, and is anatomically localized in the parietal lobes. Unilateral asomatognosias are usually related to a lesion in the nondominant parietal lobe, and include neglect of one side of the body, dressing apraxia, sensory extinction, and constructional apraxia.
- Associative level of perception* is multimodal sensory integration (visual, tactile, auditory, language, and memory) resulting in the recognition of a previously known sensory stimulus.
- Astereognosis* is the inability to identify an object by palpation despite intact primary sensory modalities, and is usually caused by a lesion of the opposite sensory cortex.
- Dejerine-Roussy syndrome* is a pain syndrome that is often delayed in onset after a posterolateral thalamic lesion, and affects all or part of the contralateral body.
- Discriminative level of perception* is the awareness of the characteristics of a unimodal sensory stimulus, such as shape, weight, color, and movement, and can be tested by two-point discrimination, cutaneous localization, figure writing (graphesthesia), and stereognosis.
- Dyspraxia* is difficulty in producing a purposeful movement in the absence of a severe disorder of sensation, strength, coordination, cognition, perception, or language.
- Gerstmann's syndrome* is a bilateral asomatognosia resulting from a dominant parietal lesion, and is characterized by finger agnosia, acalculia, agraphia, and left-right confusion.
- Ideational apraxia* is the inability to produce a purposeful movement because of loss of the plan of action; it is identified when a patient cannot correctly utilize a familiar object, and is thought to be produced by a lesion of the left angular gyrus, which affects the limbs bilaterally. (It has been likened to sensory aphasia.)
- Ideomotor apraxia* is the inability to produce a purposeful movement when commanded, and can be produced by a lesion in the region of the supramarginal gyrus involving the fibers of the left arcuate fasciculus, in the left premotor cortex (both with bilateral effects), in the corpus callosum, or in the right premotor area causing left limb apraxia. (It has been likened to conduction aphasia.)
- Impersistence* is the failure to continue a voluntary action, such as eye closure or hand gripping, for more than a few seconds, and is thought to be a disorder of attention that is usually the result of a right frontal lesion.
- Motor aphasia* (Broca's aphasia) is nonfluent, effortful speech with good comprehension and the inability to repeat.
- Primary sensory modalities* are touch, pain, temperature, and vibration.
- Prosopagnosia* is a type of visual agnosia characterized by the inability to recognize individual faces, and is usually the result of a lesion in the bilateral inferior parieto-occipital area or, rarely, with a right inferior parieto-occipital lesion.

*Sensory aphasia* (Wernicke's aphasia) is fluent, nonsensical speech (jargon speech) with impaired comprehension and the inability to repeat.

*Transcortical aphasias* are similar to motor and sensory aphasias, but with preserved repetition.

*Visual object agnosia* is the inability to recognize any object, and is usually caused by a more extensive lesion in the bilateral inferior parieto-occipital area or, rarely, with a left inferior parieto-occipital lesion.

## Clinical Examination

- Vital signs.
- Signs of trauma.
- Cardiovascular exam.
- Skin.
- Evidence of active bleeding.
- Neurological exam.
- Level of consciousness.
  - Glasgow Coma Scale (eye opening, verbal response, motor response).
- Cognition.
  - Speech (fluency and repetition).
  - Comprehension.
  - Naming.
  - Reading.
  - Writing.
  - Calculation.
  - Object recognition.
  - Copying a geometric pattern.
  - Memory.
  - Reasoning.
  - Emotional state.
- Cranial nerves.
  - Assess swallowing ability before the patient drinks.
- Motor system.
  - Inspection.
  - Strength.
  - Tone.
  - Reflexes.
  - Coordination.
- Sensation.
- National Institutes of Health Stroke Scale (NIHSS).
  - The NIHSS provides prognostic information and helps identify patients at greatest risk for intracranial hemorrhage associated with thrombolytic therapy. The NIHSS is available on the National Institute of Neurological Disorders and Stroke website at <http://www.ninds.nih.gov/doctors>.

## Diagnostic Evaluation

The emergency diagnostic evaluation for acute stroke includes the following:

- Brain computed tomography (CT) scan.
  - Because clinical features alone cannot differentiate ischemic from hemorrhagic stroke, brain imaging is needed.
  - The usual initial brain imaging test is noncontrast-enhanced CT.
  - For rtPA candidates, the goal time from arrival to CT interpretation is 45 minutes.
- Electrocardiogram.
  - Acute myocardial infarction can lead to stroke.
  - Acute stroke can lead to myocardial ischemia.
  - Atrial fibrillation can be detected.
- Blood glucose.
- Serum electrolytes.
- Renal function tests.
- Complete blood count, including platelet count.
- Prothrombin time:international normalized ratio.
- Activated partial thromboplastin time.
- Others as indicated.
  - Hepatic function study.
  - Toxicology screen.
  - Blood alcohol level.
  - Pregnancy test.
  - Arterial blood gas.
  - Lumbar puncture.
  - Electroencephalography.
  - Chest X-ray.

Other diagnostic studies can be obtained after the patient receives initial treatment.

*Doppler ultrasonography* can identify stenosis at the origin of the internal carotid artery. *Transcranial doppler* can assess anterior and posterior brain circulation, including stenotic lesions in the large intracranial arteries.

## Angiography

- If the cause of an intracerebral hemorrhage is uncertain, angiography should be considered.
- Magnetic resonance angiography, CT angiography, and catheter angiography are used.
- Catheter cerebral angiography is the standard for diagnosing cerebral aneurysms as the cause for subarachnoid hemorrhage (SAH).
- Timing of cerebral angiography depends on the patient's clinical state.

## **Multimodal Magnetic Resonance Imaging**

- *Diffusion-weighted* magnetic resonance imaging allows for early identification of ischemic regions within minutes of stroke onset because of early changes of decreased water diffusion within ischemic brain tissue. The diffusion-weighted imaging lesion contains irreversibly damaged brain, as well as the ischemic penumbra.
- *Gradient-recalled echo* magnetic resonance imaging sequences have recently been shown to be superior to CT for detecting any hemorrhage and equivalent to CT for acute hemorrhage.
- *Oxygen-15 positron-emission tomography* can identify the penumbra in stroke patients.

## **Differential Diagnosis**

- Unrecognized seizures.
- Confusional states.
- Syncope.
- Toxic or metabolic disorders, including hypoglycemia.
- Brain tumors.
- Subdural hematoma.
- Migraine.

## **Treatment**

### ***Treatment of Ischemic Stroke***

#### *General Supportive Care*

##### HOSPITALIZATION

- Most patients should be admitted to the hospital.
- Treatment is best accomplished in comprehensive stroke units, which also incorporate comprehensive rehabilitation.
- Stroke units decrease mortality and morbidity from stroke.
- The American Stroke Association (ASA; a division of the American Heart Association) recommends early mobilization and prevention of subacute complications of stroke.
- Subcutaneous administration of heparin or low-molecular-weight heparin or heparinoids, the use of intermittent external compression stocking, or aspirin for patients who cannot receive anticoagulants is strongly recommended by the ASA to prevent deep vein thrombosis among immobilized patients.

##### MAINTAIN ADEQUATE TISSUE OXYGENATION

- Monitor with pulse oximetry with target oxygen saturation level of 95% or higher.

#### LOWER ELEVATED BODY TEMPERATURE

- Treat fever with antipyretic agents and cooling devices.
- Treat the source of fever.

#### MONITOR AND MANAGE BLOOD PRESSURE

- In most patients, a decline in blood pressure occurs spontaneously.
- Withhold antihypertensive agents, unless the diastolic blood pressure is higher than 120 mmHg or the systolic blood pressure is higher than 220 mmHg (unless there is end-organ involvement or the patient is eligible for thrombolytic therapy).
- Intravenous labetalol is a good choice of drug to treat hypertension in acute ischemic stroke.
- Thrombolytic therapy is not given to patients with a diastolic blood pressure higher than 110 mmHg or a systolic blood pressure higher than 185 mmHg at the time of treatment.
- Before, during, and 24 hours following rtPA therapy, the blood pressure needs careful management.

#### CONTROL HYPERGLYCEMIA OR HYPERGLYCEMIA

- Lower elevated glucose levels to less than 300 mg/dL.

#### *Save the Penumbra (Restore or Improve Perfusion)*

The desired result of thrombolytic therapy is clot lysis with resulting recanalization and restoration of obstructed cerebral blood flow.

#### INTRAVENOUS rtPA

- Intravenous rtPA (a thrombolytic agent) is strongly recommended by the ASA for carefully selected patients who can be treated within 3 hours of onset of ischemic stroke.
- The major risk is symptomatic brain hemorrhage (6.4%).
- Intravenous rtPA leads to a complete or near-complete reversal of a stroke in about one of every three patients treated.
- Bleeding in the brain occurs in about 5.2% of patients.
- Intra-arterial rtPA is a treatment option for selected patients.
- Intra-arterial rtPA requires immediate cerebral angiography and interventional neuroradiology at an experienced stroke center.

#### *Anticoagulants*

ASA recommendations include the following:

- Urgent, routine anticoagulation is not recommended for the purpose of improving neurological outcome or preventing recurrent stroke in most patients.



- Initiation of anticoagulant therapy within 24 hours of treatment with intravenous rtPA is not recommended.
- Anticoagulants are associated with an increased risk of serious bleeding complications, including the risk of symptomatic, hemorrhagic transformation of ischemic strokes.
- Warfarin benefits patients with atrial fibrillation; however, the best time to start after an acute ischemic stroke is unclear.

### *Antiplatelet Agents*

ASA guidelines include the following:

- The primary benefit of aspirin seems to be in preventing a subsequent stroke.
- Aspirin should be given within 24 to 48 hours of ischemic stroke onset in most patients.
- Aspirin should not be given within 24 hours of the use of a thrombolytic agent.
- Aspirin should not be used as a substitute for intravenous rtPA or other acute therapies for the treatment of acute ischemic stroke.

### OTHER ANTIPLATELET REGIMENS

Common antiplatelet regimens include clopidogrel and the combination of aspirin and dipyridamole.

### *Surgery*

#### CAROTID ENDARTERECTOMY

- Although not currently recommended by the ASA for the treatment of patients with an acute ischemic stroke, studies of emergency carotid endarterectomy (CEA) have shown successful recanalization of the internal carotid artery.
- CEA reduces the risk of stroke in patients with recently symptomatic stenosis.
- The benefit of CEA is greater in men than in women, for those with stroke compared with those with a TIA, and those with hemispheric symptoms compared with those with retinal symptoms.

#### EXTRACRANIAL–INTRACRANIAL BYPASS

It is not recommended by the ASA for the treatment of patients with an acute ischemic stroke.

#### ENDOVASCULAR TREATMENT

Carotid stenting may be a reasonable alternative to CEA in patients at high risk of perioperative complications of CEA.

## ENDOVASCULAR MECHANICAL THROMBOLYSIS

- A variety of devices are available to break up and remove clots, but their efficacy is unclear.

## ***Treatment of Intracerebral Hemorrhage***

### *Reverse the Effects of Anticoagulation*

#### GENERAL SUPPORTIVE CARE

- Intubate.
  - Intubate for hypoxia ( $PO_2 < 60$  mmHg or  $PCO_2 > 50$  mmHg) or obvious risk of aspiration.
- Monitor and manage blood pressure.
  - Severe hypertension should be treated ( $>180/105$  mmHg).
  - If the patient has an intracerebral pressure (ICP) monitor; the cerebral perfusion pressure should be kept at more than 70 mmHg.
- Manage increased ICP.
  - Increased ICP is defined as 20 mmHg or more for longer than 5 minutes.
  - The goal of treatment is to have an ICP of less than 20 mmHg and cerebral perfusion pressure higher than 70 mmHg.
  - ICP monitoring is recommended by the American Heart Association in patients with a Glasgow Coma Scale score of lower than 9 and other patients thought to be deteriorating owing to an increased ICP.
  - Treatment of elevated ICP includes ventricular drains (for secondary hydrocephalus), osmotherapy, hyperventilation, and muscle relaxants.

#### SURGERY

- Patients with cerebellar hemorrhage more than 3 cm in diameter with brainstem compression or hydrocephalus are surgical candidates.
- Patients with small hemorrhages ( $<10$  cm<sup>3</sup>) are nonsurgical candidates.

## ***Treatment of Subarachnoid Hemorrhage***

- Patients with SAH should have an early referral to a treatment center.
- Treatment includes intraluminal thrombosis of an aneurysm, with coils that are delivered via a catheter or direct surgical repair, with either clipping or wrapping of the aneurysm.
- Oral nimodipine reduces poor outcome.
- Hypertension/hypervolemia/hemodilution (triple-H therapy) prevents complications of vasospasm.
- Vasospasm that is not responsive to medical therapy can be treated with transluminal angioplasty.

## **Rehabilitation**

### **Goals**

- Prevent, recognize, and manage comorbid illnesses.
- Prevent, recognize, and manage complications.
- Reduce activity restrictions (disabilities) that result from impairments.
- Reduce participation limitations (handicaps) that limit involvement in life situations.
- Maximize psychosocial adjustment to disease and disability for the patient and the family.
- Prevent recurrent stroke.

### **When**

- Start rehabilitation in the acute care hospital after the patient's medical condition has been stabilized.
- This is often within 24 to 48 hours of the stroke.
- Post-acute stroke rehabilitation is started when the stroke patient is medically stable.

### **Where**

Some patients will recover from the acute stroke and not need rehabilitation services, but those who do need rehabilitation services can receive them in a setting determined primarily by functional status and availability of social support. The settings for post-acute stroke rehabilitation include acute inpatient rehabilitation hospitals or units, subacute inpatient rehabilitation facilities, outpatient rehabilitation facilities, and home-based rehabilitation. General criteria for rehabilitation are as follows:

- Acute inpatient rehabilitation.
  - The patient has endurance sufficient to tolerate 3 hours of therapy daily.
  - The patient is medically stable but needs close medical supervision and rehabilitation nursing services.
  - The patient has significant activity restrictions in mobility and self-care.
  - The patient has the ability to learn.
- Subacute inpatient rehabilitation.
  - The patient has endurance sufficient to tolerate less intense treatment.
  - The patient is medically stable and needs general medical supervision and skilled nursing services.
  - The patient has significant activity restrictions in mobility and self-care.
  - The patient has the ability to learn.

- Outpatient-based rehabilitation.
  - The patient has sufficient function and social support to travel to an outpatient facility.
- Home-based rehabilitation.
  - This is for patients that cannot readily travel to outpatient services.

## **How**

Although stroke care in the United States is often fragmented, the importance of improving stroke care is receiving increasing emphasis. The Joint Commission on Accreditation of Healthcare Organizations awards certificates for primary stroke centers, and a list of centers can be found at <http://www.jcaho.org/dscc/dsc/certified+organizations/certified+organizations-disease.htm>. The ASA (<http://www.strokeassociation.org/>) has developed recommendations for the establishment of stroke systems of care. The Department of Veterans Affairs and Department of Defense has published a clinical practice guideline for the management of stroke rehabilitation in the primary care setting that can be accessed at [http://www.guideline.gov/summary/summary.aspx?view\\_id=1&doc\\_id=3846](http://www.guideline.gov/summary/summary.aspx?view_id=1&doc_id=3846). Patients with acute stroke should receive organized and coordinated care, which includes acute stroke treatment, secondary prevention of stroke, and rehabilitation by a multidisciplinary team. Rehabilitation involves the following assessments and interventions.

- Basic assessment.
  - Basic assessment includes an assessment of cognitive skills, severity of disability, depression, sensory deficits, communication, and swallowing deficits.
  - Tools for the measurement of disability include the Barthel Index, Functional Independence Measure, and Modified Rankin Scale.
  - Tools for the assessment of depression in the rehabilitation setting include the hospital anxiety and depression scale, the general health questionnaire-12, and for those with communication problems, the visual analog mood scale or hospital stroke aphasic depression questionnaire.
- Psychosocial assessment.
  - The patient should receive a referral to a social worker for comprehensive assessment and intervention.
- Bladder and bowel assessment and intervention.
  - Interventions include prompted voiding, bladder training (includes patient education, scheduled voiding, and positive reinforcement), and bowel management programs.
- Nutrition assessment.
  - Nutritional assessment and correction of major nutritional problems are recommended by the ASA.

- Patient and family education.
  - The rehabilitation team, the patient, and the family should develop the rehabilitation plan jointly.
  - It is important that the patient's caregivers have adequate support and training for their role.
- Secondary stroke prevention.
  - Secondary prevention of stroke includes the treatment of underlying disease, lowering blood pressure, lowering blood cholesterol with statins, management of other risk factors, CEA, carotid stenting, and antiplatelet therapy.
- Prevent and manage complications.
- Initiate rehabilitation interventions.
  - Exercise therapy includes strengthening, aerobics, stretching, and coordination and balance training.
  - Task-specific therapy seems to be the most efficacious therapy for motor function.
  - Robotic therapy can increase the intensity of therapy that involves repetitive movement and allow for the precise control and measurement of therapy that may ultimately determine the optimal dosage.
  - Consider use of partial body-weight support with treadmill training, which may improve gait.
  - Consider constraint-induced therapy (constraining the uninvolved limb and forcing use of the involved limb) for select patients.
  - Functional electrical stimulation may decrease shoulder subluxation, strengthen select muscles, and facilitate gait training.
  - Treat spasticity with nonpharmacological (remove painful stimuli, positioning, stretching, splinting, and surgery) and pharmacological (oral tizanidine, dantrolene, baclofen, injection of botulinum toxin or phenol, and intrathecal baclofen) means.
  - Consider biofeedback for select patients.
  - Prevent and manage shoulder pain.
  - Provide cognitive retraining, if needed.
  - Virtual reality and motor imagery are therapies under study.
  - Treat dysphagia.
  - Treat language and communication disorders. Higher intensity of speech therapy seems to improve speech outcome.
  - Extending therapy into the community after the initial rehabilitation can allow for continued improvement in endurance and function.

## Complications

### *Pneumonia*

- Risk factors for aspiration pneumonia are a wet-sounding quality to the voice after swallowing, incomplete mouth closure, or a high NIHSS.

- The presence of a gag reflex does not always predict protection from aspiration.
- Having the patient drink a glass of water is a useful screen for aspiration.
- A fiberoptic endoscopic evaluation of swallowing test or a videofluoroscopic modified barium swallow examination can objectively evaluate swallowing function.

### ***Deep Venous Thrombosis***

- A deep venous thrombosis can be detected in approximately one-third to one-half of patients who have a moderately severe stroke.

### ***Pulmonary Embolism***

- This accounts for approximately 10% of deaths after a stroke.
- A pulmonary embolism can be detected in about 1% of persons who have had a stroke.

### ***Pressure Sores and Palsies***

- Pressure sores usually occur over the sacrum of immobile patients, and prevention includes frequent turning, minimizing bed rest, and the use of pressure-relieving surfaces for bed and chair, as well as controlling incontinence.
- Pressure palsies can occur with the ulnar nerve in the cubital tunnel, the radial nerve as it exits the spiral groove, and the peroneal nerve at the fibular head.

### ***Contractures***

- Limitation in joint motion can usually be prevented by active or passive range of movement exercises daily, controlling spasticity, and splints, especially for the hand and ankle.

### ***Shoulder Pain***

- Shoulder pain in the involved limb is common following a stroke, and its cause is multifactorial.
- Prevention strategies include careful attention to correct handling of the paretic arm, avoiding impingement associated with overhead use of the arm, and maintaining shoulder range of movement.

### ***Neurological Complications***

- Cerebral edema and increased ICP can be seen with ischemic stroke, and are usually related to large vessel occlusions with multilobar infarctions, with brain edema peaking 3 to 5 days post-stroke.

- Seizures are more common with hemorrhagic stroke. Following ischemic stroke, seizures usually occur within 24 hours and are usually partial.
- Recurrent stroke is frequent; approximately 25% of people who recover from their first stroke will have another stroke within 5 years.
- Complications of SAH include re-bleeding, cerebral vasospasm, hydrocephalus, and hyponatremia.

## **Depression**

- The peak incidence of depression is between 6 months and 2 years post-stroke, with prevalence between 10 and 34%.
- Lesions of the left frontal pole and the pallidus are related to post-stroke depression.
- The role of antidepressant drugs or psychotherapy in the prophylaxis of depression is not clear.

The University of Massachusetts Medical School and the ASA have developed a program called “StrokeSTOP” that encourages the active prevention and treatment of stroke by future physicians. The StrokeSTOP program can be accessed online at [www.umassmed.edu/strokestop](http://www.umassmed.edu/strokestop). Information for clinicians treating acute stroke is also available from the Brain Attack Coalition website, found at <http://www.stroke-site.org/index.html>.

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