Stroke Overview

A stroke, or cerebrovascular accident (CVA), occurs when blood flow to an area of the brain is interrupted.

There are two main types of stroke: ischemic stroke, which is caused by a blockage in a blood vessel in the brain, and hemorrhagic stroke, which is caused by bleeding in the brain or surrounding area.

Strokes can cause long-lasting disability or even death; however, early treatment and preventive measures can reduce the brain damage that occurs because of stroke.

In both ischemic and hemorrhagic stroke, one or more areas of the brain can be damaged.

Depending upon the area affected, a person may lose the ability to move one side of the body, the ability to speak, or a number of other functions.

The damage from a stroke may be temporary or permanent.

A person's long-term outcome depends upon how much of the brain is damaged, how quickly treatment begins, and several other factors.

Types of Stroke

Ischemic stroke	Ischemic strokes are caused by a blockage (clog) in one of the blood vessels that supply oxygen and other important nutrients to the brain.	
	There are two main subtypes of ischemic stroke, thrombotic and embolic.	
	Thrombotic stroke	A thrombotic stroke results from a problem within an artery (blood vessel) that supplies blood to the brain.
		This is most likely to occur in arteries that are clogged with fatty deposits, called plaques.
		Plaques partially block the artery, and can rupture and bleed, forming a blood clot.
		This blood clot ("thrombus") can further clog or completely block the artery, which then slows or prevents blood flow to the area of brain fed by that artery.
		Blood clotting disorders can also cause clots to form within arteries in some people.
	Embolic stroke	An embolic stroke occurs when a blood clot or other particle breaks loose from another part of the body, often the heart or a large artery in the neck, and travels through the bloodstream to the brain where it lodges in a smaller blood vessel.

Types of Stroke (cont)

		The blood clot or particle, called an "embolus," then blocks blood flow to that area of the brain, reducing the amount of oxygen and nutrients that reach that area.
		One of the most common causes of embolic strokes is an irregular heart rhythm called "atrial fibrillation."
		Emboli can also originate in the aorta and in the arteries within the neck and head and travel further along within arteries within the brain.
	Transient ischemic attack (TIA)	Transient ischemic attacks are episodes in which a person has signs or symptoms of a stroke (eg, weakness; inability to speak) that last for a short time, but without any sign of stroke on brain scans such as MRI or CT.
		Symptoms of a TIA usually last between a few minutes and a few hours.
		A person may have one or many TIAs.
		People recover completely from the symptoms of a TIA.
Hemorrhagic stroke	Hemorrhagic strokes occur when blood vessels in the brain leak or rupture (break), causing bleeding in or around the brain.	
	There are two main subtypes of hemorrhagic stroke, intracerebral and subarachnoid.	
	Intracerebral hemorrhage	In an intracerebral hemorrhage (ICH), bleeding occurs within the brain.
		This damages the brain as blood collects and puts pressure on the surrounding tissue.
		Causes of ICH:
		• High blood pressure
		• Injury
		• Bleeding disorders
		• Deformities in blood vessels, such as an aneurysm (a weakening in the lining of the blood vessel)

Types of Stroke (cont)

Subarachnoid hemorrhage	Subarachnoid hemorrhage occurs when a blood vessel on the surface of the brain ruptures.
	The blood builds up and causes pressure in the "subarachnoid" space, which is between two layers of the tissue covering the brain.
	The most common early symptom of a subarachnoid hemorrhage is a severe headache called "thunderclap headache," which many patients describe as the worst headache of their life.

Stroke Risk Factors

Ischemic stroke risk factors

Hypertension	Diabetes
Atrial fibrillation	Prior stroke or TIA
Sex (females > males)	Physical inactivity
Ethnicity (highest risk in African Americans)	Smoking
Age > 55 years	Dyslipidemia
Atherosclerosis	Patent foramen ovale (PFO)
Sickle cell disease	Illegal drug use
Obesity	

Hemorrhagic stroke risk factors

High blood pressure	Use of warfarin or other blood thinning medicines
Smoking	Illegal drug use (especially cocaine and "crystal meth"

Stroke Symptoms

Signs and symptoms of stroke often develop suddenly and then may temporarily improve or slowly worsen, depending upon the type of stroke and area of the brain affected.

Classic symptoms

Classic stroke symptoms can be recalled with the acronym **FAST**

F	Face	Sudden weakness or droopiness of the face, or problems with vision	Ask the person to smile. Does one side droop?
A	Arm	Sudden weakness or numbness of one or both arms	Ask the person to raise both arms. it through lifestyle changes and medicine are critical to reducing stroke risks. There are several steps you can take to reduce your risk for stroke: Does one arm drift downward?

Stroke Symptoms (cont)

S	Speech	Difficulty speaking, slurred speech, or garbled speech	Ask the person to repeat a simple sentence. Are the words slurred?
T	Time	Time is very important in stroke treatment. The sooner treatment begins, the better the chances are for recovery.	If the person shows any of these signs, call 9-1-1 immediately. Stroke treatment can begin in the ambulance.

Other common signs of stroke

Sudden dizziness, trouble walking, or loss of balance or coordination

Sudden trouble seeing in one or both eyes

Sudden severe headache with no known cause

Sudden numbness of the face, arm, or leg

Sudden confusion or trouble understanding others

Stroke Diagnosis

Brain and blood vessel imaging	After doing a quick physical exam, the doctor or nurse usually sends the patient right away for an imaging test of the brain (eg, CT scan or MRI scan) and an imaging test of the blood vessels in the neck and head (eg, CT angiography or MR angiography) that supply the brain with blood.
	The imaging allows the doctor or nurse to see the area of the brain affected by the stroke, as well as to confirm the type of stroke (ischemic or hemorrhagic).
	Occasionally, a catheter must be inserted through a blood vessel in the groin and threaded up to the blood vessels of the neck, where dye is injected to highlight any areas of blockage.
Heart testing	An electrocardiogram (ECG) is performed in most people who are thought to be having a stroke.
	Because many people with ischemic strokes also have coronary artery disease, there may be a lack of blood flow (called "ischemia") in the heart during the stroke.
	Other heart testing may also be recommended, such as an echocardiogram.
	This test uses sound waves to examine the heart and the aorta (the main artery that supplies the whole body).
	In some people with embolic strokes, the heart or the aorta is the source of the blood clot that led to the stroke.

Treatment

Ensure adequate respiratory and cardiac support and determine quickly from CT scan whether the lesion is ischemic or hemorrhagic.
Evaluate ischemic stroke patients presenting within hours of symptom onset for reperfusion therapy.
Elevated blood pressure (BP) should remain untreated in the acute period (first 7 days) after ischemic stroke to avoid decreasing cerebral blood flow and worsening symptoms.
BP should be lowered if it exceeds 220/120 mm Hg or there is evidence of aortic dissection, acute myocardial infarction (MI), pulmonary edema, or hypertensive encephalopathy.
If BP is treated in the acute phase, short-acting parenteral agents (eg, labetalol, nicardipine, nitroprusside) are preferred.
Assess patients with hemorrhagic stroke to determine whether they are candidates for surgical intervention.
After the hyperacute phase, focus on preventing progressive deficits, minimizing complications, and instituting secondary prevention strategies.

Nonpharmacologic Therapy

Acute ischemic stroke	Surgical decompression is sometimes necessary to reduce intracranial pressure.
	An interprofessional team approach that includes early rehabilitation can reduce long-term disability.
	In secondary prevention, carotid endarterectomy and stenting may be effective in reducing stroke incidence and recurrence in appropriate patients.
Hemorrhagic stroke	In SAH, surgical intervention to clip or ablate the vascular abnormality reduces mortality from rebleeding.
	After primary intracerebral hemorrhage, surgical evacuation may be beneficial in some situations.
	Insertion of an external ventricular drain with monitoring of intracranial pressure is commonly performed in these patients.

Pharmacologic Therapy of Ischemic Stroke

Alteplase	(t-PA, tissue plasminogen activator) initiated within 4.5 hours of symptom onset reduces disability from ischemic stroke.
	Adherence to a strict protocol is essential to achieving positive outcomes:
	(1) activate the stroke team;
	(2) treat as early as possible within 4.5 hours of onset;
	(3) obtain CT scan to rule out hemorrhage;
	(4) meet all inclusion and no exclusion criteria;
	(5) administer alteplase 0.9 mg/kg (maximum 90 mg) infused IV over 1 hour, with 10% given as initial bolus over 1 minute;
	(6) avoid anticoagulant and antiplatelet therapy for 24 hours;
	(7) monitor the patient closely for elevated BP, response, and hemorrhage.
Aspirin	160 to 325 mg/day started between 24 and 48 hours after completion of alteplase also reduces long-term death and disability.

Drugs Used For Ischemic Stroke	
Drug	**Alteplase *(Activase)*** Injection
	Cathflo Activase (single-use 2 mg vial) used to restore function of potentially clotted central lines and devices
Dosing	**0.9 mg/kg (maximum dose 90 mg)**; give 10% of the dose as a bolus over 1 minute then infuse the remainder over 60 minutes
	Must **rule out** an **intracranial hemorrhage before use**
Contraindications	**Active internal bleeding** or bleeding diathesis (predisposition)
	History of recent stroke (within the past 3 months)
	Severe uncontrolled hypertension (BP > 185/110 mmHg)
	Any prior intracranial hemorrhage (ICH)
	Other conditions that increase bleeding risk: recent intracranial or intraspinal surgery, trauma (within the past 3 months), intracranial neoplasm, arteriovenous malformation or aneurysm
	Labs that increase bleeding risk: **INR > 1.7**, aPTT > 40 seconds, platelet count < 100,000/mm^3
	Treatment dose of **LMWH** (within the previous 24 hours), use of a **direct thrombin inhibitor or direct factor Xa inhibitor** (within the previous 48 hours)
	Blood glucose < 50 mg/dL
Side Effects	**Major bleeding (i.e., ICH)**
Monitoring	**Hgb, Hct, s/sx of bleeding**
	Neurological assessments and BP
	Head CT 24 hrs after treatment, before starting anticoagulants or antiplatelet drugs
Notes	**Contraindications** and **dosing differ** when used for **ACS** and pulmonary embolism, due to a higher risk of hemorrhagic conversion (i.e., brain bleed) in stroke
	If severe headache, acute hypertension, nausea, vomiting or worsening neurological function occurs, discontinue the infusion and obtain an emergent head CT
	The abbreviation "tPa" is prone to errors; not recommended by ISMP, but used commonly

Secondary Prevention of Ischemic Stroke	
Antiplatelets	Use antiplatelet therapy in noncardioembolic stroke.
	Aspirin, clopidogrel, and extended-release dipyridamole plus aspirin are all first-line agents
	Cilostazol is also a first-line agent, but its use has been limited by lack of data.

Secondary Prevention of Ischemic Stroke (cont)	
	Limit the combination of clopidogrel and ASA to select patients with a recent MI history or intracranial stenosis and only with ultra–low-dose ASA to minimize bleeding risk.
Anticoagulants	Oral anticoagulation is recommended for atrial fibrillation and a presumed cardiac source of embolism.
	A vitamin K antagonist (warfarin) is first line, but other oral anticoagulants (eg, dabigatran) may be recommended for some patients.
Antihypertensives	Treatment of elevated BP after ischemic stroke reduces risk of stroke recurrence.
	Treatment guidelines recommend BP reduction in patients with stroke or TIA after the acute period (first 7 days).
Statins	Reduce risk of stroke by approximately 30% in patients with coronary artery disease and elevated plasma lipids.
	Treat ischemic stroke patients, regardless of baseline cholesterol, with high-intensity statin therapy to achieve a reduction of at least 50% in LDL for secondary stroke prevention.
Low-molecular-weight heparin or low-dose subcutaneous unfractionated heparin	(5000 units three times daily) is recommended for prevention of deep vein thrombosis in hospitalized patients with decreased mobility due to stroke and should be used in all but the most minor strokes.

Antiplatelet Drugs	
Drug	**Aspirin (*Bayer, Buffferin, Ecotrin***, *Ascriptin, Durlaza*, others)
	+ omeprazole (*Yosprala*)
	OTC: tablet, chewable tablet, enteric coated tablet, suppository
	Rx: **ER** capsule (*Durlaza*), **delayed-release** tablet (*Yosprala*)
Dosing	**50-325 mg daily**
	Yosprala: 81 mg/40mg or 325 mg/40 mg daily
	Do not crush enteric-coated, delayed-release or ER products
Contra-indica-tions	NSAID or **salicylate allergy; children and teenagers** with viral infection due to risk of **Reye's syndrome** (symptoms include somnol-ence, N/V, confusion); rhinitis, nasal polyps or asthma (due to risk of urticaria, angioedema or bronchospasm)
Warnings	**Bleeding** [including GI bleed/ulceration, increase risk with heavy alcohol use or other drugs with bleeding risk (i.e., NSAIDs, antico-agulants, other antiplatelets)], **tinnitus** (salicylate **overdose**)

Antiplatelet Drugs (cont)	
Side Effects	**Dyspepsia, heartburn, bleeding**, nausea
Monitoring	Symptoms of bleeding, bruising
Notes	To decrease nausea, use EC or buffered product or take with food
	PPIs may be **used to protect the gut** with chronic NSAID use; **consider the risks** from chronic PPI use (**decrease bone density, increase infection risk**)
	Yosprala is indicated for those at risk of developing aspirin-associated gastric ulcers
Drug	**Extended-release dipyridamole/aspirin (*Aggrenox*)**
	Capsule
Dosing	200 mg/25 mg BID
	If intolerable headache: 200 mg/25 mg QHS (+ low-dose aspirin daily in the morning), then resume BID dosing within 1 week
Contra-indica-tions	As above for aspirin component plus:
Warnings	**Hypotension** and chest pain (in patients with coronary artery disease) can occur due to the vasodilatory effects of dipyridamole
Side Effects	**Headache**
Notes	**Not interchangeable** with the individual components of aspirin and dipyridamole
	Amount of aspirin provided is not adequate for prevention of cardiac events (i.e., MI)
Drug	**Clopidrogel (*Plavix*)**
	Tablet
	Indicated for ACS, recent MI, stroke and PAD
Dosing	**75 mg daily**
Boxed Warnings	Clopidogrel is a **prodrug**. Effectiveness depends on the **conversion** to an **active metabolite**, mainly by **CYP450 2C19**. Poor metabolizers of CYP2C19 exhibit higher cardiovascular events than patients with normal CYP2C19 function. **Tests to check CYP2C19 genotype** can be used as an aid in determining a therapeutic strategy. Consider alternative treatments in patients identified as CYP2C19 poor metabolizers.
Contra-indica-tions	Active **serious bleeding** (i.e., GI bleed, intracranial hemorrhage)
Warnings	**Bleeding risk: stop** 5 days **prior to elective surgery, do not use with omeprazole** or **esomeprazole**, premature discontinuation (increase risk of thrombosis), thrombotic thrombocytopenic purpura (**TTP**)
Side Effects	Generally well tolerated, unless **bleeding** occurs
Monitoring	Symptoms of bleeding, Hgb/Hct as necessary
Notes	Drug of choice in stroke/TIA if a **contraindication or allergy to aspirin**; do not use ini combination with aspirin long-term for stroke prevention

Treatment of Modifiable Risk Factors	
Hypertension	Blood pressure lowering treatment is often initiated after the first several days following a stroke.
	Thiazide diuretics, ACE inhibitors and ARBs have the best evidence for stroke risk reduction.
	A **goal BP < 130/80 mmHg** is recommended for most patients.
	Lifestyle modifications are an important part of hypertension management.
Dyslipidemia	Treat with a **high-intensity statin**, with atorvastatin 80 mg/day being preferred.
	In patients at higher risk, consider adding ezetimibe or a PCSK9 inhibitor to achieve an LDL < 70 mg/dL.
Diabetes	Patients with no established history should be screened for diabetesin the post-stroke period; an A1C is the preferred test.
	Treat diabetes according to the most recent ADA guidelines.
Atrial Fibrillation	**Cardioembolic stroke** due to **atrial fibrillation** requires **anticoagulation** to prevent future strokes.
Lifestyle Modifications	Patients should be screened for obesity and counseled on lifestyle modifications for hypertension and cardiovascular risk reduction (i.e., **smoking cessation**, diet, exercise, weight loss).
	Nutrition **Sodium restriction** to < 2.4 grams/day, or < 1.5 grams/day for greater**blood pressure reduction** and a Mediterranean-type **diet** (emphasizing vegetables, fruits, whole grains, fish, poultry, legumes, nuts and olive oil) is recommended.

Treatment of Modifiable Risk Factors (cont)

Physical activity	If capable, patients should engage in moderate-intensity exercise (at least 10 minutes four days per week) and avoid long periods of sitting.
Weight reduction	Maintain a **BMI 18.5 - 24.9 kg/m^2** and a **waist circumference < 35 inches for women** and **< 40 inches for men**.
Alcohol intake	Limit to < 2 drinks/day for males and < 1 drink/day for females.

Pharmacologic Therapy of Hemorrhagic Stroke

There are no standard pharmacologic strategies for treating intracerebral hemorrhage.

Follow medical guidelines for managing BP, increased intracranial pressure, and other medical complications in acutely ill patients in neurointensive care units.

SAH due to aneurysm rupture is often associated with delayed cerebral ischemia in the 2 weeks after the bleeding episode.

Vasospasm of the cerebral vasculature is thought to be responsible for the delayed ischemia and occurs between 3 and 21 days after the bleed.

The calcium channel blocker nimodipine 60 mg every 4 hours for 21 days, along with maintenance of intravascular volume with pressor therapy, is recommended to reduce the incidence and severity of neurologic deficits resulting from delayed ischemia.

Drugs Used For Hemorrhagic Stroke

Drug	Mannitol (*Osmitrol, Resectisol*)
	Injection
Dosing	5%, 10%, 15%, 20%, 25%
	Mannitol 20%: 0.25-1 g/kg/dose IV Q6-8H PRN
Contra-indications	Severe **renal disease** (anuria), severe hypovolemia, pulmonary edema or congestion, active intracranial bleed (except during craniotomy)
Warnings	CNS toxicity (can accumulate in the brain, causing rebound increases in ICP, if used for long periods of time as a continuous infusion; intermittent boluses preferred), extravasation (vesicant), nephrotoxicity, fluid and electrolyte imbalances (i.e., dehydration, hyperosmolar-induced hyperkalemia, acidosis, increase osmolar gap)
Side Effects	Dehydration, headache, lethargy, increase or decrease BP
Monitoring	Renal function, daily fluid intake and output, serum electrolytes, serum and urine osmolality, ICP, CPP
Notes	Maintain serum omlolality < 300-320 mOsm/kg
	Inspect for crystals before administering; if crystals are present, warm the solution to redissolve
	Use a **filter for administration**

Drug	Nimodipine (*Nymalize*)
	Capsule, oral solution

Drugs Used For Hemorrhagic Stroke (cont)	
Dosing	60 mg PO Q4H for 21 days
	Start within 96 hours of SAH onset
	Swallow capsules whole; administer on an empty stomach, at least 1 hour before or 2 hours after meals
	Cirrhosis: 30 mg PO Q4H for 21 days (closely monitor)
Boxed Warnings	**Do not administer** nimodipine **IV** or by other parenteral routes; **death and serious life-threatening adverse events** have occurred (including cardiac arrest, cardiovascular collapse, hypotension and bradycardia) when the **contents of nimodipine capsules** have been inadvertently **injected parenterally**
Contra-indica-tions	Increase risk of significant hypotension when used in combination with strong inhibitors of CYP3A4
Side Effects	**Hypotension**
Monitoring	CPP, ICP, BP, HR, neurological checks
Notes	**If capsules cannot be swallowed**, contents may be **withdrawn with a parenteral syringe**, then **transferred to an oral syringe** that cannot accept a needle and that can only administer medication orally or via nasogastric tube; **label oral syringes "For Oral Use Only" or "Not for IV Use"; the medication should be drawn up in the pharmacy to reduce medication errors