ISCHEMIC STROKE AND BRAIN HEMORRAGE

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Brain Stroke: Advances in Epidemiology, Management, and Recovery

Stroke Epidemiology

Key Points:
•**Incidence and Prevalence:** 15 million people suffer strokes annually; 5 million are permanently disabled.
•**Mortality:** Second leading cause of death globally.
•**Regional Variations:** Higher incidence in low- and middle-income countries.
•**Risk Factors:** Hypertension, diabetes, obesity, smoking, and atrial fibrillation.

Global, regional, and national burden of stroke and its risk factors, 1990–2021

Published September 18, 2024, in *The Lancet Neurology*

Pathophysiology of Stroke

Ischemic stroke

Overview:
•Caused by the obstruction of blood flow to the brain due to a thrombus or embolus.
•Accounts for approximately **87% of all strokes** globally.
Pathophysiology:
•**Thrombotic Stroke:** Formation of a clot in one of the cerebral arteries, often due to atherosclerosis.
•**Embolic Stroke:** A clot or debris forms elsewhere in the body (commonly the heart) and travels to the brain.

Hemorrhagic Stroke

Overview:
•Caused by bleeding into the brain tissue (intracerebral) or the surrounding space (subarachnoid) due to vessel rupture.
Pathophysiology:
•**Intracerebral Hemorrhage:** Rupture of small arteries, often due to uncontrolled hypertension or trauma.
•**Subarachnoid Hemorrhage:** Bleeding into the space between the brain and thin tissues covering the brain, often due to aneurysm rupture.

Stroke Classification

Types of Strokes and Clinical Presentation

Key Points:

•**Ischemic Stroke:** Thrombotic, embolic, or lacunar infarcts.
•**Hemorrhagic Stroke:** Hypertensive or aneurysmal rupture.
•**Transient Ischemic Attack (TIA):** Warning signs, resolving within 24 hours.

Acute Stroke Management

Emergency Care and Diagnosis

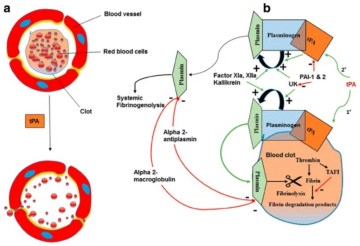
Key Points:

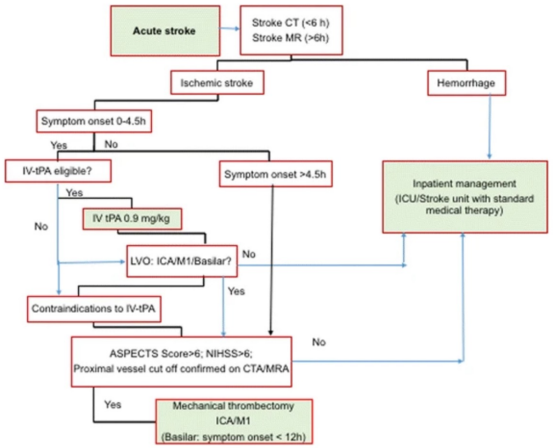
•**Early Recognition (FAST):** Face drooping, Arm weakness, Speech difficulties, Time to act.

•**Imaging:** Non-contrast CT to rule out hemorrhage; MRI for ischemia.

•**Reperfusion Therapy:**

- tPA for ischemic stroke within 4.5 hours.
- Mechanical thrombectomy within 6-24 hours.





tPA Indications

Timing: Administered within **4.5 hours** from the onset of stroke symptoms.

Eligibility:

Clinical diagnosis of ischemic stroke with measurable neurological deficit.	Imaging (CT/MRI) confirms absence of hemorrhage or extensive infarction.	Age ≥18 years (considerations for elderly depend on clinical judgment).

Key Objective: Restoration of blood flow to ischemic brain tissue and prevention of infarction expansion.

Mechanism of Action

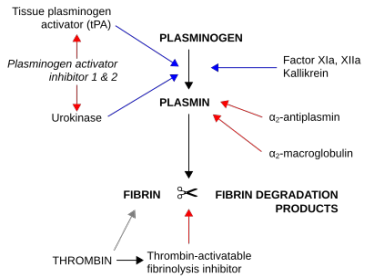
•**Primary Function:**

- Acts as a **plasminogen activator**, converting plasminogen to plasmin.
- Plasmin breaks down fibrin, dissolving thrombi within cerebral vessels.

•**Site of Action:** Clots in cerebral arteries causing ischemia.

•**Effect:** Rapid reperfusion of ischemic brain tissue, reducing damage and improving outcomes.

Visual: Diagram showing tPA binding to fibrin in a thrombus and converting plasminogen to plasmin, leading to clot dissolution.



https://www.youtube.com/watch?v=bc2_sQ3kK6U

Contraindications

•**Absolute Contraindications:**

- Intracranial hemorrhage (confirmed by imaging).
- Recent head trauma or intracranial surgery (within 3 months).
- Known bleeding disorders or active internal bleeding.
- Severe uncontrolled hypertension (SBP >185 mmHg or DBP >110 mmHg).
- Stroke or major trauma within the past 3 months.
- Platelet count <100,000/mm^3 or INR >1.7.

•**Relative Contraindications (case-specific):**

- Seizure at stroke onset with residual neurological impairments.
- Recent gastrointestinal or urinary tract hemorrhage.
- Recent use of anticoagulants with elevated lab markers.

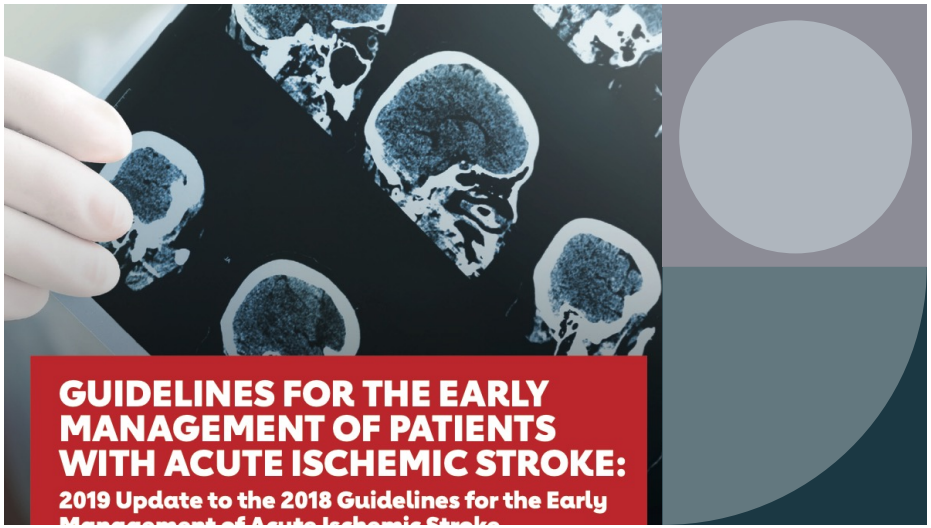
AHA/ASA Guideline

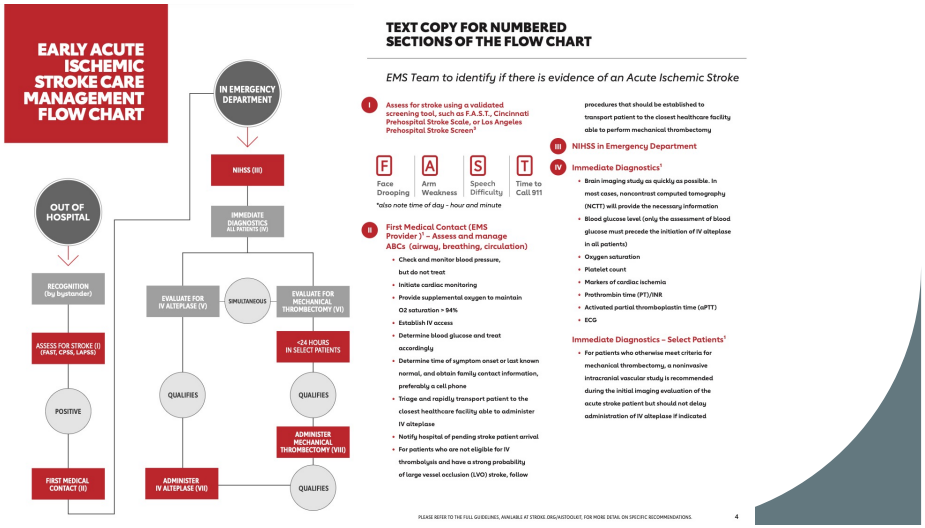
2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Updated 2019

- IV alteplase within 4.5 hours of stroke onset remains the standard of care for most ischemic stroke patients, providing the opportunity for more favorable outcomes. Patients eligible for IV alteplase should receive it, even if mechanical thrombectomy is being considered.
- Mechanical thrombectomy evaluation and treatment should occur as rapidly as possible to ensure the treatment of as many eligible patients as possible.
- Mechanical thrombectomy is recommended within 16 hours and reasonable up to 24 hours in selected patients with AIS with large vessel occlusion in the anterior circulation greater than 6 hours from symptom onset who meet certain advanced imaging criteria.
- The benefits of both IV alteplase and mechanical thrombectomy are time dependent. The earlier the treatment within the time window, the greater the benefit to patients.





V IV alteplase eligibility[1]

Indications (Class I Recommendations — Recommended Care)

- If within 3 hours of onset and:
  - < 18 years of age
  - Severe stroke
  - Mild but disabling stroke
- If 3–4.5 hours from onset, 18–80 years of age, and:
  - Without a history of both diabetes mellitus and prior stroke
  - NIHSS score <25
  - Not taking any OACs
  - Without imaging evidence of ischemic injury involving more than one third of the MCA territory
- If BP can be lowered safely and maintained < 185/110 mm Hg
- With blood glucose > 50 mg/dL
- With mild to moderate early ischemic changes on NCCT
- With antiplatelet drug monotherapy or combination therapy
- With end stage renal disease with normal aPTT

Additional Recommendations (Class IIa and IIb).

Situations requiring individual patient risk benefit assessment for which administration of IV alteplase may be considered

- If 3–4.5 hours from onset
  - >80 years of age (COR IIa)
  - Both prior stroke and diabetes mellitus (COR IIb)
  - Mild but disabling stroke (COR IIb)
  - NIHSS > 25 (COR IIb)
- Pre-existing disability (mRS ≥ 2 COR IIb)
- Pre-existing dementia (COR IIb)
- Moderate to severe ischemic stroke with early improvement but remain moderately impaired and potentially disabled (COR IIa)
- Seizure at the time of onset, if evidence suggests that residual impairments are secondary to stroke (COR IIa)
- Initial blood glucose levels <50 or >400 mg/dL that are subsequently normalized (COR IIb)
- Clinical history of potential bleeding diathesis or coagulopathy (COR IIb)
- History of warfarin use and an INR ≤1.7 or a PT <15 s (COR IIb)
- Lumbar dural puncture in the preceding 7 days (COR IIb)
- Arterial puncture of a noncompressible blood vessel in the preceding 7 days (COR IIb)
- Recent major trauma (within 14 days) not involving the head (COR IIb)
- Major surgery in the preceding 14 days (COR IIb)
- History of gastrointestinal or genitourinary bleeding (>21 days) (COR IIb)
- Women who are menstruating and do not have a history of menorrhagia (COR IIa)
- Women with recent or active history of menorrhagia without clinically significant anemia or hypotension (COR IIb)
- Recent or active vaginal bleeding causing clinically significant anemia (after emergency consultation with a gynecologist) (COR IIa)
- Extracranial cervical arterial dissection (COR IIa)
- Intracranial arterial dissection (COR IIb)
- Small or moderately-sized unruptured and unsecured intracranial aneurysm (COR IIa)
- Giant unruptured and unsecured intracranial aneurysm (COR IIb)
- Unruptured and untreated intracranial vascular malformation, if high likelihood of morbidity and mortality outweigh the anticipated risk of ICH (COR IIb)
- Small number of cerebral microbleeds (CMBs) demonstrated on MRI (COR IIa)
- Previously high burden of CMBs (>10) demonstrated on MRI if there is potential for substantial benefit (COR IIb)
- Extra-axial intracranial neoplasm (COR IIb)
- Concurrent acute MI, followed by percutaneous coronary angioplasty and stenting if indicated (COR IIa)
- MI in the past 3 months: Non-STEMI or STEMI involving the right or inferior myocardium. (COR IIa)
- MI in the past 3 months: STEMI involving the left anterior myocardium (COR IIb)
- Major AIS likely to produce severe disability and acute pericarditis (COR IIb), after urgent consultation with cardiologist
- Moderate AIS likely to produce mild disability and acute pericarditis (COR IIb)
- Major or moderate AIS likely to produce severe or mild disability and known left atrial or ventricular thrombus (COR IIb)
- Major AIS likely to produce severe disability and cardiac myxoma or papillary fibroelastoma (COR IIb)
- AIS due to complications of cardiac or cerebral angiographic procedures (COR IIa)
- Systemic malignancy and >6 month life expectancy in the absence of other contraindications (COR IIb)
- Pregnancy, when anticipated benefits of treating severe or moderate stroke outweigh increased risk of uterine bleeding (COR IIb)
- Early postpartum period (<14 days after delivery) (COR IIb)
- History of diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions but potential increased risk of visual loss should be weighed against anticipated benefits (COR IIa)
- Sickle cell disease in adults (COR IIa)
- Hyperdense middle cerebral artery sign (COR IIa)
- Illicit drug use (COR IIa)
- Stroke mimics (COR IIa)

Contraindications (Class III — Harm)

- CT reveals an acute intracranial hemorrhage
- CT brain imaging exhibits extensive regions of clear hypoattenuation
- Prior ischemic stroke within 3 months
- Recent severe head trauma within 3 months
- Acute head trauma (Posttraumatic infarction that occurs during the acute in-hospital phase)
- Intracranial/spinal surgery within the prior 3 months
- History of intracranial hemorrhage
- Symptoms and signs most consistent with an subarachnoid hemorrhage
- Structural GI malignancy
- Gastrointestinal bleeding event within 21 days
- Platelets <100 000/mm3
- INR >1.7
- aPTT >40 s
- PT >15 s
- Treatment dose of LMWH within the previous 24 hours
- Taking direct thrombin inhibitors or direct factor Xa inhibitors unless laboratory tests are normal or the patient has not received a dose of these agents for >48 hours (assuming normal renal metabolizing function)
- Symptoms consistent with infective endocarditis
- Known or suspected to be associated with aortic arch dissection
- Intra-axial intracranial neoplasm

Contraindications (Class III — No Benefit)

- Otherwise eligible patients with mild but nondisabling stroke

VI Evaluate for Mechanical Thrombectomy (< 24 hours)[1]

- Evaluation for IV alteplase and evaluation for mechanical thrombectomy happens simultaneously
- Within 6 hours:
  - Pretrokw mRS score 0–1
  - Causative occlusion of the ICA or proximal MCA (M1)
  - Age >18 years
  - NIHSS score of >6
  - ASPECTS of >6
  - Within 6–24 hours
  - Causative occlusion of the ICA or M1
  - Meets eligibility criteria for DAWN or DEFUSE3 trials

VII Administer IV alteplase[1]

- Infuse 0.9 mg/kg (maximum dose 90 mg) over 60 minutes, with 10% of the dose given as a bolus over 1 minute
- IV alteplase remains the recommended therapy, but it may be reasonable to choose tenecteplase (single IV bolus of 0.25–mg/kg, maximum 25 mg) over IV alteplase in patients without contraindications for IV fibrinolysis who are also eligible to undergo mechanical thrombectomy
- Admit the patient to an intensive care or stroke unit for monitoring for at least 24 hours
- If the patient develops severe headache, acute hypertension, nausea, or vomiting or has a worsening neurological examination, discontinue the infusion (if IV alteplase is being administered) and obtain emergent CT scan
- Measure BP and perform neurological assessments every 15 minutes during and after IV alteplase infusion for 2 hours, then every 30 minutes for 6 hours, then every hour until 24 hours after IV alteplase treatment
- Increase the frequency of BP measurements if systolic BP is >180 mm Hg or if diastolic BP is >105 mm Hg. Administer antihypertensive medications to maintain blood pressure at or below these levels
- Abciximab should not be administered concurrently with IV alteplase
- IV aspirin should not be given within 90 minutes after the start of IV alteplase
- The efficacy of IV glycoprotein IIb/IIIa inhibitors tirofiban and eptifibatide coadministered with IV alteplase is not well established (COR IIb)
- Delay placement of nasogastric tubes, indwelling bladder catheters, or intra-arterial pressure catheters if the patient can be safely managed without them
- Obtain a follow-up CT or MRI scan at 24 hours after IV alteplase before starting anticoagulants or antiplatelet agents

VIII Administer Mechanical Thrombectomy[1]

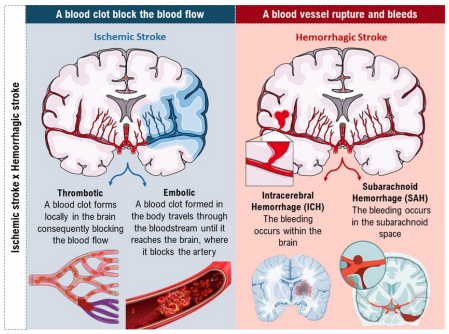
- Stent retrievers remain the recommended choice of device for mechanical thrombectomy. The use of other devices as first line may be reasonable in some circumstances. The use of a proximal balloon guide catheter or a large-bore distal-access catheter, rather than a cervical guide catheter alone, in conjunction with stent retrievers may be beneficial
- In patients who undergo mechanical thrombectomy, it is reasonable to maintain blood pressure ≤180/105 during and for 24 hours after the procedure

Stroke Treatment Strategies

Title: From Acute Care to Long-Term Management

Key Points:

- **Ischemic Stroke:** Antithrombotic therapy, statins, and BP control.
- **Hemorrhagic Stroke:** Blood pressure management, surgical intervention for large hematomas.
- **Neuroprotective Strategies:** Emerging therapies targeting oxidative stress and inflammation.

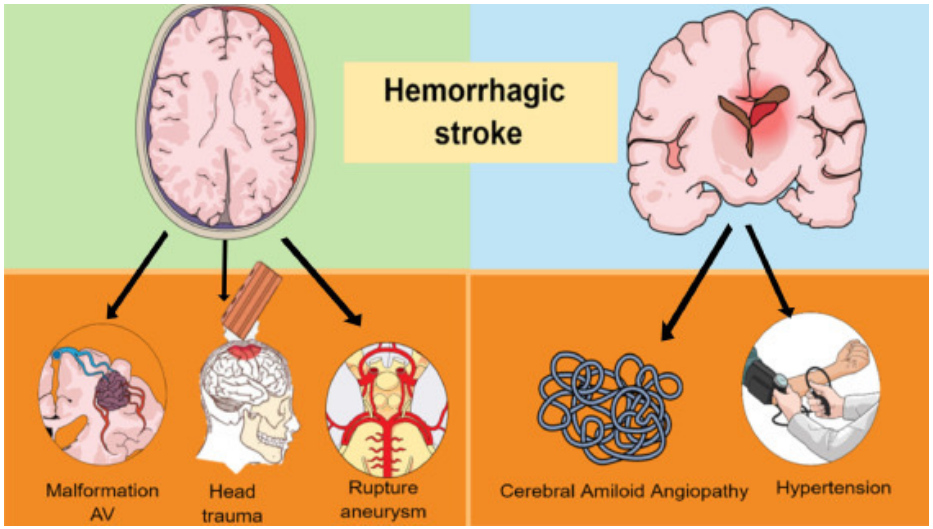


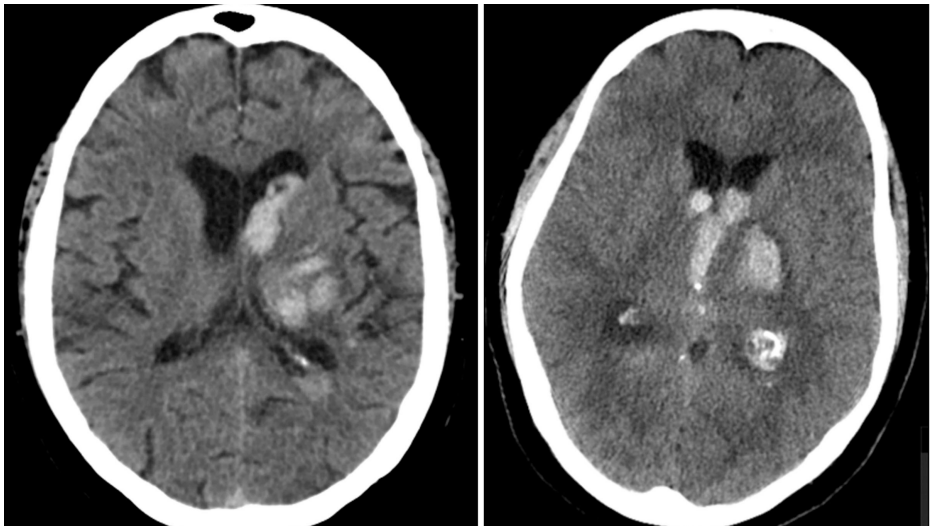
Overview of Hemorrhagic Stroke

Hemorrhagic stroke occurs when a blood vessel in the brain ruptures, leading to bleeding in or around the brain tissue. This can result in increased intracranial pressure (ICP), tissue ischemia, and direct neuronal damage.

Types of Hemorrhagic Stroke:

1. **Intracerebral Hemorrhage (ICH):** Bleeding directly into the brain parenchyma.
2. **Subarachnoid Hemorrhage (SAH):** Bleeding into the space between the brain and the arachnoid membrane, often due to aneurysm rupture.





Management Strategies

1. Blood Pressure Management

Rationale:
Elevated blood pressure is common in hemorrhagic stroke and can exacerbate bleeding or hematoma expansion. Aggressive but controlled BP management can reduce re-bleeding and limit secondary brain injury.

Key Points:

•Target BP Goals:
- For ICH: Maintain systolic blood pressure (SBP) between 140–160 mmHg.
- For SAH: Prevent vasospasm with BP maintenance tailored to individual patient needs.

•Medications Used:
- **IV Antihypertensives:** Labetalol, nicardipine, and clevidipine are first-line agents due to their rapid onset and titratability.
- **Avoidance:** Excessive lowering of BP (<120 mmHg SBP) can lead to ischemic injury in penumbral areas.

BP goals	Therapeutic Options*
Target for patients otherwise eligible for reperfusion therapy (except for high BP) is to reduce BP to <185/110 mm Hg	- **Labetalol** 10–20 mg IV over 1–2 min, may repeat 1 time or - **Nicardipine** 5 mg/h IV, titrate up by 2.5 mg/h every 5–15 min, maximum 15 mg/h; when desired BP reached, adjust to maintain to proper BP limits, or - **Clevidipine** 1–2 mg/h IV, titrate by doubling the dose every 2–5 min until desired BP reached; maximum 21mg/h - If BP is not maintained ≤185/110 mm Hg, do **not** administer alteplase
Target during and after alteplase or other emergency reperfusion therapy is to maintain BP ≤180/105 mm Hg	Monitor BP every 15 min for 2 h from the start of alteplase therapy, then every 30 min for 6 h, and then every hour for 16 h
If SBP >180–230 mmHg or DBP >105–120 mm Hg	- **Labetalol** 10 mg IV followed by continuous IV infusion 2–8 mg/min, or - **Nicardipine** 5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5–15 min, maximum 15 mg/h, or - **Clevidipine** 1–2 mg/h IV, titrate by doubling the dose every 2–5 min until desired BP reached; maximum 21mg/h - If BP not controlled or DBP >140 mm Hg, may consider IV **sodium nitroprusside.**

Figure 18. Blood pressure target and therapeutic options for patients with acute ischemic stroke. SBP, systolic blood pressure; DBP, diastolic blood pressure. Adapted from the AHA/ASA 2019 update to 2018 guidelines for the early management of acute ischemic stroke.
* Different treatment options may be appropriate in patients who have comorbid conditions that may benefit from rapid reductions in BP such as acute coronary event, acute heart failure, aortic dissection, or preeclampsia/eclampsia.

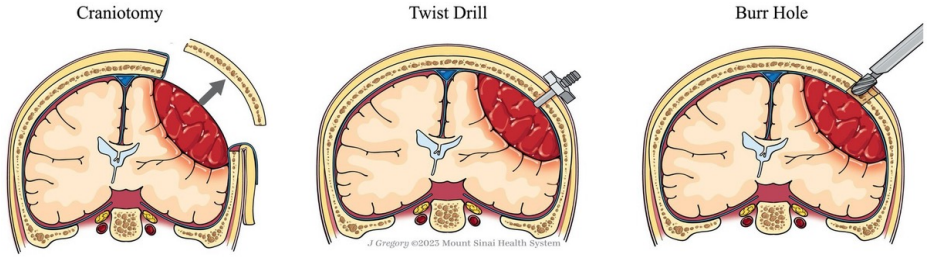
Surgical Intervention

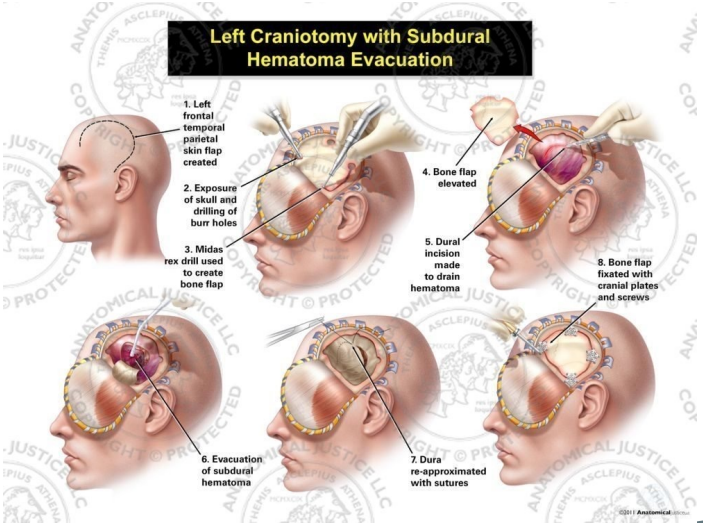
Indications for Surgery:

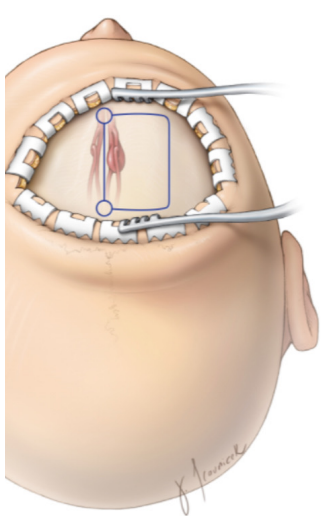
•**ICH:**
- Significant hematomas causing mass effect or midline shift.
- Hematomas >30 mL in size, especially in young patients.
- Brainstem compression or impending herniation.

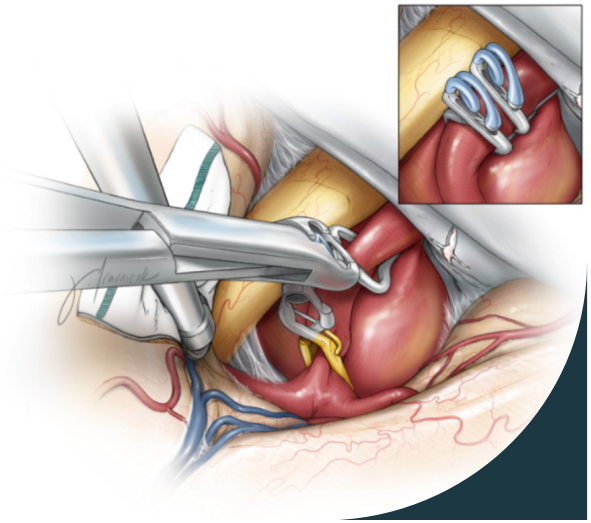
•**SAH:**
- Securing ruptured aneurysms (clipping or endovascular coiling).
- Decompressive craniectomy for refractory intracranial pressure.

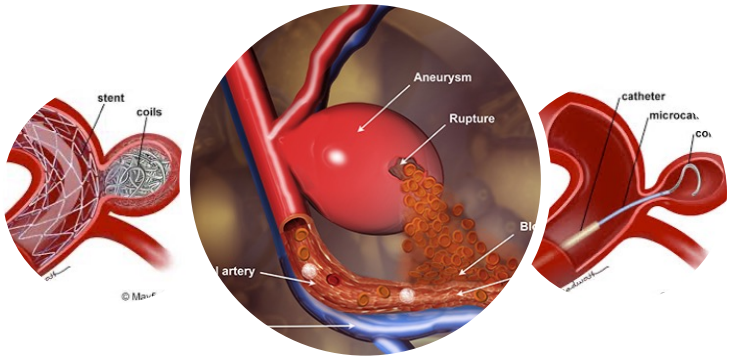
Surgical Techniques:
•**Craniotomy:** Direct removal of hematoma and repair of ruptured vessels.
•**Endovascular Coiling:** Minimally invasive procedure for aneurysm repair in SAH.
•**Ventriculostomy:** For hydrocephalus management, especially in SAH.











Intracranial Pressure (ICP) Management

Monitoring: Via ICP monitors for patients with high risk of elevated ICP.

•Therapeutic Measures:

- Elevation of the head of the bed to 30 degrees.
- Osmotic agents like mannitol or hypertonic saline.
- Sedation and neuromuscular blockade in refractory cases.

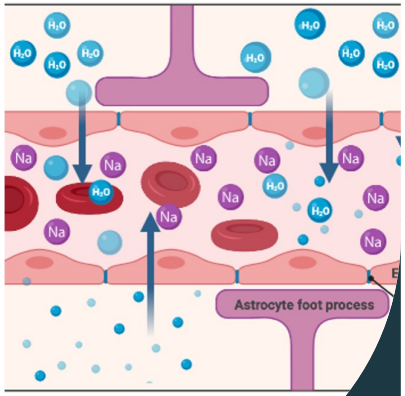
Mechanism of Action

•Mannitol:

- An osmotic diuretic that reduces ICP by creating an osmotic gradient across the blood-brain barrier (BBB).
- Pulls water out of the brain parenchyma into the vasculature, reducing brain volume.
- Enhances cerebral blood flow and improves microcirculation by reducing blood viscosity.

•Hypertonic Saline (HTS):

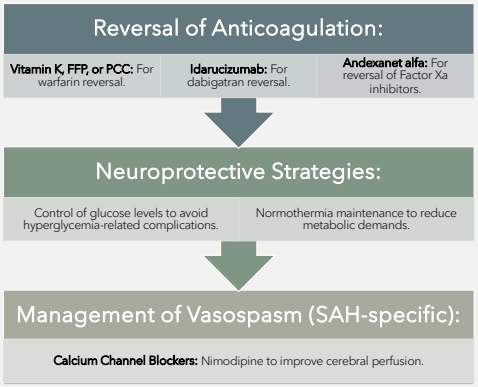
- Increases serum osmolality, drawing water out of brain tissue into the intravascular compartment.
- Helps restore circulating volume and improves cerebral perfusion pressure (CPP).
- Stabilizes cell membranes and reduces inflammation.



Osmolarity and Dose

Parameter	Mannitol	Hypertonic Saline
Osmolarity	300-320 mOsm/L	Depends on concentration (3%, 7.5%, 23.4%). 23.4% has very high osmolarity.
Common Doses	0.25-1 g/kg IV every 4-6 hours	3%: 250 mL bolus or continuous infusion; 23.4%: 30 mL bolus in emergencies.

Additional Therapies for Hemorrhagic Stroke



Calcium Channel Blockers: Nimodipine in Stroke Management
Role of Nimodipine

Nimodipine, a dihydropyridine calcium channel blocker, is specifically indicated for the prevention and treatment of cerebral vasospasm, a common and severe complication of **subarachnoid hemorrhage (SAH)**. It works by improving cerebral perfusion and reducing the risk of delayed ischemic neurological deficits.

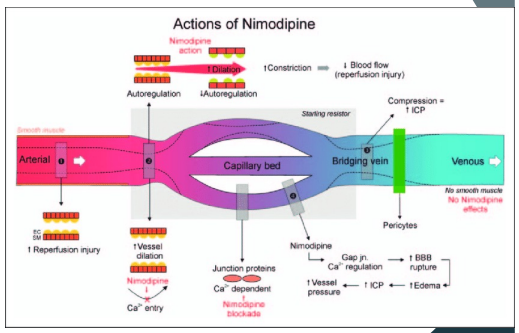
Mechanism of Action

•Selective Vasodilation:

- Nimodipine preferentially dilates cerebral blood vessels by inhibiting the influx of calcium ions into vascular smooth muscle cells.
- It reduces arterial spasm in the brain, maintaining blood flow to ischemic but viable tissue.

•Neuroprotective Effects:

- Limits neuronal calcium overload, which is implicated in cell death during ischemic injury.



Dosage and Administration

•**Standard Dosage:**

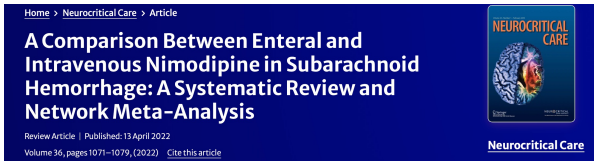
- 60 mg orally every 4 hours for 21 days, starting within 96 hours of the hemorrhagic event.

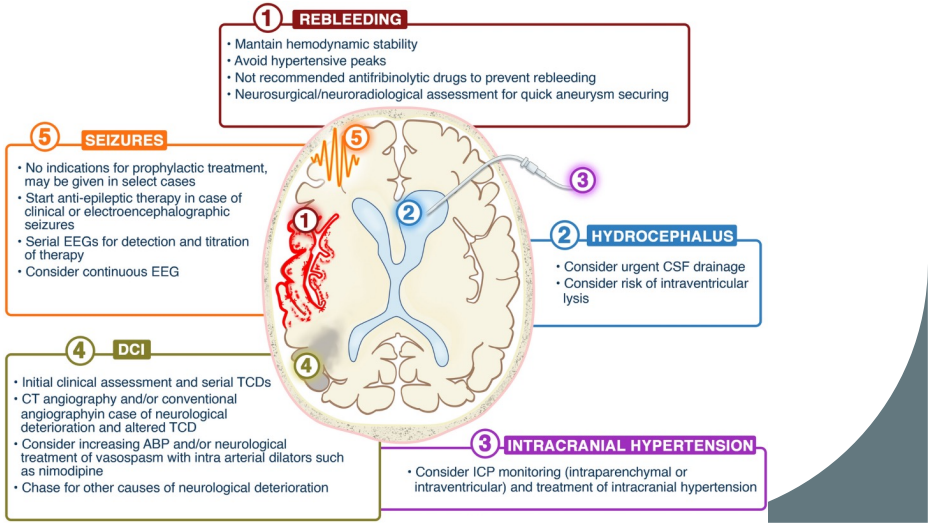
•**Alternative Dosage (for Side Effects):**

- If hypotension occurs, reduce to 30 mg every 2 hours.

•**Route of Administration:**

- Oral or via a nasogastric tube. **Intravenous use is contraindicated** due to the risk of severe hypotension.





Advanced Telemedicine Technique in Stroke Evaluation

Pre-hospital Stroke Evaluation with In-ambulance Telemedicine (PURSUIT)

Key Features:

•Real-time stroke assessments via the In-Touch RP-Xpress telemedicine device.

•Two-way audio-visual communication over 4G/LTE network.

•Remote vascular neurologists perform NIH Stroke Scale (NIHSS) evaluations during patient transport.

•Data encryption ensuring HIPAA compliance.

Advantages:

•Faster triage and treatment initiation.

•Reduced in-hospital assessment time.

•Increased accuracy and reliability of stroke diagnosis.

Stroke. 2014 August ; 45(8): 2342–2347. doi:10.1161/STROKEAHA.114.005193.

Pre-hospital Utility of Rapid Stroke evaluation Using In-ambulance Telemedicine (PURSUIT): A Pilot Feasibility Study

Tzu-Ching Wu, MD[1,*], Claude Nguyen, MD[1], Christy Ankrom, BS[1], Julian Yang, MD[2], David Persse, MD[3], Farhaan Vahidy, MD[1], James C. Grotta, MD[1], and Sean I. Savitz, MD[1]

[1] Department of Neurology, University of Texas-Health Science Center at Houston Houston, TX, USA

Technical Implementation of the PURSUIT System System Components

•**RP-Xpress Device:** Portable, high-resolution camera with zoom and wide field of view.

•**4G LTE Hotspot:** Secure connection for real-time communication.

•**Remote Workstation:** Vascular neurologists assess patients remotely.

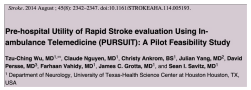
•**EMT Integration:** EMTs assist with patient positioning and data relay.

Reliability Outcomes:

•85% success rate in teleconsultations without major technical issues.

•High inter-rater reliability: Intra-class correlation (ICC) of 0.997 (real-time) and 0.993 (recorded).

•Clinical data accuracy of 96%.



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Clinical Impact and Future Implications

Impact on Stroke Care:

•Average teleconsultation time: 10 minutes.
•Potential to reduce hospital door-to-needle time.
•Facilitates early thrombolysis for ischemic stroke.

Challenges and Future Directions:
•Technical reliability in different environments.
•Training EMTs for enhanced neurological assessments.
•Expansion to live patient trials for further validation.