**Ischemic Stroke**

- Stroke is the 5th leading cause of death in America, and a leading cause of adult disability
- 87% of all strokes are ischemic strokes
- Stroke contributed to reduced mobility in more than half of stroke survivors age 65 and over

**Pathophysiology**

- Normal cerebral blood flow averages 50mL/100g → cerebral autoregulating → constrict and dilate can be impaired by atherosclerosis, chronic hypertension, and acute injury (such as stroke)
  - If reperfusion is established, symptomology will appear transient (TIA).
- **Ischemic penumbra** → tissue that is ischemic but maintains membrane integrity is referred to as the ischemic penumbra which surrounds the infarct core. Progression without perfusion will lead to cell death.
- Ischemia lowers ATP, extracellular potassium, intracellular sodium/water, leading to cell swelling and lysis. Increase in intracellular calcium that follows results in activation of lipases, proteases, and endonucleases, and release of FFA from membrane phospholipids → release of excitatory acids such as glutamate and aspartate perpetuate neuronal damage and accumulation of FFA, arachidonic acid, PG, leukotrienes, and free radicals (2-3 hours on onset of ischemia)
  - Necrotic Pathway
  - Apoptotic Pathway
    - Fever and hyperglycemia hasten destruction
- Three major mechanisms
  - Occlusion of intracranial vessel by embolus arising from a different site
  - In situ thrombosis of an intracranial arteries, usually small arteries that arise
  - Hypoperfusion cause by flow-limiting stenosis of a major extracranial or intracranial vessel
Assessment
- AHA/ASA Guideline 2018, based on existing evidence and new evidence
- National Institutes of Health Stroke Scale (NIHSS) → 13-item test, each item scored from 0-2 or 3 depending on the item, higher number indicates a higher severity

<table>
<thead>
<tr>
<th>No Stroke</th>
<th>Minor Stroke</th>
<th>Moderate Stroke</th>
<th>Moderate/Severe Stroke</th>
<th>Severe Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1-4</td>
<td>5-15</td>
<td>15-20</td>
<td>21-42</td>
</tr>
</tbody>
</table>

- Transient Ischemia Attack → 40% of people will have an actual stroke, symptoms for TIA are the same as for a stroke
  - Usually last less than 1 hour
  - ~10-15% increase of risk of stroke in the first 3 months
  - Resolution within 24 hours without evidence of brain infarction on brain imaging
  - More than >24 hours constitute a stroke, or a brain infarction is demonstrated
  - TIA, stroke risk score based on ABCD2

<table>
<thead>
<tr>
<th>Age ≥ 60 years</th>
<th>Blood Pressure</th>
<th>Clinical Symptoms</th>
<th>Duration &gt; 60 minutes vs 10-59 minutes</th>
<th>Diabetes (oral medications or insulin)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SBP &gt; 140mmHg</td>
<td>Unilateral weakness or speech disturbance</td>
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<td></td>
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<tr>
<td></td>
<td>DBP &gt; 90mmHg</td>
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- Imaging (CT or MRI), chest x-ray, electrocardiogram, urinalysis, complete blood count, erythrocyte sedimentation rate, serum electrolytes, blood urea nitrogen, creatinine, blood glucose, serum lipid profile, prothrombin (PT), partial thromboplastin time (PTT), and blood glucose.

General Recommendations
- Public health leaders should promote programs for educating the public
- Stroke assessment (Using LA prehospital stroke screen or Cincinnati Stroke Scale), initial management, and notification should be sent
- Door to needle (DTN) time goals should establish a primary goal of achieving DTN times < 60 minute or <45 minutes
- Noncontract CT provide information for acute management
  - Vs. MRI, provides very detailed imaging but expensive
  - 50% of patients will be eligible for IV alteplase or mechanical thrombectomy
  - No time → CT or MRI is not recommended to determine a time
  - AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation, obtaining CTP, DW-MRI, or MRI perfusion
- ABC’s
  - Airway should be kept patent, supplemental oxygen to maintain >94%
  - Hypotension and hypovolemia → maintain perfusion. If hypertensive, BP should be carefully lowered <185 mmHg and diastolic < 110mmHg are thresholds indicating need for pharmacologic management
Stroke Topic Discussion 3

- Lower hyperthermia if patient has a temperature of > 38°C

Pharmacotherapy

- **IV alteplase** 0.9mg/kg maximum dose of 90mg over 60 minutes, 10% given as bolus over 1 minute
  - Tissue plasminogen activator (tPA)
  - 3-4.5 hours mild treatment with possible benefits
- **IV alteplase** should not be administer to patient with LMWH within 24 hours
- Maintain blood pressure at <180/105
- Benefit of therapy is time dependent and treatment should be initiated as quickly as possible
  - 0.9 mg/kg maximum 90 mg over 60 minutes with initial 10%, ≥ 18 year of age, time is brain,
  - These patients are still eligible: antiplatelet before stroke is fine, aspirin and clopidogrel is fine, ESRD and

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindication</th>
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<tbody>
<tr>
<td>&lt;3 hour window</td>
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<tr>
<td>- ≥ 18 years</td>
<td>- Unclear time or unwitnessed time of last known baseline</td>
</tr>
<tr>
<td>- Blood pressure of &lt;180/110mmHg</td>
<td>- Acute intracranial hemorrhage or subarachnoid hemorrhage</td>
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<tr>
<td>- CT shows ischemic changes</td>
<td>- Previous stroke within 3 months</td>
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<tr>
<td></td>
<td>- Recent head trauma within 3 months</td>
</tr>
<tr>
<td>≥80 years</td>
<td>- Intracranial/intraspinal surgery within 3 months</td>
</tr>
<tr>
<td>Without history of diabetes and prior stroke</td>
<td>- GI malignancy/GI bleed within 21 days</td>
</tr>
<tr>
<td>NIHSS score ≤ 25</td>
<td>- Coagulopathy (Plts &lt;100k, INR &gt;1.7, aPTT, PT)</td>
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<tr>
<td>Not affecting more than one third of the middle cerebral artery territory</td>
<td>- Thrombin inhibitors/Xa inhibitors (may receive if coagulation labs appear normal or have not taken medication in past 48 hours)</td>
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<td></td>
<td>- Glycoprotein IIB/IIIA receptor inhibitors</td>
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<tr>
<td></td>
<td>- Infective endocarditis</td>
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<td></td>
<td>- Aortic arch dissection</td>
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<td>- Intra-axial intracranial neoplasm</td>
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- When should we stop the infusion?
  - If they develop severe headache, acute hypertension, nausea, or vomiting, or worsening neurologic exam
- BP and neurologic exam every 15 minutes during and after infusion for 2 hours than 30 minutes for 6 hours, then hourly until 24 after IV alteplase (may need more BP monitoring, follow up CT/MRI 24 hours after administration before starting anticoagulants

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Table 6. Options to Treat Arterial Hypertension in Patients With AIS Who Are Candidates for Acute Reperfusion Therapy

<table>
<thead>
<tr>
<th>Class III, LOE C-E0</th>
<th>Patient otherwise eligible for acute reperfusion therapy except that BP is &gt;185/110 mm Hg:</th>
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<tbody>
<tr>
<td></td>
<td>Labetolol 10-20 mg IV over 1-2 min, may repeat 1 time; or</td>
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<tr>
<td></td>
<td>Nicardipine 5 mg IV, titrate up by 2.5 mg/h every 5-15 min, maximum 15 mg/h; when desired BP reached, adjust to maintain proper BP limits; or</td>
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<tr>
<td></td>
<td>Clopidogrel 1-2 mg IV, titrate by doubling the dose every 2-5 min until desired BP reached; maximum 21 mg/h</td>
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<tr>
<td>Other agents (e.g., hydralazine, enalapril) may also be considered</td>
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- If BP is not maintained ≤180/110 mm Hg, do not administer alteplase

Management of BP during and after alteplase or other acute reperfusion therapy 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 systolic BP >190-200 mm Hg or diastolic BP >105-120 mm Hg:
  - Labetolol 10 mg IV followed by continuous IV infusion 2-6 mg/min; or
  - Nicardipine 5 mg IV, titrate up to desired effect by 2.5 mg/h every 5-15 min, maximum 15 mg/h; or
  - Clopidogrel 1-2 mg IV, titrate by doubling the dose every 2-5 min until desired BP reached; maximum 21 mg/h

- If BP not controlled or diastolic BP >140 mm Hg, consider IV sodium nitroprusside

AIS indicates acute ischemic stroke; BP, blood pressure; IV, Intravenous; and LOE, Level of Evidence.

*Different treatment options may be appropriate in patients who have comorbid conditions that may benefit from acute reductions in BP such as acute coronary event, acute heart failure, aortic dissection, or preeclampsia/eclampsia.

Data derived from Jauch et al.*
Alternatives
- Mechanical thrombectomy
- Intraarterial administration of tPA if under 6 hours

Post Stroke
- Aspirin is essential within 48 hours of stroke, reduction in death, clopidogrel, aspirin/extended release dipyridamole. Recommended that clopidogrel or aspirin/dipyridamole be used over aspirin alone
- Anticoagulants are not recommended if patients did not have a cardioembolic stroke
- Statin therapy is warranted, high-intensity
- Blood Pressure management to a goal of <130/80mmHg

Intracranial Hemorrhage, Hemorrhagic Stroke
Pathophysiology
- Bleeding into subdural and epidural spaces is primarily produced by trauma. While subarachnoid results from trauma or a rupture of an intracranial aneurysm or arteriovenous malformation
- Subarachnoid hemorrhage is extravasation of blood into the subarachnoid space vs intracerebral hemorrhage is bleeding into the parenchyma of the brain
- High mortality rate over next month of about 45%  
  - High risk of rebleeding 20% in first 2 weeks, 30% in first month, and 3% per year after that
- Subarachnoid Hemorrhage \( \rightarrow \) rupture of saccular aneurysm
  - Most unruptured intracranial aneurysms are completely asymptomatic
  - Larger aneurysm > 2.5cm in diameter are at a higher risk of bleeding – common terminal internal carotid artery, middle cerebral artery bifurcation, and top of the basilar artery.
  - Small ruptures and leaks of blood into subarachnoid space = sentinel bleeds. Lead to hemorrhage
- 45% most cases, severe headache associated with exertion is main complaint “worst headache of my life”, sudden onset
- Delayed neurologic deficits
  - Rerupture = \( \sim \)30%, rerupture is associated with a 60% mortality rate and poor outcome
  - Hydrocephalus = cause stupor and coma. Mitigated by placement of an external ventricular drain, over few days or weeks – drainage or can clear on own
  - Vasospasms = narrowing arteries of base of the brain causes symptomatic ischemia and infarction in 30% of patients, major cause of delayed morbidity and mortality 4-14 days will appear
    - Direct effects of clotted blood and its breakdown products within subarachnoid
    - Ultrasound to measure velocity of blood flow
    - Hyponatremia \( \rightarrow \) quickly in 2 weeks of SAH

Initial Triage
- Severity score, CT or MRI, glucose management, ABC’s of emergency medicine,
- Blood pressure presenting with 150-220mmHg systolic blood pressure should be decreased to systolic less than 140 mmHg
- Patients presenting with seizures should be treated accordingly with antiseizure drugs
- Treatment of calcium channel antagonist nimodipine 60mg PO every 4 hours improves outcomes
  - Prevention of ischemic injury, rather than reducing risk of vasospasm
  - Symptomatic cerebral vasospasm detrimental effect can be mitigated by increasing cerebral perfusion by raising mean arterial pressure through plasma expansion and IV vasopressors
- Decrease of blood pressure to lower than 140 SBP
  - SBP > 220mmHg should consider aggressive decrease in BP with continuous infusion and frequent BP monitoring
  - SBP 150 – 220mmHg acute lowering to <140 is safe and effective for improving functional outcome

Medical Treatment for ICH
• Underlying antiplatelets, anticoagulants, and coagulation deficiencies
• Formal screening for dysphagia should be performed and screening for myocardial ischemia or infarction with electrocardiogram and cardiac enzyme testing after ICH is reasonable
• Ventricular drainage is reasonable for hydrocephalus, especially those with decreased level of consciousness. Glasgow Coma Scale (GCS) less than or equal to 8 and evidence of transtentorial herniation
• Cerebral perfusion pressure may be employed for those with suspect hypoperfusion, CPP = MAP - ICP
• No corticosteroid should be used in those with high ICP in ICH
• Surgical treatment is warranted in those with certain hemorrhages in certain areas such as cerebellar area or where the brainstem is being compressed

Post ICH
• Blood pressure control of long-term goal of < 130mmHg systolic and < 80mmHg diastolic
• Lifestyle modifications such as avoidance of alcohol use of greater than 2 drinks per day, tobacco use, and illicit drug
• Anticoagulation after nonlumbar ICH and antiplatelet monotherapy might be considered
  o Avoidance for at least 4 weeks in patients without mechanical heart values may decrease ICH recurrence

References