Types of Stroke

- Ischemic Stroke
  - Small vessel (20%)
  - Large vessel (31%)
  - Embolic (32%)

- Hemorrhagic
  - Intracerebral Hemorrhage (10%)
  - Subarachnoid Hemorrhage (7%)
The Majority of Strokes are Ischemic

- Ischemic: 85%
- Lacunar: 21%
- Atherosclerotic: 17%
- Cardioembolic: 17%
- Cryptogenic: 26%
- Subarachnoid Intraparenchymal: 17%
- Other: 4%

Hemorrhagic: 15%

Event Risk Within 3 Months After TIA

Independent risk factors for stroke within 90 days after TIA:
- Age > 60 years
- Diabetes mellitus
- Duration of episode greater than 10 min
- Weakness and speech impairment with the episode

Risk Factors for Intracerebral Hemorrhage

- Hypertension
- Alcohol (greater than 60 mg alcohol [5 drinks] per day increases overall risk of stroke
- Bleeding dyscrasias
- Thrombocytopenia
- Anticoagulation use
- Thrombolytics
Primary Intracerebral Hemorrhage

- Hypertensive
  - Globus pallidus (50%)
  - Thalamus (10%)
  - Cerebellar deep nuclei (10%)
  - Deep lobar white matter (10%)
  - Pons (10%)
Intracerebral Hemorrhage (Hypertensive): Pathogenesis
Amyloid Angiopathy
Intracerebral Hemorrhage

- Thirty day mortality is >90% with hematoma volume >60-65 cubic cm (1995 study)
- Location Mortality*
  - Brainstem: 60-68%
  - Deep cerebral: 44-52%
  - Lobar: 46-58%

*Neurology 2006
Imaging

- CT of brain
  - Very sensitive for hemorrhage
  - Rapidly obtained and interpreted
  - Gives clues for etiology of the bleed based on appearance and location
Figure 84 Coronal section through the cerebral cortex shows recent cerebral hemorrhage centered on the basal ganglia in a patient with hypertension. The bleeding probably originated from a ruptured microaneurysm.

Figure 85 CT showing a typical hemorrhage into the putamen in a 43-year-old patient with undiagnosed hypertension presenting with abrupt onset of hemiplegia, hemisensory loss, hemianopia, global

Figure 86 CT showing a smaller hemorrhage in a 59-year-old patient with hypertension who presented with contralateral pure motor hemiparesis. In such cases, CT is essential for the diagnosis.
Cerebellar Hemorrhage

- Compression of Brainstem
- Vessel compression (basilar artery) leading to ischemia
- Cisterns and 4th ventricle obstruction leading to hydrocephalus and brain herniation
- Neurosurgery can be life-saving with direct evacuation and/or ventriculostomy
Figure 94 Brain viewed from the base showing hemorrhage into the right lobe of the cerebellum.

Figure 95 CT showing hemorrhage into the cerebellum, which may be caused by hypertension or amyloid angiopathy. The 62-year-old patient had poorly controlled hypertension and presented with collapse, inability to walk, occipital headache and vomiting. There was right-sided facial weakness of peripheral-type and gaze failure resulting from compression of the pons.
Subarachnoid Hemorrhage

- Berry Aneurysm
- Mortality High (50%)
- Late Vasospasm Leads to Ischemia
- Some benefit with Nimodipine 60 mg every 4 hours NGT or po
- Surgical clipping or endovascular coiling
Intracerebral Hemorrhage Summary

- Neurosurgical consultation if cerebellar or large hematoma
- Control blood pressure to reduce risk of expanding hematoma but not too low to avoid loosing perfusion pressure
- Correct coagulopathies
- Prophylaxis for DVT, GI bleed, and aspiration
Ischemic Stroke
Large Vessel Stroke

- Aorta
- Vertebral arteries
- Basilar artery
- Internal Carotid Arteries
  - Extracranial
  - Intracranial
Arterial Disorders Causing Stroke

- Atherosclerotic
- Nonatherosclerotic Noninflammatory
- Nonatherosclerotic Inflammatory
Embolic Stroke

- Arterial Atherothrombosis
- Cardiogenic
- Paradoxical (DVT with PFO)
Cardiac Sources of Cerebral Emboli
Differential Diagnosis Of Stroke

- Craniocerebral/cervical trauma
- Meningitis/encephalitis
- Intracranial Mass (SDH; Tumor)
- Seizure with persistent neurological signs
- Migraine
- Metabolic
  - Hyperglycemia
  - Hypoglycemia
  - Post-cardiac arrest ischemia
  - Drug overdose
Initial Testing For Stroke

- CT Scan
- EKG
- Electrolytes
- CBC
- Pulse Ox
- PT (INR) and PTT
- Urine drug screen
Treatment of Acute Stroke
Things To Avoid In Early Treatment of an Ischemic Stroke Victim

- Sublingual Nifedipine
- Hypotension (allow BP up to 220/110)
- Hyperglycemia
- Hypoglycemia
- IV Heparin
- Fever (>99.6)
Anticoagulants are not recommended for any subgroup of patients with acute stroke based on any presumed mechanism or location (e.g. cardioembolic, large vessel atherosclerotic, vertebrobasilar, or “progressing” stroke) because data are insufficient.
Things to Do For the Early Ischemic Stroke Victim

- Hydrate (normal saline)
- Consider Thrombolytics and/or Endovascular Intervention
- Aspirin (81 or 325 mg)
- DVT Prophylaxis
- Treat fever (acetaminophen)
- Assess swallowing (place NGT if needed)
Certified Stroke Centers

- Joint Commission established criteria 2003
- Baptist Princeton was the First Primary Stroke Center in Birmingham
- Stroke mortality at days 1 and 7, and at one year are lower than at non accredited centers
- Use of thrombolytics higher

Xian, et.al., JAMA; 305 (Jan 26, 2011): 373-380
tPA Usage at Princeton

<table>
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<th>Year</th>
<th>2008</th>
<th>2009</th>
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<td>15</td>
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Alteplase Eligible Patients at Princeton

- In 2015, 88% of patients received t-PA within 60 minutes. (Goal 75%)
- In 2015, Average Door to Needle time: 51 minutes
- 46% of patients discharged home (goal 35%).
Alteplase Use in the United States

- Only about 50% of the alteplase eligible patients receive the drug
- 6-8% of the 795,000 strokes that occur in one year in the U.S. are eligible for alteplase
- 22-31% of ischemic strokes present to ED in <3 hours
Certified Stroke Center

- Accredited by Joint Commission
- Stroke Team
- Emergency Medical Services
- Neuroimaging and laboratory
- Standardized Stroke Protocols
- Support by Medical Services
- Continuing Medical Education
### Core Stroke Measures

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<th>Measure</th>
<th>Core STK-1b</th>
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<th>Core STK-3</th>
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<td>96.1</td>
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Pre-Hospital Evaluation

Spot a Stroke

Fast

Face Drooping
Arm Weakness
Speech Difficulty
Time to Call 911

Stroke Warning Signs and Symptoms
Pre-hospital Evaluation and Treatment

- EMS personnel trained to recognize stroke
- Sensitivities for stroke about 50% in three studies
- Miss opportunities for using tPA
- Confirm “last known well”
NINDS tPA Stroke Trial

NIHSS Excellent Recovery (%)

- tPA: 31
- Placebo: 20

Total Death Rate (%)

- tPA: 9 (Hemorrhage: 8, Non-Hemorrhage: 1)
- Placebo: 20

p < .05

New England Journal, 1995
Pre-2015 Inclusion Criteria for Alteplase

- Diagnosis of ischemic stroke
- Neurological signs not minor or clearing spontaneously
- Symptoms not suggestive of SAH
- No CHT, MI, or prior stroke in past 3 months
- No GI bleed or urinary tract bleed in past 21 days
- No major surgery in past 14 days
- No arterial puncture at non-compressible site
- No current or previous ICH
Pre-2015 Inclusion Criteria for Alteplase

- No evidence of active bleeding or acute trauma
- If patient on warfarin, INR is less than or equal to 1.7
- Patient is not taking dabigatran (Pradaxa®), rivaroxaban (Xarelto), apixaban (Eliquis),
- If heparin given in last 48 hours, aPTT is normal
- Platelet count is greater than or equal to 100,000
- Serum glucose >50, or < 400 mg/dl
- No seizure with postictal residual
- CT dose not show hypodensity >1/3 of cerebral hemisphere
Expanded Use of Alteplase

- FDA approved for 0-3 hours after stroke onset
- 2013 AHA/ASA guidelines for 3-4.5 hours after onset of stroke (ECASS III protocol. NEJM 2008;)
  - Age less than 80
  - No prior history of stroke and diabetes mellitus
  - NIHSS <25
  - NO anticoagulation use, regardless of INR
Alteplase in 3-4.5 hour Window

- Favorable outcome 28% more likely with alteplase than with placebo
- sICH 2.4% in alteplase group vs 0.3% in placebo group
Age and Alteplase

- ...compared with control subjects, patients given intravenous alteplase (within 0-3 hours symptom onset) provides a better chance of being independent at 3 months across **all age groups** (Class I; Level of Evidence A).
Alteplase for Mild Stroke Symptoms

- For patients with mild but disabling stroke symptoms, intravenous alteplase is indicated within 3 hours from symptom onset of ischemic stroke. There should be no exclusion for patients with mild but nonetheless disabling stroke symptoms in the opinion of the treating physician from treatment with intravenous alteplase because there is proven clinical benefit for those patients (Class I; Level of Evidence A).

- Within 3 hours from symptom onset, treatment of patients with milder ischemic stroke symptoms that are judged as nondisabling may be considered. Treatment risks should be weighed against possible benefits; however, more study is needed to further define the risk-to-benefit ratio (Class IIb; Level of Evidence C).
Alteplase in Patient with Rapid Improvement

- Rapid improvement is one of the most common reasons for exclusion from intravenous alteplase for acute ischemic stroke, yet it is an often misinterpreted exclusion criterion. (Demaerschalk, et al. 2016)
Rapidly Improving Stroke Patient

- Intravenous alteplase treatment is reasonable for patients who present with moderate to severe ischemic stroke and demonstrate early improvement but remain moderately impaired and potentially disabled in the judgment of the examiner (Class IIa; Level of Evidence A).

- Because time from onset of symptoms to treatment has such a powerful impact on outcome, delaying treatment with intravenous alteplase to monitor for further improvement is not recommended (Class III; Level of Evidence C).
Alteplase Use in Patients on Xa Inhibitors and Direct Thrombin Inhibitors

- AHA 2016 Guidelines
  - Not recommended *unless*
    - >48 since last dose (normal renal function), or
  - If laboratory tests for Xa activity are normal (direct factor Xa inhibitors), or
  - aPTT, INR, platelet count, ecarin clotting time are normal (direct thrombin inhibitors)
Early Ischemic Changes (EIC) on CT

- ECASS I pioneered the assessment of EIC by introducing the rule of EICs in more than one third of the MCA territory.
- In the NINDS studies, extent of EICs on the baseline CT scan did not influence patient eligibility.
CT Score for Stroke

- Alberta Stroke Program Early CT Score (ASPECTS)
- Ten point score to assess cortical stroke.
AHA Scientific Rational tPA Inclusion and Exclusion Criteria

- E-publication before print (February 2016)
- Recommendations from AHA/ASA vs FDA
- FDA revised package insert 2015
February 2015 FDA Changes to Alteplase Package Insert

- Removed prior stroke within 3 months as contraindication
- Removed seizure at onset of stroke as contraindication
- Bleeding diathesis remains a contraindication, but all laboratory values and specific examples of oral anticoagulants removed
- Removed prior history of ICH contraindication and replaced with a warning
- Contraindication to severe uncontrolled BP remains, but specific BP values removed
February 2015 FDA Changes to Alteplase Package Insert (cont’d)

- Blood glucose exclusion removed entirely
- Warning for NIHSS >22 removed entirely
- Warning for minor deficit stroke removed entirely
- Warning of major early infarct sign on CT removed entirely
- Contraindication to suspicion of SAH changed to contraindication in SAH
- Category C warning in pregnancy unchanged
- Emphasized use for patients >18. Safety in children unknown
February 2015 FDA Changes to Aleplase Package Insert (cont’d)

- Unknown risk to nursing mothers (previously not mentioned)
- Warning for advanced age (>75) replaced with warning that age >77 was one of several pt characteristics associated with increased risk of ICH; efficacy results suggest a reduced but still favorable clinical outcome
- Warning for GI or GU bleed within 21 days of stroke changed to warning with GI or GU bleeding
Benefit of Alteplase at 3 Months

- Chance of favorable outcome (mRS 0-1)
  - 2.55 if treatment 0-90 minutes
  - 1.64 if treatment 91-180 minutes
  - 1.34 if treatment 181-270 minutes
  - 1.22 if treatment 271-360 minutes

Lees, KR, Lancet, 2010;375;1695-1703
Further Testing For Ischemic Stroke Victim

- CT Angiography (head and Neck)
- Carotid Ultrasound
- MRI with diffusion weighted imaging
- MRA (head and neck)
- TEE or TTE
- Four Vessel Cerebral Angiogram
Early Interventions For Ischemic Stroke Victim

- Intravenous TPA
- Intra-arterial TPA
- Mechanical disruption of clot
Mechanical Embolus Removal in Cerebral Ischemia (MERCI)
Intra-arterial Treatment for Acute Ischemic Stroke

- Proximal intracranial arterial occlusion in the anterior circulation
  - Confirmed vessel imaging before randomization
  - Treatment initiated within 6 hours of stroke onset
- 81% of patients treated with a retrievable stent vs. usual treatment (89% had IV tPA for intervention)
- Modified Rankin Scale 0-2 in 32.6% vs. 19.1% in favor of intervention
  - No significant difference in mortality or symptomatic ICH
Other Intra-arterial Intervention Trials

Stent Retriever
It may be useful for primary stroke centers and other healthcare facilities that provide initial emergency care, including administration of intravenous r-tPA, to develop the capability of performing emergency noninvasive intracranial vascular imaging to most appropriately select patients for transfer for endovascular intervention and to reduce the time to endovascular treatment (Class IIb; Level of Evidence C). (Revised from the 2013 guideline) Powers, et. al. Focused Update on Treatment of Ischemic Stroke and Endovascular Treatment, 2015.
Secondary Stoke Prevention (Medical)

- Antiplatelets (ASA, clopidogrel, ticlopidine, dipyridamole/asa combination)
- ACE-I (Ramipril+thiazide; perindopril+indapamide)
- Blood Pressure Control
- Anticoagulation (warfarin, dabigatran, apixaban, rivaroxaban)
- HMG-CoA Reductase Inhibitors (pravastatin (Pravachol®), simvastatin (Zocor®), and atorvastatin (Lipitor®))
Benefits of Carotid Endarterectomy

- Well Established in Symptomatic (>70%) and asymptomatic (>60%) Carotid Stenosis
- Effective for ulcerative plaques with or without significant stenosis
- Low surgical risk in high volume centers (operative risk of death 2.8% in asymptomatic stenosis, and 5% in symptomatic TIA patients, and 7% risk in stroke patients)
- Absolute Risk Reduction of Recurrent Stroke: 17% at 5 years
Endarterectomy for Extracranial Carotid Artery Atherosclerosis
Benefits of Carotid Stenting

- Less invasive than CEA
- Can be used extracranially or intracranially
- No risk of cranial nerve injury
- Useful in patients s/p CEA with severe stenosis
- Useful in patients with severe medical comorbidity
- Useful in radiation arteriopathy
Cerebrovascular Emboli Protection Device
Stroke 2017

- Stroke is the 5th leading cause of death in the United States (behind heart disease, cancer, chronic lower respiratory diseases, and accidents)