Stroke

Causes, Symptoms, Diagnosis, & Treatment

OLLI Lecture
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Objectives

• Better understanding of stroke mechanisms contributing to stroke etiology
• Recognize the heterogeneous nature of stroke and the variability of stroke symptoms
• Develop a familiarity with the diagnostic approaches to facilitate expeditious identification of patients eligible for acute therapies.
• Learn the principles behind the rationale for acute stroke reperfusion therapies
• Become familiar with some of the more common modifiable stroke risk factors
Apoplexy
  - First described by Hippocrates
  - From Greek: “struck down with violence”

In 1599 English literature
  - “stroke of God’s hand”

In 1600s, Johann Jakob Wepfer,
  - Apoplexy due to effects of bleeding in the brain.
Mechanism of Brain Tissue Injury in Stroke

Stroke: Acute injury to brain by an abnormality of blood supply

**Ischemic Stroke**  
~ 80%

Lack of or diminished blood flow

**Hemorrhagic Stroke**  
~20%

Release of blood into the brain & extravascular spaces within the cranium or skull
Cerebrovascular Arterial Circulation

- Basilar artery
- Internal carotid arteries
- Vertebral arteries
- Circle of Willis
- External carotid arteries
- Common carotid arteries
- Subclavian arteries
- Innominate artery
- Aorta
Cerebrovascular Arterial Circulation: Large Vessels

Anterior Circulation

- Pericallosal artery
- Anterior cerebral artery
- Recurrent artery of Heubner
- Anterior choroidal artery
- Middle cerebral artery
- Ophthalmic artery
- Internal carotid artery

Posterior Circulation

- Posterior cerebral artery
- Superior cerebellar artery
- Anterior inferior cerebellar artery
- Vertebral artery
- Basilar artery

Lateral view

- Pericallosal artery
- Ophthalmic artery
- Posterior cerebral artery
- Internal carotid artery
- Anterior choroidal artery
- Superior cerebellar artery
- Basilar artery
- Anterior inferior cerebellar artery
- Posterior inferior cerebellar artery
- Vertebral artery

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The Numbers

• U.S.
  – ~800,000 new annual stroke cases with ~600,000 first-time strokes
  – *Fifth* cause of death with ~130,000 stroke-related deaths per year
  – Women have a higher lifetime risk of stroke than men
    • Affects 3 times as many women as breast CA and receives much less public attention
  – Stroke morbidity and mortality disproportionately affects minority populations
  – Between 2012 and 2030 the total direct medical stroke-related costs are projected to triple, from $71.6 to $184.1 billion

• Globally
  – In 2013, *second*-leading cause of death (after heart disease)
  – In 2010, 33 million strokes with 16.9 million as a first stroke
  – Burden of stroke now disproportionately affects those living in lower-income countries

• Both in U.S. and globally
  – A leading cause of disability

Mozzafarrian et al. 2016
Ischemic Stroke Mechanisms

- **Thrombosis**
  - Localized in situ obstruction

- **Embolism**
  - Material formed elsewhere

- **Hypoperfusion**
  - ↓ systemic perfusion = ↓ cerebral perfusion
Transient Ischemic Attack (TIA)

• “A brief episode of neurological dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than an hour, and without evidence of acute infarction.”

• Transient reduction of blood flow to a region in brain in the absence of infarction on brain imaging

• Most TIAs last only a few minutes and the great majority less than an hour.
  • Those lasting longer than an hour often associated with brain infarction on MRI DWI
Transient Ischemic Attack (TIA)

- Mechanisms for TIA are similar to ischemic stroke

- Reconstitution of flow to the hypoperfused region results in the resolution of symptoms

- Significance of TIAs is increased risk of ischemic stroke after a TIA specifically early on after a TIA

- Prompt evaluation of mechanism and appropriate treatment
Stroke Symptoms

SPOT A STROKE

FACE DROOPING
ARM WEAKNESS
SPEECH DIFFICULTY
TIME TO CALL 911

Stroke Warning Signs and Symptoms
Seven “Suddens” of Stroke

• New and sudden onset of neurologic symptoms including:
  • **Sudden weakness** in face, arm, leg on *one side* of the body
  • **Sudden numbness** in face, arm, leg on *one side* of the body
  • **Sudden difficulty** speaking
    – Both slurring (dysarthria) and word-finding difficulty (aphasia)
  • **Sudden difficulty** seeing
    – Dimness, blurriness, double vision, loss of vision
  • **Sudden difficulty** with balance
    – Vertigo, loss of balance, or incoordination
  • **Sudden severe headache** without a cause
  • **Sudden confusion or** altered level of consciousness
What to do in case of experiencing stroke?

- Someone you know is experiencing sudden-onset of L facial drooping and dragging their L arm and leg, what should they do?
  
  A: sleep it off, may be it will get better
  B: “toughen up”!!
  C: call primary care provider
  D: drive to the nearest hospital
  E: Call 9-1-1
Acute Stroke System of Care Workflow

Pre-Hospital/Arrival (1) → Diagnosis (2) → Treatment (3)
Acute Stroke System of Care Workflow
Step 1: Arrival 9-1-1 ... to ... Stroke Center

*Stroke Centers*: Hospitals certified by The Joint Commission as designated centers capable of rapid diagnosis and treatment of acute stroke
Rationale for Emergent Treatment of Acute Ischemic Stroke

• Acute Reperfusion Therapy
  – Treatment intended to emergently restoring blood flow in the acutely occluded cerebral artery.
    • Pharmacologic – IV tPA, and/or
    • Mechanical – Endovascular mechanical thrombectomy
  – Time-dependent
    • Can only be delivered for a certain time-frame after symptom-onset
    • Faster treatment times = Better outcomes
Pharmacologic Treatment

• Recombinant tissue plasminogen activator (tPA)
  – Time-dependent
  – Strict clinical criteria
  – Considered ‘Standard of Care’

• The only FDA-approved pharmacologic treatment for acute ischemic stroke (1996)
  – Up to 3 hours from symptom onset time

• Recommended by AHA/ASA
  – Up to 4.5 hours from symptom onset time
  – Selected patient population
  – NOT FDA-approved

• Other experimental agents
  – Desmoteplase, Tenecteplase
The greatest population benefit would occur by treating more patients early.
## Table 3. Binary Clinical Outcomes in Patients With Documented National Institutes of Health Stroke Scale Scores With Onset-to-Treatment Times 0 to 90, 91 to 180, and 181 to 270 Minutes (n = 51,158)

<table>
<thead>
<tr>
<th>Outcome, No. of Patients (%)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-90 vs 91-180</td>
<td>0-90 vs 181-270</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>.58 (.46-0.73)</td>
<td>.66 (0.54-0.81)</td>
</tr>
<tr>
<td>TPA complications</td>
<td>.10 (.08-0.13)</td>
<td>.18 (0.15-0.21)</td>
</tr>
<tr>
<td>Symptomatic intracranial hemorrhage</td>
<td>.02 (.01-0.03)</td>
<td>.04 (0.03-0.05)</td>
</tr>
<tr>
<td>Serious systemic hemorrhage</td>
<td>.17 (.15-0.20)</td>
<td>.19 (0.17-0.22)</td>
</tr>
<tr>
<td>Ambulation independent at discharge</td>
<td>.77 (.75-0.79)</td>
<td>.76 (0.74-0.78)</td>
</tr>
<tr>
<td>Discharge home</td>
<td>.06 (.04-0.08)</td>
<td>.06 (0.05-0.07)</td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; OTT, onset-to-treatment; TPA, tissue-type plasminogen activator.
Mechanical Reperfusion
Thrombectomy or embolectomy or intra-arterial

- Catheter-based delivery of mechanical devices
Endovascular Therapies

- Five positive endovascular RCTs for treatment of acute ischemic stroke
  - Endovascular therapy ± IV rtPA

<table>
<thead>
<tr>
<th>Study Title</th>
<th>Country; Year</th>
<th>Number of Patients Enrolled</th>
<th>Time Window (Symptom Onset to Groin Puncture)</th>
<th>Parenchymal Imaging Selection</th>
<th>Vascular Imaging Selection</th>
<th>Recanalization (TICI 2b/3)</th>
<th>Minutes to Reperfusion (Range)</th>
<th>Reperfusion at 24 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN)</td>
<td>Netherlands; 2010-2014</td>
<td>N = 500</td>
<td>6 hours</td>
<td>NCT</td>
<td>CTA/MRA/DSA</td>
<td>58.7%</td>
<td>332 (275-354)</td>
<td>75.4% versus 32.9%</td>
</tr>
<tr>
<td>Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times (ESCAPE)</td>
<td>Canada, United States, South Korea, Ireland, United Kingdom; 2013-2014</td>
<td>N = 316</td>
<td>12 hours</td>
<td>NCT (ASPECTS ≥6)</td>
<td>Multiphase CTA (collateral filling of ≥50% of middle cerebral artery-pia)</td>
<td>72.4%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Extending the Time for Thrombolysis in Emergency Neurological Deficit: Intra-Arterial (EXTEND IA)</td>
<td>Australia, New Zealand; 2012-2014</td>
<td>N = 70</td>
<td>6 hours (90 minutes from image to groin puncture)</td>
<td>CT/MR diffusion-perfusion; Tmax &gt;6-second delay perfusion volume and rCBF or DWI for ischemic core (using RAPID software); Included mismatch ratio &gt;1.2, absolute mismatch volume &gt;10 mL, ischemic core &lt;70 mL.</td>
<td>CTA/MRA</td>
<td>86.0%</td>
<td>248 (204-277)</td>
<td>89% versus 34%</td>
</tr>
<tr>
<td>Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment Trial (SWIFT PRIME)</td>
<td>United States; 2012-2014</td>
<td>N = 197</td>
<td>6 hours (90 minutes from image to groin puncture)</td>
<td>NCT (ASPECTS ≥7) CT/MR diffusion-perfusion; Tmax &gt;10-second delay perfusion volume and rCBF or DWI for ischemic core (RAPID); Included mismatch ratio &gt;1.8, absolute mismatch volume ≥15 mL, ischemic core ≤50 mL.</td>
<td>CTA/MRA</td>
<td>88.0%</td>
<td>Not reported</td>
<td>Reperfusion at 27 hours; 83% versus 40%</td>
</tr>
<tr>
<td>Randomized Trial of Revascularization With Solitaire FR Device Versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting Within 8 Hours of Symptom Onset (REVASCAT)</td>
<td>Spain; 2012-2014</td>
<td>N = 206</td>
<td>8 hours</td>
<td>NCT (ASPECTS ≥7)</td>
<td>CTA/MRA</td>
<td>66.0%</td>
<td>355 (269-430)</td>
<td>Not reported</td>
</tr>
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Endovascular Therapies

AHA/ASA Guideline

2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment

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

- Patients **eligible** for intravenous r-tPA should receive **intravenous r-tPA** even if endovascular treatments are being considered (Class I; Level of Evidence A).

- Patients should receive **endovascular therapy** with a **stent retriever** if they meet all the following criteria (Class I; Level of Evidence A). (New recommendation):
  - Prestroke mRS score 0 to 1,
  - Acute ischemic stroke receiving intravenous r-tpa within 4.5 hours of onset according to guidelines from professional medical societies,
  - Causative occlusion of the ICA or proximal MCA (M1),
  - Age ≥18 years,
  - NIHSS score of ≥6,
  - ASPECTS of ≥6, and
  - Treatment can be initiated (groin puncture) within 6 hours of symptom onset

- In carefully selected patients with anterior circulation occlusion who have **contraindications to intravenous r-tpa**, endovascular therapy with stent retrievers completed within 6 hours of stroke onset is reasonable (class iia; level of evidence C). (New recommendation)
Acute Stroke System of Care Workflow

Pre-Hospital/Arrival (1)

Primary Stroke Center Comprehensive Stroke Center

Diagnosis (2)

Treatment (3)

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**Stroke Diagnosis**

### Heart Attack

- **Symptoms**
  - Chest pain
- **Diagnosis**
  - ECG
  - Cardiac Enzymes

### Stroke (i.e. Brain Attack)

- **Symptoms**
  - Heterogeneous and variable
  - **Sudden weakness** in face, arm, or leg on one side of the body
  - **Sudden numbness** in face, arm, or leg on one side of the body
  - **Sudden difficulty** speaking
  - **Sudden difficulty** seeing
  - **Sudden difficulty** with balance
  - **Sudden confusion**
  - **Sudden severe headache** without a cause

- **Diagnosis**
  - History and exam
  - Imaging
    - CT – sometimes
    - MRI - sometimes
History

• **Time**
  – Symptom onset-time available
    • Use of cues
  – Last well-known time (LKWT)
  – Awaken with symptoms
  – Reset after TIA

• **Nature of symptom onset**
  – Sudden and maximal : embolic
  – Gradual and progressive : thrombotic

• **Other significant medical history**
Neurologic Examination:
The NIH Stroke Scale (NIHSS)

- National Institute of Health Stroke Scale (NIHSS)
  - Scores range from normal of 0 to maximal score of 42
  - Predicts short-term and long-term neurologic outcomes
  - May provide information regarding the likelihood of identifying a large vessel occlusion
  - Does not include a detailed assessment of CNs
  - Milder deficits may escape detection
  - Higher stroke severity in dominant vs non-dominant hemispheres

- NIHSS should not take the place of a focused and thorough neurologic evaluation
# Differential Diagnosis

- **Intracerebral hemorrhage vs Stroke mimics**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure (Post-ictal)</td>
<td>Focal deficits. Spontaneous resolution over hours (may last up to 48 hours)</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Aphasia or hemiplegia. Variable drowsiness or obtundation. Blood glucose usually &lt;45 mg/dL. Resolution of symptoms (immediate to hours) with IV glucose.</td>
</tr>
<tr>
<td>Migraine</td>
<td>Symptoms begin in one region and gradually spread to involve other areas.</td>
</tr>
<tr>
<td>Mass lesions/Tumor</td>
<td>Duration of symptoms. Associated symptoms.</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>Headache, thunderclap headache.</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>Hypertensive, hyperosmolar hyperglycemia, hyponatremia, hepatic. Associated with altered LOC, poor attention, or disorientation</td>
</tr>
<tr>
<td>Peripheral vestibulopathy</td>
<td>Vertigo, nystagmus on exam, nausea, emesis.</td>
</tr>
<tr>
<td>Reactivation of prior deficits</td>
<td>Imaging evidence or history of remove stroke. Previous deficits may have resolved completely.</td>
</tr>
<tr>
<td>Conversion reaction</td>
<td>Diagnosis of exclusion. Comorbid psychiatric problems are common. Paresis, paralysis, and movement disorders are common.</td>
</tr>
</tbody>
</table>
Acute Stroke Neuroimaging

- Initial imaging of brain parenchyma
  - Exclude hemorrhagic stroke: CT or MRI
Acute Stroke Neuroimaging

- For acute intracerebral hemorrhage
  - accuracy of MRI (GRE sequences) is equal to that of CT. (Kidwell et al, 2004)
Acute Stroke Neuroimaging
CT vs MRI

• CT
  • Advantages: Fast acquisition time, widely available, sensitive to hemorrhage
  • Disadvantages: Limited sensitivity to infarct size, location of early ischemia

• MRI (DWI sequence)
  • Advantage: Sensitive to early ischemia, fast acquisition time, high conspicuity of lesion
  • Disadvantage: Lack of availability, patient contraindication (eg, metals, claustrophobia), long acquisition time
Acute Stroke Neuroimaging

- Imaging of the early ischemic changes: CT or MRI

- Non-contrast CT (within 6-8 hour)
  - Specificity: 56-100%
  - Sensitivity: 20-75%
  - Worse in posterior fossa ischemia

- MRI DWI sequence (within <6 hours)
  - Specificity: 86-100%
  - Sensitivity: 91-100%
Multimodal Neuroimaging

- Potential to improve patient selection criteria to guide therapy

- Noninvasive multimodal CT and MR
  - Angiography (A): vessel imaging (CTA, MRA)
  - Perfusion (P): tissue viability, cerebral perfusion (CTP, MRP)

- Multimodal MRI parenchymal sequences
  - Diffusion-weighted imaging (DWI)
  - Apparent diffusion coefficient (ADC)
  - Fluid-attenuated inversion recovery (FLAIR)
  - Gradient recoiled echo (GRE)
  - Susceptibility-weighted imaging (SWI)

- No standardized imaging protocols for acute stroke exist

- Advanced neuroimaging should not delay the administration of IV rtPA
Guidelines for Imaging

- **Emergency imaging of the brain** is recommended **before any specific treatment** for acute stroke is initiated (Class I; Level of Evidence A). In most instances, nonenhanced CT will provide the necessary information to make decisions about emergency management.

- If endovascular therapy is contemplated, a **noninvasive intracranial vascular study** is strongly recommended during the **initial imaging evaluation** of the acute stroke patient but **should not delay intravenous r-tPA** if indicated. For patients who qualify for intravenous r-tPA according to guidelines from professional medical societies, initiating intravenous r-tPA before noninvasive vascular imaging is recommended for patients who have not had noninvasive vascular imaging as part of their initial imaging assessment for stroke. Noninvasive intracranial vascular imaging should then be obtained as quickly as possible (Class I; Level of Evidence A). (New recommendation)

- The **benefits of additional imaging** beyond CT and CTA or MRI and MRA such as CT perfusion or diffusion- and perfusion-weighted imaging for selecting patients for endovascular therapy are **unknown** (Class IIb; Level of Evidence C). (New recommendation)
Treatment Timeline Goals

• IV tPA within 60 minutes of arrival to ED (Door-to-Needle Time)
  – Evaluation by ED physician (10 minutes)
  – Evaluation by stroke/neurologist (15 minutes)
  – Non-contrast CT scan is completed (25 minutes)
  – CT is interpreted (45 minutes)

• Endovascular thrombectomy within 90 minutes of arrival to ED (Door-to-Puncture Time)

• Faster treatment = Better outcomes

*Time is Brain*
Acute Stroke System of Care Workflow

Pre-Hospital/Arrival (1)

Primary Stroke Center
Comprehensive Stroke Center

Diagnosis (2)

Treatment (3)

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Pre-hospital

• 49 yo M w/o any PMH w/LKWT ~ 09:50 a.m while at work, slipped off his chair

• Co-workers called 9-1-1

• Paramedic determined possible Stroke
  • R-sided gaze preference, dysarthria, L-hemiparesis, L-sided neglect
  • GCS 15

• Patient taken to SNRC-OSH
At OSH

- NIHSS score of 17 on arrival at OSH
- At OSH pt was deemed a candidate for IV tPA
- Patient received IV tPA at OSH @11:03
- CTA at OSH showed R MCA thrombosis
From OSH to UCI

• OSH contacted UCI neuro-interventional team requesting a transfer

• Pt transferred to UCI for possible endovascular thrombectomy

• Timeline of arrival and evaluation at UCI
  • Arrival to ED 12:12pm
  • Stroke Team at bedside 12:12pm
  • Neuro-interventional Team at bedside 12:12pm
At UCI Comprehensive Stroke Center

• NIHSS score of 6 on arrival at UCI (improved from 17 at FVH)
  • Mild dysarthria
  • R-sided gaze preference
  • L-sided central facial weakness
  • L-hemisensory disturbances
  • L-sided neglect

• Timeline of imaging evaluation & assessment
  • CT completed 12:25pm (13min)
  • CT interpretation 12:25pm (13min)
  • CTP completed 12:38pm (26 min)
  • CTP interpretation 12:48pm (36 min)
At UCI Comprehensive Stroke Center

- CTP (perfusion) demonstrated large area of penumbra
At UCI Comprehensive Stroke Center

- Pt deemed appropriate for endovascular thrombectomy
- Left ED for angiography suite at 1:15pm
- R MCA thrombectomy w/groin puncture time at 1:34pm
  - Door-to-Puncture time: 82 minutes (goal of <90 minutes)
  - Mechanical thrombectomy w/Penumbra

- Results:
  - TICI 2b: Complete recanalization
  - Clinical improvement: NIHSS 6(pre) → 0(post)
At UCI Comprehensive Stroke Center

CTP: *Pre*-Thrombectomy

MRI: *Post*-Thrombectomy
Discharge & Follow Up

- NIHSS score of 0 at time of discharge
- ~ 4 weeks after discharge reported
  - Some fatigue
  - Some mild incoordination with L hand when typing on computer.
- Remained with a NIHSS score of 0
- Back to work and fully functional in his daily activities

**Time is Brain!**
### Current Reperfusion Limitations or Future Directions

**IV tPA**

- Low utilization rate: 5-9%
  - Limited therapeutic window
  - ~15-30% stroke patients awaken with deficits or have unclear onset times
- 6% risk of hemorrhage
- Less effective in large vessel occlusion
  - Successful in dissolving larger proximal clots only 15-25% of the time

**Mechanical Interventions**

- Low utilization rate: < 5%
- Criteria for patient selection
- Require extremely specialized resource-intensive hospital setting
- Role of endothelial trauma and potential for vessel perforations
- Distal embolization
  - Reported in up to 9% in some of the recent trials
Stroke is Preventable

• Despite significant progress in care and treatment, stroke remains one of the leading causes of disability

• ~80% of strokes are preventable!

• Know your stroke risk factors
Modifiable Stroke Risk Factors: 

**Hypertension**

- Most common modifiable risk factor for stroke
- AHA recommendations
  - age not a factor in the decision to treat BP
  - Treat anyone with BPs in (140 – 159) / (90 – 99)
- Emphasis on lifestyle changes: diet and exercises
- AHA/ASA do not recommend specific regimen
  - Diuretics and ACEi – most studied
  - Consideration of specific patient characteristics
- Avoid BP medications that lead to variability
  - Visit-to-visit variability in SBP increases risk of stroke sixfold
    - Metoprolol: ↑ variability
    - Amlodipine: ↓ variability
Modifiable Stroke Risk Factors:  

*High Cholesterol*

- **Primary prevention** with focus on treatment with statins that are likely to lower cholesterol by
  - 50% or more (high-potency)
  - 30% to 50% (moderate-potency)
- **Secondary prevention**
  - Consideration of atherosclerotic origin of stroke or TIA
  - If LDL > 100 w or w/o evidence of clinical atherosclerotic cardiovascular disease
- **Intolerance to statins, myopathy or general muscle pain**
  - Varies from 7% to 29% in the literature
  - Addressed by stopping the medications, checking for muscle enzymes, and reducing the dose upon reinitiating
Modifiable Stroke Risk Factors:

**Diet and Nutrition**

- **Mediterranean diet** is associated with **lower** risk of stroke
  - High intake: olive oil, fruits and vegetables, nuts and whole grains;
  - Moderate intake: fish and poultry
  - Low intake: dairy, red and processed meats, and sweets

- **Nurse’s Health Study and Health Professionals Follow-Up Study**
  - Single serving of caffeinated or decaffeinated **coffee decreased** stroke risk by ~10%
  - Daily servings of **soda increase** the risk of ischemic stroke per daily serving by
    - 13% with sugar-sweetened soda
    - 7% with low-calorie soda
Modifiable Stroke Risk Factors:

• Diabetes Mellitus
  – Key risk factor for first-ever and recurrent ischemic stroke
  – Lifestyle and pharmacologic management with aim of hemoglobin A1C < 7%

• Tobacco Use
  – Cigarette smoking at least doubles the risk of stroke
  – Secondhand smoke increases risk of stroke by 30% in nonsmokers
  – Risk from smokeless tobacco products and e-cigarettes less clear, but still advocate for cessation of all forms of tobacco and nicotine
Modifiable Stroke Risk Factors:

• Obesity
  – Every 1 unit increase in BMI increases risk of ischemic stroke by ~5%

• Physical Activity
  – AHA/ASA recommendations
    • Patients with stroke should engage in
      – 3-4 session per week
      – Sessions lasting average of 40 minutes
      – Moderate-to-vigorous intensity aerobic exercise
Summary

• A leading cause of disability and death both in the US and globally

• Acute stroke treatment requires emergent and streamlined evaluation in a certified stroke center

• IV tPA is considered standard of care

• Endovascular mechanical thrombectomy has also become a standard of care for selected patients

• A great portion of strokes are preventable!
QUESTIONS???

**Stroke is an Emergency: Time is Brain**

- PSA
  - New and sudden onset of neurologic symptoms including:
    - **Sudden weakness** in face, arm, leg on *one side* of the body
    - **Sudden numbness** in face, arm, leg on *one side* of the body
    - **Sudden difficulty** speaking
      » Both slurring (dysarthria) and word-finding difficulty (aphasia)
    - **Sudden difficulty** seeing
      » Dimness, blurriness, double vision, loss of vision
    - **Sudden difficulty** with balance
      » Vertigo, loss of balance, or incoordination
    - **Sudden severe headache** without a cause
    - **Sudden confusion or** altered level of consciousness
  - CALL 9-1-1
### Neurologic Examination: The NIH Stroke Scale (NIHSS)

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<tr>
<th>Category</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1a. LOC</td>
<td>0 = Alert 1 = Not alert, arousable 2 = Not alert, obtunded 3 = Unresponsive</td>
<td>5a. L motor arm</td>
<td>0=No drift 1=Drift before 10 seconds 2=Falls before 10 seconds 3=No effort against gravity 4=No movement</td>
<td>7. Ataxia</td>
<td>0=Absent 1=One limb 2=Two limbs</td>
</tr>
<tr>
<td>1b. Questions</td>
<td>0 = Answers both correctly 1=Answers one correctly 2=Answers neither correctly</td>
<td>5b. R motor arm</td>
<td>0=No drift 1=Drift before 10 seconds 2=Falls before 10 seconds 3=No effort against gravity 4=No movement</td>
<td>8. Sensory</td>
<td>0=Normal 1=Mild loss 2=Severe loss</td>
</tr>
<tr>
<td>1c. Commands</td>
<td>0=Performs both tasks correctly 1=Performs one task correctly 2=Performs neither task</td>
<td>6a. L motor leg</td>
<td>0=No drift 1=Drift before 10 seconds 2=Falls before 10 seconds 3=No effort against gravity 4=No movement</td>
<td>9. Language</td>
<td>0=Normal 1=Mild aphasia 2=Severe aphasia 3=Mute or global aphasia</td>
</tr>
<tr>
<td>2. Gaze</td>
<td>0=Normal 1=Partial gaze palsy 2=Total gaze palsy</td>
<td>6b. R motor leg</td>
<td>0=No drift 1=Drift before 10 seconds 2=Falls before 10 seconds 3=No effort against gravity 4=No movement</td>
<td>10. Dysarthria</td>
<td>0=Normal 1=Mild 2=Severe</td>
</tr>
<tr>
<td>3. Visual fields</td>
<td>0=No visual loss 1=Partial gaze palsy 2=Total gaze palsy</td>
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<td>4. Facial Palsy</td>
<td>0=Normal 1=Minor paralysis 2=Partial paralysis 3=Complete paralysis</td>
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BOX 1-1  IV rtPA Exclusion and Relative Contraindication Criteria

Key IV rtPA Exclusion Criteria

- Stroke or significant head trauma within 3 months
- Major surgery or serious trauma within 14 days
- Gastrointestinal or urinary hemorrhage within 21 days
- Arterial puncture at a noncompressible site within 7 days
- History of intracranial hemorrhage
- Intracranial neoplasm, arteriovenous malformation, or aneurysm
  - Some experts consider treating patients with remotely secured or unruptured aneurysms
- Symptoms of subarachnoid hemorrhage
- Active internal bleeding
- Pretreatment blood pressure with systolic >185 mm Hg or diastolic >110 mm Hg
- Clear and large hypodensity on CT scan
- Current bleeding diathesis including
  - International normalized ratio (INR) >1.7
  - Heparin within 48 hours resulting in abnormal partial thromboplastin time (PTT)
  - Platelets <100,000/mm³
  - Direct thrombin inhibitor (eg, dabigatran) or factor Xa inhibitor (eg, rivaroxaban, apixaban) use within 48 hours
  - Optimal laboratory testing thresholds for safe IV recombinant tissue-type plasminogen activator (rtPA) use in this setting remain to be determined and are an area of active investigation.
- Serum glucose <50
  - If persistent symptoms after correction, or infarct is verified/supported by imaging, most experts would consider IV rtPA treatment.

Relative Contraindications for IV rtPA

- Minor deficit
  - Rapidly improving deficits should not be considered a contraindication unless the remaining deficit is minor.²³
  - A common definition of minor deficits is an NIH Stroke Scale (NIHSS) score ≤5 and not clearly disabling.
  - A consensus definition of deficits that should typically be considered disabling (regardless of total NIHSS score) is shown in Table 1-1.
- Myocardial infarction in the past 3 months
  - Some experienced centers treat this as a contraindication only if the myocardial infarction is subacute and transmural, or other signs suggest a high risk of hemothorax, such as clinical or ECG evidence of pericarditis.
  - Concurrent acute myocardial infarction may benefit from IV rtPA as well and should be considered on a case-by-case basis.
BOX 1-1  IV rtPA Exclusion and Relative Contraindication Criteria (continued)

Additional Exclusion Criteria for IV rtPA Within the 3- to 4.5-Hour Time Window\(^1\)
- History of stroke AND diabetes mellitus
- NIHSS score >25
- Age >80 years old
- On warfarin (regardless of INR value)
Ancillary Testing

- Blood glucose (Finger stick is acceptable)
  - The only lab result needed for administration of IV tPA

- Administration of IV tPA should NOT be delayed while awaiting results of the following lab results:
  - Complete blood count (CBC)
    - Unless clinical suspicion of a bleeding abnormality or thrombocytopenia
    - < 3/1000 will have unsuspected thrombocytopenia (Cucchiara et al, 2007)
  - Coagulation panel (PT/INR/PTT)
    - Patient has received heparin or warfarin,
    - Patient has received other anticoagulants
    - <4/1000 will have an unsuspected INR>1.7 (Rost et al, 2009)
  - Chemistry panel (Chem7)
  - Cardiac enzymes
  - CXR
  - 12-lead ECG
Post-Reperfusion Therapy

- Standard post-tPA management for the first 24 hours:
  - Admission to Stroke Unit ICU level of care
  - NPO until dysphagia screening to avoid aspiration PNA
  - Isotonic IV fluids (not dextrose containing because of risk of hyperglycemia)
  - BP and neurologic monitoring
    - Q15min x 2 hrs, then
    - Q30min x 6 hrs, then
    - Q60min x 16 hrs
  - Aggressive BP treatment
    - If SBP>180 mmHg or DBP >105 mmHg
  - Emergent CT scan if neurologic decline, acute increase in BP, N/V, new HA
  - Repeat brain imaging at 24 hours to assess for asymptomatic hemorrhage