Stroke Update

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Outline and Learning Objectives

• Review epidemiology
• Review polyvascular disease
• Discuss new definitions of TIA
• Review medical interventions
  – Antihypertensives
  – Statin therapy
  – Anticoagulants
  – Antiplatelet therapy
• Review barriers to improve outcomes
• Discuss promotion of stroke centers
• Review stroke workup

Stroke in the US

• 795,000 people experience a new or recurrent stroke.
  – Approximately 610,000 of these are first attacks, and 185,000 are recurrent attacks.
• 137,000 stroke deaths annually in the United States.
• Leading cause of serious, long-term disability
• Third leading cause of death in the U.S.; second leading cause worldwide
• Second-leading cause of hospital admission among older adults

Stroke. 2011;42:849-877

Atherothrombosis Significantly Shortens Life Expectancy

Average remaining life expectancy at age 60 (men)

<table>
<thead>
<tr>
<th>Years</th>
<th>Healthy</th>
<th>CV disease</th>
<th>MI</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 yrs</td>
<td></td>
<td>12.3 yrs</td>
<td>10.8 yrs</td>
<td>8 yrs</td>
</tr>
</tbody>
</table>

Analysis of data from the Framingham Heart Study.
Estimated Outcomes After Ischemic Stroke

Ischemic Stroke: Common Causes

- Atherothrombosis
  - Large-vessel
    - Extracranial
    - Aortic
    - Cervical ICA
    - Cervical CCA
  - Intracranial
    - ICA
    - MCA
    - Vertebrobasilar arteries
- Small vessel
  - Lacunar
- Cardiac source
  - Atrial fibrillation
  - Dilated cardiomyopathy
  - Nonatherosclerotic arteriopathies, eg:
    - Vasculitis
    - Migraine
- Prothrombotic disorders

Prevalence of Ischemic Stroke

REACH Registry
Overlap of Serious Vascular Disease in the Stroke Patient

- Reduction of Atherothrombosis for Continued Health (REACH) Registry
  - www.reachregistry.org
- CVD population: N=18,957
  - TIA: N=8,741 (48%)
  - Stroke: N=10,216 (73%)
- 40.2% of the total CVD population has more than 1 disease location
  - 34.3% have 2 disease locations
  - 5.9% have 3 disease locations

The Prevalence of PAD in Ischemic Stroke Patients

A study of 852 patients with TIA or ischemic stroke found 54.8% of patients had a form of PAD. This included:
- 50.8% of the total population had an ABI <0.9
- 10.0% of the total population had intermittent claudication

Risk Factors for Stroke

Modifiable
- Hypertension
- Diabetes
- Cardiac disease
- Atrial fibrillation
- TIAs/prior stroke
- Metabolic syndrome
- Dyslipidemia
- Cigarette smoking
- Alcohol abuse
- Obesity
- Physical inactivity
- Carotid stenosis

Nonmodifiable
- Age
- Gender
- Race/ethnicity
- Heredity
INTERSTROKE: Population-attributable risk for common risk factors

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Population-attributable risk, % (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>34.6 (30.4–39.1)</td>
</tr>
<tr>
<td>Smoking</td>
<td>18.9 (15.3–23.1)</td>
</tr>
<tr>
<td>Waist-to-hip ratio (tertile 2 vs tertile 1)</td>
<td>26.5 (18.8–36.0)</td>
</tr>
<tr>
<td>Dietary risk score (tertile 2 vs tertile 1)</td>
<td>18.8 (11.2–29.7)</td>
</tr>
<tr>
<td>Regular physical activity</td>
<td>28.5 (14.5–48.5)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5.0 (2.6–9.5)</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td>3.8 (0.9–14.4)</td>
</tr>
<tr>
<td>Cardiac causes</td>
<td>6.7 (4.8–9.1)</td>
</tr>
<tr>
<td>Ratio of apolipoprotein B to A1 (tertile 2 vs tertile 1)</td>
<td>24.9 (15.7–37.1)</td>
</tr>
<tr>
<td>Psychological factors</td>
<td></td>
</tr>
<tr>
<td>Stress</td>
<td>4.6 (2.1–9.6)</td>
</tr>
<tr>
<td>Depression</td>
<td>5.2 (2.7–9.8)</td>
</tr>
</tbody>
</table>

For all parameters other than physical activity, the population-attributable risk is provided for individuals who do not participate in regular physical activity.


Prevalence of Stroke by Age

Total Number of Elderly by Age Group: 1900 to 2050

Geographical Variation

Stroke mortality, 2010

Estimated Cost of Stroke in the US

Historic Definition
Temporary focal brain or retinal deficits caused by vascular disease that *resolve within 24 hours*
**New Definition of TIA**

TIA is a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, and without evidence of acute infarction.


**ABCD² of TIA**
- Patients with TIA score points for each of the following factors:
  - Age 60 years (1 point)
  - Blood pressure 140/90 mm Hg on first evaluation (1 point)
  - Clinical symptoms of focal weakness with the spell (2 points) or speech impairment without weakness (1 point)
  - Duration 60 minutes (2 points) or 10 to 59 minutes (1 point)
  - Diabetes (1 point).
  - 2-day risk of stroke:
    - 0% for scores of 0 - 1
    - 1.3% for 2 - 3
    - 3.4% for 4 - 5
    - 8.1% for 6 - 7


**Working up TIA**
- Neuroimaging evaluation within 24 hours of symptom onset.
  - MRI, including DWI, is the preferred brain diagnostic imaging modality.
- Noninvasive imaging of the cervicocephalic vessels should be performed routinely as part of the evaluation.
- Noninvasive testing of the intracranial vasculature reliably excludes the presence of intracranial stenosis.
- Patients with suspected TIA should be evaluated as soon as possible after an event.
  - ECG/ECHO

**Admit to the Hospital?**
- Reasonable to hospitalize patients with TIA if they present within 72 hours of the event and any of the following criteria are present:
  - ABCD² score of 3 or greater
  - ABCD² score of 0-2 and uncertainty that diagnostic workup can be completed within 2 days as an outpatient


**Evaluation of Tissue Status: Noncontrast Head CT**
- **Advantages**
  - Almost universally available
  - Rapid
  - High sensitivity for detection of hemorrhage (100% ICH, 90% SAH)
- **Disadvantages**
  - Often normal in hyperacute phase
  - Insensitive to lacunar and posterior fossa strokes

Evaluation of Tissue Status: Multimodal MRI (including DWI)

**Advantages**
- More sensitive to acute ischemia
- More sensitive to posterior fossa lesions
- More sensitive to small vessel, lacunar lesions

**Disadvantages**
- Not universally available
- Longer scanning time
- Patient contraindications (e.g. pacemaker)

MRI - Tissue Status: Ischemia

- CT
- DWI

Evaluation of Vessel Status

1. CT Angiography
2. MR Angiography
3. Ultrasound Techniques
4. Catheter Angiography

CT Angiography

- Requires injection of intravenous contrast agent
- New generation helical scanners allow rapid evaluation of aortic arch, neck, and intracranial vessels with 1 injection
- 80-100% accuracy compared with catheter angiography
- Disadvantages: iodinated contrast agent, radiation exposure

CTA: Carotid Stenosis

CTA: MCA Stenosis
**MR Angiography**

- Noninvasive means to evaluate neck and intracranial vessels
- Time of flight technique may overestimate stenoses
- Not reliable in identifying distal or branch intracranial occlusions
- Sensitivity and specificity 70-100% compared to catheter angiography
- Power-injector, contrast-enhanced techniques – increased sensitivity
- Subject to limitations of standard MRI

**AHA Guidelines for the Use of Imaging in Acute Stroke**

- Brain imaging is required to guide the selection of acute interventions to treat patients with stroke
- CT remains the most important brain imaging test
- New studies suggest that MRI could be an alternative to CT
  - May be used to detect acute ICH

**Evidence-based guideline: The role of diffusion and perfusion MRI for the diagnosis of acute ischemic stroke**

- DWI should be considered superior to noncontrast CT scan for the diagnosis of acute ischemic stroke in patients presenting within 12 hours of symptom onset (Level A).
- There is insufficient evidence to support or refute the value of PWI in diagnosing acute ischemic stroke (Level U).
- Baseline DWI volume should be considered useful in predicting baseline clinical stroke severity and final infarct volume in anterior-circulation stroke syndromes (Level B).
- Baseline DWI volume may be considered not useful in predicting baseline NIHSS score in posterior-circulation stroke syndromes (Level C).
- Baseline DWI volume may be considered useful in predicting clinical outcome as measured by the NIHSS and Barthel index (Level C).
- Baseline PWI volume may be considered useful in predicting baseline clinical stroke severity (Level C).

**rtPA for Acute Stroke**

- Only FDA-approved therapy
- Can reverse effects of stroke
- Only used in about 4% of cases
  - Time limit: must be administered within 3 hours of stroke onset
  - Rapid identification and treatment
- Utility of rt-PA is limited due to:
  - Three hours time window
  - Associated with a significant risk of ICH

**Overall Benefits and Risks of IV tPA for Stroke**

- Benefit: Neurologically normal at 3 months
  - 55% relative increase; 12% absolute increase
- Robust effect:
  - NNT to cure=7
- Risk of symptomatic ICH: 6.4%
- Overall benefits in spite of the ICHs
- Risk of ICH can be reduced by closely following tPA protocol

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1. NINDS rt-PA Stroke Study Group. 
Empirical Characteristics of Litigation Involving Tissue Plasminogen Activator and Ischemic Stroke

Study objective:
- The use of tissue plasminogen activator (tPA) in potential stroke victims by emergency physicians is controversial. One factor that may represent a barrier to use is medicolegal concerns resulting from adverse outcomes.

Results:
- Thirty-three cases were found involving tPA ischemic stroke therapy. In 29 (88%) of these cases, patient injury was claimed to have resulted from failure to treat with tPA.
- Emergency physicians were the most common physician defendants. Defendants prevailed in 21 (64%) cases, and among the 12 with results favorable to the plaintiff, 10 (83%) involved failure to treat and 2 (17%) claimed injury from treatment with tPA.

Acute Ischemic Stroke:
ASA/AAN/ACCP Guidelines

- Pharmacotherapies
  - tPA (tissue plasminogen activator) within 3 hours of stroke onset
  - Aspirin for acute stroke (within 48 hours of symptom onset): 160 to 325 mg/day to reduce stroke mortality and decrease morbidity; ONLY if no contraindications or if patient will not be given tPA
  - Heparin and low molecular weight heparin (LMWH): not indicated and may increase bleeding complications;
  - LMWH and heparinoids may be considered for DVT prophylaxis in at-risk patients
- Early consultation by neurologist or stroke team critical

An Advisory Statement from the Stroke Council, American Heart Association and American Stroke Association

EXPANSION OF THE TIME WINDOW FOR TREATMENT OF ACUTE ISCHEMIC STROKE WITH INTRAVENOUS TISSUE PLASMINOGEN ACTIVATOR

Gregory J. del Zoppo, MD, MS, FAHA; Jeffrey L. Saver, MD, FAHA; Edward C. Jauch, M.D, MS, FAHA; Harold P. Adams, Jr., MD, FAHA

This science advisory reflects a consensus of expert opinion following thorough literature review that consisted of a look at clinical trials and other evidence related to the management of acute ischemic strokes.

ECASS - 3

DESIGN AND METHODS
- Multicenter, prospective, placebo-controlled RCT
- Usual criteria for rt-PA eligibility within 3 hrs, exclusion criteria included:
  - older than 80 years; baseline NIH Stroke Scale score >25; on oral anticoagulants; combo of a previous stroke & DM
- rt-PA (n = 418) or placebo (n = 403) given at 3.0 - 4.5 hrs from stroke symptom onset
- Dose = 0.9 mg/kg (max 90 mg); 10% as initial bolus & remainder infused over 1 hr.
- Primary outcome: modified Rankin Scale Score 0-1 (minimal or no disability) at 90 days after Tx.

RESULTS
Primary Outcome:
- mRS 0-1: rt-PA (52.4%) vs placebo (45.2%) (OR 1.34, 95% CI = 1.02-1.76; p = 0.04)

Secondary Outcome:
Global Favorable Outcome
- mRS of 0-1, Barthel Index score >95, an NIHSS score of 0-18, Glasgow Outcome Score of 1
- ECASS – 3 = OR 1.28, 95% CI = 1.00-1.65 vs NINDS pool pts (enrolled 0-3hrs) = OR1.9, 95% CI 1.2-2.9

Symptomatic ICH (ECASS-3 definition) occurred in rt-PA n = 10 (2.4%) vs placebo n = 1 (0.2%) (OR 9.85, 95% CI 1.26-77.32, p = 0.008)

ECASS - 3

RESULTS
Symptomatic ICH (NINDS study definition) occurred in rt-PA n = 33 (7.9%) vs placebo n = 14 (3.5%) (OR 2.38, 95% CI = 1.25-4.52, p = 0.006)

Increased incidence of symptomatic ICH is consistent with the experience with rt-PA in other clinical trials with rt-PA
- Mortality in the two treatment groups did not differ significantly, although it was nominally higher among the subjects treated with placebo (7.7% vs. 8.4%, p=0.68)
Recommendations

- rt-PA should be administered to eligible pts within 3.0–4.5 hours after stroke (Class I Recommendation, LOE B)
- Eligibility criteria in this time period are similar to those for persons treated at earlier time periods with the following additional exclusion criteria:
  - Age > 80 years; Oral anticoagulant use with INR ≤ 1.7*
  - baseline NIH Stroke Scale score > 25; a history of stroke and diabetes (*For the 3.0 – 4.5 hr window all pts receiving oral anticoagulant are excluded whatever their INR).
- The efficacy of IV rt-PA within 3.0 – 4.5 hours after stroke in pts with these exclusion criteria is not well-established & requires further study. (Class Ib Recommendation, LOE C)

Physician Resistance to rtPA

- Skill set for correct diagnosis
- Establishment of onset time necessary/difficult
- Alteplase protocol vs lack of existing protocols
- Lack of communication/understanding between EDs, neurologists, PCPs
- Difficulty in implementing standing orders in hospital setting

INTRA-ARTERIAL ADMINISTRATION OF THROMBOLYTIC AGENTS

- Potential advantages
  - Higher concentration of medication at site
  - Lower systemic doses might improve safety
- Potential disadvantages
  - Facilities not widely available
  - Time required to mobilize resources
- No head-to-head comparisons with IV therapy

Times for thrombolysis

- ≤ 3 hours for IV TPA - FDA approved
- ≥ 3 – 4.5 hours for IV TPA – Not FDA approved
- Time of onset to 6 hours – Not FDA approved with device or IA thrombolytics

HYPERTENSION

7th Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
<th>Initial Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120 and &lt;80</td>
<td>Encourage</td>
<td>Drug(s) for compelling indications</td>
</tr>
<tr>
<td>Pre-hypertension</td>
<td>120–139 or 80–89</td>
<td>Yes</td>
<td>Non-hypertensiv vs-drug indicated</td>
</tr>
<tr>
<td>Stage 1 Hypertension</td>
<td>140–159 or 90–99</td>
<td>Yes</td>
<td>Thiazide-type diuretics</td>
</tr>
<tr>
<td>Stage 2 Hypertension</td>
<td>≥160 or ≥100</td>
<td>Yes</td>
<td>2-drug combination therapy</td>
</tr>
</tbody>
</table>

*Treatment determined by highest category
†These patients with chronic kidney disease or diabetes is BP goal of <130/80 mm Hg. They also consider ARB, CCB, or combination.
‡May consider ACEI, ARB, BB, or combination.
ASA Treatment Guidelines for 2007: Ischemic Stroke Not Eligible for Thrombolytic Therapy

<table>
<thead>
<tr>
<th>BP Level (mm Hg)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP &lt;220 OR DBP &lt;120</td>
<td>No treatment unless end-organ involvement</td>
</tr>
<tr>
<td>SBP &gt;220 OR DBP &lt;121-140</td>
<td>Nicardipine or labetalol to 10%-15% ↓ in BP</td>
</tr>
<tr>
<td>DBP &gt;140</td>
<td>Nitroprusside to 10%-15% ↓ in BP</td>
</tr>
</tbody>
</table>

ASA = American Stroke Association; IS = ischemic stroke; SBP = systolic blood pressure; DBP = diastolic blood pressure.


ASA Treatment Guidelines for 2007: Ischemic Stroke Eligible for Thrombolytic Therapy

<table>
<thead>
<tr>
<th>BP Level (mm Hg)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pretreatment</td>
<td>Labetalol (may repeat once), nitropaste, or nicardipine</td>
</tr>
<tr>
<td>SBP &gt;185 or DBP &gt;110</td>
<td>If BP not reduced and maintained, do not administer rt-PA</td>
</tr>
<tr>
<td>During and after rt-PA</td>
<td>Labetalol</td>
</tr>
<tr>
<td>SBP 180-230 OR DBP 105-120</td>
<td>Nicardipine or labetalol</td>
</tr>
<tr>
<td>SBP &gt;230 OR DBP 121-140</td>
<td>If BP not controlled, consider nitroprusside</td>
</tr>
</tbody>
</table>

rt-PA = recombinant tissue plasminogen activator.


Blood Pressure and Stroke
What to Conclude

- All studies support detection and aggressive treatment of blood pressure for both primary and secondary prevention
- Reduction of stroke by 35%-40% possible
- Thiazide-type diuretic recommended as first therapeutic agent
- ACEI and ARBs are more effective in reducing progression of renal disease and are recommended as first-choice medications for patients with diabetes


Antiplatelets

ATC
Efficacy of Aspirin at Various Doses in Reducing Vascular Events in High-risk Patients

<table>
<thead>
<tr>
<th>Aspirin Dose</th>
<th>No. of Trials</th>
<th>OR (%)</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 mg-1500 mg</td>
<td>34</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>160 mg-325 mg</td>
<td>19</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>75 mg-150 mg</td>
<td>12</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>&lt;75 mg</td>
<td>3</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Any aspirin</td>
<td>65</td>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

*Vascular events included nonfatal MI, nonfatal stroke, and death from vascular causes. Treatment after P=0.001.


European Stroke Prevention Study (ESPS-2)

<table>
<thead>
<tr>
<th>Design</th>
<th>2 x 2 factorial design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke (75%) or TIA (24%)</td>
<td></td>
</tr>
<tr>
<td>Endpoints</td>
<td>Primary: Stroke, death, stroke and death</td>
</tr>
<tr>
<td>Secondary: TIA, MI</td>
<td></td>
</tr>
<tr>
<td>Follow-up: 2 years</td>
<td></td>
</tr>
<tr>
<td>DP-XR 200 mg BID 1,664 patients</td>
<td></td>
</tr>
<tr>
<td>ASA 25 mg BID 1,664 patients</td>
<td></td>
</tr>
<tr>
<td>Placebo 1,664 patients</td>
<td></td>
</tr>
</tbody>
</table>

**Risk Reduction for Stroke or Death**

<table>
<thead>
<tr>
<th>Pairwise Comparisons</th>
<th>Relative Risk Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stroke</td>
</tr>
<tr>
<td>ASA vs placebo</td>
<td>0.013</td>
</tr>
<tr>
<td>DP vs placebo</td>
<td>0.039</td>
</tr>
<tr>
<td>DP + ASA vs placebo</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DP + ASA vs ASA</td>
<td>0.006</td>
</tr>
<tr>
<td>DP + ASA vs DP</td>
<td>0.002</td>
</tr>
</tbody>
</table>

ASA = aspirin 25 mg bid; DP = modified-release dipyridamole 200 mg bid.

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**CAPRIE**

**Clopidogrel vs Aspirin in Patients at Risk for Ischemic Events**

**Objective**
To test the relative efficacy of clopidogrel and aspirin for prevention of stroke, MI, or vascular death.

**Study Design**
Randomized, blinded, prospective, international trials at 304 study centers in 16 countries.

**Patient Population**
19,185 patients with
- Recent MI
- Recent ischemic stroke
- Established PAD

**Treatment**
Patients were randomized to
- Clopidogrel bisulfate: 75 mg/d
- Aspirin: 325 mg/d

**Treatment duration** lasted up to 3 years (mean 1.6 y).

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**2008 AHA/ASA Guideline Recommendations for Antiplatelet Therapy in Stroke and TIA**

"For patients with noncardioembolic ischemic stroke or TIA, antplatelet agents rather than oral anticoagulation are recommended to reduce the risk of recurrent stroke and other cardiovascular events (Class I, Level of Evidence A)."

"Aspirin (50 to 325 mg/d) monotherapy, the combination of aspirin and extended-release dipyridamole, and clopidogrel monotherapy are all acceptable options for initial therapy (Class I, Level of Evidence A)."

Stroke. 2008;39:1647

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**PRoFESS® Results Announced at XVII European Stroke Conference**

**Recurrent stroke event rates**
- **DP + ASA**: 9.0%
- **clopidogrel**: 8.8%
- **HR 1.01, 95% CI 0.92-1.11**

- The study did not meet its primary endpoint of non-inferiority for DP + ASA versus clopidogrel.

**Secondary endpoint of the composite of stroke, MI or vascular death**
- **13.1%**

**Hemorrhagic strokes**
- **0.8%**

**Benefit-risk ratio expressed as the combination of recurrent stroke and major hemorrhage**
- **11.7%**
- **HR 1.03, 95% CI 0.95-1.11**

ASA = aspirin 25 mg bid; DP = modified-release dipyridamole 200 mg bid.
PRoFESS® Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>DP + ASA</th>
<th>clopidogrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of randomized pts</td>
<td>10,181</td>
<td>10,151</td>
</tr>
<tr>
<td>Headache with permanent discontinuation</td>
<td>600 (5.95%)</td>
<td>88 (0.9%)</td>
</tr>
<tr>
<td>Dizziness or lightheadedness</td>
<td>1365 (13.6%)</td>
<td>908 (9.1%)</td>
</tr>
<tr>
<td>Fainting</td>
<td>149 (1.5%)</td>
<td>76 (0.8%)</td>
</tr>
<tr>
<td>Migraine during first 6 months of study</td>
<td>562 (5.9%)</td>
<td>314 (3.3%)</td>
</tr>
</tbody>
</table>

ASA = aspirin 25 mg bid; DP = modified-release dipyridamole 200 mg bid


Newer treatments for nonvalvular Afib

- **Warfarin**
  - Inhibits synthesis of vitamin K dependent clotting factors

- **Dabigatran**
  - Direct thrombin inhibitor

- **Rivaroxaban**
  - Direct factor Xa inhibitor

Reversal of Treatments

- **Warfarin**
  - Vitamin K
  - Fresh frozen plasma
  - Protein complex concentrates

- **Dabigatran**
  - No antidote
  - Hemodialysis

- **Rivaroxaban**
  - Hemostatics PCC, rFVIIa may be considered but not been evaluated
  - NOT dialyzable

Effect of statins on all strokes, fatal stroke, and hemorrhagic stroke

<table>
<thead>
<tr>
<th>Studies</th>
<th>Relative risk reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stroke (total)</td>
<td>0.82 (0.77–0.87)</td>
</tr>
<tr>
<td>All stroke (primary-prevention studies)</td>
<td>0.91 (0.75–0.87)</td>
</tr>
<tr>
<td>All stroke (secondary prevention: SPARCL, HPS, LIPID, and CARE)</td>
<td>0.88 (0.78–0.99)</td>
</tr>
<tr>
<td>Fatal stroke (total)</td>
<td>0.97 (0.73–1.33)</td>
</tr>
<tr>
<td>Fatal stroke (primary-prevention studies)</td>
<td>0.90 (0.76–1.09)</td>
</tr>
<tr>
<td>Fatal stroke (secondary prevention: SPARCL)</td>
<td>0.98 (0.36–2.97)</td>
</tr>
<tr>
<td>Hemorrhagic stroke (total)</td>
<td>1.03 (0.75–1.41)</td>
</tr>
<tr>
<td>Hemorrhagic stroke (primary-prevention studies)</td>
<td>0.91 (0.65–1.28)</td>
</tr>
<tr>
<td>Hemorrhagic stroke (secondary prevention: SPARCL and HPS)</td>
<td>1.73 (1.19–2.50)</td>
</tr>
</tbody>
</table>


Effect of High-dose Atorvastatin After Stroke or TIA

<table>
<thead>
<tr>
<th>No. at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin 2365 2148 2023 1903 1873 871 129</td>
</tr>
</tbody>
</table>

HR, 0.77 (95% CI, 0.67–0.88)  P<0.001

SPARCL=Stroke Prevention by Aggressive Reduction in Cholesterol Levels.

2008 AHA/ASA Recommendations for Lipid Management

- Ischemic stroke or TIA patients with elevated cholesterol, comorbid coronary artery disease, or evidence of an atherosclerotic origin should be managed according to NCEP III guidelines, which include lifestyle modification, dietary guidelines, and medication recommendations. Class I, Level A

- Statin agents are recommended, and the target goal for cholesterol lowering for those with CHD or symptomatic atherosclerotic disease is an LDL-C level of 100 mg/dL. An LDL-C 70 mg/dL is recommended for very high-risk persons with multiple risk factors. Class I, Level A


Adjusted risk for death or dependence associated with statin withdrawal

<table>
<thead>
<tr>
<th>Statin-withdrawal group, n (%)</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
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<tbody>
<tr>
<td>27 (60)</td>
<td>4.66</td>
<td>1.46–14.91</td>
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Individuals who stop statin treatment after hospitalization for ischemic stroke have nearly a fivefold increased risk for death or dependence within three months poststroke

Awareness Is Not Enough!

NCEP, National Cholesterol Education Program

Awareness Is Not Enough!

Impact of PROTECT pilot phase on Treatment Rates at Discharge

PROTECT: Incidence of Recurrent Stroke

A significant difference was observed at 90 days with regard to the incidence of recurrent strokes

Work-up of TIA and Ischemic Stroke

All Patients
- Brain Imaging
- Neurovascular imaging
- Blood glucose
- Serum electrolytes
- CBC w/ Platelets
- PT/PTT/INR
- 12 lead EKG/ROMI
- Holter monitoring
- TTE/TEE
- Supplemental O₂
- Fever reduction
- Lipids

Selected Patients
- Hepatic functions
- Toxicology
- Blood alcohol level
- Pregnancy
- Hypercoagulable w/u
- EEG
- LP

Discharged with:
- Blood pressure control
  - Diabetics ACEI/ARBs
- Antiplatelets
- Statins
- Lifestyle changes

Review of Learning Objectives
- Review Epidemiology
- Review polyvascular disease
- Discuss new definitions of TIA
- Review medical interventions
  - Antihypertensives
  - Statin therapy
  - Anticoagulants
  - Antiplatelet therapy
- Review barriers to improve outcomes
- Discuss promotion of stroke centers
- Review stroke workup

Thank you for your Attention

- All who drink of this treatment recover within a short time, except in those who do not.

Therefore, it fails only in incurable cases - Galen