Case 1

- A 54 year-old woman with a history of HTN presented to the ED after being found at a park not moving her right side.
- Exam shows an expressive aphasia, R face and arm plegia as well as L gaze deviation and R homonymous hemianopsia.
- Her symptoms began at noon, it is now 5:15 p.m. There are no contraindications to tPA.

What treatment should you initiate?

A. IV t-PA
B. IV heparin
C. Antiplatelets
D. Mechanical Embolectomy
E. Intra-arterial t-PA
The 2011 Acute Stroke Timeline

• Time of onset = last time seen normal
  0-4.5 Hours  IV-tPA
  0-6 Hours  IA-tPA
  0-8 Hours  Mechanical Embolectomy
  Greater than 8 hours  Anticoagulants or Antiplatelets

UCSF “Stroke Protocol” CT

• Obtained at UCSF in all suspected acute stroke and TIA patients
  1. Non-contrast CT of the head
  2. CT Angiography from aortic arch/heart through Circle of Willis
  3. CT Perfusion study
  4. Post-contrast CT of the head

Future Directions

• Perfusion-Based Time Window
  • Ultrasound-enhanced thrombolysis
    – With IV t-PA in 4.5 hour window
  • Drip and Ship
  • Combination Approaches
Case 2

- A 78 year-old man with a history of DM, HTN presents with 3 days of R sided weakness
- Examination shows R hemiparesis of face and arm greater than leg along with sensory deficits
- The patient is on clopidogrel daily

Which of the following is not part of the standard stroke workup?
A. Echocardiogram
B. Extended cardiac telemetry
C. Lipid panel
D. B12, TSH, RPR, ESR
E. Carotid evaluation

Standard Large-Vessel Stroke Workup
- Cardioembolic: afib, clot in heart, paradoxical embolus
  - 1. Telemetry
  - 2. TEE with bubble study
- Aortic Arch
  - 2. TEE with bubble study
- Carotids
  - 3. Carotid Imaging (CTA, US, MRA, angio)
- Intracranial Vessels
  - 4. Intracranial Imaging (CTA, MRA, angio)

And evaluate stroke risk factors
TEE vs. TTE

- 231 consecutive TIA and stroke patients of unknown etiology underwent TTE and TEE
- 127 found to have a cardiac cause of emboli, 90 of which (71 percent) only seen on TEE
- 38 of 46 “major risk factors” only found on TEE (most left atrial thrombi)
- TEE superior to TTE for: LA appendage, R to L shunt, examination of aortic arch


Atrial Fibrillation Detection

- EKG
- 48 Hours of Telemetry
- 30 day cardiac event monitor
  - 20% of patients with cryptogenic stroke otherwise unexplained had afib detected
  - Clearly changes management

Approach to Stroke Treatment

Acute Stroke Therapy?

No

Anticoagulants?

No

Antiplatelets

Shrinking Indications for Anticoagulation in Stroke

1. Atrial Fibrillation
2. Some other cardioembolic sources
   - Thrombus seen in heart
   - EF<35
   - PFO with associated Atrial Septal Aneurysm
3. Vertebral dissection
   - 2009: Questionable in carotid dissection
4. Rare hypercoagulable states: APLA

Afib with anticoagulation contraindicated

• ACTIVE trial (5/09)
  – 7500 patients randomized to ASA vs ASA + Clopidogrel
  – Decreased rate of stroke on combination therapy after mean 3.6 years (2.4% vs 3.3%, p<0.001) with increased major hemorrhage
• Concern re: decreased rates of anticoagulation after this study
  – Don’t forget ACTIVE W (Lancet 2006)

Case 3

- A 62 year-old man with a history of HTN, DM, smoking presents with 14 hours of right-sided weakness.
- The patient is on ASA 81mg daily

Stroke workup is unrevealing.

Your Treatment?

A. Increase ASA to 325mg daily
B. Add Plavix
C. Stop ASA, start Plavix
D. Anticoagulate
E. Stop ASA, start Aggrenox

Approach to Stroke Treatment

Acute Stroke Therapy?

<table>
<thead>
<tr>
<th>No</th>
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<tr>
<td>Anticoagulants?</td>
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<td>No</td>
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<td>Antiplatelets</td>
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Antiplatelet Options

• 1. ASA
  – 50mg to 1.5g equal efficacy long-term
• 2. Aggrenox
  – 25mg ASA/200mg ER Dipyridamole
    • ESPS-2, ESPRIT (Lancet 5/06)
• 3. Clopidogrel (Plavix)
  • MATCH (Lancet 7/04)
  • FASTER (Lancet Neurol 10/07)

Aggrenox vs. Plavix

• Aggrenox
  – Headache in first 2 weeks: 30% discontinue
  – Perhaps not compatible with cardiac antiplatelet goals
    or with unstable angina
  – Cannot be crushed in FT
• Plavix
  – Less evidence directly from stroke trials (until 2008)
  – Concerns regarding use in combination with ASA

PRoFESS Trial

• Randomized, double-blind trial of Aggrenox versus Plavix in over 20,000 patients with ischemic stroke
• Recurrent 4-year event rates basically identical between the two medications
  – HR for Aggrenox 1.01 (95% CI, 0.92-1.11)
  – Composite of stroke, MI, vascular death: 13.1% in each
  – Major hemorrhagic events higher in Aggrenox group

Antiplatelet Options

- If on no antiplatelet medication
  - ASA or Plavix vs. Aggrenox
- If already on ASA
  - Switch to Plavix vs. Aggrenox
- If already on Plavix or Aggrenox
  - ???

Other Acute Stroke Management

- Statins for (almost) all
  - SPARCL (NEJM 8/06), 80mg atorvastatin in stroke and TIA if LDL>100
- Permissive HTN
  - To at least 220/120 (unless IV t-PA): Mortality and morbidity increases if lower acutely
    - New 2011 evidence!
- Tight Glucose and Fever control
- Enoxaparin for DVT prophylaxis
  - PREVAIL trial (Lancet 2007)
  - CLOTS trial 1 (Lancet 2009): Compression Stockings

Case 4

- A 61 year-old man with HTN, DM comes to the ED after a 15 minute episode of right arm weakness that has since resolved.
- Exam is normal except bp 160/80
What would be your triage?

A. Admit to the hospital floor
B. Admit to the ICU
C. Send home and f/u with PCP in 1-2 weeks
D. Send home with f/u the next day
E. No f/u required

Differential for Transient Focal Neurologic Deficit

• The Big Three
  – 1. Stroke/TIA
  – 2. Seizure
  – 3. Complicated Migraine

TIA versus Stroke

• Up to 50% of TIA have infarct on imaging
• Conceptually the same disorder
  – Same workup, same treatment
• Pendulum swing
  – Pre-2001: Much more aggressive with Stroke
  – 2002-2007: TIA and Stroke equally aggressive
  – 2008-present: Moving to more aggressive approach with TIA
Risk of Future Stroke with TIA: 

**ABCD² Score**

- 7-day risk overall 8.6-10.5 percent
- **Age**
  - >60 = 1 point
- **Blood Pressure**
  - SBP>140 or DBP>90 = 1 point
- **Clinical Features**
  - Unilateral weakness = 2 points
  - Speech disturbance without weakness = 1 point
- **Duration**
  - >60 minutes = 2 points
  - 10-59 minutes = 1 point
- **Diabetes** = 1 point


**ABCD² Score**

- 2-day risk of stroke
  - Score 6-7: 8.1 percent (high risk)
  - Score 4-5: 4.1 percent (moderate risk)
  - Score 0-3: 1.0 percent (low risk)


Aggressive Therapy for TIA

- Two key studies in October 2007
- 1. SOS-TIA trial
  - 1085 patients with TIA admitted to a 24-hour center
  - All treated with standard therapy
  - 74 percent discharged on same day, stroke risk reduced 80 percent from ABCD² prediction
- 2. EXPRESS study
  - 80 percent reduction in risk with urgent TIA clinic visit versus usual primary care visit in 1278 patients

What treatment should you initiate?

A. Aggressive Medical Management  
B. Endarterectomy (CEA)  
C. Carotid Stenting

When to Fix the Carotid?

- NASCET in early 1990s
  - Benefit of endarterectomy in patients with symptoms ipsilateral to 70-99% stenosis
    - Comparison: best medical management at the time
  - 50-69% symptomatic stenosis revascularization has limited benefit, especially in women
- In stroke management don’t miss carotid disease or atrial fibrillation

How to Fix the Carotid?

- Stenting +/- distal protection
  - SAPHIRE (NEJM 10/04 and 4/08) in high-risk patients
  - Other small trials compare with NASCET data
  - Currently widely practiced: NeuroIR, vascular surgeons, BodyIR, Cardiologists
  - Unique risks: Hypotension, Bradycardia
Randomized Trial Results

- SPACE Trial (Lancet 10/06)
  - 1200 patients with recent stroke/TIA randomized to CEA vs. stenting
- EVA-3S (NEJM 10/06)
  - 527 patients with recent stroke/TIA randomized
  - Both failed to demonstrate non-inferiority
  - In EVA-3S, stenting associated with significantly more short-term stroke and death

New Confusing Data from 2010

- CREST (NEJM 2010): 1321 symptomatic and 1181 asymptomatic patients
  - Combined endpoint the same of stroke, MI, vascular death
  - More strokes in first 90 days in stenting group, more MIs in surgical group
- ICSS (Lancet 2010): 1713 symptomatic pts
  - Combined endpoint higher in stenting group
Case 5

- A 54 year-old man with a history of HTN comes to your office concerned as his mother just died after an ischemic stroke. He wants to know what primary preventative interventions can reduce his chances of having a similar event.

2011 Primary Prevention Guidelines

- Risk estimation schemes
- Treat vascular risk factors
- Anticoagulants for afib
  - CHADS2 score
    - 1-2=medium risk
    - 3 or higher=high risk
Asymptomatic Carotid Stenosis

- Some benefit for endarterectomy in asymptomatic stenosis
  - >60% or >80% cut-offs
  - Must have a very low perioperative risk of stroke and death to realize benefit (3%)
- Data much less convincing than symptomatic trials
- When to screen? Who to screen?

Does aspirin prevent stroke?

- 2009 Meta-analysis of serious vascular event primary prevention trials
- 95,000 individuals at low-average risk
- ASA offered 12% reduction in vascular risk but mainly driven by MI
- Stroke risk reduction not significant (0.20% per year vs. 0.21% per year, p=0.4)


Transcranial Doppler to Predict Stroke risk

- 2-year study of nearly 500 patients with asymptomatic (>70%) carotid stenosis
- Embolic signals on TCD predicted risk of stroke
  - Hazard ratio of ipsilateral stroke with emboli compared to without: 5.57
  - Annual risk of stroke 3.6% vs. 0.7%
- Can we stratify those with greatest chance of benefit from surgery/stenting?

Markus HS et al: Lancet Neurol 9:663, 2010
Folic Acid Supplementation

- Really doesn’t work for MI or Dementia
- Meta-analysis of 8 randomized with stroke as an end-point published
- Reduced risk of stroke by 18% (RR 0.82)
- Greater effects seen with
  - >36 months of treatment
  - Decreased homocysteine by >20 percent
  - No fortification or little fortification of grain
  - No history of stroke

Lancet 369:1876, 2007