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 2:15 p.m. There are no contraindications to tPA.

The 2012 Acute Stroke Timeline

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

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
  - Probably cost effective

Kamel H et al: Stroke 41:1514, 2010

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

The Excitement Over the Demise of Warfarin

- We hope oral direct thrombin and Xa inhibitors lead to more patients with afib and risk factors being anticoagulated
- Stroke-specific concerns
  - Contraindications to tPA
  - What do we do with ICH patients or those who need rapid surgery?
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

Approach to Stroke Treatment

Acute Stroke Therapy?
- No

Anticoagulants?
- No

Antiplatelets

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


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**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
  - ???

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**Other Acute Stroke Management**

- Statins for (almost) all
  - SPARCL (NEJM 8/06), 80mg atorvastatin in stroke and TIA if LDL>100
- Tight Glucose and Fever control
- Enoxaparin for DVT prophylaxis
  - PREVAIL trial (Lancet 2007)
  - CLOTS trial 1 (Lancet 2009): Compression Stockings

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**Permissive Hypertension**

- National Guidelines
  - To at least 220/120: Morbidity increases if lower in the acute setting
  - After IV tPA: less than 185 systolic for 24 hours
- Randomized trial of 2020 patients with acute stroke: candesartan vs placebo for 7d
  - Lower pressures with candesartan
  - No benefit to treatment
  - Higher risk of poor functional outcome with candesartan

Permissive Hypertension

- When to stop remains controversial
- Situations where more important
  - Large Vessel Occlusion
  - Fluctuating Symptoms
- We begin a medicine before discharge (~72h) and aim for normotension over a matter of weeks
  - Choose thiazides and ACEI first

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

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


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

CREST Trial Results

- 4-year study of 1321 symptomatic and 1181 asymptomatic patients randomized to CEA or carotid stenting
- Combined endpoint of stroke, MI, death not significantly different
  - More strokes in first 90 days in stenting group, more MIs in surgical group
  - After 90 days, similar endpoints

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?
**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?


**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)