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.

What treatment should you initiate?

A. IV t-PA
B. IV heparin
C. Antiplatelets
D. Mechanical Embolectomy
E. Intra-arterial t-PA

The 2014 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
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


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**Atrial Fibrillation Detection**

- EKG
- 48 Hours of Telemetry
- 30 day cardiac event monitor
  - 15-20% of patients with cryptogenic stroke otherwise unexplained had afib detected
  - Clearly changes management
  - Probably cost effective


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**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

Stroke workup is unrevealing. Your Treatment?

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

3. Clopidogrel (Plavix)
   - Multiple secondary prevention studies (CHARISMA, SPS3) show no benefit in combination with ASA

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
  - 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
  - Plavix vs. Aggrenox (or ASA)
- If already on ASA
  - Switch to Plavix vs. Aggrenox
- If already on Plavix or Aggrenox
  - ???

Clopidogrel + ASA: Ever A Winning Combination?

- CHANCE trial
  - 5170 TIA or Minor Stroke patients assigned to daily ASA + Placebo versus daily ASA + Clopidogrel following 300mg load
  - Primary outcome was stroke at 90 days
    - NNT=29 to prevent 1 stroke
    - Similar safety endpoints
- Generalizability?
  - Await POINT trial results

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

Permissive Hypertension

- National Guidelines
  - To at least 220/120
  - 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
- We typically stop all meds except half-dose β-blockers


CATIS Trial

- Over 2000 patients in China randomized within 48 hours of stroke to...
  - 1. HTN treatment to lower bp by 10-25% in the first 24 hours after randomization, with goal <140/90 mmHg within 7 days
  - 2. Stop all anti-HTN meds during hospitalization (control)
- Primary end point: Likelihood of death and major disability at 14d or at discharge


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

Other than TIA, what is the most common neurologic diagnosis here?
A. Conversion disorder
B. Migraine
C. Focal Seizure
D. UTI
E. Cervical spine lesion

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: Moved 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


Aggressive Therapy for TIA

- Two key studies
- 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 as good as endarterectomy
  - Became widely practiced: NeuroIR, vascular surgeons, BodyIR, Cardiologists
  - Unique risks: Hypotension, Bradycardia
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

![Guidelines for the Primary Prevention of Stroke](https://www.strokejournal.org/ AJHA/ASA_Guideline.pdf)
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)