83 yo RH F with PMhx of Dementia, HTN, HLD, hypothyroid presents to UPMC Hamot on 9/24/16 as regional stroke alert for sudden onset left-sided flaccidity and right gaze preference.

- Last seen well at approximately 7:30 am
- At 8:15 am she was noted to be walking into the wall
- She developed left-sided weakness and right gaze preference
- She was evaluated at OSH, reported NIH was 21
- Head ct reported to be without ICH and patient was given iv tpa at 10:17 am
- No CD of images performed was sent with patient

- On arrival she has LUE weakness, moved BL LE to commands
- Fixed R gaze, and was mute. NIH = 24
- She had SBP in 170s and appeared to be in no acute respiratory distress
## Neurologic Examination (NIH Stroke Scale)

| 0 | Level of consciousness (alert=0, arouses minor=1, arouses pain=2, unresponsive=3) |
| 0 | Ask patient current month and age (answers both=0, one=1, neither=2) |
| 0 | Ask patient to open and close eyes (performs both=0, one task=1, neither=2) |
| 0 | Best gaze (normal=0, partial gaze palsy=1, forced deviation=2) |
| 0 | Visual field testing (no loss=0, partial HA=1, complete HA=2, bilateral HA=3) |
| 0 | Facial palsy (normal=0, minor ie. smile=1, partial ie. lower face=2, complete=3) |
| 0 | Motor function left arm (no drift=0, drift=1, gravity=2, no gravity=3, no movement=4) |
| 0 | Motor function right arm (no drift=0, drift=1, gravity=2, no gravity=3, no movement=4) |
| 0 | Motor function left leg (no drift=0, drift=1, gravity=2, no gravity=3, no movement=4) |
| 0 | Motor function right leg (no drift=0, drift=1, gravity=2, no gravity=3, no movement=4) |
| 0 | Limb ataxia (absent=0, present 1 limb=1, present 2 limbs=2) |
| 0 | Sensory (normal=0, diminished=1, total=2) |
| 0 | Best language (no aphasia=0, mild=1, severe=2, global/mute=3) |
| 0 | Dysarthria (none=0, mild/mod=1, inintelligible=2) |
| 0 | Extinction and inattention (normal=0, inattention=1, profound=2) |

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| 0 | Total score |

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**Case 1**

No CD of images performed was sent with patient
Case 1

POD#4 NIHSS=4
Overview

- Background
- Does Size Matter?
- Small vessel occlusion?
- Large vessel occlusion?
- Additional Comments
Background

- The US Food and Drug Administration approval of IV tPA in 1996

- The concept of stroke as a treatable emergency was a major shift in clinical practice

- Following tPA approval
  - in-hospital stroke code teams were formed
  - primary and comprehensive stroke centers were developed and proliferated
  - vascular neurology emerged as a discrete specialty
Effects of Stroke Centers

- maximize the number of patients treated with tPA
- minimize delays to initiation of tPA treatment
- held hospitals to evidence-based standards for inpatient management across the spectrum of cerebrovascular diseases
- developed emergency medical systems (EMS) stroke protocols & guidelines
  - transport patients to stroke centers where they were most likely to receive tPA with the shortest delays

Background

Effects of Stroke Centers (cont)

- Public education campaigns for the recognition of stroke signs and urgency of calling 911
  - now more common on billboards and public service announcements
- Tele-stroke programs were developed to direct stroke thrombolysis decisions at hospitals without the in-house expertise
- Developed large stroke registries to track tPA statistics and performance metrics
  - provided insights about stroke risk factors, demographics, prevention, and outcomes
- More recently, established the efficacy of endovascular thrombectomy for reducing disability from large artery ischemic stroke
Background

Evolution of Thrombectomy Approaches and Devices

Does Size Matter?
• 114 patients acute M1-MCA stroke & hyperdense MCA sign
• Confirmed CT angiography or conventional angiogram
• Ten patients were excluded due to unavailable or uninterpretable follow-up scans; half (5/10) had symptomatic hemorrhage
• Among 104 patients, 28 patients were treated conservatively and 76 with thrombolysis

Studied showed that resolution of a HMCAS confirmed to be M1-MCA thrombus on CT angiography is highly length dependent

Disappearance of the HMCAS on the follow up scans was noted in 43 (41%) patients and was length dependent with thrombus length <10mm showing nearly 70% resolution ($P < .001$) and volume dependent ($P < .002$)

In all treatment groups, shorter thrombus length and smaller volumes were associated with a greater probability of resolution at follow-up.
Small vessel occlusion?

Lacunar Infarction: small subcortical infarcts that result from occlusion of a single perforating artery.

- Typically caused by intrinsic disease of small vessels called lipohyalinosis, resulting from HTN and DM
- Literature demonstrates that emboli can too be the cause of lacunes
- Most lacunar infarcts do not present with stroke. That is, unrecognized ("silent") lacunar infarcts are at least 5 times more common than symptomatic infarcts

When symptomatic, lacunar infarcts present with lacunar syndromes, 5 of which are well documented:
- pure motor stroke,
- pure sensory stroke,
- sensorimotor stroke,
- ataxic hemiparesis,
- and dysarthria (ie, clumsy hand)
Large vessel occlusion?

Large Vessel Stroke
“Treatment Helps Patients With Worst Kind of Stroke”

10 randomized controlled trials enrolling 2925 patients with ischemic stroke
- pooled analysis of these trials yielded statistically significant and clinically relevant effects
- statistically significant heterogeneity was found among the results of the studies

Heterogeneity was driven by
- differences in methodological and clinical features between studies
- disparities in inclusion criteria and in the interventions considered
- the proportion of patients who underwent intravenous thrombolysis & adjunctive i-a mechanical thrombectomy
- the type of devices used for thrombectomy

BMJ 2016: 353:i1754

Systematic Review of Recent Trials
- Endovascular treatment versus medical care -
Systematic Review of Recent Trials
- Endovascular treatment versus medical care -

Allowed posterior circulation strokes
Included strokes within the internal carotid artery and/or M1 and/or M2 portions of the middle cerebral artery
Utilized perfusion imaging depicting potentially salvageable brain tissue

In the intervention arm, use of intravenous rt-PA ranged from 0% in SYNTHESIS to 100% in IMS III, EXTEND-IA, SWIFT PRIME, THERAPY, and THRACE.

In SYNTHESIS, intravenous rt-PA was not administered owing to the study design (the study compared endovascular treatments, such as intra-arterial rt-PA and thrombectomy, with intravenous thrombolysis).
Systematic Review of Recent Trials
- Endovascular treatment versus medical care -

### Table 3 | Characteristics of intervention within treatment arms

<table>
<thead>
<tr>
<th>Trial</th>
<th>Both arms</th>
<th>AMIT arm</th>
<th>Medical care (IV rt-PA) arm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No of patients</td>
<td>% IV rt-PA</td>
<td>No (%) receiving thrombectomy</td>
</tr>
<tr>
<td>SYNTHESIZE³⁰</td>
<td>656</td>
<td>65% (45%)</td>
<td>434 (67% (39%))</td>
</tr>
<tr>
<td>MR RESCUE³⁰</td>
<td>117</td>
<td>44 (34.6%)</td>
<td>70 (61 (87.1%))</td>
</tr>
<tr>
<td>MR CLEAN⁵⁰</td>
<td>500</td>
<td>46% (88%)</td>
<td>233 (91% (87.1%))</td>
</tr>
<tr>
<td>ESCAPE³</td>
<td>315</td>
<td>238 (76%)</td>
<td>165 (51 (91.5%))</td>
</tr>
<tr>
<td>EXTEND A³⁷</td>
<td>70</td>
<td>70 (100%)</td>
<td>35 (27% (77.1%))</td>
</tr>
<tr>
<td>SWIFT PRIME³⁰⁰</td>
<td>98</td>
<td>98 (100%)</td>
<td>98 (100%)</td>
</tr>
<tr>
<td>REVASCAT³⁷</td>
<td>296</td>
<td>150 (52%)</td>
<td>103 (98.5%)</td>
</tr>
<tr>
<td>THERAPY³⁰</td>
<td>108</td>
<td>108 (100%)</td>
<td>55 (50%)</td>
</tr>
<tr>
<td>HRACE³⁰</td>
<td>285</td>
<td>285 (100%)</td>
<td>190 (66.9%)</td>
</tr>
</tbody>
</table>

Note: Intra arterial mechanical thrombectomy; IA = intra arterial; AMIT = no stent retrievers were used.

Most 2015 studies the rate of stent retriever use (such as Solitaire FR, Solitaire 2, Trevo, CathX) was more than 86% (86.1% to 100%) Recanalization rates varied between 25.0% - 88.0% according to a score of ≥2b/3 (perfusion of half or greater of the vascular distribution of the occluded artery) Recanalization rates greater than 56% observed in MR CLEAN, ESCAPE, EXTEND-A, SWIFT PRIME, REVASCAT, and THERAPY (most were treated with stent retrievers)

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Systematic Review of Recent Trials
- Good functional outcomes & Mortality at 90 days -

Overall, 1129 out of 2907 patients (38.8%) achieved a good functional outcome at 90 days

Pooled risk ratio for 2015 trials was 1.56, representing an increase of 167 patients attaining a good outcome (modified Rankin scale score ≤2) for each 1000 additional patients receiving endovascular treatment compared with medical care alone.

BMJ 2016: 353:i1754
Systematic Review of Recent Trials
- Good functional outcomes & Mortality at 90 days -

At 90 days, 482 out of 2880 participants (16.7%) died, without differences between arms in all cause mortality.

Overall, 129 out of 2526 patients (5.1%) experienced symptomatic intracerebral hemorrhage, with no significant differences between treatment groups. Furthermore, there were no significant differences between the results of trials published in 2013 and 2015.

Pivotal factors explaining statistically significant and clinically relevant results of 2015 randomized controlled trials (but not among the 2013 trials):

- focus on large vessel occlusion scenarios
- the selection of patients with less extensive brain tissue damage
- the use of two simultaneous endovascular reperfusion techniques (IV rt-PA and thrombectomy)
- the use of more efficient devices
Weaknesses of current trials despite multicenter RCT

- Not powered enough to evaluate the safety of endovascular treatment  
  - including adjunctive intra-arterial mechanical thrombectomy.
- Observational studies may be more adequate than RCT to evaluate safety  
  - as these may include patients who are usually excluded from RCT, and follow-up is often longer
- Lastly, the magnitude of effects may have been exaggerated  
  - by stricter patient selection  
  - by a higher level of study site selection  
  - by increased interventionist proficiency compared with the real world

Systematic Review of Recent Trials  
- Endovascular treatment versus medical care -

Considering the pathophysiology of ischemic stroke

- Faster, more efficient recanalization is of paramount importance  
  - reduce the infarction of penumbral brain tissue  
  - contribute to improved clinical outcomes
- Prompt administering of intravenous rt-PA as well as timely intravascular intervention like achieved in the 2015 studies may have contributed to less brain tissue damage
- Patients undergoing adjunctive intra-arterial mechanical thrombectomy for anterior LVO are  
  - twice as likely to be without disability  
  - 1.5 times as likely to be functionally independent 90 days
Endovascular Therapy in Acute Ischemic Stroke: Challenges and Transition From Trials to Bedside
Meryam Goyal, MD; Amy Y. Yu, MD; Bjoerk E. M. Wester, MD; Emmanuel W. J. Dippel, MD; Werner Hacke, MD; Stephen M. Davis, MD; Marc Fieschi, MD; Elijah E. Yacub, MD; Francesco Turan, MD; Jeffrey Ross, MD; Shinsa Yotsumoto, MD; Zhengxiang Mao, MD; Rohit Bhatt, MD; Muhammad Al-Hekail, MD; Yuchi Hayama, MD; Suni P. Sathia, MD; Jeffrey L. Saver, MD; Andrew M. Bechtle, MD; Michael J. Bill, MD

Comments and Opinions

Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials (HERMES collaboration)
Pooled individual patient data from the 5 positive trials

Investigate efficacy in subgroups too small to be conclusive in the individual trials

Study results showed no heterogeneity of the treatment effect across pre-specified subgroups

Number needed to treat with thrombectomy of 2.6 patients to achieve a reduction in disability of at least 1 level on the modified Rankin score
Several clinically important areas are under-represented in HERMES.

Although older patients (better represented than in previous trials)
- only 15% were 80 years of age or older
- same proportion had contraindications to IV thrombolysis

The trials covered only a very narrow range, onset-to-treatment time
- only 208 patients were randomized later than 5 h from onset
- and only 69 patients beyond 6 h

Questions regarding technical issues (remain unanswered)
- the place for aspiration techniques
- need for balloon guiding catheter
- the need for additional intra-arterial thrombolytic drugs

'faster is better' — it's all about speed.
Pooled data from 1287 patients (5 Trials)
- 634 who received endovascular thrombectomy plus thrombolysis
- 653 who received thrombolysis alone
- time from symptom onset to randomization = 196 minutes (~3 hrs)

In the endovascular group,
- mean time: symptom onset to arterial puncture = 238 minutes (~4 hrs)
- mean time: symptom onset to reperfusion = 286 minutes (~5 hrs)

At 90 days, the mean mRS score was
- 2.9 in the endovascular group and
- 3.6 in the thrombolysis-alone group

"faster is better" — it's all about speed.

Among every 1000 patients achieving substantial endovascular reperfusion…

… for every 15-minute faster emergency department door-to-reperfusion time:

- an estimated 39 patients would have a less-disabled outcome at 3 months
- including 25 more who would achieve functional independence (mRS 0-2)
The odds of better disability outcomes at 90 days (mRS distribution) declined with longer time from symptom onset to arterial puncture:

Odds ratio (OR)
- 3 hours = 2.79
- 6 hours = 1.98
- 8 hours = 1.57

Statistical significance was retained through 7 hours and 18 minutes (438 minutes).

Rates of functional independence after thrombectomy

- 64% with reperfusion at 3 hours
- 46% with reperfusion at 8 hours

Among 390 patients who achieved substantial reperfusion with endovascular thrombectomy…

… each 1-hour delay to reperfusion was associated with
- less favorable degree of disability (OR, 0.84)
- less functional independence (OR, 0.81)
- no significant change in mortality
Considering outcome distributions across all mRS health states, for every 9-minute delay in symptom onset-to–substantial endovascular reperfusion time, 1 of every 100 treated patients had a worse disability outcome (higher score by 1 or more levels on the mRS).

The probability of functional independence (mRS 0-2) at 3 months declined from 64.1% with symptom onset-to-reperfusion time of 180 minutes to 46.1% with symptom onset-to-reperfusion time of 480 minutes.

Distribution of mRS scores by treatment population at 90 days

For the primary outcome, pooled data showed reduced chance of disability at 90 days in patients assigned to thrombectomy versus those assigned to control (adjusted cOR 2·49, 95% CI 1·76–3·53; p<0·0001)

The number needed to treat for one patient to have reduced disability of at least 1 point on mRS was 2.6
Mortality at 90 days and risk of parenchymal hematoma type 2 and symptomatic intracranial hemorrhage did not differ between populations

<table>
<thead>
<tr>
<th>Intervention population</th>
<th>Control population</th>
<th>Risk difference (%)</th>
<th>Odds ratio (95% CI)</th>
<th>Adjusted odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic intracranial hemorrhage</td>
<td>4.4% (20/454)</td>
<td>4.9% (23/473)</td>
<td>-0.51</td>
<td>1.05 (0.63-1.78)</td>
</tr>
<tr>
<td>Parenchymal hematoma type 2</td>
<td>5.1% (10/197)</td>
<td>5.3% (14/264)</td>
<td>-0.2</td>
<td>0.99 (0.61-1.61)</td>
</tr>
<tr>
<td>Mortality</td>
<td>15.1% (9/60)</td>
<td>18.9% (122/646)</td>
<td>-1.96</td>
<td>0.82 (0.44-1.50)</td>
</tr>
</tbody>
</table>

Data show the proportion of patients with outcome (n%), unless otherwise stated.

Table 4: Safety outcomes at 90 days

Lancet Apr 2016 Vol 387

? Eligibility by Time and by Imaging

Mechanical thrombectomy ≤6 hours after symptom onset is the new standard of care

- However, when faced with the scenario of a patient presenting at 10 hours after symptom onset who fulfills the imaging and clinical criteria, should this patient be offered endovascular treatment?

- Does time of onset or neuroimaging determine patient eligibility for endovascular treatment?
  - The best answer would be a combination of both features
  - The ischemic tissue core grows with time
Case 2

- 57 y.o. white male with PMH of HTN, HLD, PVD with peripheral stents who presented to the ED as a stroke alert from home.
- Per EMS, patient went to bed at 6PM, around 11:00PM wife was up and heard him coughing in the bedroom, and then heard a thud. She found him on the ground next to the bed.
- He was not able to get up and would not answer her and that is when she called 911.
- On arrival (11:28PM), he is awake, alert but globally aphasic, not speaking or following commands.
- He has obvious right facial droop and right sided weakness.
- He has diminished pain response on the right.
- NIH 21
- CTA showed a left MCA trifurcation clot. Neurointervention was called.
Case 2

Next morning NIHSS=3
Discharge (day 2) NIHSS=1

NIHSS=21
One interesting finding is that patients with cervical carotid artery occlusive lesion in addition to the intracranial occlusion showed a dramatic treatment effect:

- **ESCAPE** = cOR 9.6 in favor of the endovascular treatment
- **REVASCAT** = cOR 4.3 in favor of the endovascular treatment

Optimal management of the cervical carotid artery occlusion is still unclear:

1. Formal assessment for revascularization by CEA or CAS at a later time
2. Immediate angioplasty/stenting of the lesion before attending the intracranial occlusion
3. Angioplasty/stenting of the lesion after attending the intracranial occlusion

The efficacy and safety of periprocedural antiplatelet management of patients with carotid artery stents is also uncertain.

**Tandem Extracranial and Intracranial Lesions**

...recommends thrombectomy for patients:
- Patients who are free from disability prior to the stroke
- Have occlusion of the internal carotid artery or proximal middle cerebral artery
- Received treatment with tPA within 4.5 hours from onset (if eligible)
- Have clinical severity of 6 or greater on the National Institutes of Health Stroke Scale
- Have a small infarct core defined as a score of 6 or greater (ASPECTS)
- Can have the procedure (arterial puncture) initiated < 6 hours from symptom onset

The guidelines also include recommendations about:
- The need to optimize systems of care to increase access
- Reduce times to treatment, without a specific prescription for how to do so
Additional Comments

Additional comments

- Transfers from local hospitals to endovascular-capable stroke centers must increase and must be accomplished with the utmost speed

- Sharing of vascular imaging by video links between the referring facilities and receiving facilities could potentially save an estimated 30 to 45 minutes by allowing for patients to be transported directly to the angiography suite

- Patients transferred between facilities had a delay of 2 hours compared with those taken straight to an endovascular center

- Less than 5% of all stroke patients may be candidates for endovascular thrombectomy therapy, new triage approaches for stroke need to be evaluated, as has previously occurred in the successful evolution of care for trauma and acute coronary syndrome.
Additional comments

• Meta analysis provides evidence that potentially supports strengthening of recommendations for treatment from 6 through 7 hours 18 minutes after symptom onset

• The potential benefit of earlier times to thrombectomy require substantial system changes to reduce workflow delays.

• Aggressive goals of Endovascular-capable stroke centers
  - 60 minutes from hospital arrival to arterial puncture
  - 90 minutes from hospital arrival to achievement of substantial reperfusion

Case 3

• symptom onset 13:15
• pre hospital stroke alert called at 13:47
• patient arrived 14:21
• blood glucose 97
• ct clear 14:33
• tpa started 14:47
• thrombectomy procedure start time 15:33
Case 3

- 74 year old female with no known past medical history.
- She denies any medical history or medications.
- She was an event today with her daughter and had a witnessed onset of sudden left sided flaccidity and facial droop. This occurred at precisely 1315.
- At that time she dropped her purse and the bags she was carrying.
- She admits to having a headache but denies chest pain, sob or palpitations.
- She has never had symptoms such as these before.
- Air transferred to UPMC and arrived as a prehospital stroke alert.
- NIHSS=17
Case 3

NIHSS=1
Questions?

"Mr. Osborn, may I be excused? My brain is full."

UPMC