Pregnancy and Stroke

Steven Feske, M.D.
Director, Stroke Division
Brigham and Women’s Hospital

October 28, 2016
Disclosures

I have no financial relationships with the developers of any of the products discussed.

NINDS
• SPOTRIAS
• NeuSTART
• IRIS (and Takeda Pharmaceuticals)
• ATACH II
• POINT
• StrokeNET
• DEFUSE-3

Covidien
• SWIFT PRIME
Morbidity of Stroke in Pregnancy and the Puerperium

Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality  N = 9 million discharges 2000-2001

- Stroke Rate  34 per 100,000
- Mortality Rate  1.4 per 100,000 = 4.1%

Disability estimates

- Long-term disability in ~2/3 survivors, greater in women
- Depression in 11-68%
- Major depression in 10-27%

Bousser M-G Circulation 1999;99:463
<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Rate per 10^5 Age 15-24</th>
<th>Rate per 10^5 Age 25-34</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accident</td>
<td>6.0</td>
<td>37.5</td>
</tr>
<tr>
<td>Homocide</td>
<td>0.8</td>
<td>13.0</td>
</tr>
<tr>
<td>Suicide</td>
<td>10.0</td>
<td>12.4</td>
</tr>
<tr>
<td>Cancer</td>
<td>4.1</td>
<td>9.0</td>
</tr>
<tr>
<td>Heart disease</td>
<td>2.7</td>
<td>8.1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>0.5</td>
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</table>
Rate of Stroke in Pregnancy and the Puerperium
Is It Increasing?

![Bar chart showing the rate of antenatal and postpartum stroke in 1994-5 and 2006-7. The rate per 100,000 is as follows:

- Antenatal Stroke:
  - 1994-5: 15
  - 2006-7: 22

- Postpartum Stroke:
  - 1994-5: 12
  - 2006-7: 22

Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality

*Stroke 2011;42:2564*
Increase in Rate of Stroke Follows Increases in Rates of HTN and Chronic Heart Disease

Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality

Stroke 2011;42:2564
Case
A 34-year-old woman began having headaches several days after delivery of her first child. The pregnancy and delivery had been normal, and the baby was healthy. Her headaches were diffuse, worse at night. Four days after onset, her husband witnessed a grand mal seizure. She had no history of prior seizures. On initial examination her pulse was 80 and regular, BP 115/70; she was aphasic and had mild right hemiparesis.
Head CT without contrast
## Causes of Hemorrhagic Stroke in Pregnancy

Percent of All Hemorrhages

<table>
<thead>
<tr>
<th></th>
<th>Preeclampsia</th>
<th>Eclampsia</th>
<th>Unknown</th>
<th>AVM</th>
<th>Aneurysm</th>
<th>Other</th>
<th>Cavernous Malformation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feske 2009</td>
<td>42</td>
<td>11</td>
<td>14</td>
<td>14</td>
<td>17</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Liang 2006</td>
<td>24</td>
<td>24</td>
<td>19</td>
<td>10</td>
<td>24</td>
<td>--</td>
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</tr>
<tr>
<td>Jeng 2004</td>
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<tr>
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<td>--</td>
<td>23</td>
<td>38</td>
<td>23</td>
<td>15</td>
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</tr>
<tr>
<td>Kittner 1996</td>
<td>15</td>
<td>31</td>
<td>23</td>
<td>--</td>
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<td>Sharshar 1995</td>
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Goals of Neuroimaging in Pregnancy

1. Provide standard of care imaging able to answer important diagnostic questions.
2. Minimize risks to the fetus.
3. Use radiation doses as low as reasonably achievable for potential stochastic effects.
4. Use doses below exposure thresholds for deterministic effects.
Goals of Neuroimaging in Pregnancy

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4. *Use doses below exposure thresholds for deterministic effects.*

- **Stochastic effects** – *May occur after any dose of radiation; higher doses increase risk.*
  - Mutagenesis
  - Childhood malignancy

- **Deterministic effects** – *Predictably occur above specific exposure thresholds.*
  - Cataract formation
  - Infertility
Considerations in Neuroimaging in Pregnancy

1. Radiation dose absorbed
2. Rate of dose absorption
3. Fetal gestational age
4. Urgency of diagnostic need
Considerations in Neuroimaging in Pregnancy

1. **Radiation dose and rate absorbed**
   1. E.g. Estimate 6% increase in risk of childhood cancer per 100 rad.
   2. Fetal exposure to indirect radiation from CT is to be < 0.01 rad.
   3. Fetal exposure to direct radiation from pelvic CT may reach 3 rad.

2. **Fetal gestational age**

3. **Urgency of diagnostic need**
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   1. 0-4 weeks – Increase risk of miscarriage with doses > 10 rad.
   2. 5-10 weeks – Fetal malformation, growth retardation, and death possible with doses > 5-10 rad.
   3. 6 weeks – birth – Mental retardation with doses > 5-10 rad.
      1. Very low risk after 15 weeks

3. **Urgency of diagnostic need**
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3. Urgency of diagnostic need
For potential stroke in pregnancy:

• **Degree of urgency is high.**

• **Exposure is indirect and doses are low.**

• **Events occur late in pregnancy when fetal risks are minimal.**
Further Considerations in Neuroimaging in Pregnancy

1. *MRI*

2. *Iodinated Contrast Agents*

3. *Gadolinium*
Further Considerations in Neuroimaging in Pregnancy

1. **MRI is felt to be safe.**
   1. No conclusive evidence of fetal harm from exposure up to 3 T.
   2. **Theoretical concerns**
      1. Noise exposure
      2. Strong magnetic fields
      3. Increase in body temperature

2. **Iodinated contrast agents should be avoided, except when no alternative.**
   1. **Theoretical concerns**
      1. Neonatal hypothyroidism
      2. Renal injury

3. **Gadolinium should be avoided.**
   1. **Theoretical concerns**
      1. Miscarriage
      2. Developmental abnormalities
CT without contrast
Empty Delta Sign

CT with contrast
How should we treat her?
Case

28-year-old RH woman 30-weeks pregnant without prior complications

• 10:00 AM last seen well

• 10:50 AM found on ground by her husband, eyes open, mute, weak on R

• Brought to a local hospital
  • Alert without gaze deviation
  • Dense motor aphasia, mute
  • Dense right hemiplegia
  • No signs of trauma
  • Normal CBC, platelets, INR, PTT
  • Head CT normal (or subtle change of acute stroke; no hemorrhage)
  • MRI early acute stroke left basal ganglia
PMH
• G2 P1
• G1 2009; stat C-section at term for concerning fetal heart tracing
• G2 current @ 30 weeks;
  • Rh− received Rhogam at 28 weeks
  • Observed briefly for preterm contractions at 28 weeks
• No miscarriages
• No pre-eclampsia-eclampsia
• No prior abnormal thrombosis
• No trauma
• Nonsmoker; no alcohol or drug abuse

FH
• 2 maternal uncles and one aunt with DVT/PE; ?FVIII excess
• No family history of arterial dissection, aneurysm, or AVM
• Father estranged and history unknown
On Arrival at Local Hospital

11:50 AM
1 hr 50 min

CT without contrast
MRI at Local Hospital

12:33 PM
2 hr 33 min

DWI
ADC
dark so acute infarct

FLAIR
Not yet bright, so early

MRI at Local Hospital

12:33 PM
2 hr 33 min
What imaging study would you get?
MRA at BWH

Left M1 occlusion
Open left ICA without evidence of dissection
How should we treat her?
Case
A 36-year-old woman complained of headaches and was found to have new HTN 10 days after delivery of twins by C-section. Initial head CT and MRI were normal. Headaches persisted, and she had a grand mal seizure and developed aphasia and right hemiparesis.
What is the diagnosis?
How should we treat her?
Changes in Coagulability during Pregnancy

• Physical changes
  • Compression of the IVC
  • Compression of the aorta
  • Compression of uterine arteries and veins
  • Decreased venous compliance

• Increases in procoagulant factors
  • Increase in factors I, VII, VIII, IX, X, XII, and XIII
  • No change in factors II, V, XI

• Decreases in coagulation inhibitors
  • Decreased AT III
  • Decreased protein S
  • Functional protein C resistance

• Thrombin generation and fibrinolysis
  • Increased thrombin generation
  • Increased fibrinogen and fibrinolysis
  • Platelet consumption
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Changes in Coagulability during Pregnancy

Intrinsic pathway

- XII
- XIIa
- XI
- Xla
- IX
- IXa
- VIIIa
- VIII
- Va
- Prothrombin II
- V
- Fibrinogen I
- Activated Protein C
- Protein S
- Protein C
- Thrombomodulin

Extrinsic pathway

- VIIa
- VII
- Tissue factor
- Antithrombin III
- X
- Xa
- X
- Thrombin IIa
- Fibrin la
- Cross-linked fibrin clot
- FDP
- Plasmin

Increased
Decreased
Is Iron Deficiency a Thrombophilic State?

<table>
<thead>
<tr>
<th>Cases</th>
<th>No.</th>
<th>female</th>
<th>male</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pediatric cases</strong></td>
<td>12</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Arterial ischemic strokes</td>
<td>6</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Cerebral venous sinus thrombosis</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Central retinal artery occlusion</td>
<td>1</td>
<td>1</td>
<td>--</td>
</tr>
<tr>
<td><strong>Adult cases</strong></td>
<td>14</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Arterial ischemic strokes</td>
<td>7</td>
<td>7</td>
<td>--</td>
</tr>
<tr>
<td>Cerebral venous sinus thrombosis</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Central retinal vein occlusion</td>
<td>3</td>
<td>3</td>
<td>--</td>
</tr>
<tr>
<td>Non-arteritic ischemic optic neuropathy</td>
<td>1</td>
<td>1</td>
<td>--</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>--</td>
<td>1</td>
</tr>
</tbody>
</table>
Is Iron Deficiency a Thrombophilic State?

**Possible mechanisms**

- Thrombocytosis – many patients had normal or near normal platelet counts
- Cytokines – not elevated when studied
- Erythropoietin elevation
- High flow turbulence – does not explain venous events
- Associated disease, such as tumor – not found
- Female predominance is likely related to female predominance of iron deficiency – does not explain predominance in children
Acute Hemorrhage is a Thrombophilic State!

- Thrombosis and hemorrhage are well-known complications of trauma

- Increased high molecular weight fibrinogen after delivery as part of the acute phase reaction

- The mild “DIC” state:
  - Increased thrombin generation

  - Increased fibrinolysis
    - increased FDP
    - increased D-dimer
    - Fibrinogen consumption

  - Platelet consumption

Postpartum Thrombophilia

1,687,930 Californian women hospitalizations for delivery from Jan 2005 to June 2010

Thrombotic events: Stroke, MI, VTE

Risk factors
• Older
• White or African American v Hispanic or Asian
• No private insurance
• Other risk factors for thrombosis
  • Age > 35 yr
  • Eclampsia
  • Primary hypercoagulable state
  • Smoking
  • Cesarean delivery

Kamel NEJM 2014;370:1307
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  • Age > 35 yr
  • Eclampsia
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  • Smoking
  • Cesarean delivery
• Physiologic protein S deficiency
• Acute blood loss and trauma of labor
• Iron deficiency anemia
• Dehydration

Kamel NEJM 2014;370:1307
Risk of Thrombosis
During 3-week Intervals after Delivery

At 13-15 weeks
OR = 2.0 (95% CI, 1.1-3.6)
## Risk of Stroke Based on Time After Delivery

<table>
<thead>
<tr>
<th>Time after Delivery</th>
<th>Case Period Rate per 100,000 deliveries</th>
<th>Crossover Period Rate</th>
<th>Absolute Risk Difference</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks 0-6</td>
<td>7.1</td>
<td>0.8</td>
<td>6.2</td>
<td>8.5 (4.9 - 14.8)</td>
</tr>
<tr>
<td>Weeks 7-12</td>
<td>0.9</td>
<td>0.5</td>
<td>0.4</td>
<td>1.7 (0.7 - 3.8)</td>
</tr>
<tr>
<td>Weeks 13-18</td>
<td>0.5</td>
<td>0.5</td>
<td>0</td>
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</tr>
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<td>Weeks 19-24</td>
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Kamel NEJM 2014;370:1307
# Risk of Thrombotic Event Based on Time After Delivery

**Odds Ratios**

<table>
<thead>
<tr>
<th>Time after Delivery</th>
<th>Stroke</th>
<th>MI</th>
<th>VTE</th>
<th>Composite</th>
<th>All</th>
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<tr>
<td>Weeks 0-6</td>
<td>8.5</td>
<td>13.0</td>
<td>12.1</td>
<td>10.8</td>
<td>22.8</td>
</tr>
<tr>
<td>Weeks 7-12</td>
<td>1.7</td>
<td>4.0</td>
<td>2.2</td>
<td>2.2</td>
<td>2.1</td>
</tr>
<tr>
<td>Weeks 13-18</td>
<td>1.0</td>
<td>1.0</td>
<td>1.6</td>
<td>1.4</td>
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<td>2.5</td>
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**Clear increase in risk for at least 12 weeks; though small after 6 weeks...**

Kamel NEJM 2014;370:1307
## Risk of Thrombotic Event Based on Time After Delivery

### Absolute Risk

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<td>Weeks 0-6</td>
<td>6.2</td>
<td>0.7</td>
<td>15.2</td>
<td>22.1</td>
<td>127.6</td>
</tr>
<tr>
<td>Weeks 7-12</td>
<td>0.4</td>
<td>0.4</td>
<td>2.3</td>
<td>3.0</td>
<td>6.1</td>
</tr>
<tr>
<td>Weeks 13-18</td>
<td>0</td>
<td>0</td>
<td>0.9</td>
<td>0.9</td>
<td>0.2</td>
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<tr>
<td>Weeks 19-24</td>
<td>0.1</td>
<td>0.2</td>
<td>-0.3</td>
<td>-0.1</td>
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**Clinical importance:** VTE > Stroke > MI

Kamel NEJM 2014;370:1307
## Major Series of Stroke in Pregnancy

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Location</th>
<th>Time Interval</th>
<th>No. Pregnancies</th>
<th>No. Events</th>
<th>Ischemic Strokes</th>
<th>Hemorrhagic Strokes</th>
</tr>
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<tbody>
<tr>
<td>Weibers 1985</td>
<td>Rochester, MN population-based</td>
<td>1955-79</td>
<td>26,099</td>
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<td>53</td>
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## Stroke Proportions and Rates

### Hospital-based Studies (raw proportion)

<table>
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<tr>
<th>Study</th>
<th>N</th>
<th>Total Events</th>
<th>Ischemic</th>
<th>Hemorrhagic</th>
<th>Total per 10^5</th>
</tr>
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<tbody>
<tr>
<td>Feske 2009</td>
<td>101,570</td>
<td>52*</td>
<td>15.8</td>
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<td>79,301</td>
<td>20</td>
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### Population-based Studies (incidence)

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<th>N</th>
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<td>Sharshar 1995</td>
<td>348,295</td>
<td>4.3 4.6</td>
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* Strokes only; single TIA not included.
# Stroke Proportions and Rates

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<tr>
<th>Study</th>
<th>N</th>
<th>Total Events</th>
<th>Ischemic</th>
<th>Hemorrhagic</th>
<th>Total per 10⁵</th>
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<td>Feske 2009</td>
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<td><strong>Population-based Studies (incidence)</strong></td>
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* Strokes only; single TIA not included.
Relative Risk of Stroke in Pregnancy and the Puerperium

<table>
<thead>
<tr>
<th>Stroke Type</th>
<th>Relative Risk of Stroke during Pregnancy</th>
<th>Relative Risk of Stroke during the Puerperium (6 wk)</th>
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<tr>
<td>Cerebral infarction</td>
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<tr>
<td>Cerebral hemorrhage</td>
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Rate of Stroke in Pregnancy and the Puerperium
Is It Increasing?

<table>
<thead>
<tr>
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<tr>
<td>Antenatal Stroke</td>
<td>15</td>
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<td>Postpartum Stroke</td>
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Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality

Stroke 2011;42:2564
## Mechanisms of Ischemic Stroke in Pregnancy

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>% Cardio-embolism</th>
<th>% PEE</th>
<th>% Peripartum Angiopathy</th>
<th>% CVT</th>
<th>Unknown</th>
<th>% Other</th>
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<tr>
<td>Awada 1995</td>
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<td>--</td>
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<tr>
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<td>39</td>
<td>--</td>
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<td>Boston</td>
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<td></td>
<td></td>
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</tbody>
</table>
Stroke Subtypes: BWH Jan 1996-Dec 2005

Pregnancy-related diagnoses
N = 101,570

Stroke events
N = 53

Ischemic events
N = 17
- Venous thrombosis without hemorrhage
  N = 3
- Arterial events
  N = 14
  - Embolism
    N = 8
  - Large vessel disease
    N = 1
  - Non-specific/Other
    N = 4
  - TIA
    N = 1

Hemorrhagic events
N = 36
- Venous thrombosis with hemorrhage
  N = 6
- Eclampsia-associated
  N = 15
- Vascular malformation
  N = 11
- Ruptured aneurysm
  N = 5
- Ruptured AVM
  N = 5
- Cavernous malformation
  N = 1
- Non-specific
  N = 4

Total CVT = 9

Feske Stroke 2009;40(4):e183
Rare Causes of Stroke in Pregnancy

**Choriocarcinoma**
- Malignant transformation of trophoblasts
- Molar pregnancy; also term, abortion, ectopic
- Early metastases to lungs, brain, liver, vagina
- Vascular invasion causing thrombosis and hemorrhage

**Amniotic Fluid Embolism**
- Dyspnea
- Hypotension
- Cardiorespiratory collapse
- DIC
- Neurologic deficits

**Risks**
- Difficult labor
- Multiparity
- Greater gestational age
- Advanced maternal age

**Air Embolism**
- C-section
- Vaginal insufflation

**Sheehan Syndrome**
- Anterior pituitary hypertrophy
- Limited blood supply
- Hemorrhage and hypotension
Choriocarcinoma

Subintimal tumor

Tumor free in lumen

Choriocarcinoma in Vertebral Artery

... in MCA

Aguilar MJ. Neurology 1964;14:933
Choriocarcinoma

Hemorrhage and hemorrhagic infarction

Aguilar MJ. Neurology 1964;14:933
Stroke Subtypes: BWH Jan 1996-Dec 2005

Pregnancy-related diagnoses
N = 101,570

Stroke events
N = 53

Ischemic events
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- Non-specific
  N = 4

Total CVT = 9

Feske Stroke 2009;40(4):e183
10 of 14 women with arterial strokes had major predisposing conditions:

- 6 hypercoagulable states
  - APAS, DIC, SLE, MTHFR mutation, Crohn’s disease
  - strong family history of early stroke

- 1 congenital heart disease and mechanical heart valve

- 1 fibromuscular dysplasia and vertebral artery dissection

- 1 delayed vasospasm (possible postpartum PEE/postpartum vasculopathy)

- 1 HELLP syndrome and cardiac arrest

6 of 14 women with arterial ischemic strokes had PEE
Underlying Causes of Stroke: Cerebral Venous Thrombosis

8 of 9 women with CVT had major predisposing conditions:

- 6 hypercoagulable state
  - prior DVT
  - strong family history of venous thrombosis
  - APAS
  - protein S deficiency
  - MTHFR mutation
  - sickle cell trait

- 1 family history of early CAD (1)

- 1 HELLP syndrome (1)
Timing of Events

Timing of arterial ischemic events

Timing of cerebral venous thrombosis

Timing of cerebral hemorrhages associated with preeclampsia/eclampsia

Timing of cerebral hemorrhages associated vascular malformations

Feske Stroke 2009;40(4):e183
Case
A 37-year-old woman 27 weeks pregnant developed a sudden, severe headache and nausea and vomiting and neck stiffness. On initial examination her pulse was 100 and regular, BP 145/70; she was initially alert and then slightly drowsy. Otherwise mental state and the rest of the neurologic examination were normal.
Conventional Angiogram

L Vertebral Injection AP
Conventional Angiogram

3D Reconstruction
Conventional Angiogram

Before

L Vertebral Injection AP

After Coiling
Importance of Hemorrhagic Stroke in Pregnancy

<p>| | |</p>
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<tr>
<td>Absolute risk</td>
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<td>Relative risk</td>
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<tr>
<td>Mortality</td>
<td>5-12%</td>
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<tr>
<td>Author/Year</td>
<td>% AVM</td>
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<td>Sharshar 1995</td>
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<td>Kittner 1996</td>
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<tr>
<td>Witlin 1997</td>
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<td>Jeng 2004</td>
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* 6 CVT not included
## Mechanisms of Hemorrhagic Stroke in Pregnancy

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<th>Author/Year</th>
<th>% AVM</th>
<th>% Aneurysm</th>
<th>% CM</th>
<th>% PEE</th>
<th>% Unknown</th>
<th>% Other</th>
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<td>Boston N = 30</td>
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</tbody>
</table>

* 6 CVT not included
Timing of cerebral hemorrhages associated with preeclampsia/eclampsia

Feske 2009
Timing of cerebral hemorrhages associated with vascular malformations

AVM

SAH

CM

Feske 2009
Treatment of aneurysms

**Risks**

- Increasing risk of recurrent hemorrhage with progression of pregnancy; peaks at 30-34 weeks

- High risk of recurrent hemorrhage if an initial bleeding aneurysm goes unsecured: 33-50%

- High maternal and fetal mortality; great benefit of surgery
  - Overall: mother 35%; fetus 17%
  - With no surgery: mother 63%; fetus 27%
  - With surgery: mother 11%; fetus 5%

**Recommendations**

- Secure aneurysm as soon as possible after rupture by open or endovascular surgery.

- If cannot, because urgent obstetrical issues prevent it, then proceed to C-section and then secure aneurysm.

Dias Neurosurgery 1990;27:855
Treatment of AVMs

Risks
- Some authors have found increased risk of AVM hemorrhage during pregnancy, others have not.
- Analysis of risk of rupture per day shows many-fold increase of risk on day of delivery.
- Risk is greatly increased after hemorrhage during pregnancy; to about 26% (vs 6% risk if hemorrhage before pregnancy).

Recommendations
- If known AVM, address before pregnancy.
- If AVM found during pregnancy without hemorrhage, “controlled delivery” with plan to treat AVM after delivery.
- If AVM bleeds during pregnancy, treat definitively based on neurosurgical principles (based on grading of AVM).

Ogilvy Stroke 2001;32:1458
Treatment of CVT
Treatment of CVT


Heparin for Venous Sinus Thrombosis

Mean Severity Score vs Time (days)

- Control
- Heparin

Einhäupl Lancet 1991;338:597
Heparin for Venous Sinus Thrombosis
3-month Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control (N=10)</th>
<th>Heparin (N=10)</th>
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<tbody>
<tr>
<td>Complete recovery</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Slight neurologic deficit</td>
<td>6</td>
<td>2</td>
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<tr>
<td>Death</td>
<td>3</td>
<td>0</td>
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</table>

Einhäupl Lancet 1991;338:597
Overall Benefit or Harm of Heparin, Outcome: Death

<table>
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<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
<th>Weight</th>
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<tbody>
<tr>
<td>Einhaupl 1991</td>
<td>0/10</td>
<td>3/10</td>
<td>46.2%</td>
<td>0.14 [0.01, 2.45]</td>
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<td>CVST Group 1999</td>
<td>2/30</td>
<td>4/29</td>
<td>53.8%</td>
<td>0.48 [0.10, 2.44]</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>40</strong></td>
<td><strong>39</strong></td>
<td>100.0%</td>
<td><strong>0.33 [0.08, 1.28]</strong></td>
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</table>

Total events: 2 (Treatment), 7 (Control)
Heterogeneity: Chi² = 0.55, df = 1 (P = 0.46); I² =0.0%
Test for overall effect: Z = 1.60 (P = 0.11)

Overall Benefit or Harm of Heparin, Outcome: Death and Dependency

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
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<td>Einhaupl 1991</td>
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<tr>
<td>CVST Group 1999</td>
<td>4/30</td>
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<td>63.5%</td>
<td>0.64 [0.20, 2.05]</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>40</strong></td>
<td><strong>39</strong></td>
<td>100.0%</td>
<td><strong>0.46 [0.16, 1.31]</strong></td>
</tr>
</tbody>
</table>

Total events: 4 (Treatment), 9 (Control)
Heterogeneity: Chi² = 0.97, df = 1 (P = 0.32); I² =0.0%
Test for overall effect: Z = 1.45 (P = 0.15)

Cochrane Rev 2002
6. For patients with CVT, *initial anticoagulation with UFH or LMWH in full anticoagulant doses is reasonable, followed by warfarin, regardless of the presence of ICH* (Class IIa; Level B)

8. In patients with CVT and increased ICP it is reasonable to initiate treatment with acetazolamide (Class IIa; Level C)

9. Endovascular intervention may be considered if deterioration occurs despite intensive anticoagulation treatment (Class IIb; Level C)

10. In patients with neurological deterioration due to severe mass effect or ICH causing intractable intracranial hypertension, decompressive hemicraniectomy may be considered (Class IIb; Level C)

Saposnik G et al. Stroke 2011;42:1158
Treatment of Acute Ischemic Stroke
NINDS Study of IV rt-PA for Acute Ischemic Stroke Outcome

Modified Rankin Scale

<table>
<thead>
<tr>
<th></th>
<th>0-1</th>
<th>2-3</th>
<th>4-5</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>26</td>
<td>25</td>
<td>27</td>
<td>21</td>
</tr>
<tr>
<td>rt-PA</td>
<td>39</td>
<td>21</td>
<td>23</td>
<td>17</td>
</tr>
</tbody>
</table>

ARR = 13 %
NNT = 8
NNH = 20 (sICH 6 vs 0.6 %)
(Harm as sICH)

The NINDS Stroke Study Group NEJM 1995;333:1581
IV tPA in 3-4.5 hr Window

ECASS III Results: Primary Endpoint

Modified Rankin Scale at 90 days

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>rt-PA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>45</td>
<td>52</td>
</tr>
<tr>
<td>2-3</td>
<td>28</td>
<td>23</td>
</tr>
<tr>
<td>4-5</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>Death</td>
<td>7</td>
<td>8</td>
</tr>
</tbody>
</table>

ARR = 7 %
NNT = 14
NNH = 45 (sICH 2.4 v 0.2 %)

OR = 1.34
P-value = 0.04

ECASS III NEJM 2008;359:1317
TREVO Stentriever

SOLITAIRE Flow Restoration

MERCI devices

Mechanical Clot Retrieval Devices

TREVO Stentriever
Dense Left MCA Sign

CT without contrast
Occlusion of the Terminal LICA
Angiogram

Before clot extraction

After clot extraction

Angiogram
Stent Retriever with Extracted Clot
Final Stroke

DWI
Final Stroke

This...

Not This!
### Randomized Clinical Trials of Endovascular Therapy for Acute Ischemic Stroke 2015

<table>
<thead>
<tr>
<th>Trial</th>
<th>Country</th>
<th>Good Outcome (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR CLEAN</td>
<td>Netherlands</td>
<td>33</td>
</tr>
<tr>
<td>ESCAPE</td>
<td>Canada</td>
<td>53</td>
</tr>
<tr>
<td>EXTEND-IA</td>
<td>Australia</td>
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<td>SWIFT PRIME</td>
<td>USA</td>
<td>60</td>
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<tr>
<td>REVASCAT</td>
<td>Spain</td>
<td>44</td>
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<td>THRACE</td>
<td>France</td>
<td>53</td>
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<tr>
<td>PISTE</td>
<td>UK</td>
<td>28</td>
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</table>

**Medical**: 19, 29, 40, 35, 28