Pregnancy and Stroke

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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
• ARCADIA

Covidien
• SWIFT PRIME
Topics

I. Importance of stroke in pregnancy
II. Pathophysiology of stroke in pregnancy
III. Cerebral venous thrombosis
IV. Acute ischemic stroke
V. Subarachnoid hemorrhage
VI. PRES and RCVS
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
# Leading Causes of Death in Adolescents and Young Adults

<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>
<td>1.4</td>
</tr>
</tbody>
</table>
Summary of Risks

Non-pregnancy women of childbearing age
• The annual risk of stroke in non-pregnant women ages 15-44 is low (10/10^5). However, the risk may be rising (Ban 25/10^5). (up to age 49)

Pregnancy-associated
• 42% of strokes in women 15-44 y/o are associated with pregnancy.

All Strokes
• Considering ALL STROKES (ICH + AIS): There is a small increase in ALL STROKES during pregnancy driven by hemorrhagic stroke.
• There is a marked increase in ALL STROKES during the early postpartum period.

During pregnancy
• There is no increase in the risk of ISCHEMIC STROKES during pregnancy. (Ban found slight decrease.)
• There is an increase in the risk of HEMORRHAGIC STROKES during pregnancy (Kittner 2.5-fold, Ban increased SAH)

During the early postpartum period
• There is an increased risk of ISCHEMIC STROKES in the early postpartum period (up to 6 weeks). (Kittner 8.7-fold)
• There is an increased risk of HEMORRHAGIC STROKES in the early postpartum period (up to 6 weeks). (Kittner 28.5-fold, Ban increased ICH and SAH)
Rate of Stroke in Pregnancy and the Puerperium
Is It Increasing?

<table>
<thead>
<tr>
<th>Year</th>
<th>94-5</th>
<th>06-7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal Stroke</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td>Postpartum Stroke</td>
<td>12</td>
<td>22</td>
</tr>
</tbody>
</table>

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

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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>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral infarction</td>
<td>0.7</td>
<td>8.7</td>
</tr>
<tr>
<td>Cerebral hemorrhage</td>
<td>2.5</td>
<td>28.5</td>
</tr>
</tbody>
</table>

Major References: Epidemiology


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
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
- X → Xa

Extrinsic pathway

- VIIa → VII
- Tissue factor

Prothrombin II

Activated Protein C

Antithrombin III

Fibrinogen I

Fibrin Ia

Plasmin

FDP

Cross-linked fibrin clot

Protein S

Protein C Thrombomodulin

Intrinsic pathway

- XII → XIIa
- XI → Xla
- IX → IXa VIIIa
- X → Xa

Extrinsic pathway

- VIIa → VII
- Tissue factor

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Antithrombin III

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Fibrin Ia

Plasmin

FDP

Cross-linked fibrin clot

Protein S

Protein C Thrombomodulin
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
Risk of Thrombosis
During 3-week Intervals after Delivery

At 13-15 weeks
\( OR = 2.0 \) (95% CI, 1.1-3.6)

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

<table>
<thead>
<tr>
<th>Time after Delivery</th>
<th>Case Period</th>
<th>Crossover Period</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>0.0</td>
<td>1.0 (0.4 – 2.5)</td>
</tr>
<tr>
<td>Weeks 19-24</td>
<td>0.9</td>
<td>0.9</td>
<td>0.1</td>
<td>1.1 (0.5- 2.2)</td>
</tr>
</tbody>
</table>

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>
</tr>
</thead>
<tbody>
<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>
<td>1.0</td>
</tr>
<tr>
<td>Weeks 19-24</td>
<td>1.1</td>
<td>2.5</td>
<td>0.9</td>
<td>1.0</td>
<td>0.9</td>
</tr>
</tbody>
</table>

*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**

<table>
<thead>
<tr>
<th>Time after Delivery</th>
<th>Stroke</th>
<th>MI</th>
<th>VTE</th>
<th>Composite</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absolute Risk Difference</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<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>
</tr>
<tr>
<td>Weeks 19-24</td>
<td>0.1</td>
<td>0.2</td>
<td>-0.3</td>
<td>-0.1</td>
<td>-0.9</td>
</tr>
</tbody>
</table>

**Clinical importance:** VTE > Stroke > MI

Kamel NEJM 2014;370:1307
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.
### 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><strong>Feske 2009</strong></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><strong>Liang 2006</strong></td>
<td>24</td>
<td>24</td>
<td>19</td>
<td>10</td>
<td>24</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>Jeng 2004</strong></td>
<td>32</td>
<td>--</td>
<td>23</td>
<td>14</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>Jaigobin 2000</strong></td>
<td>--</td>
<td>23</td>
<td>38</td>
<td>23</td>
<td>15</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>Kittner 1996</strong></td>
<td>15</td>
<td>31</td>
<td>23</td>
<td>--</td>
<td>31</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>Sharshar 1995</strong></td>
<td>44</td>
<td>19</td>
<td>13</td>
<td>13</td>
<td>--</td>
<td>13</td>
<td>--</td>
</tr>
</tbody>
</table>
### Causes of Hemorrhagic Stroke in Pregnancy

#### Percent of All Hemorrhages

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<thead>
<tr>
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<th>Preeclampsia</th>
<th>Eclampsia</th>
<th>Unknown</th>
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<th>CVT</th>
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<td><strong>Feske 2009</strong></td>
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<td>11</td>
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<td>13</td>
<td>--</td>
<td>13</td>
<td>--</td>
</tr>
</tbody>
</table>
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.

- **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 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**
   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**
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
Left Transverse Sinus Thrombosis

Normal MR Venogram
How should we treat her?
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>
</tr>
</thead>
<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>
</tr>
<tr>
<td>Death</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

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

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

Total events: 2 (Treatment), 7 (Control)
Heterogeneity: Chi² = 0.55, df = 1 (P = 0.46); I² = 0%
Test for overall effect: Z = 1.60 (P = 0.11)

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

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<th>Control n/N</th>
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<td></td>
<td>36.5</td>
<td>0.14 [ 0.01, 2.45 ]</td>
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<tr>
<td>CVST Group 1999</td>
<td>4/30</td>
<td>6/29</td>
<td></td>
<td>63.5</td>
<td>0.64 [ 0.20, 2.05 ]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>40</strong></td>
<td><strong>39</strong></td>
<td></td>
<td><strong>100.0</strong></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%
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
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
Case

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

CT without contrast

11:50 AM
1 hr 50 mim
On Arrival at Local Hospital

CT without contrast

11:50 AM
1 hr 50 min
What would you do now?
What additional imaging studies would you get?
MRA at BWH

Left M1 occlusion
Open left ICA without evidence of dissection
## Mechanisms of Ischemic Stroke in Pregnancy

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>% Cardioembolism</th>
<th>% PEE</th>
<th>% Peripartum Angiopathy</th>
<th>% CVT</th>
<th>% Unknown</th>
<th>% Other</th>
</tr>
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<tbody>
<tr>
<td>Awada 1995, Saudi Arabia</td>
<td>33</td>
<td>11</td>
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<td>44</td>
<td>11</td>
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<td>Sharshar 1995, Ile de France</td>
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<td>7</td>
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<td><strong>27</strong></td>
<td><strong>20</strong></td>
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<tr>
<td>Kittner 1996, Md/Wash DC</td>
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<td>25</td>
<td><strong>13</strong></td>
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<td>Witlin 1997, Memphis</td>
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<td>Jiagobin 2000, Toronto</td>
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<td>Jeng 2004, Taiwan</td>
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<td>--</td>
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<td>Liang 2006, Taiwan</td>
<td>36</td>
<td>18</td>
<td>--</td>
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<td>--</td>
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<tr>
<td>Feske 2009, Boston</td>
<td>35</td>
<td>26</td>
<td>--</td>
<td>39</td>
<td>--</td>
<td>22</td>
</tr>
</tbody>
</table>
How should we treat her?
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 v 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>
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<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
SOLITAIRE Flow Restoration

MERCI devices

TREVO Stentriever

Mechanical Clot Retrieval Devices
Dense Left MCA Sign

CT without contrast
Occlusion of the Terminal LICA
Stent Retriever with Extracted Clot
Final Stroke

DWI
Final Stroke

This...

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

Good Outcome (%) Independence at 90 days

<table>
<thead>
<tr>
<th>Trial</th>
<th>Medical</th>
<th>Endovascular</th>
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</thead>
<tbody>
<tr>
<td>MR CLEAN</td>
<td>33</td>
<td>19</td>
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<tr>
<td>Canada</td>
<td>53</td>
<td>29</td>
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<tr>
<td>Australia</td>
<td>71</td>
<td>40</td>
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<tr>
<td>USA</td>
<td>60</td>
<td>35</td>
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<tr>
<td>Spain</td>
<td>44</td>
<td>28</td>
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<tr>
<td>France</td>
<td>192</td>
<td>94</td>
</tr>
<tr>
<td>UK</td>
<td>94</td>
<td>32</td>
</tr>
</tbody>
</table>

Netherlands Canada Australia USA Spain

Endovascular Medical
Randomized Clinical Trials of Endovascular Therapy for Acute Ischemic Stroke in Late Window 2018

Good Outcome (%)

Independence at 90 days

DAWN USA
Endovascular 49
Medical 13
NNT 3

DEFUSE 3 USA
Endovascular 45
Medical 17
NNT 4
<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Wk</th>
<th>Gestation</th>
<th>Indication</th>
<th>Outcome Mother</th>
<th>Outcome Fetus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baudo 1990</td>
<td>35</td>
<td>PE 1</td>
<td>No cx</td>
<td>No cx</td>
<td>No cx</td>
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<tr>
<td>Flossdorf 1990</td>
<td>31</td>
<td>PE 1</td>
<td>No cx</td>
<td>No cx</td>
<td>No cx</td>
</tr>
<tr>
<td>Azzano 1995</td>
<td>16</td>
<td>Valve 1</td>
<td>Severe bleeding rethrombosis</td>
<td>Fetal death after</td>
<td></td>
</tr>
<tr>
<td>Schumacher 1996</td>
<td>21</td>
<td>MI 1</td>
<td>No cx</td>
<td>No cx</td>
<td>No cx</td>
</tr>
<tr>
<td>Fleyfe 1997</td>
<td>28</td>
<td>Valve 1</td>
<td>No cx</td>
<td>No cx</td>
<td>No cx</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>5</strong></td>
<td></td>
<td><strong>1 bleeding</strong></td>
<td><strong>1 death</strong></td>
</tr>
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</table>

From Ahearn Arch Intern Med 2002;162:1221
### IV tPA Use for Stroke in Pregnancy

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Maternal/Gestational Age</th>
<th>Maternal Outcome</th>
<th>Fetal Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapprich 2002</td>
<td>-- / 12 wk</td>
<td>minor ICH</td>
<td>No Cx</td>
</tr>
<tr>
<td>Weise 2006</td>
<td>33 yr / 13 wk</td>
<td>No Cx</td>
<td>No Cx</td>
</tr>
<tr>
<td>Leonhardt 2006</td>
<td>26 yr / 23 wk</td>
<td>No Cx</td>
<td>No Cx</td>
</tr>
<tr>
<td>Murugappan 2006</td>
<td>37 yr / 12 wk</td>
<td>minor uterine hematoma</td>
<td>MTP*</td>
</tr>
<tr>
<td>Murugappan 2006</td>
<td>31 yr / 4 wk</td>
<td>No Cx</td>
<td>MTP*</td>
</tr>
<tr>
<td>Murugappan 2006</td>
<td>29 yr / 6 wk</td>
<td>died**</td>
<td>died</td>
</tr>
<tr>
<td>Yamaguchi 2010</td>
<td>36 yr / 18 wk</td>
<td>No Cx</td>
<td>No Cx</td>
</tr>
<tr>
<td>Hori 2013</td>
<td>35 yr / 4 mos</td>
<td>no Cx</td>
<td>No Cx</td>
</tr>
<tr>
<td>Tassi 2013</td>
<td>28 yr / 16 wk</td>
<td>no Cx</td>
<td>No Cx</td>
</tr>
<tr>
<td>Ritter 2014</td>
<td>32 yr / 36 wk</td>
<td>no Cx</td>
<td>No Cx</td>
</tr>
</tbody>
</table>

*MTP = medical termination of pregnancy

** died from arterial dissection complicating angioplasty

- Dapprich Cerebrovasc Dis 2002;13:290
- Wiese Stroke 2006;37:2168
- Leonhardt J Throm Thrombolys 2006;21:271
- Murugappan Neurology 2006;66:768
- Yamaguchi Rinsho Shinkeigaku 2010;50:315
- Hori Rinsho Shinkeigaku 2013;53:212
- Ritter J Neurol 2014;261:632
## IA tPA Use for Stroke in Pregnancy

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Maternal/Gestational Age</th>
<th>Maternal Outcome</th>
<th>Fetal Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elfort 2002</td>
<td>28 / 1wk (after IVF)</td>
<td>minor ICH</td>
<td>No Cx</td>
</tr>
<tr>
<td>Johnson 2005</td>
<td>39 yr / 37 wk</td>
<td>No Cx</td>
<td>No Cx</td>
</tr>
<tr>
<td>Murugappan 2006</td>
<td>43 yr / 37 wk</td>
<td>No Cx</td>
<td>No Cx</td>
</tr>
<tr>
<td>Murugappan 2006</td>
<td>28 yr / 6 wk</td>
<td>buttock hematoma</td>
<td>No Cx</td>
</tr>
<tr>
<td>Murugappan 2006</td>
<td>25 yr / 1st trimester</td>
<td>minor ICH</td>
<td>Miscarriage*</td>
</tr>
<tr>
<td>Li 2012</td>
<td>24 yr / 11 wk</td>
<td>No Cx</td>
<td>No Cx</td>
</tr>
</tbody>
</table>

* Mother had bacterial endocarditis

Elfort Neurology 2002;59:1270  
Johnson Stroke 2005;36:e53  
Murugappan Neurology 2006;66:768  
Li Neurologist 2012;18:44
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

<table>
<thead>
<tr>
<th>Type</th>
<th>Value</th>
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<tbody>
<tr>
<td>Absolute risk</td>
<td>0.006</td>
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<tr>
<td>Relative risk</td>
<td>28.5</td>
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<tr>
<td>Mortality</td>
<td>5-12%</td>
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</table>
### Mechanisms of Hemorrhagic Stroke in Pregnancy

<table>
<thead>
<tr>
<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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<tr>
<td>Sharshar 1995</td>
<td>13</td>
<td>13</td>
<td>13</td>
<td>44</td>
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<tr>
<td>Ile de France N = 16</td>
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<tr>
<td>Kittner 1996</td>
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<td>15</td>
<td>31</td>
<td>31</td>
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<tr>
<td>Md/Wash DC N = 13</td>
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<tr>
<td>Witlin 1997</td>
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<td>--</td>
<td>--</td>
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<td>Memphis N = 6</td>
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<td>Jiagobin 2000</td>
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<td>23</td>
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<td>Toronto N = 13</td>
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<tr>
<td>Jeng 2004</td>
<td>23</td>
<td>14</td>
<td>--</td>
<td>32</td>
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<td>--</td>
</tr>
<tr>
<td>Taiwan N = 22</td>
<td></td>
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<td></td>
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<td>Liang 2006</td>
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<td>10</td>
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<td>24</td>
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<td>Taiwan N = 21</td>
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<tr>
<td>Feske 2009*</td>
<td>17</td>
<td>17</td>
<td>3</td>
<td>50</td>
<td>13</td>
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<tr>
<td>Boston N = 30</td>
<td></td>
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</tbody>
</table>

* 6 CVT not included
### Mechanisms of Hemorrhagic Stroke in Pregnancy

<table>
<thead>
<tr>
<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>15</td>
<td>31</td>
<td>31</td>
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<td>Md/Wash DC N = 13</td>
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<td>Memphis N = 6</td>
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<tr>
<td>Toronto N = 13</td>
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<td>Liang 2006</td>
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<tr>
<td>Feske 2009*</td>
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<td>17</td>
<td>3</td>
<td>50</td>
<td>13</td>
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<tr>
<td>Boston N = 30</td>
<td></td>
<td></td>
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</tr>
</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.
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
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.
Singhal AB NEJM 2009;360:1126
Singhal AB NEJM 2009;360:1126
What is the diagnosis?
How should we treat her?
## MgSO4 versus Phenytoin for Eclampsia

**Recurrent convulsions**
- MgSO4 5.7%
- Phenytoin 17.1%
- $P < 0.00001$
- 67% relative risk reduction

### Chart

<table>
<thead>
<tr>
<th>No. of recurrent convulsions</th>
<th>MgSO4</th>
<th>Phenytoin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
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<tr>
<td>&gt;5</td>
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</table>

Eclampsia Trial Collaborative Group Lancet 1995;345:1455