Stroke in Pregnancy

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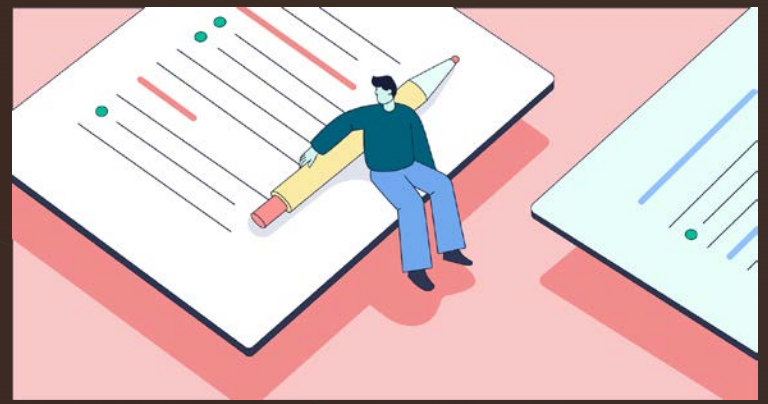
Objectives

- Maternal Mortality & Incidence of Stroke in Peripartum
- When It happens
- Why it happens
- What to do
- How you prevent it
- Call to action



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Mortality

Maternal Mortality

- Pregnancy Mortality Surveillance System – Pregnancy related death within 1 year of end of pregnancy
- Pregnancy related deaths on the rise
  - 7.2/100,000 in 1987
  - 33.2/100,000 in 2021

[1]CDC

Maternal Mortality

- Racial/Ethnic disparities (deaths/100,000) in 2021
  - 118.7 American Indian or Alaska Native persons
  - 111.7 among Native Hawaiian or other Pacific Islander persons
  - 69.3 Non-Hispanic Black persons
  - 31.4 Hispanic persons
  - 24.3 White persons
  - 22.4 Asian persons

[1]CDC

Maternal Mortality

- Pregnancy mortality urban vs rural (deaths/100,000)
  - 29.9 large metro – central
  - 25.4 large metro – fringe
  - 36.7 medium metro
  - 36.4 small metro
  - 42.6 micropolitan
  - 41.4 “noncore” (<10,000 residents)

[1]CDC

Maternal Mortality

- 1/3 deaths are cardiovascular related[2]
- 1/12 Deaths maternal deaths in the US are due to stroke[3]

[2] Elgendy
[3] Miller

Limited Data for Stroke in Pregnancy/Postpartum

- Difficult to study
- Lack of data
- “Stroke” definitions vary
- “Postpartum period” definitions vary

[3] Miller

How often does stroke in pregnancy setting occur?

- 18% of strokes women ages 12-35
- Increase over the last 30 years[3]
  - From 1994/5-2006/7 up 47% antenatal, 83% postpartum[4]
- Occurs 30-34/100,000 delivers [2,5,11]
  - Compared with approx. 10/100,000 nonpregnant women of similar age[6]
- May be as high 1/500 delivers for pregnant persons with high risk comorbidities

[2] Elgendy
[3] Miller
[4]Kuklina
[5]Too
[6]Hong
[11] Swartz

When do they happen?

- Approx 1 day prior to birth to 2 weeks after delivery[2,3]
- Many happen outside of the hospital
- Healthcare Cost and Utilization Project's Nationwide Readmissions Database 2013-2014 – retrospective cohort study looking at readmission for stroke within 2 months of discharge. [4]
  - 6,272,136 deliveries
  - 1505 patients readmitted for stroke, majority within 10 days.

[2]Elgendy
[3] Miller
[4]Too
[11]Swartz

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Why do pregnant women have strokes?

Risk Factors-Nonpregnancy Related

- APLS
- AVM
- Cardiac disease
- Chronic HTN
- CKD
- Diabetes
- Genetic stroke syndromes
- Infection
- Migraine
- Obesity
- Primary hypercoagulable state
- Race
- Sickle cell disease
- Social determinants of health
- Smoking
- SLE

[2]Elgendy
[3]Miller

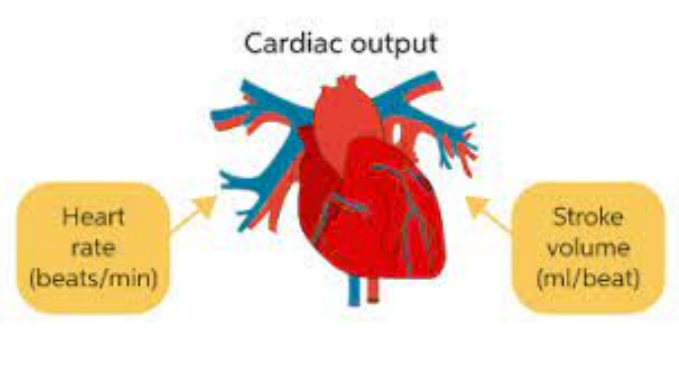
Pregnancy Related Risk Factors

- Assistance with reproductive technology
- Cesarean delivery
- Hypertensive disorders of pregnancy[2]
  - Gestational HTN
  - HELLP
  - Preeclampsia/eclampsia
  - Chronic HTN
- Metastatic choriocarcinoma
- Peripartum Cardiomyopathy

[2] Elgendy
[3]Miller

Why do strokes occur in pregnancy?

- Cardiovascular adaptation
  - Increase 50% cardiac output
  - Cardiac remodeling – LA dilation, LV mass increase
  - Increase risk of arrhythmias, especially with underlying cardiac conditions
  - Systemic vasodilation, vascular compliance, venous capacitance -> increased risk of VTE
  - Sympathetic vasomotor activation-> increased risk of RCVS



[3] Miller
[9] Miller

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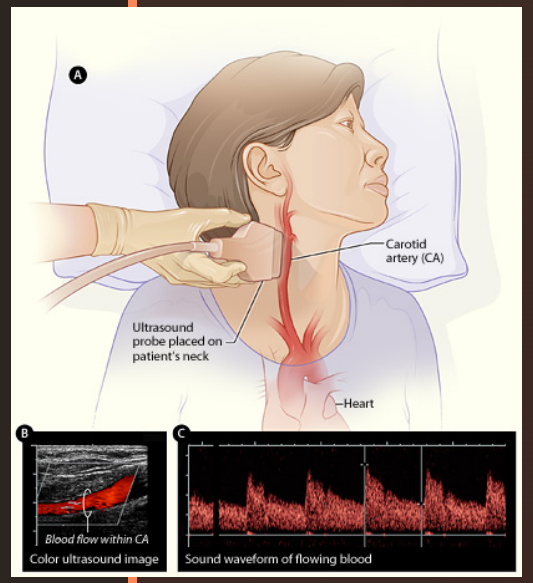
Why do strokes occur in pregnancy?

- Arterial Remodeling & BBB
  - Increase in carotid stiffness in healthy pregnant women as compared with nonpregnant controls [7]
  - Remodeling of cerebral arterioles and resistance to systematic vasoconstrictors, permeability of BBB
  - Failure of physiologic changes may account for increased risk of stroke in preeclampsia



[3]Miller
[7]Yuan
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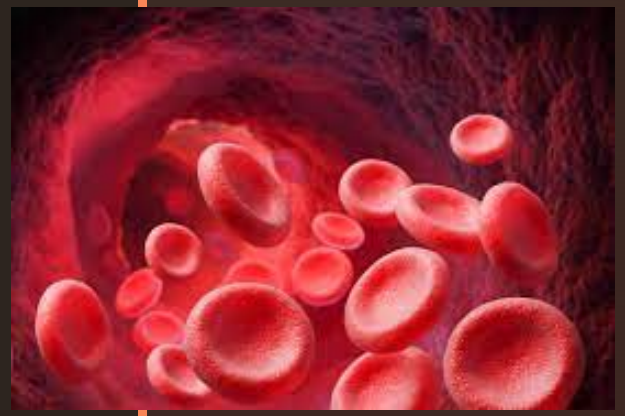
Why do strokes occur in pregnancy?

- Hematologic adaptation
  - Increased volume-> dilutional anemia, decreased clotting factors
  - Increased von Willebrand factor, Factor V, Factor VIII, and fibrinogen, acquired resistance to activated protein C.
  - Placenta produces antifibrinolytics



[2] Elgendy
[3]Miller
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Why do strokes occur in pregnancy?

- Immunomodulation and inflammatory changes
  - 1st trimester high inflammatory milieu, high levels of Thelper activity, IL-6, CRP, and TNF alpha which affect endothelial function – increase thrombus formation
  - 2nd trimester immune quiescent state
  - Near delivery proinflammatory state returns increased transcription factor nuclear factor kappa
  - Dysregulation of immunomodulatory response implicated in preterm births, preeclampsia, peripartum cardiomyopathy

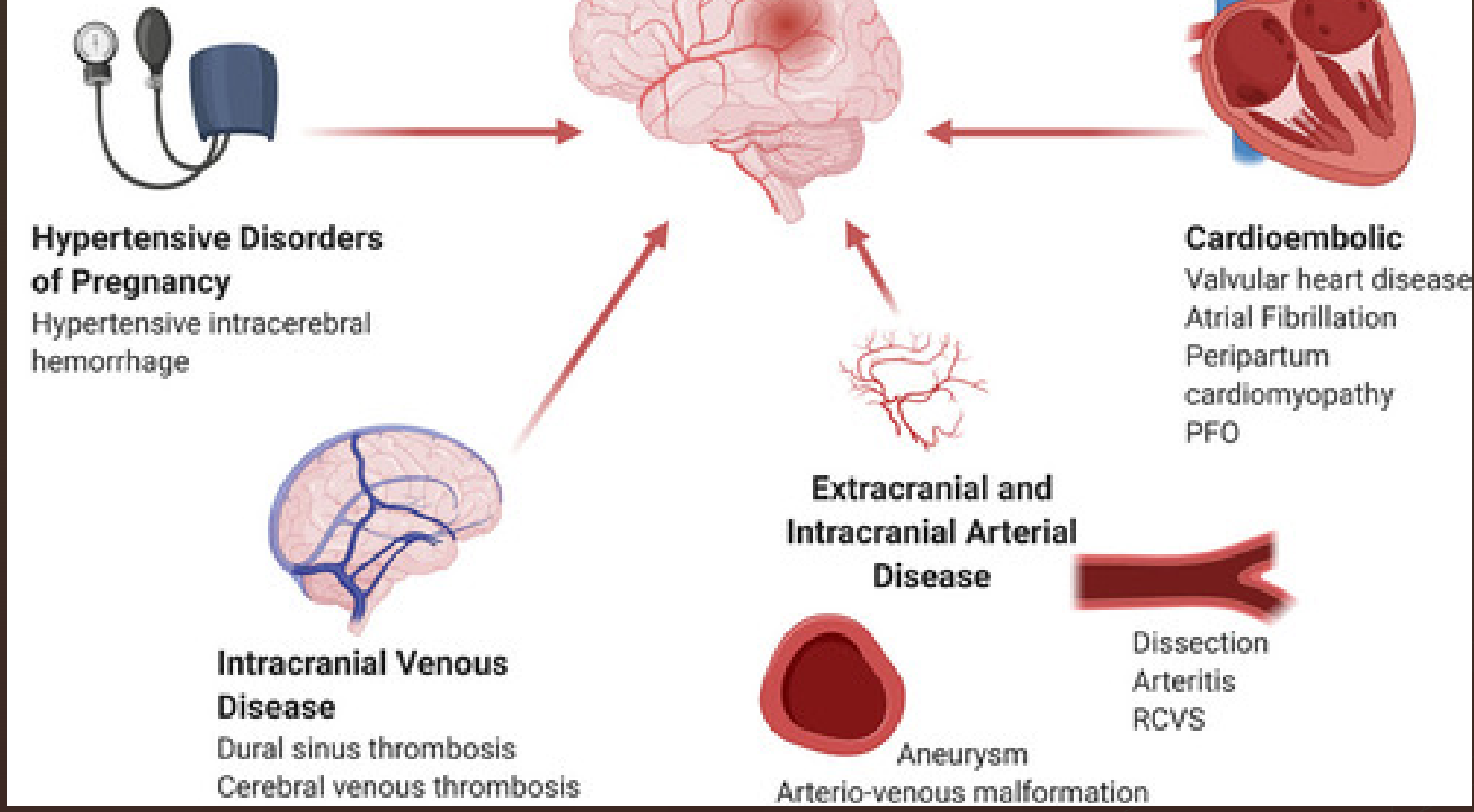
[3]Miller

Ischemic vs Hemorrhagic

- ~60% hemorrhagic[2]
  - Compared with 13% of general population

[2] Elgendy
[3]Miller

Mechanisms of Pregnancy-Associated Stroke



Hypertensive Disorders of Pregnancy
Hypertensive intracerebral hemorrhage

Cardioembolic
Valvular heart disease
Atrial Fibrillation
Peripartum cardiomyopathy
PFO

Intracranial Venous Disease
Dural sinus thrombosis
Cerebral venous thrombosis

Extracranial and Intracranial Arterial Disease

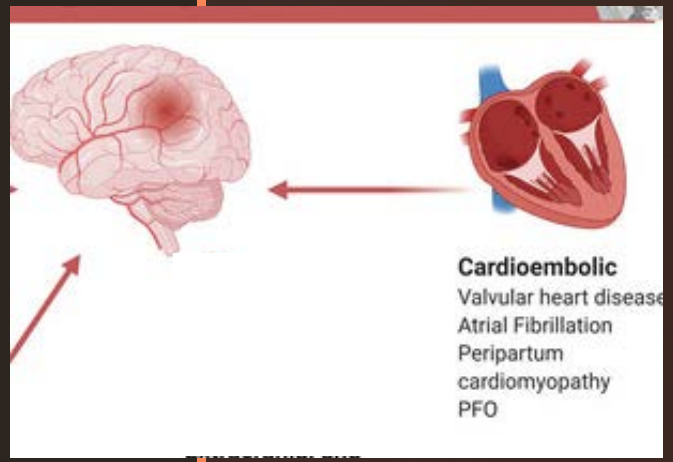
Dissection
Arteritis
RCVS

Aneurysm
Arterio-venous malformation

Photo from [2]Elgendy

Causes of Ischemic Stroke in Peripartum

- Cardioembolic
  - Paradoxical Emboli with PFO or pulmonary shunt
  - Preexisting cardiac disease
  - Peripartum cardiomyopathy

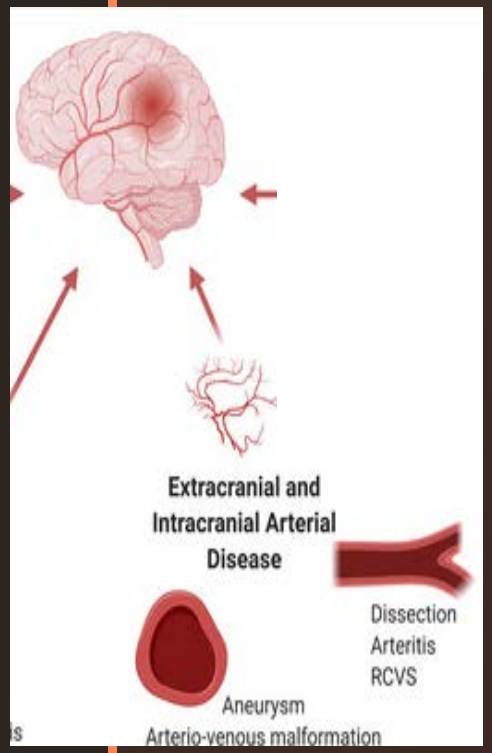


[2] Elgendy
[3]Miller
[9] Miller

Photo from [2]Elgendy

Causes of Ischemic Stroke in Peripartum

- Dissection
  - 5x more likely in setting of pregnancy
  - More often in setting of HTN or postpartum RCVS
  - Trauma
    - Partner violence increased in pregnancy and postpartum

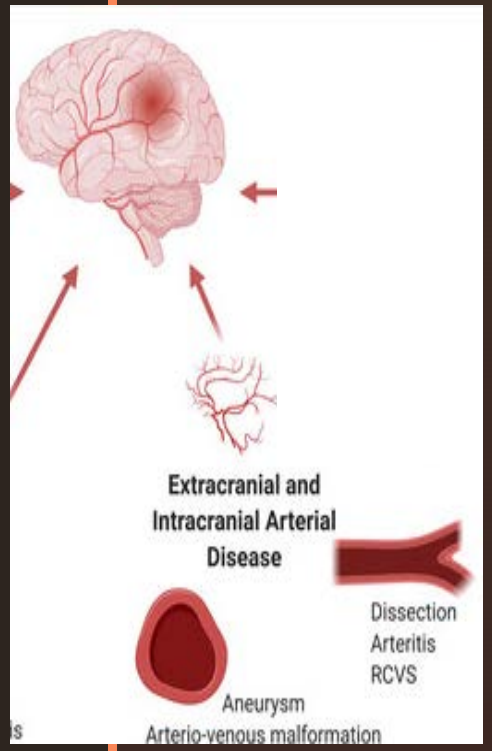


[2] Elgendy
[3] Miller

Photo from [2] Elgendy

Causes of Ischemic/Hemorrhagic Stroke in Peripartum

- Reversible Cerebral Vasoconstriction Syndrome (RCVS)
  - Nonvasculitic vasospasm of medium and large cerebral arteries
  - Postpartum state accounts for up to 20% of cases
  - Ischemic, SAH, and/or ICH
  - More common in preeclampsia



[2] Elgendy
[3] Miller

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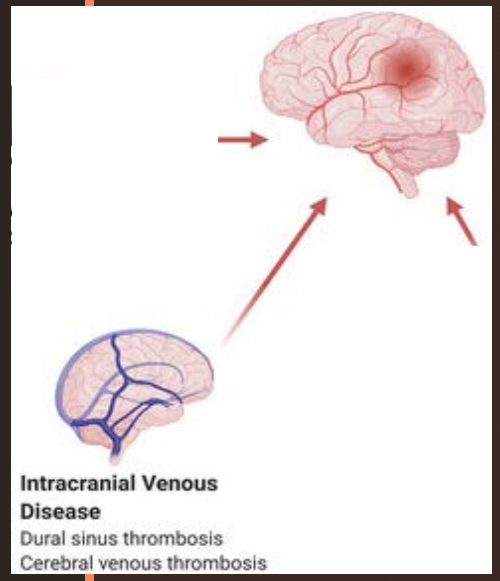
Causes of Ischemic/Hemorrhagic Stroke in Peripartum

- Posterior Reversible Encephalopathy Syndrome (PRES)
  - Vasogenic brain edema
  - Endothelial dysfunction
  - HTN
  - Eclampsia

[2] Elgendy
[3] Miller

Causes of Ischemic/Hemorrhagic Stroke in Peripartum

- Cerebral Venous Thrombosis
  - Venous clot with resultant congestion, edema
  - Can lead to venous infarct or ICH
  - 1/3 pregnancy related strokes
  - ¾ of postpartum strokes
  - Risk Factors – Obesity, preeclampsia, infection, dehydration, thrombophilias

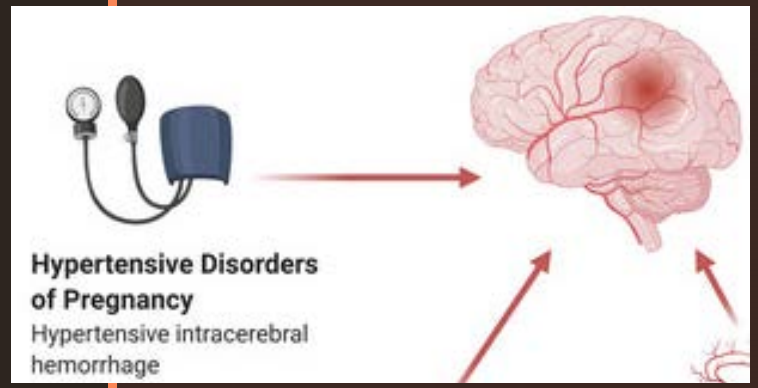


[2] Elgendy
[3]Miller
[9] Miller

Photo from [2]Elgendy

Causes of Hemorrhagic Stroke in Peripartum

- Hypertensive
  - ICH direct cause of death in ½ of preeclampsia deaths



[2] Elgendy
[3]Miller
Photo from [2]Elgendy

Causes of Hemorrhagic Stroke in Peripartum

- Vascular Lesions
  - AVM
  - Aneurysms (SAH)
  - Cavernous Malformations
  - Moyamoya

[2] Elgendy
[3]Miller
[9] Miller

Acute Evaluation and Treatment

Acute Evaluation

- Stroke evaluation - follow current guidelines
- Get the noncontrast head CT – fastest, ok for baby
- Get CTA if concern for LVO or hemorrhage – life threatening
- MRI without GAD reasonable if needed
- No need to stop breastfeeding or pump & dump with contrast

[2] Elgendy
[3] Miller
[9] Miller

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Acute Treatment- Ischemic

- IV Thrombolysis – has been done successfully
  - AHA/ASA doesn't consider pregnancy to be a contraindication
  - Less data to support postpartum (48 hours) thrombolytics, can be considered
  - Should not cross placenta
  - Get OB/Gyn on board (Consider MFM, OB anesthesia, NICU)

[2] Elgendy
[3]Miller
[9]MIller

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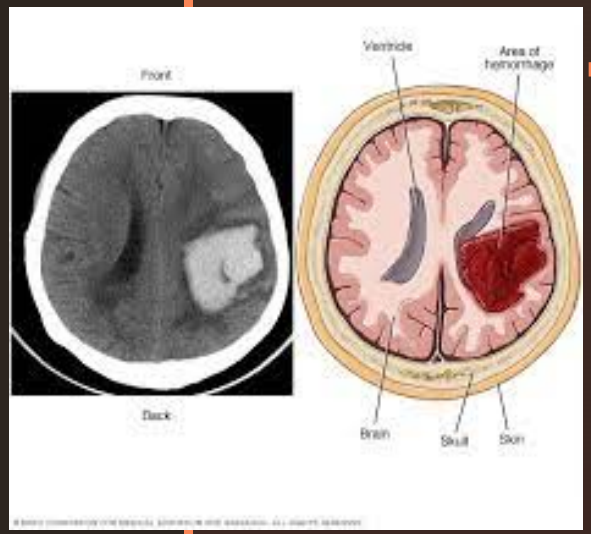
Acute Treatment - Ischemic

- Mechanical thrombectomy – should be discussed with NIR
  - If NIR agreeable, I would offer it
- Life-threatening risk of stroke vs theoretical risk of neonatal hypothyroidism as well as radiation exposure

[2] Elgendy
[3]Miller
[9]MIller

Acute Treatment - Hemorrhagic

- ABCs
- Blood pressure management (SBP130-150 per AHA/ASA guidelines)
- Reverse coagulopathy
- Treat complications – vasospasm, intracranial hypertension, hydrocephalus, seizures



[2] Elgendy
[3]Miller
[9]MIller

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Acute Treatment – Hemorrhagic SAH

- If aneurysm identified – call NSG, intervention shouldn't be delayed due to pregnancy
- Get bleeding to stop - TXA can be used
- Lower BP – labetalol, methyldopa, long acting nifedipine
- Nimodipine and nicardipine can also be used in pregnancy and lactation
- Don't forget to put a monitor on baby

[2] Elgendy
[3]Miller
[9]MIller

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Acute Treatment – Hemorrhagic ICH

- Lower BP to AHA/ASA goal of SBP 130-150
- If due to hypertensive disorders of pregnancy, may need to emergently deliver fetus
- If due to vascular lesion – source control, should not be delayed due to pregnancy status but try to minimize fetal risk

[2] Elgendy
[3]Miller
[9]MIller

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Acute Treatment - Complications

- ABCs – intubate if needed
- Seizures in setting of preeclampsia – magnesium
- High ICP – elevated HOB, head midline, left lateral displacement of uterus
  - Low dose of mannitol (0.25 g/kg to 0.5g/kg)[3]
  - Hypertonic saline safety not clear[3]
  - Consider OB anesthesia

[2] Elgendy
[3]Miller
[6]Hong
[9]MIller

Outcomes

- 7.4% -7.7%of maternal strokes are fatal[2,8]
- Residual Deficits
  - 1/3 ischemic stroke patients
  - ½ hemorrhagic stroke patients
- Please involve PMR

[2]Elgendy
[3] Miller
[8]Liu

Delivery and Breastfeeding

Mode of Delivery

- Stroke doesn’t preclude vaginal delivery
- If mild ICP increase is ok – can try vaginal birth
- If ICP is concern – consider assisted vaginal delivery
- If ICH, high risk of ICH – consider Cesarean delivery

[9]MIller

Breastfeeding

- Study 300,000 Chinese women showed breastfeeding for at least 6 months was associated with reduced risk of cardiovascular disease and stroke later in life[11]
- Risk inversely proportional to length of time breast feeding

[9]MIller
[10]Peters

Prevention

How do we prevent it? Primary Prevention

- Close BP monitoring – especially in postpartum period
- Targeted risk reduction with known risk factors
  - Migraine
  - HTN
  - Thrombophilias
  - Known cerebrovascular lesions

[3] Miller

How do we prevent it? Secondary Prevention

- Treat etiology of stroke
- Aggressive BP management
  - Safe pregnancy and lactation
    - Labetalol, long acting nifedipine, verapamil, methyldopa, hydralazine
  - Safe lactation only
    - ACE (benazepril, captopril, enalapril, quinapril)
    - ARB (limited data for candesartan)

[3] Miller

How do we prevent it? Secondary Prevention

- Antiplatelets
  - ASA 81mg – safe after 12 weeks, reasonable for secondary prevention 0-12 weeks, ok in lactation
  - Clopidogrel – insufficient data of safety in both pregnancy and lactation, consider on case by case
  - Ticagrelor – insufficient evidence of safety

[3] Miller

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How do we prevent it? Secondary Prevention

- Anticoagulation
  - LMWH and unfractionated heparin – safe in pregnancy and lactation
  - Warfarin – Teratogenic esp 6-12 weeks, consider in mechanical heart valve after week 12 at low dose, ok in lactation

Dabigatran, apixaban, and rivaroxaban – insufficient evidence of safety in pregnancy and lactation

[3] Miller

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How do we prevent it? Secondary Prevention

- Statins
  - Insufficient evidence of safety in both pregnancy and lactation

[3] Miller

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Will it happen again?

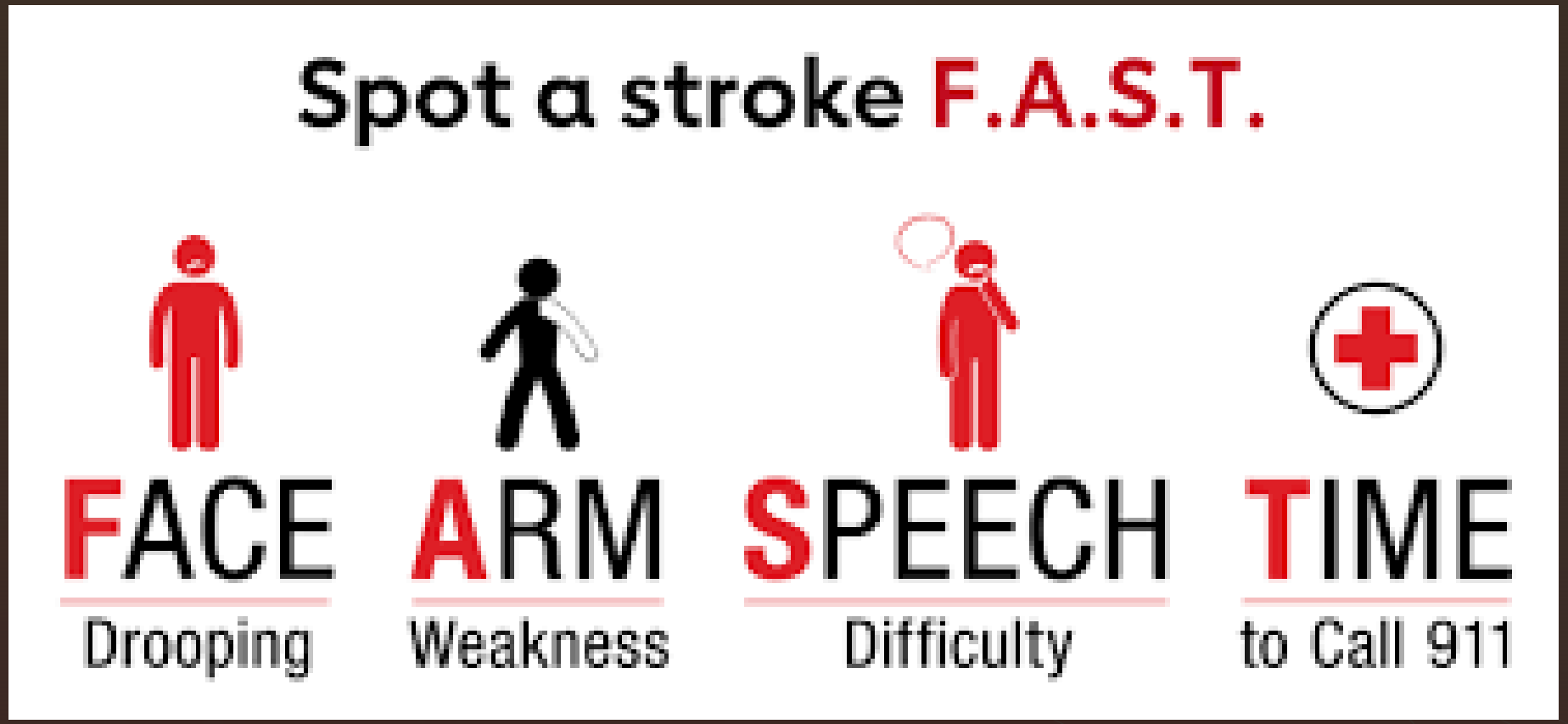
- Pregnancy related risk of recurrence – 2% ischemic stroke, 2.2% CVST
- FUTURE study women with previous stroke had more pregnancy complications/adverse outcomes, no recurrent stroke
- Maternal stroke is not a contraindication for subsequent pregnancy
  - If CVST – consider LMWH ppx

[2]Elgendy
[3] Miller
[9] Miller

Call to Action

- Please obtain obstetric history, screen for pregnancy complications
- If you treat people who can carry children – review red flag headache symptoms & discuss cardiovascular risk factors
  - Aggressively treat BPs
  - Discuss contraceptives
- Increase rural access to care and address systemic racism

Questions?



Borrowed from American Stroke Association

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