Common Neurologic Consults in Pregnancy

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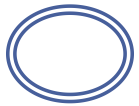
Disclosures



- I do consultant work for Crico and Teladocs
- I receive royalties from Springer and Oxford Press

Objectives

Use Cases to:

- Review the pathophysiology of some common neurologic disorders seen in pregnancy
- Discuss the importance of planning pregnancy
- Describe treatment specific concerns around pregnancy

Migraine, Stroke, IIH, Low pressure headache, Postpartum Neuropathy

Issues to discuss when caring for Women in their Reproductive years

- Family planning- the key question
- Discussion of medication risks in pregnancy
- Effects of pregnancy on the underlying disease
- Effects of the underlying disease on pregnancy

FDA Pharmaceutical Pregnancy Categories

A Adequate and well controlled human studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no risk in later trimesters).

B Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well controlled studies in pregnant women OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester.

C Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

D There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks

X Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits

Case

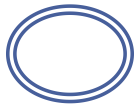
- A 35 -year-old woman G1 P0 at 31 and 5/7 weeks of gestation woke with a severe headache. She began seeing visual spots, and a half hour later she completely lost her vision.

- Shortly thereafter, she developed the worst headache of her life and blacked out. At the outside hospital her blood pressure was 170/120. She was transferred to our hospital.

Which one of these etiologies is the most likely cause?

A. Migraine without aura
B. Subdural hematoma
C. Migraine with aura
D. Preeclampsia
E. Idiopathic intracranial hypertension

Answer is D



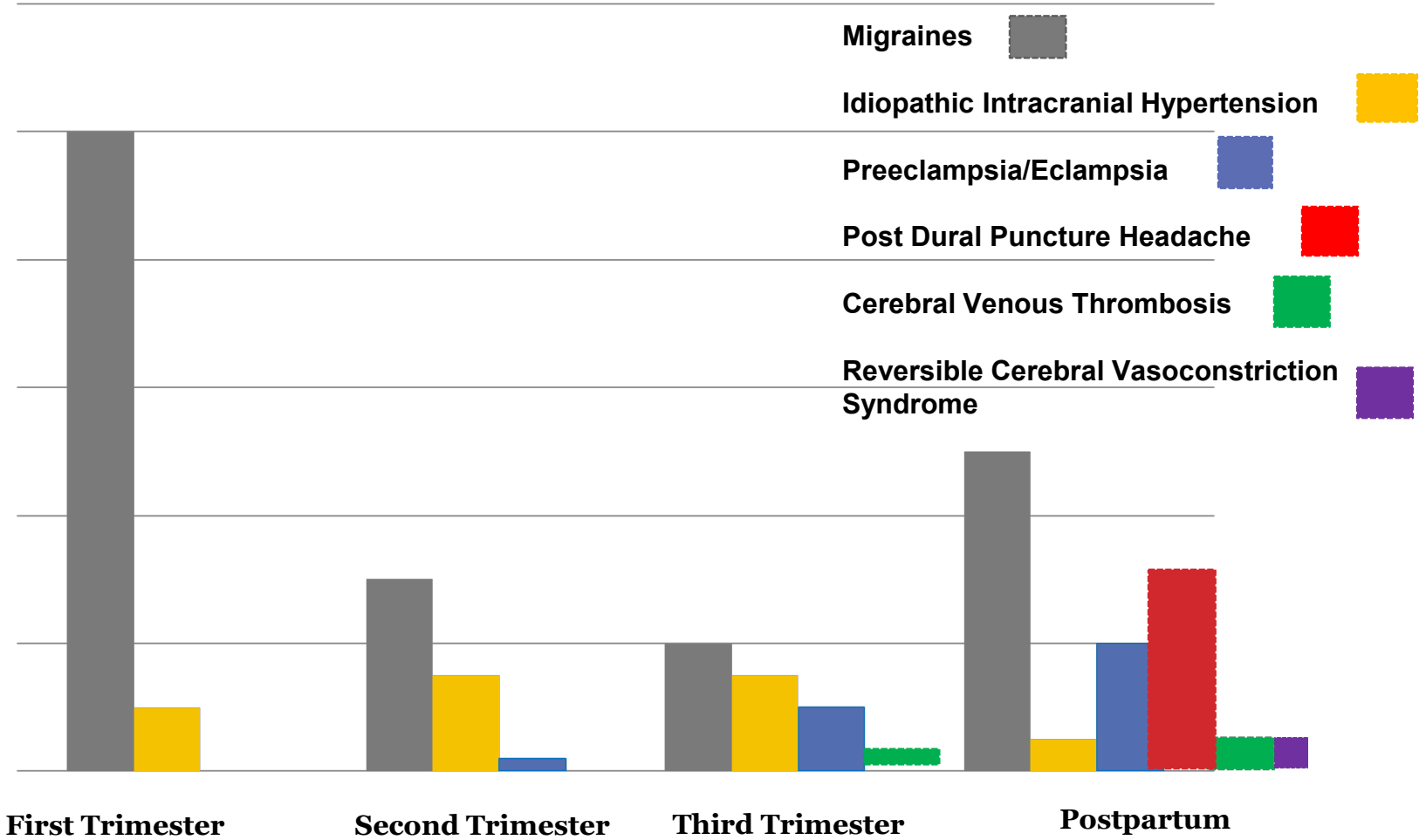
A. Migraine without aura
B. Subdural hematoma
C. Migraine with aura
D. **Preeclampsia**
E. Idiopathic intracranial hypertension

Red Flags

- Change in headache character or pattern
- Headaches with characteristics of elevated ICP
- New headaches
- Associated with elevated BP
- Unusually severe headache
- Abnormal neurologic exam
- Headaches associated with systemic disorders

Historical features	Headache type	Helpful radiographic studies depending on gestational age
Thunderclap onset	SAH, RCVS, CVT, Pituitary apoplexy, Dissection	MRI,MRV,MRA, CT, CTA, CTV
Postural	PDPH, IIH	Brain MRI with gadolinium (gadolinium is not usually used in pregnancy)
First Trimester	Likely migraine or Tension type	None (except if the headaches have any red flags)
Prior similar headache	Benign	Not needed
Hypertension, proteinuria	PEE/Eclampsia	MRI

Frequency and Headache Type by Trimester



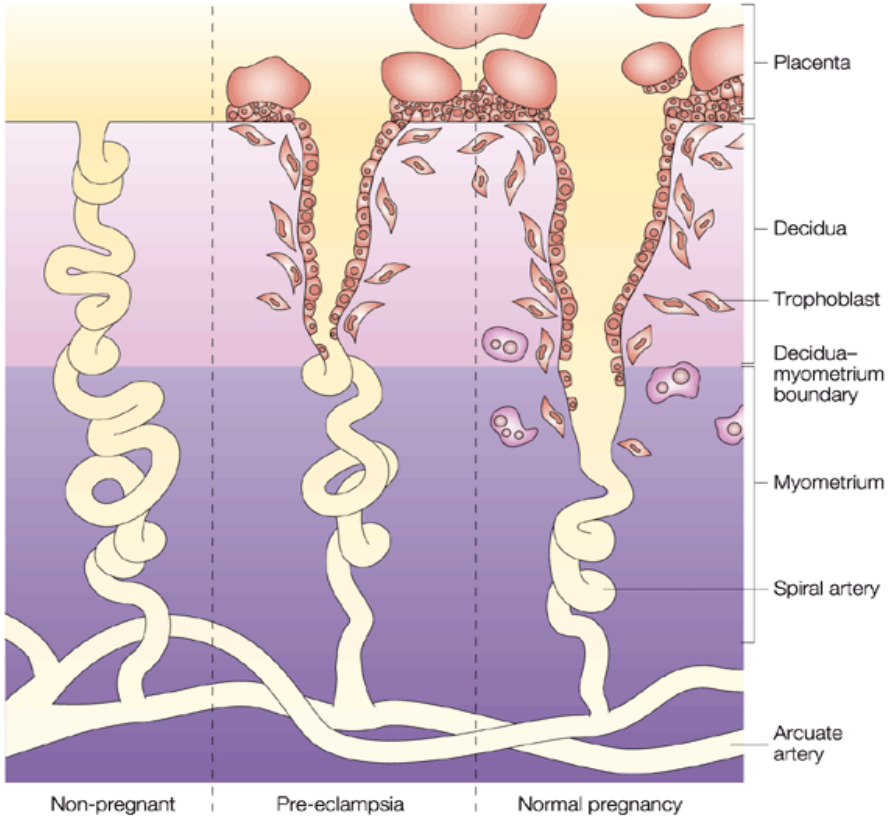
O'Neal MA.Headaches complicating pregnancy and the postpartum period. Pract Neurol 2017: 17:191-202

Pre-eclampsia/Eclampsia Definition

Diagnosed when a pregnant woman develops

- High blood pressure (two separate readings taken at least six hours apart of 140 or more in systolic blood pressure and/or 90 or more in diastolic blood pressure)
- 300 mg of protein in a 24-hour urine sample (proteinuria- no longer required)
- Onset of seizures and change in mental status defines eclampsia

Pathogenesis of Eclampsia



Nature Reviews | Immunology

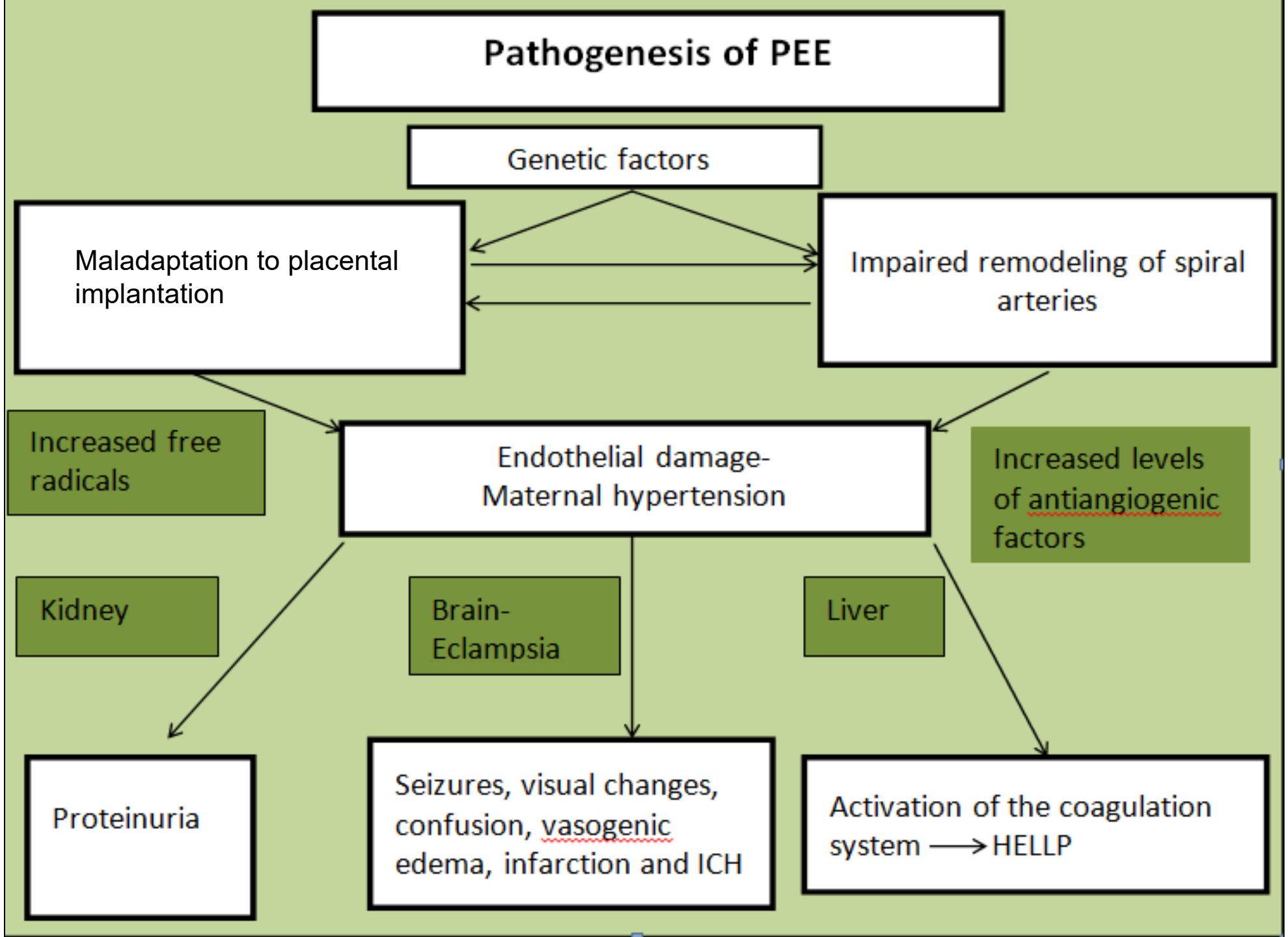
Sibai B, Dekkar G, Kupferminc M. Pre-eclampsia. Lancet 2005; 365:785-799

Pre-eclampsia/ Eclampsia

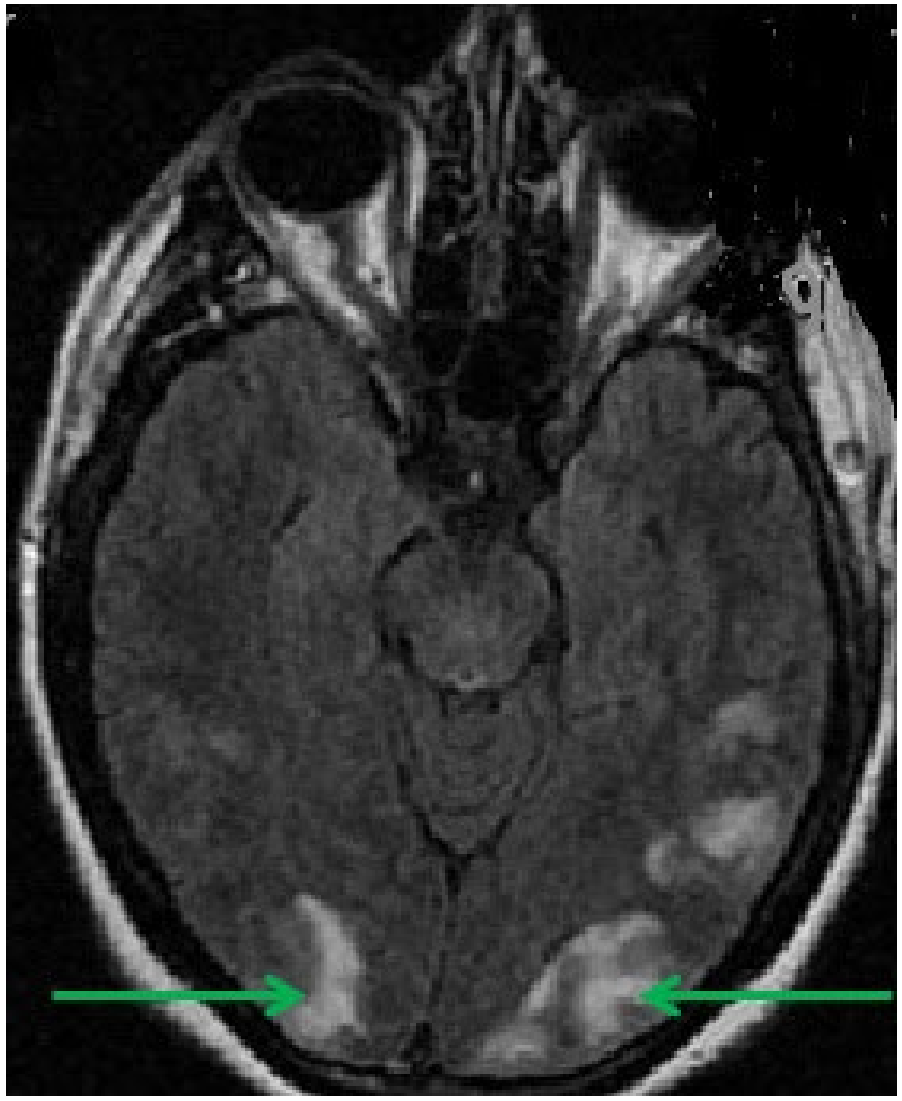
- PE/E is associated with both significant maternal and fetal morbidity and mortality
- Maternal complications include abruption placentae, disseminated coagulopathy, acute renal failure, stroke, hemorrhage, death and long- term cardiovascular morbidity
- Fetal complications include premature delivery, low birth weight, hypoxic neurologic injury, and death.

Khan KS, Wojdyla D, Say L, Gulmezoglu AM, Van Look PFA.WHO analysis of causes of maternal death:systematic review. Lancet 2006; 367: 1066–1074.

Task force on hypertension in pregnancy. Hypertension in Pregnancy 2013. American College of Obstetricians and Gynecologists


Pathogenesis of PEE
Genetic factors
Maladaptation to placental implantation
Impaired remodeling of spiral arteries
Increased free radicals
Endothelial damage-
Maternal hypertension
Increased levels of antiangiogenic factors
Kidney
Brain-
Eclampsia
Liver
Proteinuria
Seizures, visual changes, confusion, vasogenic edema, infarction and ICH
Activation of the coagulation system ⟶ HELLP

Axial Flair MRI-PRES



Hinchey J, Chaves C, Appignani B, Breen J, Pao L et al. A Reversible Posterior Leukoencephalopathy Syndrome. NEJM 1996; 334:494-500

Treatment of Pre-eclampsia/Eclampsia

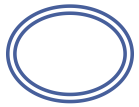
- Blood Pressure control

- Magnesium Sulfate

Altman D, et al. Do women with pre=eclampsia, and their babies , benefit form magnesium sulphate? The Magpie Trial: a randomized placebo-controlled trial. Lancet 2002, 359(9321):1877-1890.

Lucas et al. A comparison of magnesium sulfate and phenytoin for the prevention of eclampsia.
N Engl J Med 1995;333:201–5.

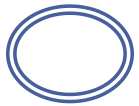
Case



- A 23- year-old women with migraine without aura is now 8 weeks pregnant. Her migraines had been well controlled with sumatriptan.

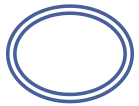
- She’s now having her usual headaches with nausea and vomiting 2-3 times a week.

Which of these migraine medications is safest to use throughout pregnancy?



A. Sumatriptan
B. Topiramate
C. Dihydroergotamine
D. Naprosyn
E. Lasmiditan

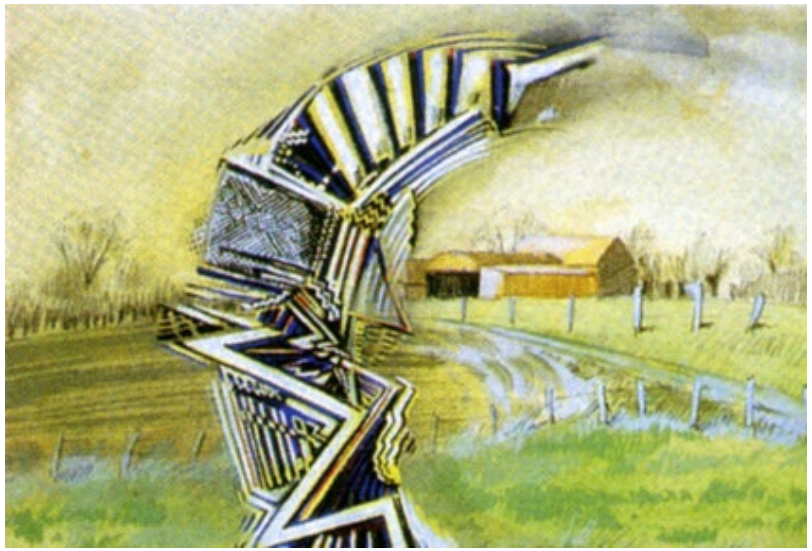
Answer is A



A. Sumatriptan
B. Topiramate
C. Dihydroergotamine
D. Naprosyn
E. Lasmiditan

Migraine Treatment around Pregnancy

- Planning
- Symptomatic therapy
- Other



Other Therapies

- Physical, chiropractic and massage therapy
- Trigger Management
- Acupuncture
- Occipital nerve blocks

Migraine during Pregnancy

- 60-70 % migraines undergo remission
- Small percent of new onset migraine during pregnancy
- Increased risk of preeclampsia/eclampsia

Kvisvik EV, et al. Headache and migraine during pregnancy and puerperium: the MIGRA-study. J Headache Pain Aug 2011; 12(4):443–451

Adeney KL,et al. Risk of preeclampsia in relation to maternal history of migraine headaches. J Matern Fetal Neonatal Med 2005; 18(3):167-172

Symptomatic Therapies

Generic Name	Level of Risk in Pregnancy	Breastfeeding- Hale Lactation Rating
Acetaminophen	B	L1
NSAIDS	B (D in 3rd trimester)	L1-L2
Metoclopramide IV	B	L2
Prochlorperazine	C	L3
Dihydroergotamine	X	L4
Magnesium IV	A (D)	L1
Triptans	C	L1
Ditans; Lasmiditan	No data in humans (adverse effects noted in animals)	No data
Gepants; Ubrogepant, Rimegepant, Zavegepant NS	No data in humans (adverse effects noted in animals)	No data

Preventative Medications

Drug Class	Generic Name	Level of Risk in Pregnancy	Breastfeeding
Beta- blockers	Atenolol Propranolol	D C (D at term)	Caution Compatible
Antiepileptics	Gabapentin Topiramate Valproate	C D X	Compatible Caution Caution
Tricyclics	Amitriptyline	C	Compatible
SNRIs	Duloxetine Venlafaxine	C C	Little data Little data
CGRP inhibitors	Erenumab Fremanezumab Galcanezumab Eptinezumab	No data	No data
Gepants	Rimegepant Atogepant	No data	No data Safe
Supplements	Magnesium Coenzyme Q10	Safe	

Triptans and Pregnancy

- Data from the Sumatriptan/Naratriptan Pregnancy Registry

- Data from Norwegian Mother and Child Cohort

Ephross SA, Sinclair SM. Final results from the 16-year sumatriptan, naratriptan, and treximet pregnancy registry. Headache 2014;54(7):1158–1172.
-Spielmann K, Kayser A, Beck E, et al. Pregnancy outcome after anti-migraine triptan use: a prospective observational cohort study. Cephalalgia 2019;38(6):1181–1092
-Nezvalová-Henriksen K, Spigset O, et al. Triptan safety during pregnancy: a Norwegian population registry study. European Journal of Epidemiology 2013; 28(9): 759–769.

Emergency Treatment of Migraine in Pregnancy

A sequential algorithm for migraine treatment:

- IVF- suggest NS at 20-30 mg/kg over 1-2 hours and 500 mg- 1 gm of IV magnesium sulfate
- Metoclopramide 10 mg IV or Prochloperazine 5-10 mg IV
- Methylprednisolone 1 gm IV or 6 mg SQ Sumatriptan
- Analgesics

1. Cete Y, Dora B, Ertan C et al. A randomized prospective placebo-controlled study of intravenous magnesium sulfate vs. metoclopramide in the management of acute migraine attacks in the emergency department. Cephalalgia 2005; 25(3): 199-204.

2. Nezalova-Henriksen et al.Triptan exposure during pregnancy and the risk of major congenital malformations and adverse pregnancy outcomes: results from the Norwegian Mother and Child Cohort Study. Headache 2010; 50(4): 563-575.

Migraine and Lactation

- Triptans considered safe

- Several Preventative drugs also safe

Lactmed

Case

- A 28-year-old woman G2P1 at 30 weeks gestation was last seen well at 10 am. She was found on the ground not speaking or moving her right side at 10:50 am.
- On initial exam at noon, she was mute with left gaze deviation and dense right hemiplegia.

NIHSS* was 15.

Question

Which of the following statements is true of ischemic stroke during pregnancy and postpartum?

a. Brain MRI, Brain and Neck MRA are the best imaging modalities
b. IV thrombolytics should not be used in pregnancy due to fetal risk
c. Head CT and CTA of neck and brain are the most appropriate imaging modalities
d. The causes of ischemic stroke during pregnancy and postpartum are similar to those that occur outside of pregnancy

Answer

Which of the following statements is true of ischemic stroke in pregnancy and postpartum?

a. Brain MRI, Brain and Neck MRA are the best imaging modalities
b. IV tPA, TNK should not be used in pregnancy due to fetal risk
c. Head CT and CTA of neck and brain are the most appropriate imaging modalities
d. The causes of ischemic stroke during pregnancy and postpartum are similar to those that occur outside of pregnancy

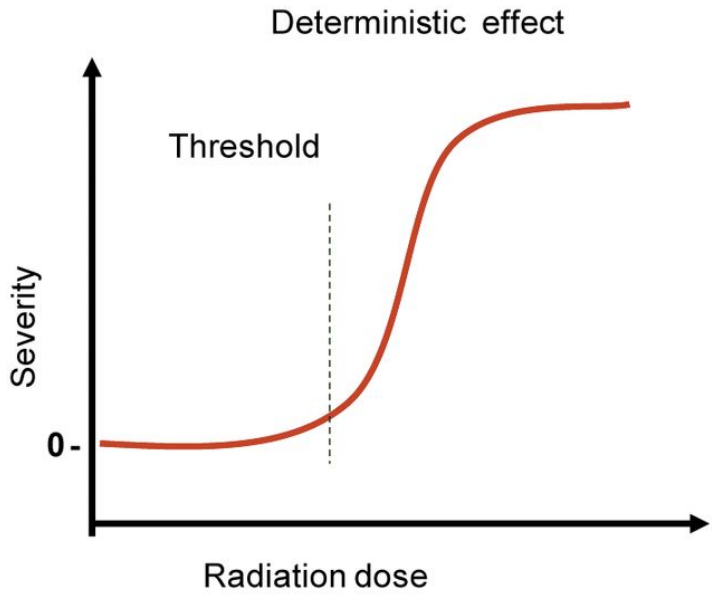
The evaluation and treatment of stroke during pregnancy should be, in most cases, the same as in the non-pregnant state

How should you treat this lady?

- Imaging- Head CT vs Brain MRI, Vessel Imaging
- IV t-PA or TNK
- Thrombectomy

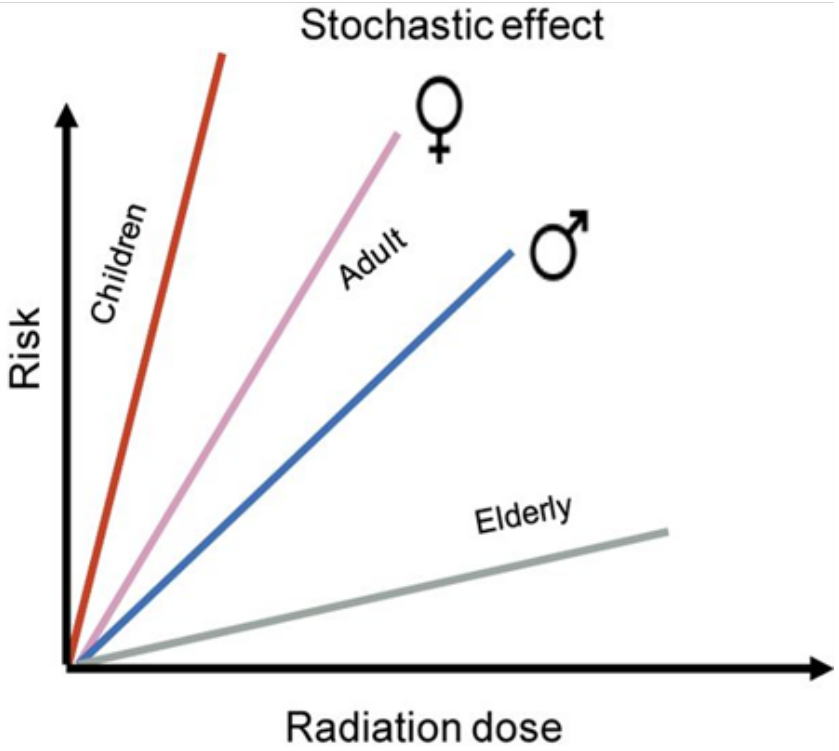
Radiation Exposure

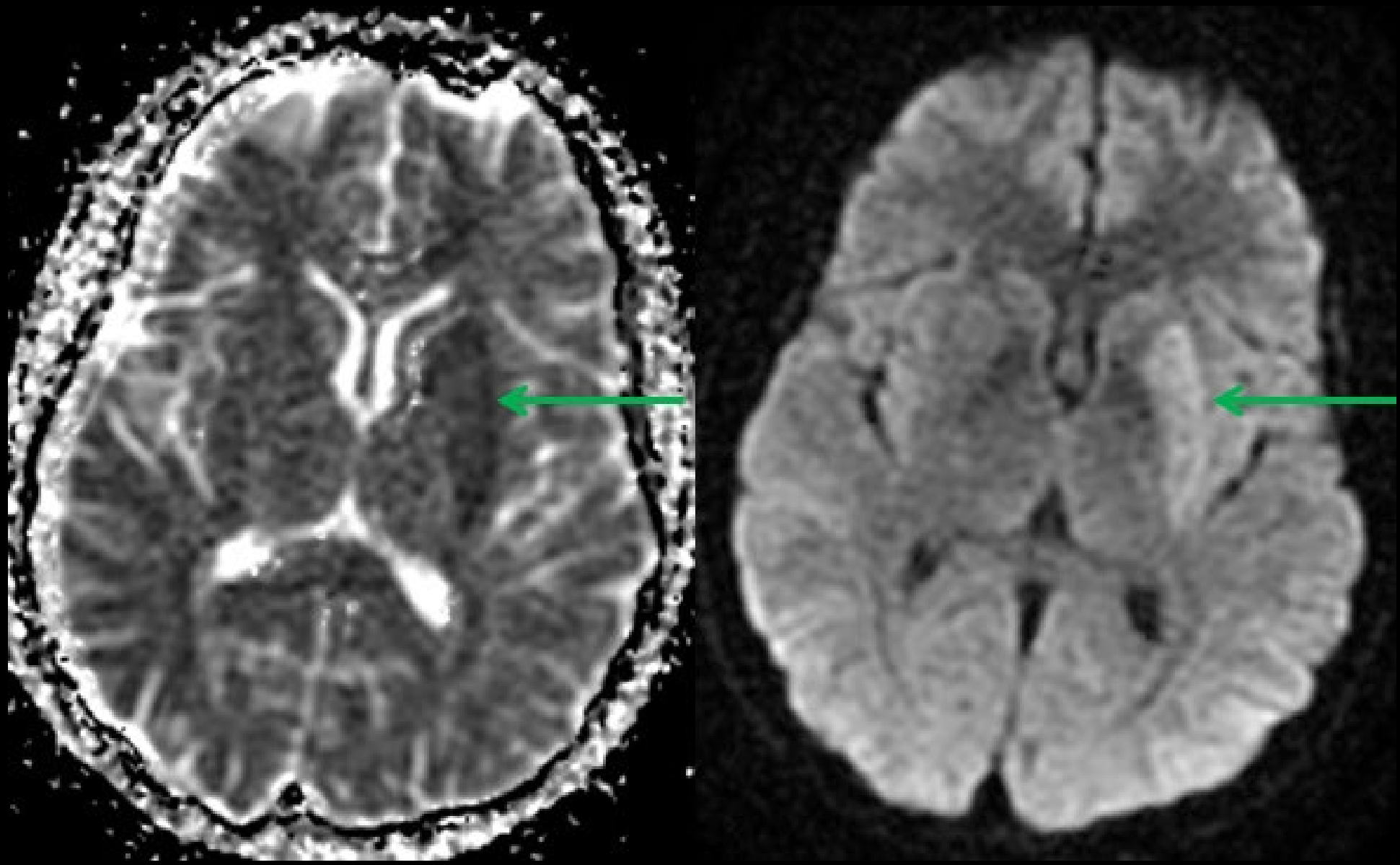
- DETERMINISTIC EFFECTS

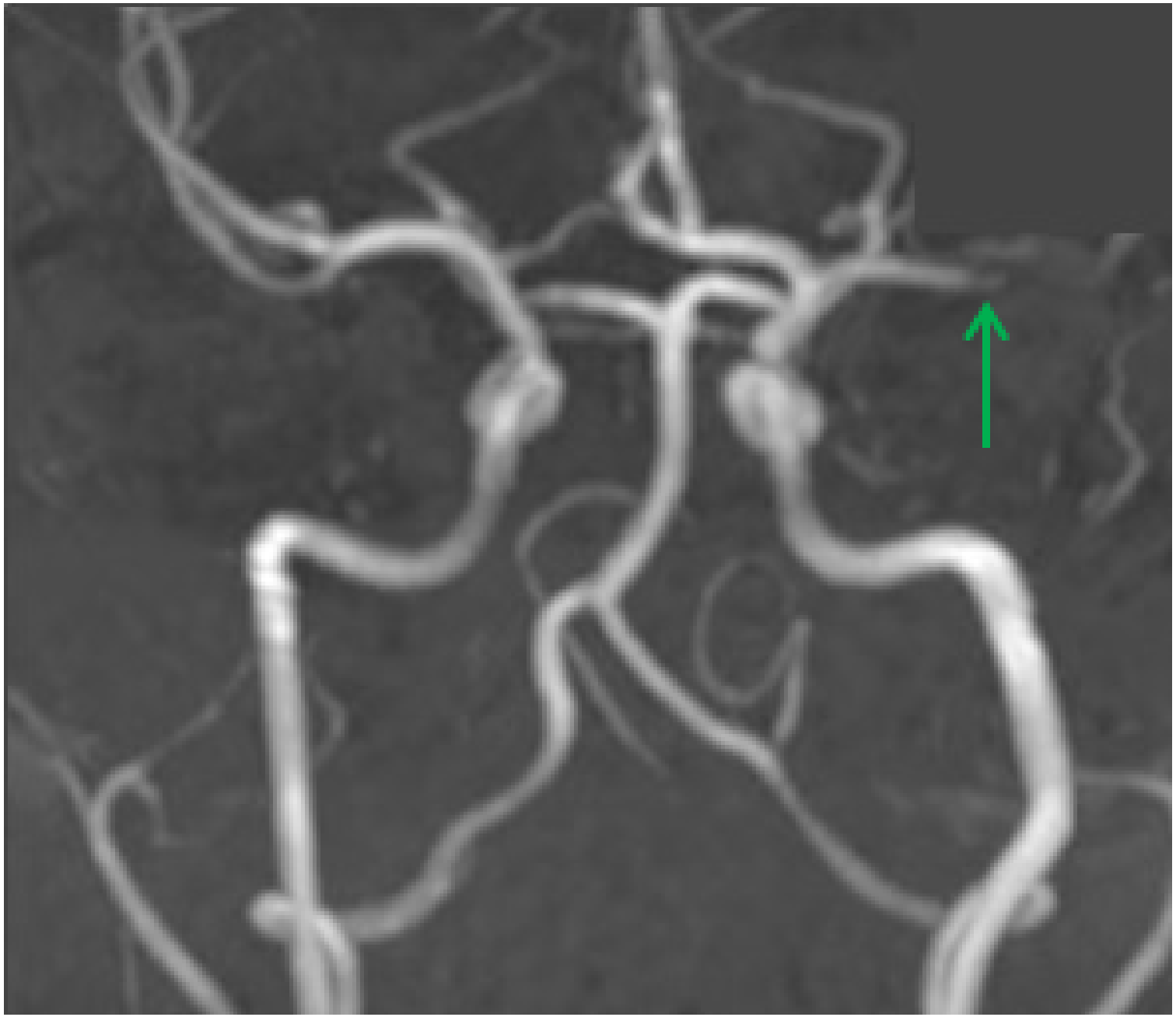


Radiation Exposure

- STOCHASIC EFFECTS







Case Reports of IV tPA in Pregnancy

Author/yr	# Cases	Gestational age	Maternal Outcome	Fetal Outcome
Dapprich/2002	1	12 weeks	Near complete	Healthy
Weatherby/2003	1	9 weeks	Full	Healthy
Leonhardt/2006	1	23 weeks	Full	Healthy
Wiese/2006	1	13 weeks	NIHSS-4	Healthy
Murugappan/2006	4	12 weeks 4 weeks 6 weeks 37 weeks	Healthy Healthy Death-complic of angio Healthy	Pregnancy terminated Pregnancy terminated Death Healthy
Yamaguchi/2010	1	18 weeks	Full	Healthy
Hori/2012	1	13 weeks	NIHSS-1	Healthy
Tassi/2013	1	16 weeks	NIHSS-1	Healthy
Ritter/2014	1	36 weeks	NIHSS-3	Healthy
Ritchie/2015	1	39 weeks	Full	Healthy
Tversky/2016	1	5 weeks	Full	Not available
Festa/2017	1	5 weeks	NIHSS-1	Healthy
Khan/2017	1	9 weeks	NIHSS-4	Fetal demise
Jiang/2018	1	31 weeks	Full	Healthy
Laudais/2018	1	13 weeks	NIHSS-1	Healthy

Case Reports of Thrombectomy for Pregnant Women

Author/yr	# of Cases	Gestational Age	Maternal Outcome	Fetal Outcome
Aaron/2016	2	3rd trimester 37 weeks	NIHSS-1 NIHSS-4	Healthy Healthy
Bhogal/2017	2	24 weeks 25 weeks	NIHSS-1 Full	Healthy Not available

Dicpinigaitis AJ, et al. Endovascular Thrombectomy for Treatment of Acute Ischemic Stroke During Pregnancy and the Early Postpartum Period. Stroke. 2021 Sep 20.

Causes of Ischemic Stroke in Pregnancy

- Cardiac emboli
- Dissection
- Pre- eclampsia/ Eclampsia
- Coagulopathy
- Cerebral Venous Thrombosis
- Reversible Cerebral Vasoconstriction Syndrome
- Other

Case

22- year-old lady 26 weeks pregnant who comes in for evaluation of headaches. She has gained 47 lbs. from her pre- pregnancy weight. She is currently having headaches mostly in the morning. She denies any visual symptoms.

Exam: She has bilateral disc edema

What tests would you do next?

A. Head CT

B. Brain MRI with gadolinium

C. Brain MRI and MRA

D. Brain MRI and MRV without gadolinium

Answer is D

A. Head CT

B. Brain MRI with gadolinium

C. Brain MRI and MRA

D. Brain MRI and MRV without gadolinium

Idiopathic Intracranial Hypertension

- Worsening headache with recumbency
  - Improves while upright and the worst upon awakening from sleep
  - Behaves like tumor associated headache (pseudotumor cerebri)
- CSF pressure greater than 250 mm water
- Transient visual obscurations
  - Sudden loss of vision lasting less than 30 seconds involving one or both eyes, and are followed by full visual recovery.
- Vomiting, often projectile, tends to improve headaches
- Pulsatile tinnitus can occur in 52% of IIH patients.[11]

Mathew PG, Najib U, Krel R, Rizzoli PB. Idiopathic Intracranial Hypertension: Papilledema and Neuro-Ophthalmology Referral Patterns. Practical Neurology. October 2016: 43-45.

Epidemiology of IIH

- Up 21/100,000
- 90% of patients are obese
- Female predominance 4:1

IIH in Pregnancy

- Onset during pregnancy - 14 weeks
- Reactivation of IIH later second trimester- 20 weeks

- No increased obstetric complications
- Visual outcomes the same as in the non-pregnant patients

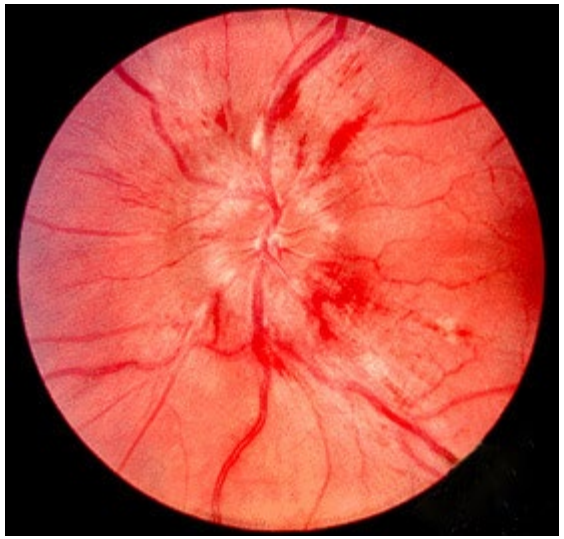
Digre K et al, Pseudotumor cerebri and pregnancy, Neurology 1984;34:721-9.

Symptoms of IIH

- Headache 92%
- Transient visual obscurations 72%
- Pulsatile Tinnitus 60%
- Photopsia
- Retrobulbar pain
- Diploplia
- Sustained visual loss 26%

Evaluation

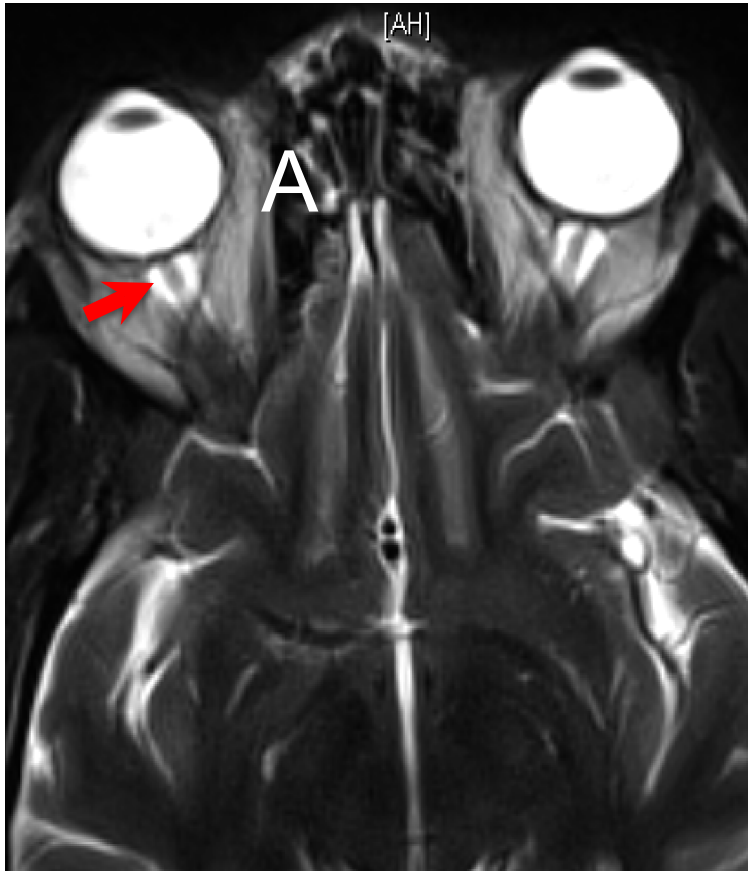
- Brain MRI/ MRV
- Lumbar Puncture
- Ophthalmological Evaluation
- Nutrition Consult

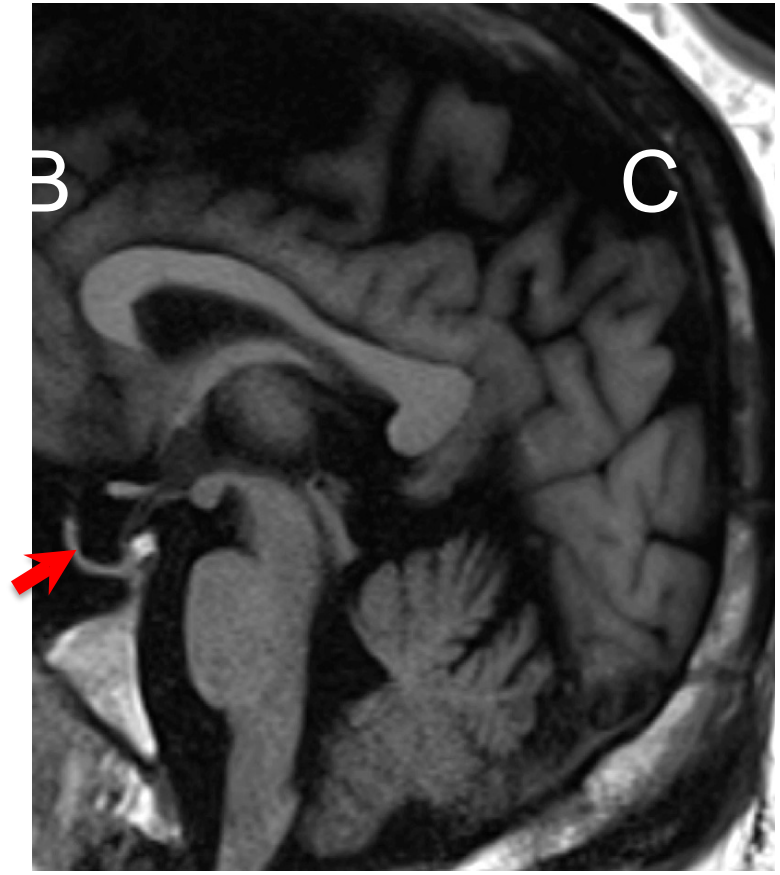


Idiopathic Intracranial Hypertension

- MRI Findings
  - Prominent subarachnoid space around the optic
  - Papilledema
    - flattening of the posterior sclera
    - intraocular protrusion of the optic nerve head
  - Enhancement of the prelaminar (intra-ocular) optic nerves
  - Partial empty sella turcica
  - slitlike ventricles (relatively uncommon compared to other findings)
  - Increased subcutaneous fat thickness in the scalp and neck [17]

MRI findings in IIH

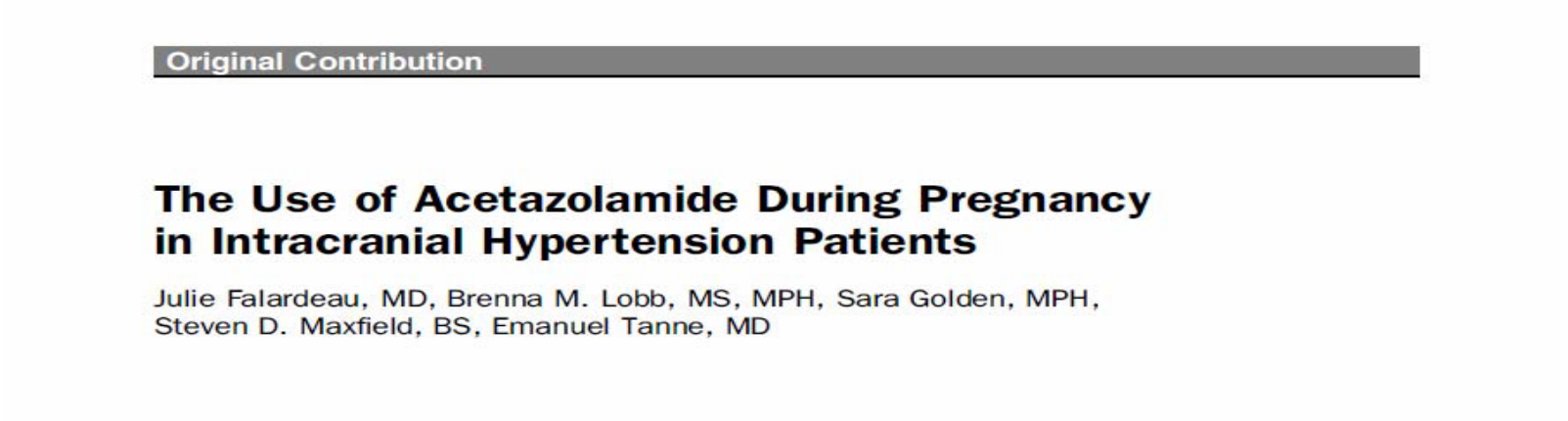




IIH Management Issues in Pregnancy

- Weight control
- Medications
- Serial lumbar punctures
- Surgery

Thaller M et al. Managing idiopathic intracranial hypertension in pregnancy: practical advice. Pract Neurol. 2022 Aug;22(4):295-300.


Original Contribution

The Use of Acetazolamide During Pregnancy in Intracranial Hypertension Patients

Julie Falardeau, MD, Brenna M. Lobb, MS, MPH, Sara Golden, MPH, Steven D. Maxfield, BS, Emanuel Tanne, MD

Results: 101 women with IIH (158 pregnancies)

acetazolamide usage before 13 week of gestation 50 pregnancies

1. Similar risk of spontaneous abortion
2. No major complication in the offspring

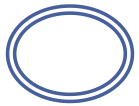
Management of Labor

- C-section – for Obstetric concerns
- Adequate labor analgesia –Uterine contractions increase ICP
- Neuroaxial anesthesia preferred

Case

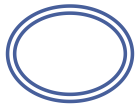
- 26- year- old lady 2 days after a vaginal delivery with epidural anesthesia is seen for a holocephalic headache which is worse with sitting or standing and relieved with lying down.

Which of these are risk factors for low pressure headache?



A. Female sex
B. Size of the needle
C. Operator experience
D. Low BMI
E. All of the above

Answer is E



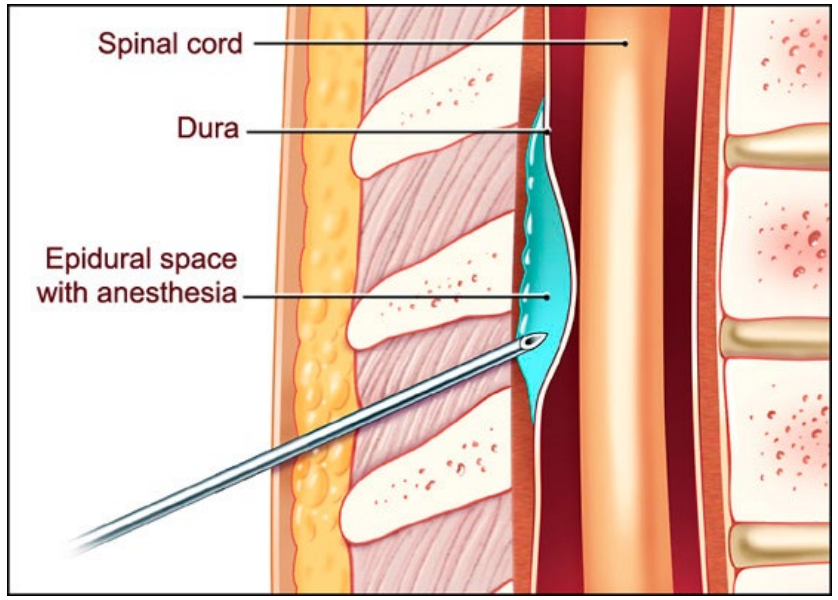
A. Female sex
B. Size of the needle
C. Operator experience
D. Low BMI
E. All of the above

Risk Factors

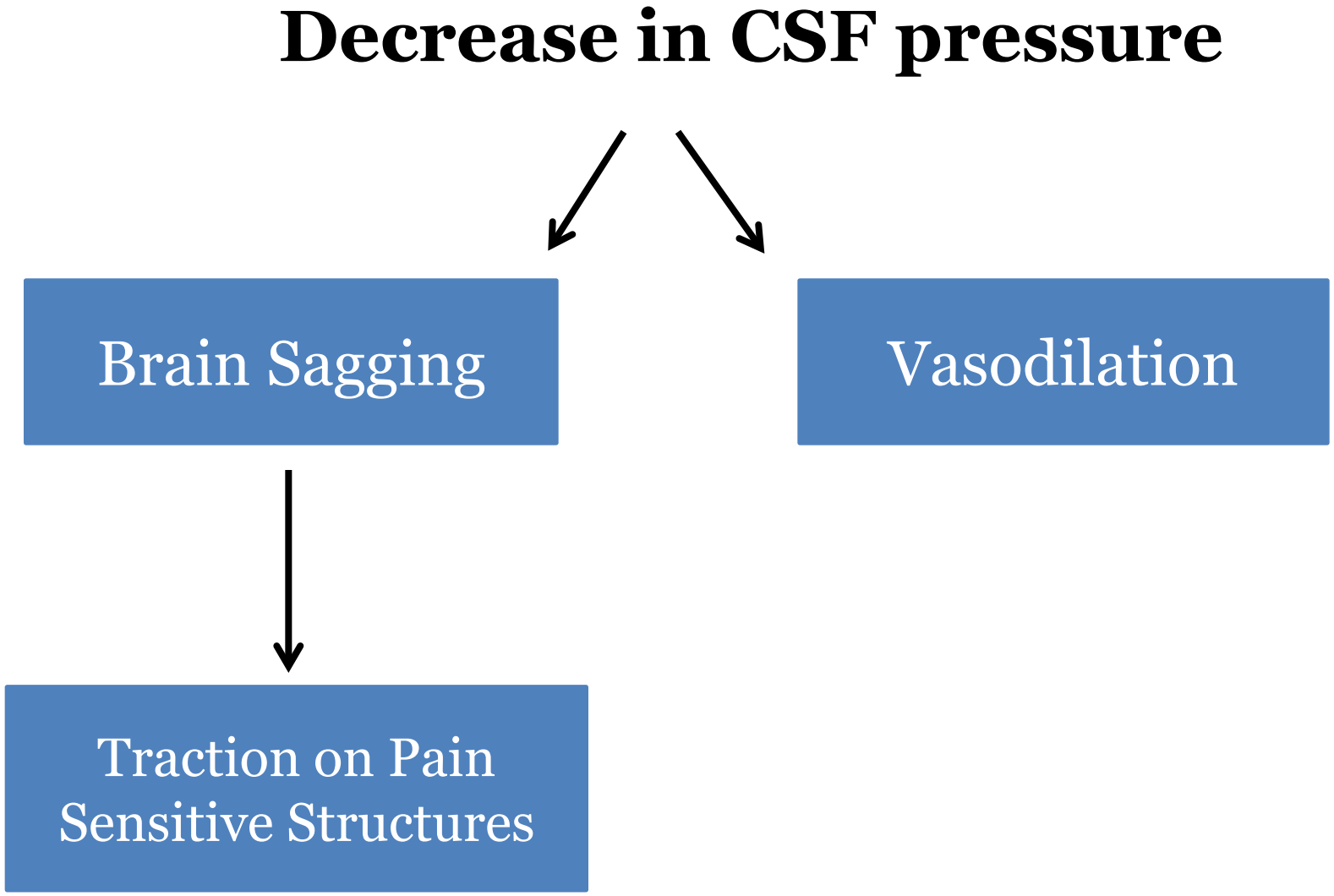
Nonmodifiable	vs	Modifiable
1. Age 2. Sex 3. Low BMI 4. History prior postdural puncture headache 5. History of chronic headache		1. Needle shape 2. Bevel orientation and angle of insertion 3. Size of spinal needle 4. Stylet replacement 5. Operator experience

Clinical Features

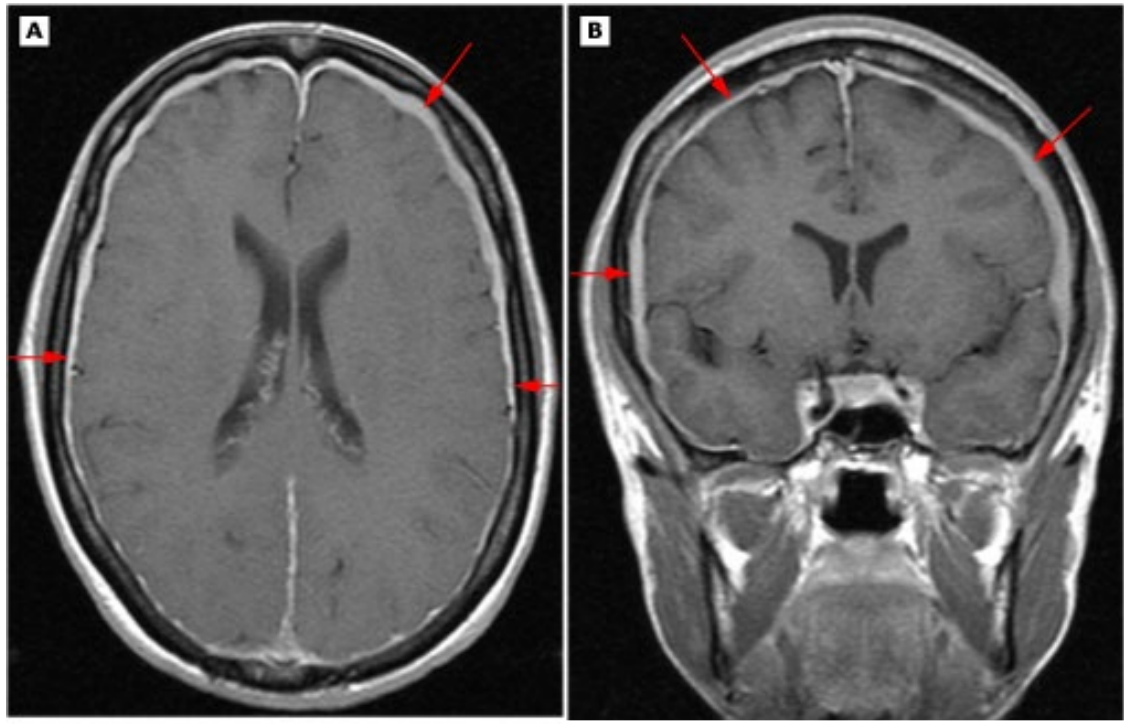
- Headache
- Nausea/Vomiting
- Neck Pain
- Tinnitus
- Visual changes
- Vertigo/Gait problems



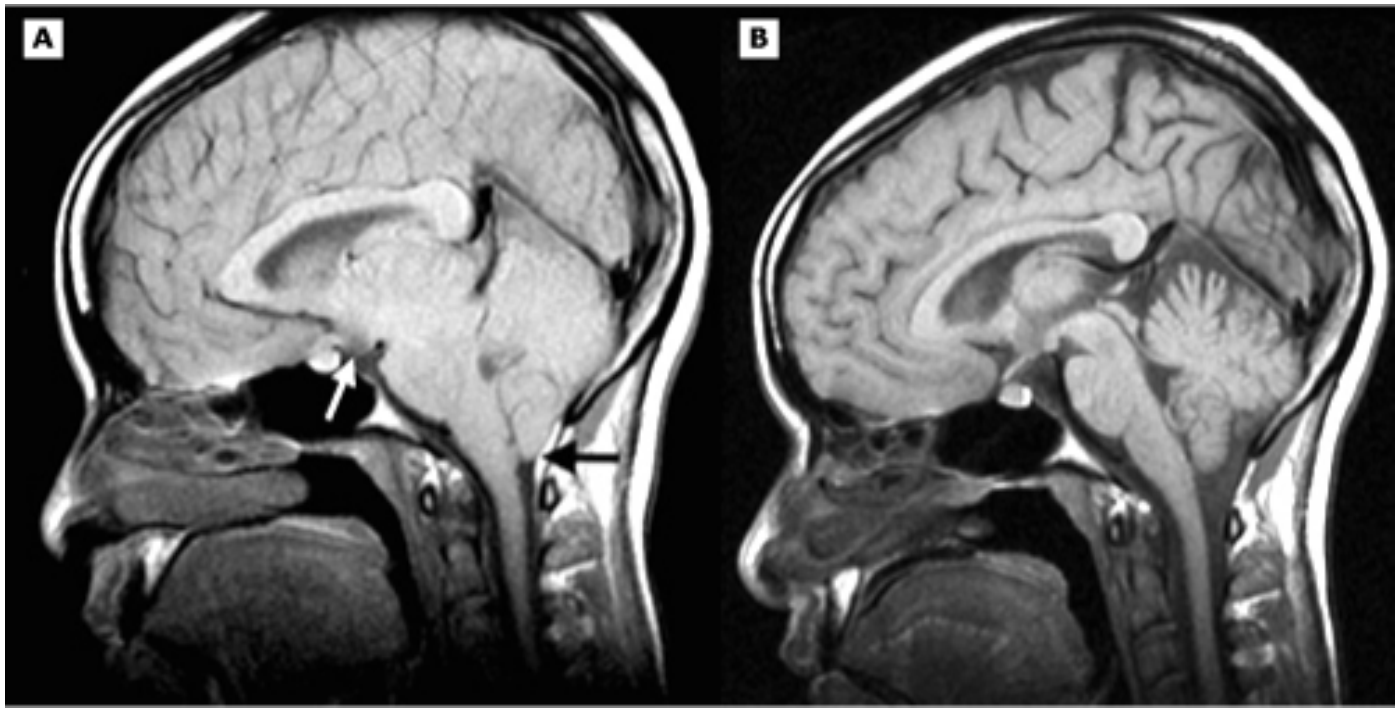
Pathophysiology



Diffuse Meningeal Enhancement



MRI findings in low pressure headache



Treatment of Post-lumbar Puncture Headache

- Conservative
- Caffeine
- Epidural Blood Patch

Controlled trials of medication in treatment of PDPH

Study	Patient Number	Regimen	Outcome
Camann 1990	40 Randomized	Caffeine 300 mg Assessed 4 & 24 hours	4 hours- 30% improvement
Sechzer 1978	41 Randomized	Caffeine 500mg IV given and repeated if headache persisted	1-2 hours 75% improvement Overall, 70 % improvement
Wu 2018	126 Randomized	Aminophylline 250 mg IV	8 hours significant improvement in headache severity

Case

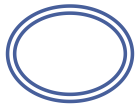
- The neurology service was asked to evaluate a 32-year-old woman G1P1 for right leg weakness two days postpartum. She had an uneventful vaginal delivery of a 3266-g baby with epidural analgesia. She noted right leg numbness and knee weakness. On the first postpartum day, her leg buckled and she fell when she stood to move to the bathroom. She had no back pain or leg pain.

- On exam: 4/5 weakness in right hip flexion and knee extension, diminished right patellar DTR, and sensory loss in her medial thigh and calf. Her back was not tender and back range of motion was normal. She had some tenderness over the right inguinal ligament.

What is the most likely diagnosis?

A. Epidural hematoma
B. A sciatic nerve injury
C. A lateral femoral cutaneous neuropathy
D. A femoral nerve injury
E. Epidural abscess

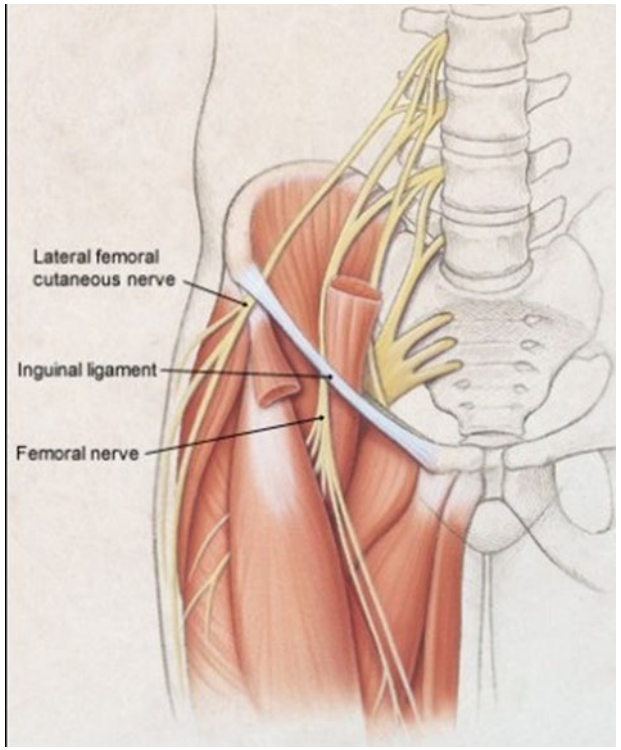
Answer is D



A. Epidural hematoma
B. A sciatic nerve injury
C. A lateral femoral cutaneous neuropathy
D. A femoral nerve injury
E. Epidural abscess

Femoral Neuropathy

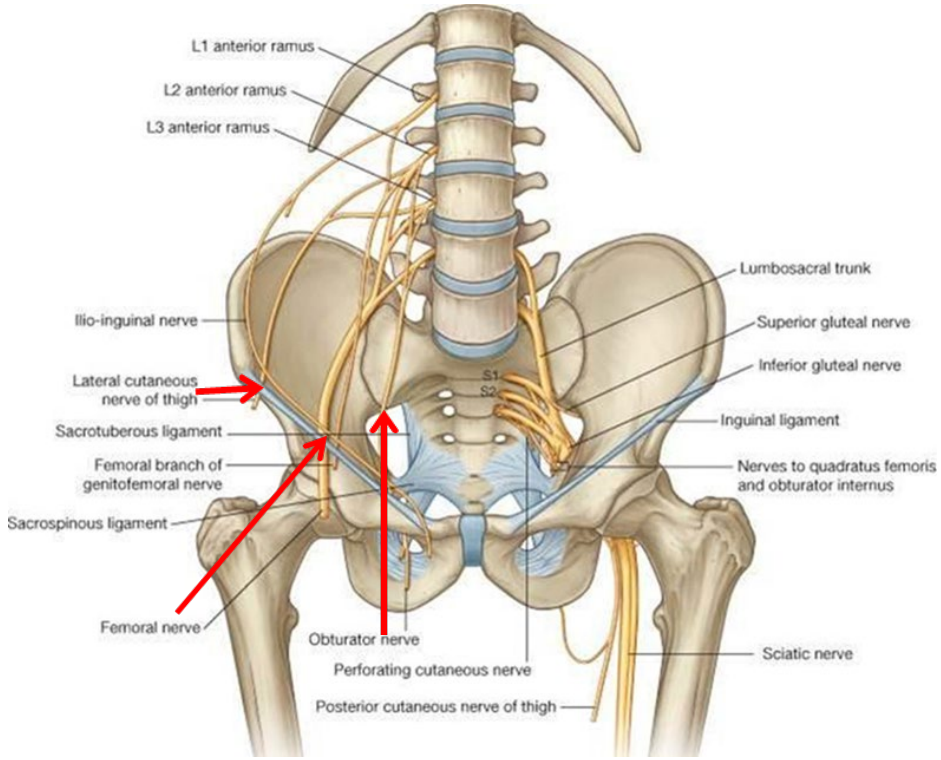
- Incidence 2.8/100,000
- 25% are bilateral
- Findings
- Risk factors



Massey E. W, Guidon A C, Peripheral Neuropathies in Pregnancy. Continuum Neurology 2014; 20 (1): 100-114.

Peripheral Nerves of the leg

- Lateral Femoral Cutaneous Neuropathy
- Femoral Neuropathy
- Peroneal Neuropathy
- Lumbosacral Plexopathy
- Obturator nerve injury



O'Neal MA et al. Postpartum spinal cord, root, plexus and peripheral nerve injuries involving the lower extremities: a practical approach. Anesth Analg. 2015 Jan;120(1):141-148.

Summary

- Discussed some common reasons for neurologic consultation in pregnancy
- Reviewed the importance of planning and use of appropriate imaging
- Described disease treatment specific to pregnancy

“This is a teaching hospital”