




# Headache in pregnant women

Dr. behnaz ansari

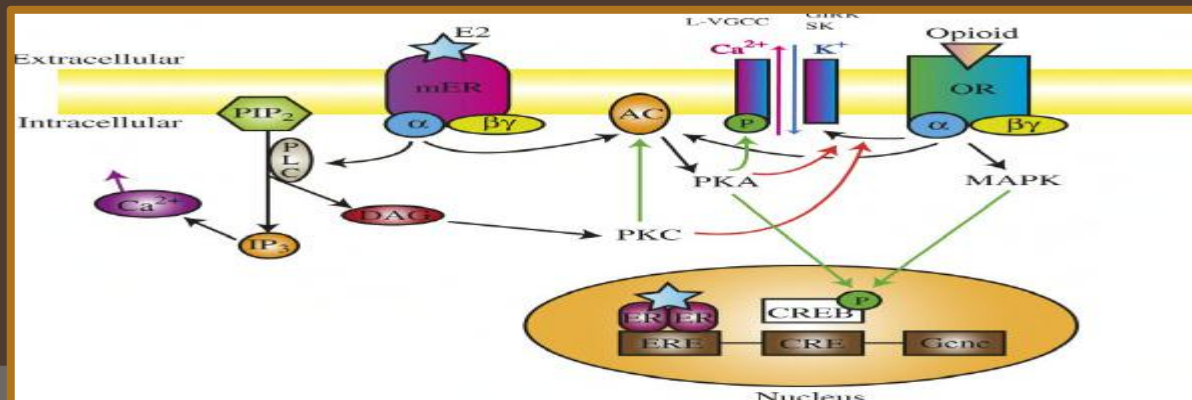
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- ◎ **Case:** A 22 y.o. gravida 1, at 28 wks. gestation presents for daily headaches which began after 16 weeks gestation. Headaches are present when she wakes up in the morning and tend to decrease but not resolve with acetaminophen.
  - ◎ She has no prior h/o headaches and is otherwise healthy. Pertinent features in exam include a BMI of 37, BP 128/88 and a normal neurologic exam (including fundoscopy).



- Headaches are common among women in their childbearing years. Tension-type headache and migraine are most common, while cluster headache is much less common .
- Estradiol receptors** are located in close proximity to 50 to 80 percent of catecholamine receptor sites in the brain, suggesting estrogen may affect the function of pain pathways .



The International Headache Society broadly categorizes headaches as primary or secondary:



➔ **primary headache** (such as migraine headaches, tension headaches and cluster headaches, chronic daily headaches or medication overuse headaches) account for majority of the cases of headache seen in pregnancy.

➔ **Secondary headaches** are headaches attributable to another underlying cause. Certain causes of secondary headaches deserve special consideration in pregnancy as they might be either unique to pregnancy or be exacerbated by physiologic changes of the gravid state.



- When headaches first present during pregnancy or postpartum, a diagnostic evaluation is indicated and should consider the possibility that the headache is related to a complication of pregnancy.

**severe preeclampsia/eclampsia always needs to be excluded in women over 20 weeks of gestation.**





- ◎ In most cases, pregnant women with primary headache syndromes have been diagnosed before pregnancy, but as many as 10 percent initially present or are first diagnosed during gestation.
- ◎ Among pregnant women with the onset of new or atypical headache, one third have **migraine**, one third have **preeclampsia/eclampsia-related headache**, and the remaining one third have a variety of **other causes** of headache



these characteristics increase the probability of a serious underlying disorder:

- Sudden onset of severe headache ("worst headache of my life")
- New-onset migrainous headaches
- Headache in immunosuppressed women
- Worsening headaches
- Headache characteristic (eg, pain, pattern) different from usual headaches
- Headache related to exertion
- Headache with fever
- Headache with altered mental status, seizures, papilledema, changes in vision, stiff neck, or focal neurological signs/symptoms
- Headache unrelieved by pain medication





**The major consideration is to "do no harm" since a history of headaches does not appear to adversely affect pregnancy outcome.**





**What investigations, if any, should be performed in this patient? What radiologic testing can be performed safely in pregnancy?**





## ADVANCED IMAGING IN THE PREGNANT PATIENT:

- ⦿ Magnetic resonance imaging (MRI) does not expose the fetus to ionizing radiation and has not been associated with adverse fetal effects. Use of gadolinium is typically avoided.
- ⦿ Computed tomography (CT) involves ionizing radiation, but **fetal radiation exposure from scatter is minimal during maternal head CT** . The estimated fetal radiation dose from a head CT is very low, <1 rad.



- In general, MRI is preferable to CT for assessing nontraumatic or nonhemorrhagic craniospinal pathology, such as edema, vascular disease, mass lesions, or local infection.
- Suspected arterial vascular lesions can be detected by MR angiography without gadolinium contrast.
- MR venogram is the standard for detecting venous thrombosis and can be performed without the use of gadolinium.



- ⦿ Lumbar puncture **is not contraindicated** during pregnancy.
- ⦿ **blood pressure measurement** is critical in pregnant women **over 20 weeks** of gestation. If blood pressure is elevated, urine protein and laboratory studies should be determined to evaluate for preeclampsia.





**What is the differential diagnosis of new onset headache in the second half of pregnancy?**





- ◎ Pregnancy is associated with a physiologic increase in blood volume and vasodilatation, that peaks around 26–28 weeks gestation.
- ◎ Previously asymptomatic arteriovenous malformations (AVMs) or aneurysms can therefore present at this time with headaches or cerebrovascular accidents.
- ◎ In patients presenting with prolonged debilitating headaches, worse with supine position, idiopathic intracranial hypertension (pseudotumor cerebri) is an important consideration.



- ⦿ In patients with pituitary adenomas, particularly macroadenomas, tumor growth can occur with pregnancy progression, and may present as headache.
- ⦿ Pregnancy is a hypercoagulable state and although ischemic stroke is rare, cerebral vein thrombosis can be seen in pregnancy, particularly in the third trimester and postpartum period.
- ⦿ Finally, preeclampsia, which can complicate 5–10% of pregnancies.



# How are headaches best managed in pregnancy?





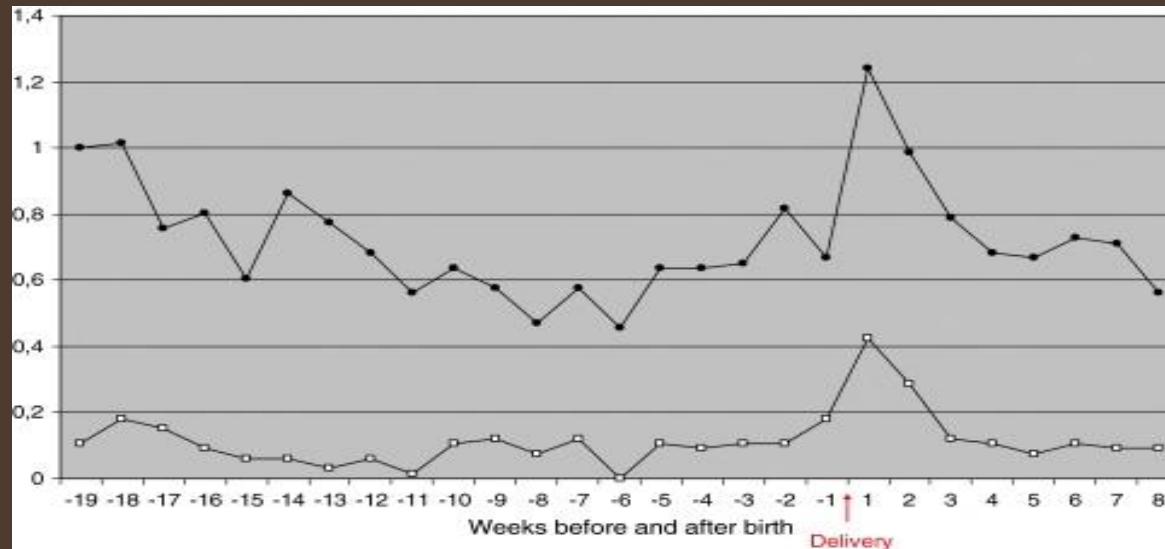


# Migraine:

- ⦿ A migraine occurring during pregnancy can generally be differentiated from a preeclampsia headache by assessment of the patient's blood pressure, urine protein, laboratory studies, gestational age, and whether she reports similar headaches prior to pregnancy.
- ⦿ Approximately 2 percent of women develop their first migraine during pregnancy, usually in the first trimester



- The occurrence of migraine is modulated by fluctuations in estrogen levels. Most women (60 to 70 percent) with a history of migraine report improvement over the course of pregnancy, approximately 5 percent describe worsening, and the remainder report no change.





→ a prospective cohort study found that the risk of developing hypertensive disorders of pregnancy was almost three-fold higher in migraineurs than in non-migraineurs (9.1 versus 3.1 percent; adjusted OR 2.85, 95% CI 1.40-5.81)

→ There appears to be an increased risk of stroke associated with migraine, particularly in women who have migraine with aura. However, the absolute increase in the risk of stroke is small and the effect of pregnancy is unclear as stroke is rare in pregnant/postpartum women .



# Treatment of acute migraine :

- The treatment of migraine in pregnant women differs somewhat from treatment of nonpregnant women because of concerns about adverse fetal drug effects.
- We initiate therapy with **acetaminophen**. Acetaminophen (1000 mg) can be an effective treatment of migraine .
- Migraine that does not respond to **acetaminophen** alone may be relieved with combination therapy such as acetaminophen (650 to 1000 mg) and **metoclopramide** (10 mg); **acetaminophen-codeine**.



- ⦿ Nonsteroidal antiinflammatory drugs (NSAIDs), such as **naproxen** or **ibuprofen**, are a second-line option, and safest in the second trimester.
- ⦿ Aspirin is generally avoided in the third trimester because of its effects on maternal and fetal platelets and risk of premature closure of the ductus arteriosus.
- ⦿ Opioids (eg, **oxycodone**, **hydromorphone**, **meperidine**, **morphine**) are a third-tier option. thus, they should not be used for prolonged periods of time.



- For moderate to severe symptoms in patients who do not respond to other drugs, triptans can be considered . **Sumatriptan** (100 mg orally, 4 to 6 mg subcutaneously, or 5 to 25 mg intranasally), **rizatriptan**, and **naratriptan** are selective serotonin agonists that are highly effective in treating migraine headaches.

➔ **Frovatriptan** is less desirable than other triptans because of its longer half-life.



- ⦿ **Ergotamine** is **absolutely contraindicated** during pregnancy because of the potential to induce hypertonic uterine contractions and vasospasm/vasoconstriction, which could cause adverse fetal effects.
- ⦿ Although the safety of **magnesium sulfate** is well established in pregnancy, its efficacy for treatment of acute migraine in adults has not been clearly established, with conflicting findings among studies.
- ⦿ An older antihistamine agent, **ciproheptadine**, can be used for acute or prophylactic therapy.

# Prophylactic treatment :




- ◉ Women with frequent migraine headaches often benefit from preventative therapy.
- ◉ Beta-blockers such as **propranolol** and **metoprolol** are not teratogens, but fetal/neonatal effects from beta-blockade are possible with prolonged use and include: mild fetal growth restriction; mild transient neonatal bradycardia, respiratory depression, hyperbilirubinemia, and/or hypoglycemia.
- ◉ Short and long acting calcium channel blockers are commonly used in the third trimester for treatment of hypertension and preterm labor, without adverse fetal/pregnancy effects. **verapamil** is the preferred agent because it is relatively safe, and has good tolerability and ease of use.





- Low dose antidepressants, such as selective serotonin reuptake inhibitors (SSRI), serotonin–norepinephrine reuptake inhibitors (SNRIs), or tricyclic antidepressants (TCA), may be considered in refractory patients.
- magnesium 400 to 800 mg daily, riboflavin 400 mg daily, or extract of butterbur root 50 to 100 mg twice daily may be considered.
- There isn't sufficient data to support the safety of Coenzyme Q10. so it has been shown to reduce the risk of preeclampsia.



If migraine prophylaxis is considered during pregnancy the lowest effective doses of propranolol or metoprolol are the first-line recommendation.

Amitriptyline is also an option.



Table 1. Headache Medications, and Their Use In Pregnancy

Class of meds	Use in pregnancy justifiable in most circumstances	Use in pregnancy justified in some circumstances
Medications for acute relief of headache	Acetaminophen Metoclopramide Promethazine Prochlorperazine Caffeine	Ibuprofen Butalbital Sumatriptan Opioids
Medications for preventive therapy	Amitriptyline Nortriptyline Metoprolol Magnesium Verapamil	

1 From Micromedex, accessed Mar 21, 2014

**TABLE 7-3** Drugs Used for Acute Treatment of Headache During P

Drug	FDA Pregnancy Category <sup>a</sup>	Notes
<b>Analgesics</b>		
Acetaminophen	B	First-line; amounts in breast milk are much less than doses usually given to infants
Aspirin	C	Second line; use in first and second trimesters only; category D in third trimester
Diclofenac	B	Second line; use in first and second trimesters only; category D in third trimester
Ibuprofen	B	Second line; nonsteroidal anti-inflammatory drug of choice; use in first and second trimesters only; category D in third trimester
Indomethacin	C	Use in first and second trimesters only; avoid from 30 weeks; category D in third trimester
Mefenamic acid	C	Use in first and second trimesters; avoid from 30 weeks; category D in third trimester
Naproxen	B	Use in first and second trimesters only; avoid from 30 weeks; category D in third trimester
<b>Antiemetics</b>		
Metoclopramide	B	
Prochlorperazine	C	
Promethazine	C	
<b>Barbiturates</b>		
Butalbital	C	Category D if used in high doses at term or for prolonged periods
<b>Ergots</b>		
Dihydroergotamine	X	
Ergotamine	X	
<b>Opiates</b>		
Codeine	C	Opiates not recommended for migraine
Meperidine	B	Category D if used in high doses at term or for prolonged periods
Morphine	C	
Tramadol	C	
<b>Triptans</b>		
Almotriptan	C	
Eletriptan	C	
Frovatriptan	C	
Naratriptan	C	
Rizatriptan	C	
Sumatriptan	C	Third line; consider for severe unresponsive attacks
Zolmitriptan	C	
<b>Other drugs</b>		
Prednisone or prednisolone	C	

**TABLE 7-5** Drugs Used for Prophylaxis of Headache

Drug	FDA Pregnancy Category <sup>a</sup>	Notes
<b>Angiotensin-converting enzyme inhibitors</b>		
Lisinopril	D	Category C in first trimester
<b>Angiotensin receptor blockers</b>		
Candesartan	D	Category C in first trimester
<b>Antiepileptics</b>		
Gabapentin	C	
Topiramate	D	
Valproic acid	X	Teratogenic
<b>Antiplatelet drugs</b>		
Aspirin	C	Doses $\leq 150$ mg/d
<b>Beta-blockers</b>		
Atenolol	D	Propranolol or metoprolol preferred
Metoprolol	C	
Nadolol	C	Propranolol or metoprolol preferred
Propranolol	C	Beta-blocker of choice
Timolol	C	Propranolol or metoprolol preferred
<b>Calcium channel blockers</b>		
Nifedipine	C	
Verapamil	C	No data on high doses in pregnancy
<b>SSRIs/SNRIs</b>		Amitriptyline or nortriptyline preferred
Citalopram	C	
Escitalopram	C	
Fluoxetine	C	
Sertraline...	C	
<b>Tricyclics</b>		
Amitriptyline	C	
Nortriptyline	C	
<b>Other drugs</b>		
Botulinum toxin	C	
Lithium	D	Teratogenic



## EMERGENCY TREATMENT OF HEADACHE IN PREGNANCY:

- Prochlorperazine 10 mg or chlorpromazine 25 mg to 50 mg IM together with IV fluid.
- Magnesium sulfate 1 gr IV over 15 minutes was effective randomized, placebo-controlled trial of migraine.
- continuous administration of magnesium sulfate beyond 5 to 7 days in pregnancy should be avoided because of hypocalcemia.
- Glucocorticoids may be useful in intractable cases.(prednisone 20 mg orally four times daily for two days or methylprednisolone 4 mg orally,21 tablets over six days).





- ◎ **Case (continued):** The patient did not have preeclampsia and was treated with acetaminophen and caffeine for symptomatic relief. She was also placed on metoprolol 12.5 mg po twice daily for prophylaxis and at a follow-up visit 4 weeks later reported improvement.





# Tension-type headache :

- In contrast to migraine, the frequency of tension-type headaches usually does not change during pregnancy since these headaches are not hormonally mediated.







- ◎ **Acetaminophen** is the first-line analgesic for treatment of tension-type headaches during pregnancy and NSAIDs are a second-line medical therapy.
- ◎ If monotherapy is ineffective, a combination of **acetaminophen** 500 mg and **caffeine** 100 mg is a reasonable third tier. **Amitriptyline** is the drug of the first choice for prophylaxis.
- ◎ Nonpharmacologic interventions include heat, ice, massage, rest, maintaining a regular meal and sleep pattern, and biofeedback are useful in managing chronic tension-type headaches.

# Cluster headache :



- Cluster headaches are probably not affected by reproductive events .
- In most patients, acute cluster headaches can be aborted by inhalation of 100 percent oxygen. If this is unsuccessful, subcutaneous or intranasal **sumatriptan** is a reasonable option.
- If response to these therapies is suboptimal, 0.5 mL **lidocaine** 4% (pregnancy category B) can be placed inside the nostril on the affected side of the head.

**Ergotamine** is effective but absolutely contraindicated during pregnancy.



when preventive therapy is indicated, the two best options during pregnancy are **verapamil** and glucocorticoids.

- Alternative treatments after the first trimester of pregnancy include **lithium** (first trimester exposure has been associated with Ebstein's anomaly in the fetus and third trimester exposure has been associated with signs of lithium toxicity in neonates) and **topiramate** (first trimester exposure has been associated with cleft lip and/or palate).
- Third-line agents include **pizotifen**, **gabapentin**, intranasal application of **capsaicin**, and oral melatonin . Pizotifen and gabapentin should not be used in the first trimester.



## EVALUATION FOR PREECLAMPSIA :

- Preeclampsia is defined as hypertension (systolic blood pressure  $>140\text{mmHg}$  OR diastolic blood pressure  $>90\text{mmHg}$ ) *and* proteinuria ( $>0.3\text{g}$  protein in a 24-hour urine collection) at  $>20$  weeks GA in a woman who was known to be normotensive prior to pregnancy. Preeclampsia occurs in approximately 2-8% of healthy nulliparous pregnancies.
- the risk of developing pre-eclampsia in women with migraines during pregnancy is **threefold** higher than the risk in pregnant women without migraines.
- The evaluation for preeclampsia should include an evaluation for **HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome with complete blood count and liver function tests.**



- The cause of headache in severe preeclampsia/eclampsia is not known, but may be related to increased cerebral perfusion pressure (eg, hypertensive encephalopathy) , cerebral ischemia from vasoconstriction , posterior reversible encephalopathy syndrome (PRES) , cerebral edema, or microhemorrhages.

➔ **Cerebral venous thrombosis** should be considered in any woman with severe preeclampsia or eclampsia who complains of **unremitting headaches**



- Typical dosing of **Magnesium sulfate** consists of a 4-6g load infused over 15-20 minutes followed by 2g/hr infusion. Patients who are not actively seizing may not require loading.
- Antihypertensives should also be given to maintain blood pressures of 140-155/90-105 mmHg. Recommended agents include hydralazine and labetalol.
- Delivery of the fetus should be considered if the gestational age is appropriate or if cerebral symptoms or severe uncontrolled blood pressures persist despite maximum antihypertensive and magnesium therapy, regardless of gestational age.

# Do all woman with eclampsia need neuroimaging studies?

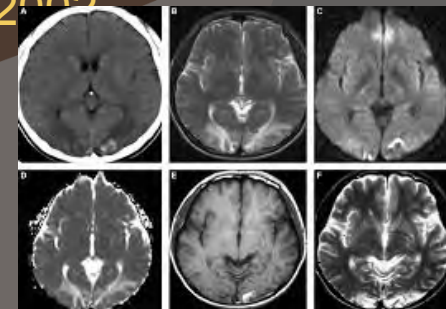


Woman with a severe headache and:

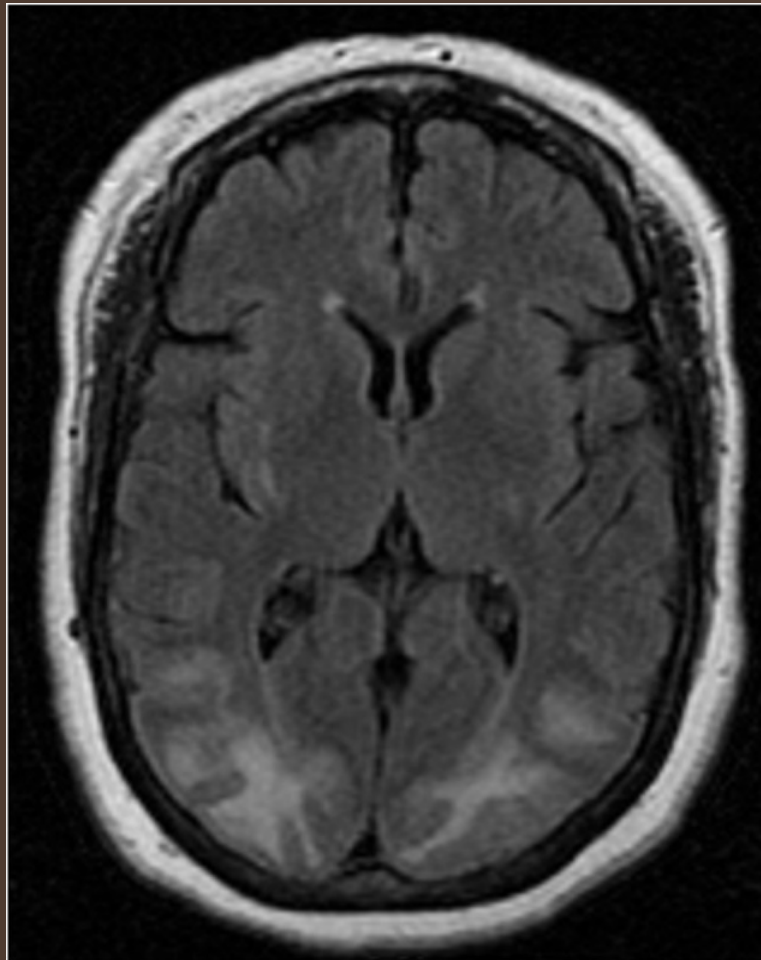
- History of acute cerebral vascular hemorrhage that occurred during pregnancy.
- Malignant hypertension
- Severe preeclampsia in setting of preexisting cerebral aneurysm or arteriovenous malformation
- Focal neurological signs, prolonged coma, atypical convulsions and who have a prolonged return to complete recovery following delivery

Up to date 2014

and Sibai BM. Hypertension and obstetric Churchill Livingstone. 2002



Symmetrical posterior edema on MRI T2 FLAIR images characteristic of posterior reversible encephalopathy syndrome (PRES) in preeclampsia woman who presented with seizure:







## Cerebral venous thrombosis :

- The risk of cerebral venous thrombosis (CVT) is increased in the prothrombotic pregnant state. Most pregnancy-related CVT occurs in the third trimester. Common presenting complaints include headache, focal neurologic deficit, seizure, altered mental status, and signs of elevated intracranial pressure (ICP) such as papilledema.
- The headache is typically sub-acute, although thunderclap headache has been reported.
- The diagnosis of CVT is based on neuroimaging.



- Anticoagulation is the standard of care for management of CVT. **Low molecular weight heparin (LMWH)** does not cross the placenta and is the first-line treatment for anticoagulation in pregnancy. Anticoagulation should be continued **throughout the pregnancy and post-partum for a minimum of six weeks for a total minimum duration of therapy of three to six months.** Although warfarin is contraindicated in pregnancy, post-partum patients may be safely transitioned to oral warfarin.
- Caesarean section may be necessary if CVT has occurred before or during labor. If it occurs early in the pregnancy, labor can be allowed spontaneously.(Aminoff's 2014)

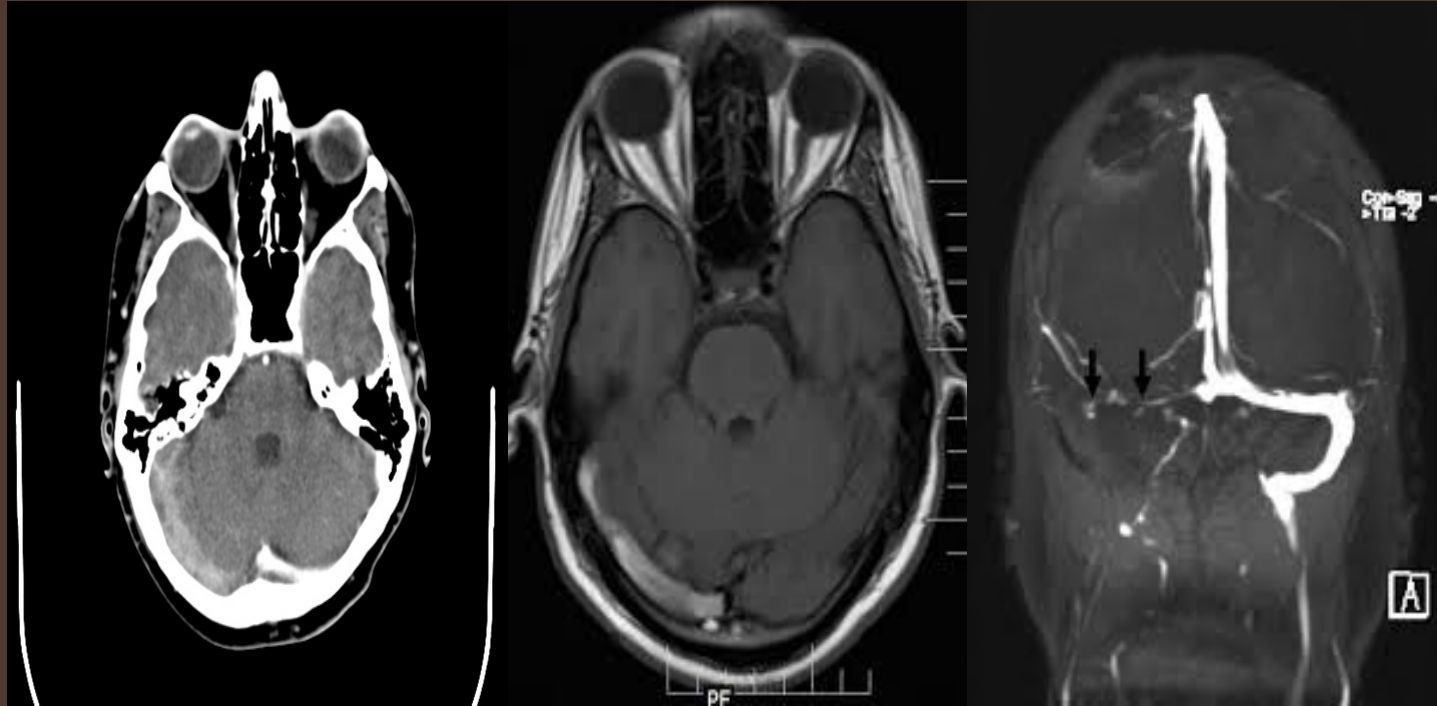


## Case (Conclusion):

- She returned at 37 wks. gestation with severe intractable headache, borderline hypertension and labs suggestive of preeclampsia. She was started on a magnesium sulfate drip and a decision was made to induce labor. On postpartum day 7, after an uneventful delivery, she returned with a severe persistent headache and generalized malaise. Slight weakness in the right leg was noted. An MRV showed right sagittal vein thrombosis. She was started on low molecular weight heparin and subsequently transitioned to oral anticoagulation, with planned treatment duration of 6 months.



# Right sagittal vein thrombosis:



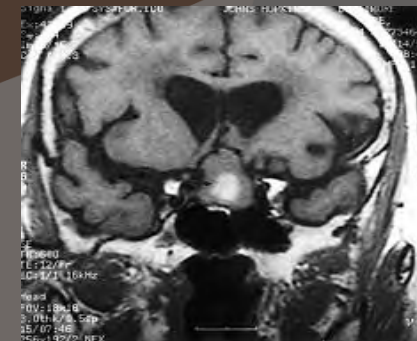


# Pituitary apoplexy :

- Pituitary apoplexy is caused by acute ischemic or hemorrhagic infarction as the pituitary gland expands and outgrows its blood supply or compresses the vessels against the sella.
- Although rare, the massive hyperplasia of lactotrophs that occurs in pregnancy causes the pituitary gland to grow by as much as 130% putting pregnant patients at risk.
- Patients will present most commonly with sudden onset severe headache and nausea and vomiting and less commonly with visual symptoms, altered mental status, or coma. Secondary adrenal insufficiency can occur, causing severe hypotension and hyponatremia which can be life-threatening.



- CT may demonstrate a recent bleed or hyperdense lesion in the pituitary. MRI is more sensitive for delineating the relationship between the pituitary and surrounding structures.
- Pituitary apoplexy patients with persistent visual symptoms, neurologic deficit, or altered mental status require **urgent surgical decompression**. Secondary adrenal insufficiency should be treated immediately with **fluid and electrolyte replacement and hydrocortisone**.

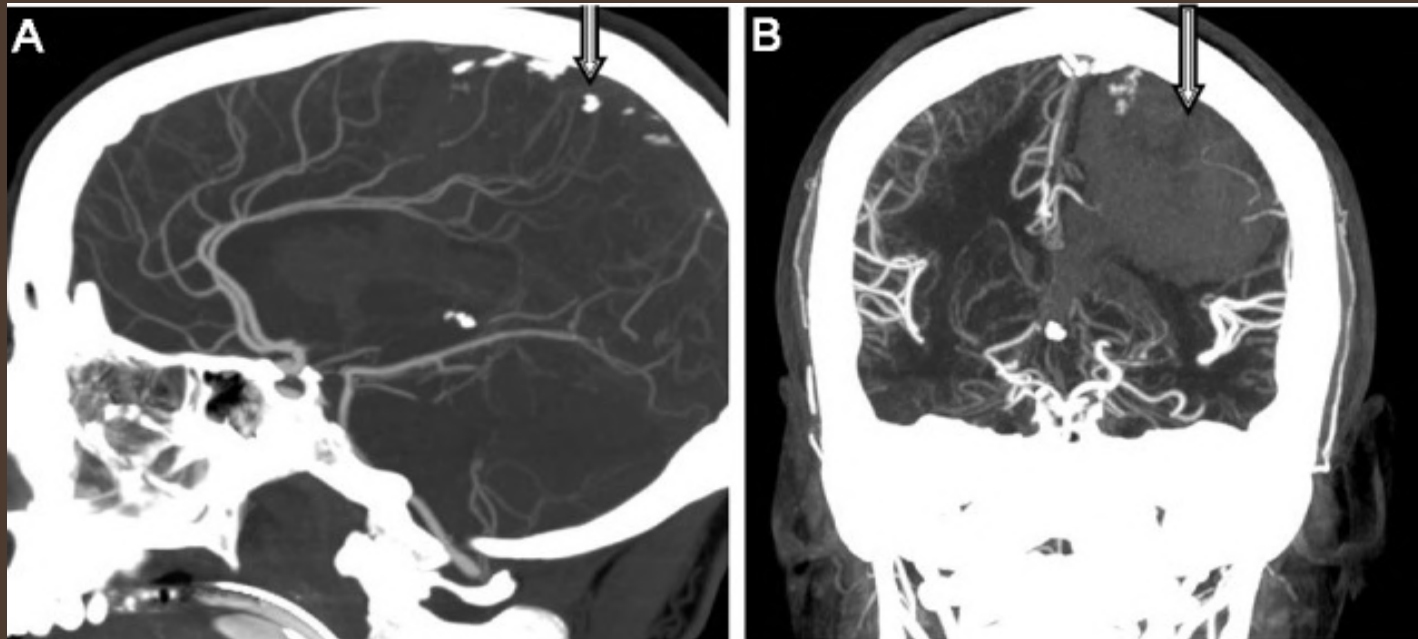




# Subarachnoid hemorrhage :

- Subarachnoid hemorrhage occurs most commonly as the result of a ruptured aneurysm or arterial-venous malformation (AVM). In pregnancy, AVM rupture typically occurs early (15- 20 weeks GA) and in younger women (20-25 years), while aneurysm rupture usually occurs later (30-40 weeks GA) and in older women (30-35 years).
- A theoretical increased risk in pregnancy has been proposed. The cardiac output and blood volume peak of the third trimester is thought to increase the risk of aneurysm rupture. However, other studies suggest there is no increased risk of SAH in pregnancy, labor, or delivery.

A ruptured arteriovenous malformations (AVM) in a 41-year-old woman in the 23rd week of pregnancy







# Arterial dissection:

- ⊙ Pregnancy theoretically increases the risk for spontaneous dissection. In pregnancy, high progesterone and/or decreased collagen synthesis is thought to weaken the arterial wall. This, together with increased shear stress on the vessel wall caused by increased intravascular volume and cardiac output, is thought to increase the risk of dissection in the pregnant population.

**Non-contrast MRA** is the preferred modality in the pregnant patient, however.



- As in CVT, **anticoagulation** is the standard of care for management of arterial dissection. LMWH is again the first-line treatment and the duration of anticoagulation is the same as for CVT. Post-partum patients may be transitioned to oral warfarin. **Anticoagulation is contraindicated in patients with intracranial extension of the dissection, intracranial aneurysm, or infarction with hemorrhagic transformation or mass effect.**
- Patients without ischemic symptoms may be treated with an antiplatelet agent only. Aspirin (pregnancy category D) has been demonstrated safe and effective at low doses (< 100mg<sub>day</sub>).
- Endovascular repair or stenting in stable patients should be reserved for those in whom anticoagulation is contraindicated.



# Idiopathic Intracranial Hypertension :

- Idiopathic intracranial hypertension (IIH), formerly pseudotumor cerebri, is defined as an opening pressure of **>250 mmH<sup>2</sup>O** with normal CSF. Occurrence rates are estimated at 5% in the pregnant population.
- Papilledema is almost universally present and can occasionally be unilateral. In patients without papilledema, a history of headache with visual disturbances, tinnitus, or sixth-nerve palsies is very suggestive of IIH.

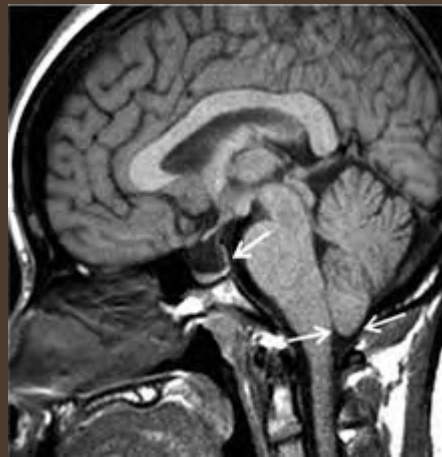
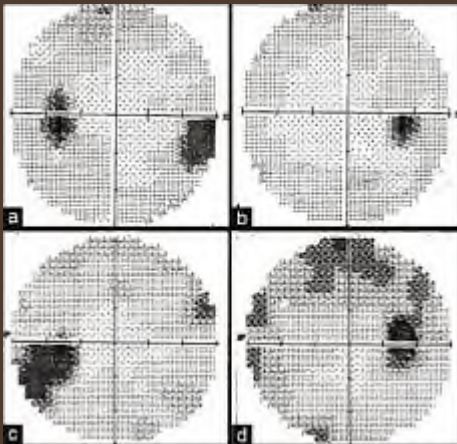
a diagnosis of CVT should be excluded in these patients.



- ⊙ **First-line therapy** for IIH in pregnancy is **diet and weight control**.
- ⊙ **Second-line therapies** include **serial LPs and/or acetazolamide** (category C). Some physicians recommended restricting its use until after 20 weeks 'gestation.
- ⊙ The use of **other diuretics** is **controversial** because of the potential for decreased placental blood flow.
- ⊙ **Steroids** (category C) are reserved for **urgent short-term** treatment in patients awaiting surgery.
- ⊙ **Surgical therapy** is recommended for those with severe or progressive visual loss despite medical management. Optic nerve sheath fenestration creates a window in the optic nerve sheath allowing CSF to drain into the retrobulbar space, directly protecting the optic nerve. Lumboperitoneal or ventriculoperitoneal shunting is also an option .

- Labor may be allowed and cesarean delivery is performed for obstetric indications. If contemplating a vaginal delivery, adequate labor analgesia is recommended.
- If a cesarean delivery is being considered, regional anesthesia is preferred.
- There is an exception, however. Spinal anesthesia is not preferred for use in patients who have a lumbo-peritoneal shunt.

Medscape





# Meningitis:

- ◎ *Streptococcus pneumoniae* and *Listeria monocytogenes* are the most common causative organisms and are associated with a very high mortality rate (28%).
- ◎ Empiric antimicrobial therapy for meningitis consists of a third-generation cephalosporin, such as **cefotaxime or ceftriaxone** (category B), and **vancomycin** (category C). Because *Listeria* infection is common in pregnancy, **ampicillin** (category B) should also be given. If viral causes are suspected, add acyclovir (category B).



## REVIEW ARTICLE

# Headache in Pregnancy: An Approach to Emergency Department Evaluation and Management

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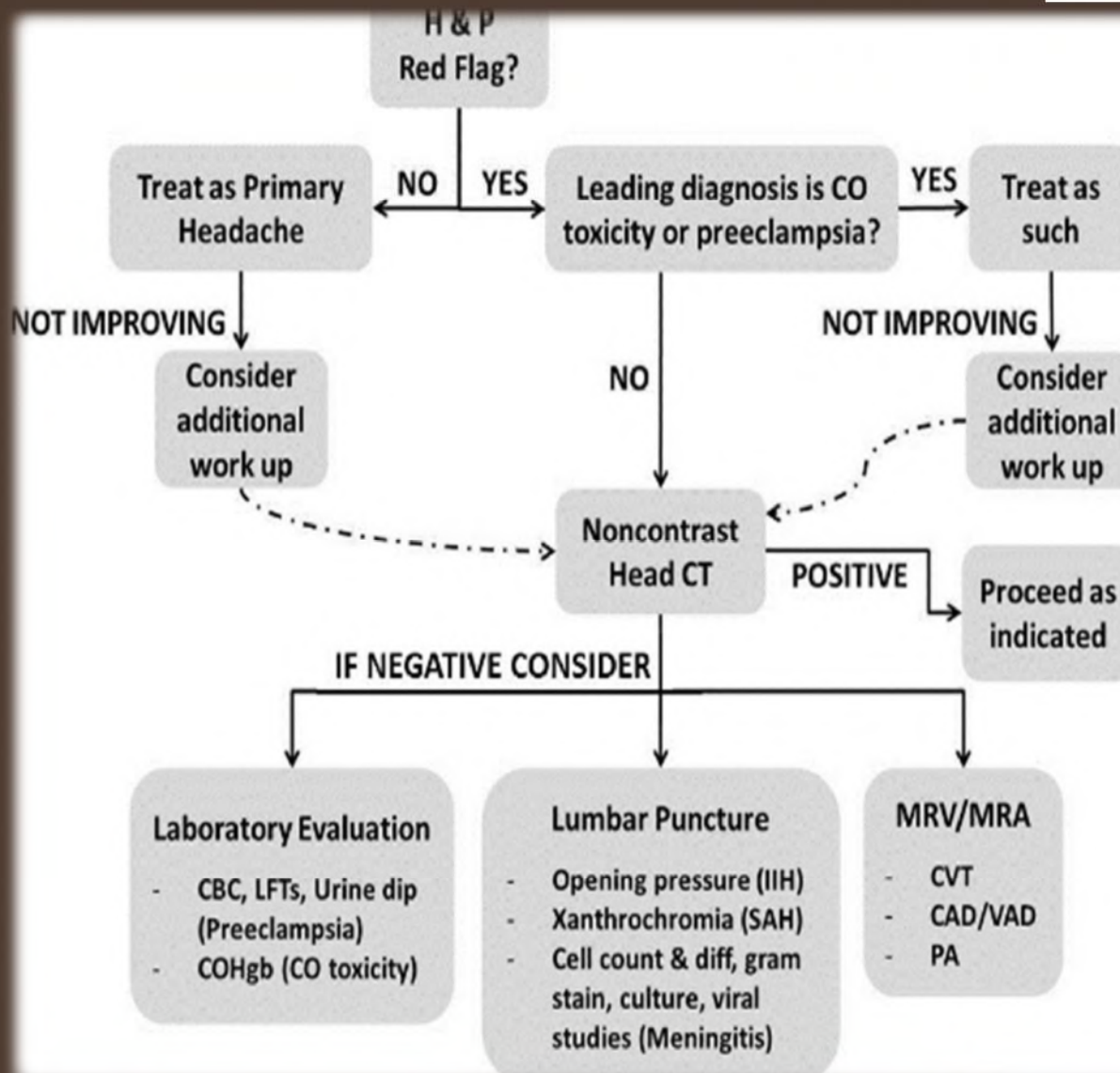
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### Red Flags:

#### History

- Headache differs from baseline
- New onset headache
- Rapidly increasing headache frequency
- Thunderclap headache
- Nausea/Vomiting
- Visual disturbance

#### Physical Exam

- BP > 140/90 at >20 weeks GA
- Fever
- Nuchal rigidity
- Papilledema
- Neurologic deficit
- Seizure/Altered mental status



# SUMMARY:



- ⦿ The objective of the ED evaluation of headache is to rule out ominous secondary causes.
- ⦿ Physiologic changes induced by pregnancy increase the risk of CVT, dissection, and pituitary apoplexy. Preeclampsia must also be considered.
- ⦿ Primary headaches should be a diagnosis of exclusion.
- ⦿ When advanced imaging is indicated, MRI should be used whenever possible to reduce radiation exposure. If CT is necessary, imaging of the head rarely exceeds fetal radiation danger thresholds. Contrast agents do cause adverse fetal effects and should be avoided unless absolutely necessary for accurate diagnosis.
- ⦿ Medical therapy should be selected with careful consideration of adverse fetal effects.
- ⦿ **Don't forget preeclampsia and CVT**



Thanks for your attention

