Headaches in pregnancy

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With your basket and my basket the people will live

Naku to rourou nau te rourou ka ora ai te iwi

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Disclosures

- I am a Generalist
- I am not a Researcher, Neurologist, Headache or Pain specialist
- I have no financial conflicts of interest

- I HATE HEADACHES!

I feel your pain

Why is it so hard?

- Don’t want to miss something serious
- Overlap of symptoms between conditions is wide
- Chronic symptoms can change in pregnancy
- Addition of pregnancy-specific conditions to the mix
- Extra considerations around appropriate imaging

Plan of Attack

1: Know the enemy

- Epidemiology
- Classification of Headaches

2: Assess the threat

- Red flags
- Secondary headache presentations
- Which symptoms matter?

3: Battle Plans

- Algorithm(s)
- Safety of treatments in pregnancy
- Focus on Primary headache disorder management

Epidemiology

- 25% of women will experience migraine
- 88% will experience tension headache
- Headaches occur 3x more commonly in women
  - Migraines in particular linked to hormonal triggers
- 35% of women report headaches in pregnancy
- Headache is the most frequent indication for neuroimaging during pregnancy (70%)

Martin SR & Foley MR *Approach to the Pregnant Patient with Headache* Clin. O&G 2005; 48(1) 2-11

Epidemiology

General:

- 7th highest cause of Years Lost to Disability (YLD)
- 3 billion people have primary headache disorders
- Burden highest in women aged 15-49yrs
  - 20.3billion YLD from migraine

In Pregnancy:

- >50% presented in the third trimester
- 65% Primary, 35% Secondary

1. Stovner LJ, Nichols E, Steiner TJ, Abd-Allah F, Abdelalim A, Al-Raddadi RM, et al. Global, regional, and national burden of migraine and tension-type headache, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet Neurology. 2018;17(11):954-76.
2. Robbins MS, Farmakidis C, Dayal AK, Lipton RB. Acute headache diagnosis in pregnant women: a hospital-based study. Neurology. 2015;85(12):1024-30.

Classification of headaches

Primary	Frequency
Tension	V. Common
Migraine	Common
Cluster	Rare
Specific headaches	Variable

Secondary	Eg.
Head trauma	MVA, Dom viol.
Vascular	SAH, HTN
Intracranial	ICP, tumour meningitis
Substance use/withdrawal	Alcohol, narcotics
Metabolic disorders	Hypoglycemia, hypoxia
Cranial structural disorders	Tooth, eye, neck conditions
Neuralgias of face/skull	TGN, PHN

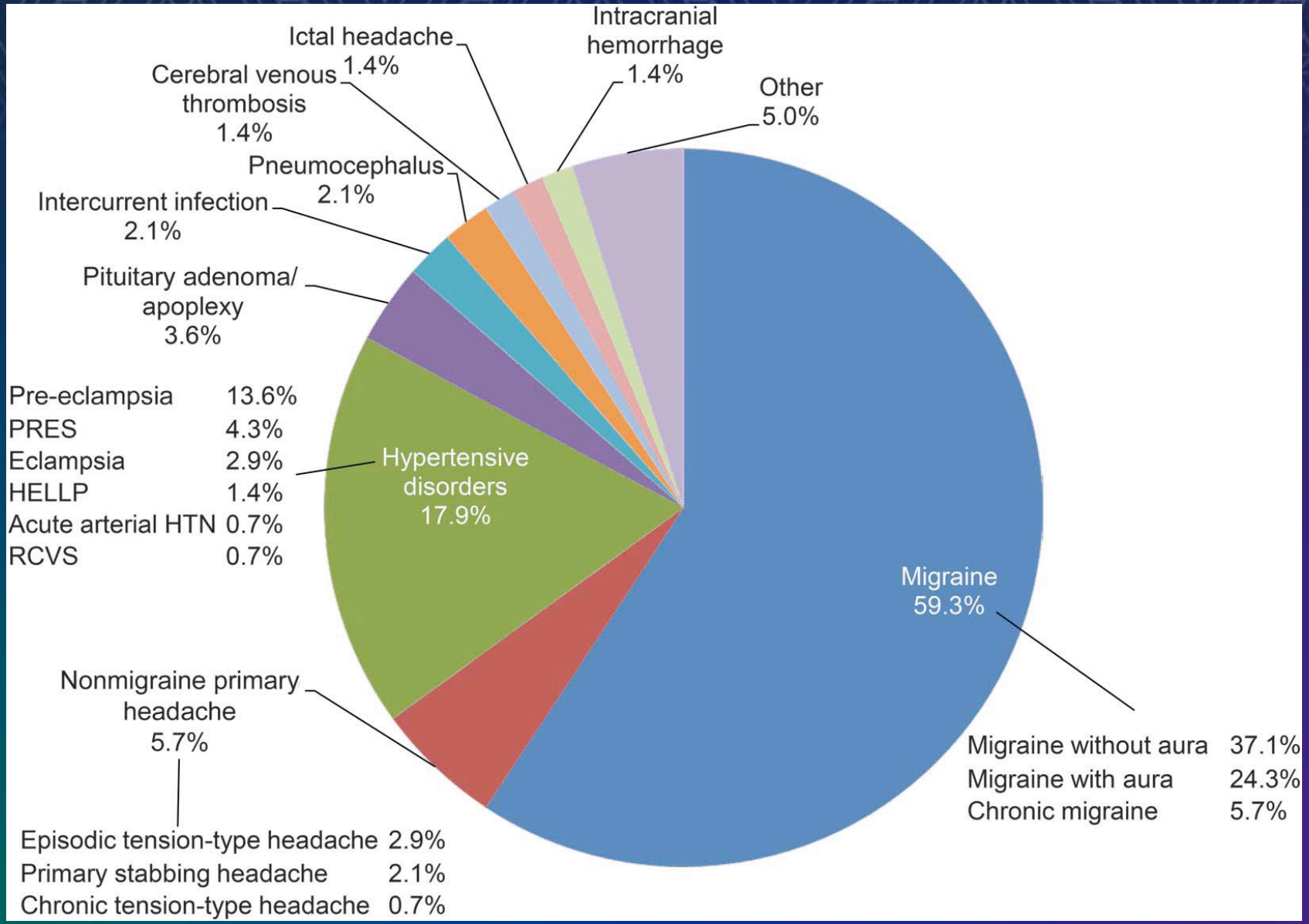
Headache Classification Committee of the IHS, *The International Classification of Headache Disorders, 3rd ed. (beta version),* Cephalalgia 2013 33(9) 629-808

Pregnancy-Related Headaches

Either directly related, or more common in pregnancy

- Pre-eclampsia
- Eclampsia
- Post dural puncture headache
- Cerebral venous sinus thrombosis
- Idiopathic intracranial hypertension
- Reversible cerebral vasoconstriction syndrome (RCVS)
- Pituitary apoplexy
- Subarachnoid haemorrhage*

Causes of Acute Headache Presentation in 140 Pregnant women



Robbins MS, Farmakidis C, Dayal AK, Lipton RB. Acute headache diagnosis in pregnant women: a hospital-based study. Neurology. 2015;85(12):1024-30.

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Comparative frequencies of secondary headaches

TABLE 1 Comparative frequencies of secondary headaches.

Ramchandren et al. (1)	Raffaelli et al. (4)	Raffaelli et al. (2)	Robbins et al. (3)
CVT (6%)	Viral infections (17.2%)	ICH (28.6%)	Preeclampsia (13.6%)
RCVS (6%)	Sinusitis (12.5%)	CVT (23.8%)	PRES (4.3%)
IIH (3%)	Preeclampsia (9.4%)	Acute stroke (14.3%)	Eclampsia (2.9%)
ICH (3%)	PRES (6.3%)	PRES (19%)	ICH (1.4%), CVT (1.4%)
Sinusitis (8%)	HELLP (4.7%)	Sinusitis (14.3%)	Pituitary apoplexy (3.6%)

CVT, cerebral venous thrombosis; RCVS, reversible cerebral vasoconstriction syndrome; IIH, idiopathic intracranial hypertension; ICH, intracranial hemorrhage; PRES, posterior reversible encephalopathy syndrome; HELLP, hemolysis, elevated liver enzymes, and low platelet count.

Khoromi S. Secondary headaches in pregnancy and the puerperium. Front Neurol. 2023;14:1239078


SHOULD I BE WORRIED
OR NOT.....
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Headache “Red Flags”

- Sudden onset headache “thunderclap”
- Worst ever headache
- Morning waking headache
- Significant change in pattern of chronic headache
- Neurologic signs or symptoms
- Change in LOC, personality, cognition
- New headache in patient over 40yrs
- Headache precipitated or exacerbated by Valsalva’s manoeuvre
- Meningeal signs (neck stiffness)
- History of recent trauma to head and neck
- History of hypertension or endocrine disease

TABLE 2 Headache red flags in pregnancy and the puerperium.

Signs and symptomss	Differential diagnosis	Work up
"Thunderclap" headache*	Aneurysmal SAH, RCVS, PRES, cerebral artery dissection, CVT, PA	Neuroimaging, LP, blood test, endocrine tests & visual testing
Focal neurological signs	ICH, stroke, CVT, intracranial mass lesion	Neuroimaging
Elevated blood pressure	Preeclampsia, RCVS, PRES, HELLP	Blood test**, urine test***, Neuroimaging
Fever	CNS infection, sinusitis	Blood test, Neuroimaging, LP
Gestational age 3rd trimester	preeclampsia, ICH, CVT, PRES	Blood test**, urine test***, Neuroimaging
Increased LFTs, ↑/↓ platelets, ↑ CRP	Preeclampsia, CVT	Blood test**, urine test***, Neuroimaging (CVT)
New onset of severe headache or worsening of previous headache in pregnancy or postpartum	CVT, carotid artery dissection, ICH, RCVS, PRES, PA, space occupying lesion	Neuroimaging
Papilledema	CVT, IIH, intracranial mass lesion, meningitis	Neuroimaging, LP, visual testing (eg, HVF if IIH is suspected)
Seizure	Eclampsia, ICH, PRES, RCVS, CNS infection, stroke, intracranial mass lesion	Neuroimaging, blood test

Khoromi S. Secondary headaches in pregnancy and the puerperium. Front Neurol. 2023;14:1239078

Differential Diagnosis Secondary Headache - 1

Condition	Important symptoms/signs	Investigations
Sinusitis	Fever, facial pain, rhinorrhoea	
Dehydration	History of decreased oral intake Negative JVP	
Cerebral venous sinus thrombosis	New onset, progressive, associated nausea, papilloedema, seizures, focal neurological deficits	MRI brain/MRV
Intracranial haemorrhage or subarachnoid haemorrhage	Thunderclap headache, vomiting, neck stiffness, impaired consciousness or sudden collapse, focal neurological deficits	CT brain Lumbar puncture
Ischaemic stroke	focal neurological deficits	Neuroimaging
Brain tumour/SOL	Am headache, insidious, focal neurological deficits	Neuroimaging

Differential Diagnosis Secondary Headaches - 2

Condition	Important symptoms/signs	Investigations
Meningitis/ encephalitis	Fever, meningism, confusion, altered level of consciousness	CT brain Lumbar puncture
Intracranial hypotension (dural puncture)	Post epidural (24 hours) frontal and postural	Blood patch
Idiopathic intracranial hypertension	Sub acute/chronic HA with visual disturbance Association with OCP and obesity Papilloedema, nonfocal exam	Neuroimaging is negative Lumbar puncture (CSF pressure is increased)
Preeclampsia	Hypertension, hyperreflexia, vasospasm on optic fundoscopy, proteinuria	Urinary protein Urate, creatinine, LFTs, FBC, Foetal USS
RCVS (Reversible cerebral vasoconstriction syndrome)	Post partum; thunderclap HA, relapses, resolves within 6-12 weeks	Neuroimaging with angio & venography; vasogenic oedema

Reality…

DACHES

Sinus eadache	Exertion Headache
discoloured discharge ased sense of pain	• Pulsating pain at both sides of the head during or after a workout 
r ial sinus on 	• Overexertion • Exercising in hot weather or at high altitudes

Which symptoms matter?

- PET headache described as 2/3 of:
  - Bilateral
  - Throbbing
  - Aggravated by physical activity

- In patients with 1º headache disorder, longer attack duration associated with new 2º cause

Which symptoms matter?

- Raffaelli et al multivariate logistic regression analysis
  - 2º headache history
  - Hypertension
  - Fever
  - Abnormal neuro exam

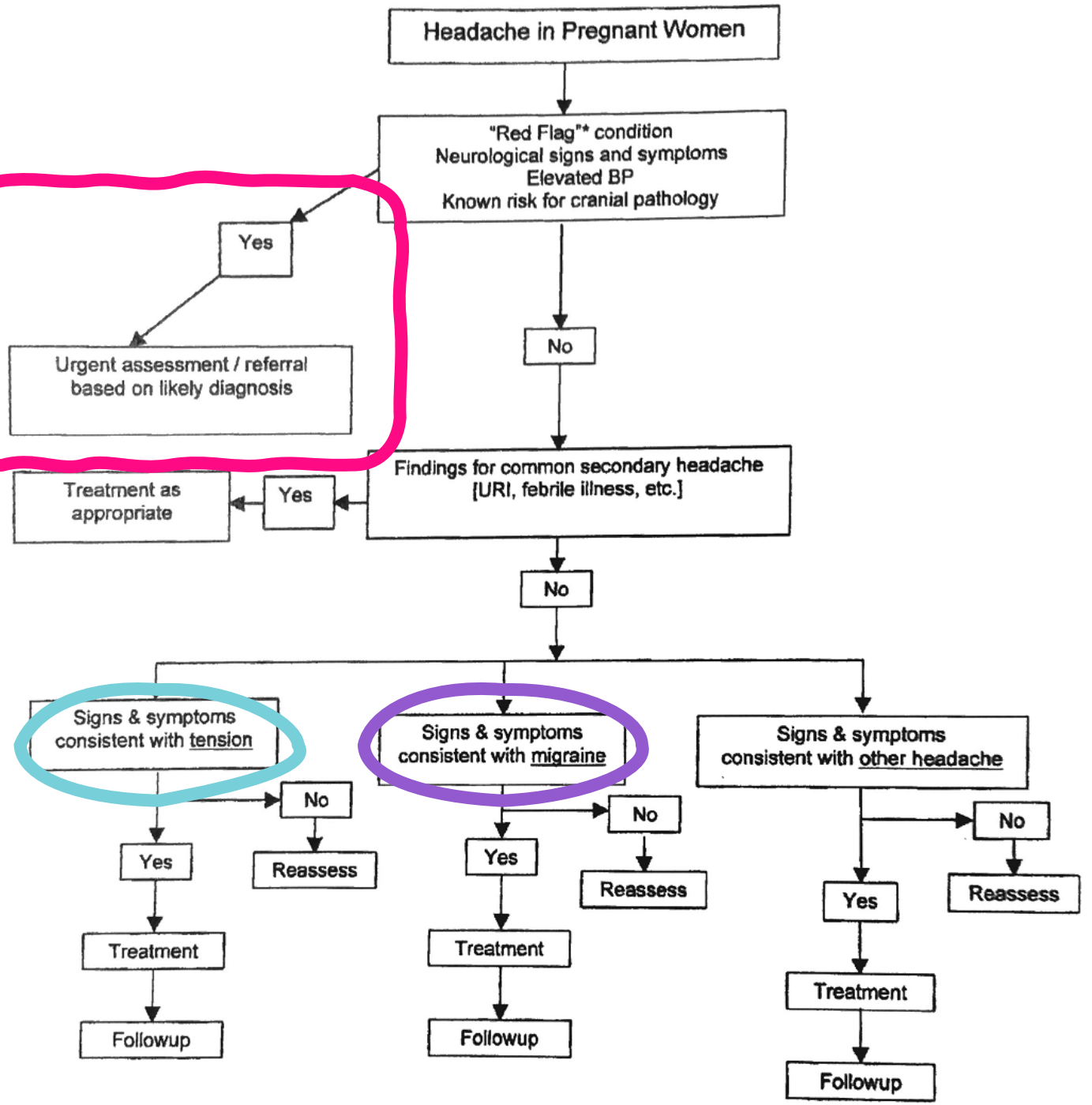
  } Independent predictors of 2º headache

- Robbins et al univariate analysis
  - Lack of headache history*
  - Hypertension*
  - Fever
  - Abnormal neuro exam

1. Raffaelli B, Siebert E, Körner J, Liman T, Reuter U, Neeb L. Characteristics and diagnoses of acute headache in pregnant women - a retrospective cross-sectional study. J Headache Pain. 2017;18(1):114
2. Robbins MS, Farmakidis C, Dayal AK, Lipton RB. Acute headache diagnosis in pregnant women: a hospital-based study. Neurology. 2015;85(12):1024-30.

Starting to put it all together

Von Wald et al, *Headache during Pregnancy, Obstet & Gyn Survey 2002; 57(3) 179-185*



Investigations

Targeted approach depending on headache history

Basic investigations for secondary causes:

- PET Bloods/Urinalysis
- Septic screen
- Blood glucose measurement

Imaging

- Non-contrast CT brain/sinuses
- MRI
- MRA/MRV

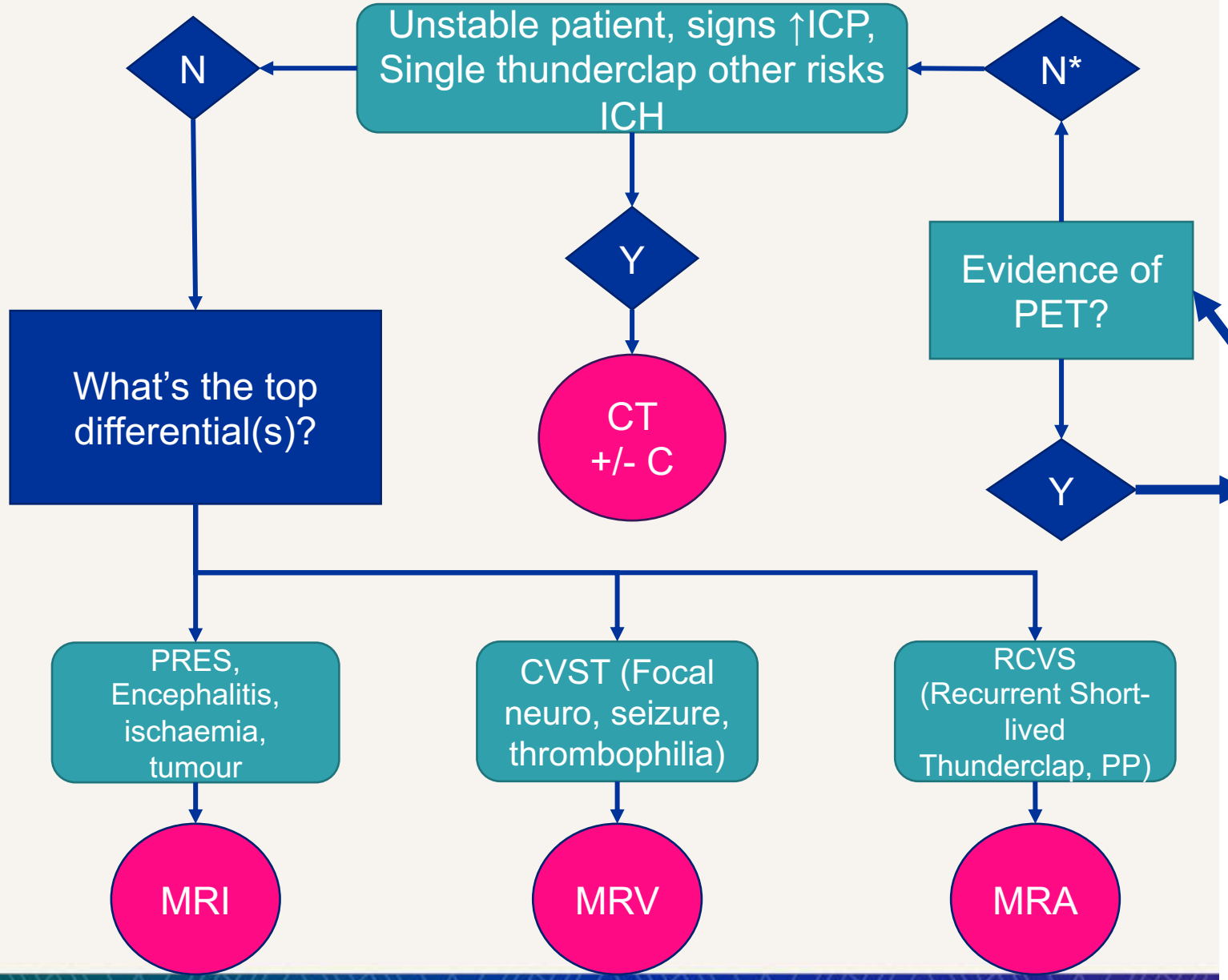
LP

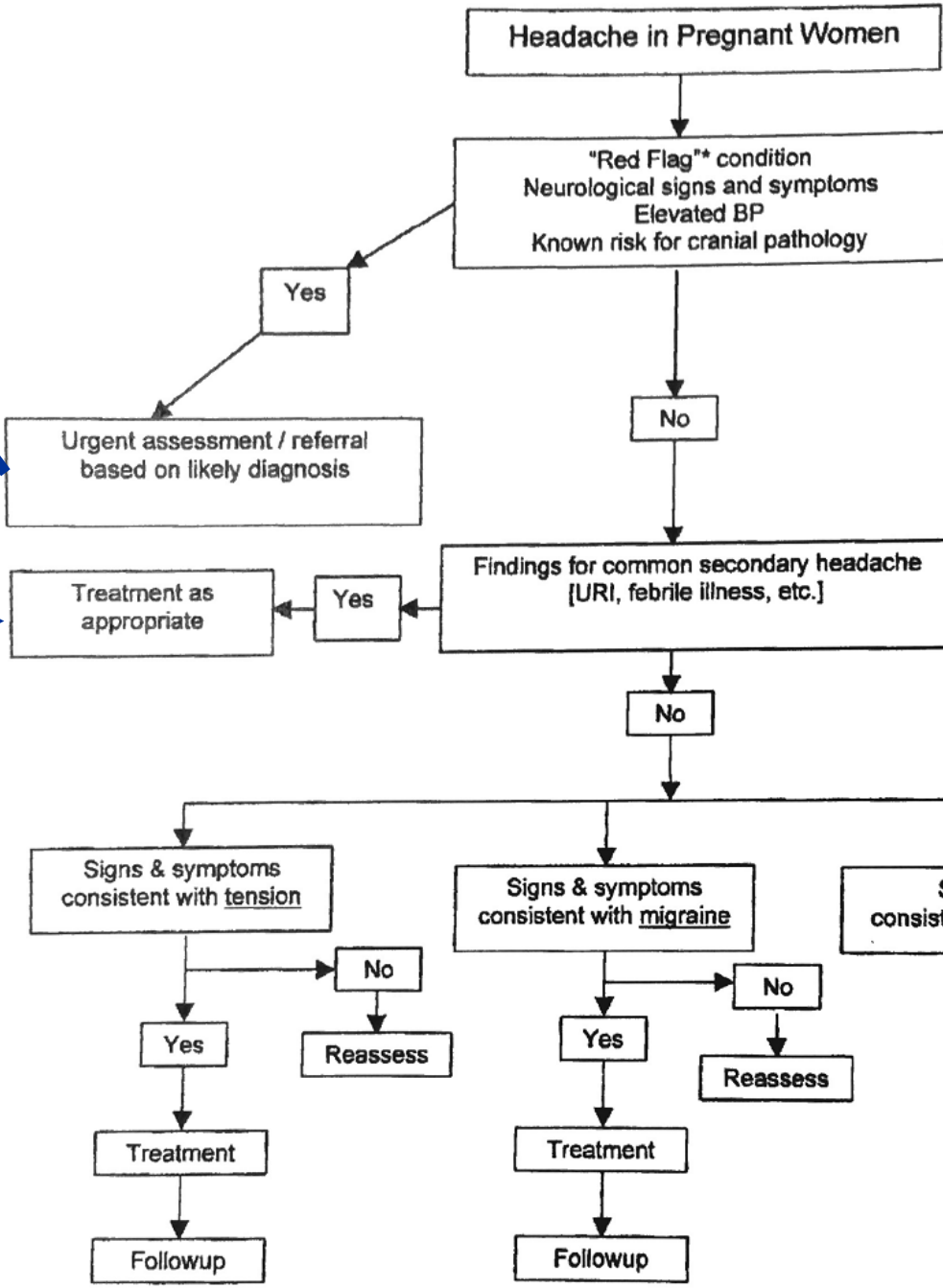
- Intracranial infection
- SAH (>24 hrs)
- IIH (after CT)

Neuroimaging

Non-contrast CT	**Often easiest and quickest to get** **Best for acute haemorrhage** **Fetal radiation exposure <0.001Gy**
Non-contrast MRI	**Probably safe, but still not recommended in 1st trimester** **Better for identifying ischaemia, tumours,encephalitis, PRES**
MRV	**Best for cerebral venous sinus thrombosis**
MRA	**Best for non-acute haemorrhage, RCVS**

1. Zamora C, Castillo M. Role of MRI and CT in the Evaluation of Headache in Pregnancy and the Postpartum Period. Neurol Clin. 2022 Aug;40(3):661-677.
2. Semere LG, McElrath TF, Klein AM. Neuroimaging in pregnancy: a review of clinical indications and obstetric outcomes. J Matern Fetal Neonatal Med. 2013 Sep;26(14):1371-9.


Unstable patient, signs ↑ICP, Single thunderclap other risks ICH
N
N*
Y
What's the top differential(s)?
CT +/- C
Evidence of PET?
Y
PRES, Encephalitis, ischaemia, tumour
CVST (Focal neuro, seizure, thrombophilia)
RCVS (Recurrent Short-lived Thunderclap, PP)
MRI
MRV
MRA
* Or doesn't explain symptoms / concern for PRES


Headache in Pregnant Women
"Red Flag"* condition
Neurological signs and symptoms
Elevated BP
Known risk for cranial pathology
Yes
No
Urgent assessment / referral based on likely diagnosis
Findings for common secondary headache [URI, febrile illness, etc.]
Yes
Treatment as appropriate
No
Signs & symptoms consistent with tension
Signs & symptoms consistent with migraine
No
Yes
Reassess
Yes
No
Reassess
Treatment
Followup
Treatment
Followup

Tension Headache

Headache features

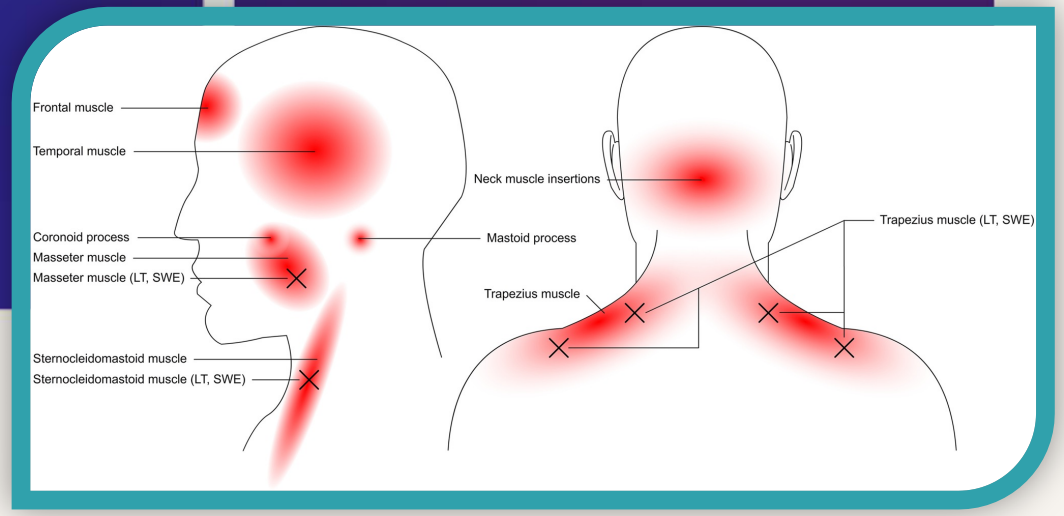
- Bilateral
- Pressing/tightening (non-pulsatile) quality
- Mild/moderate
- No change with activity
- Onset later in the day
- Lasts >30min

Associated symptoms

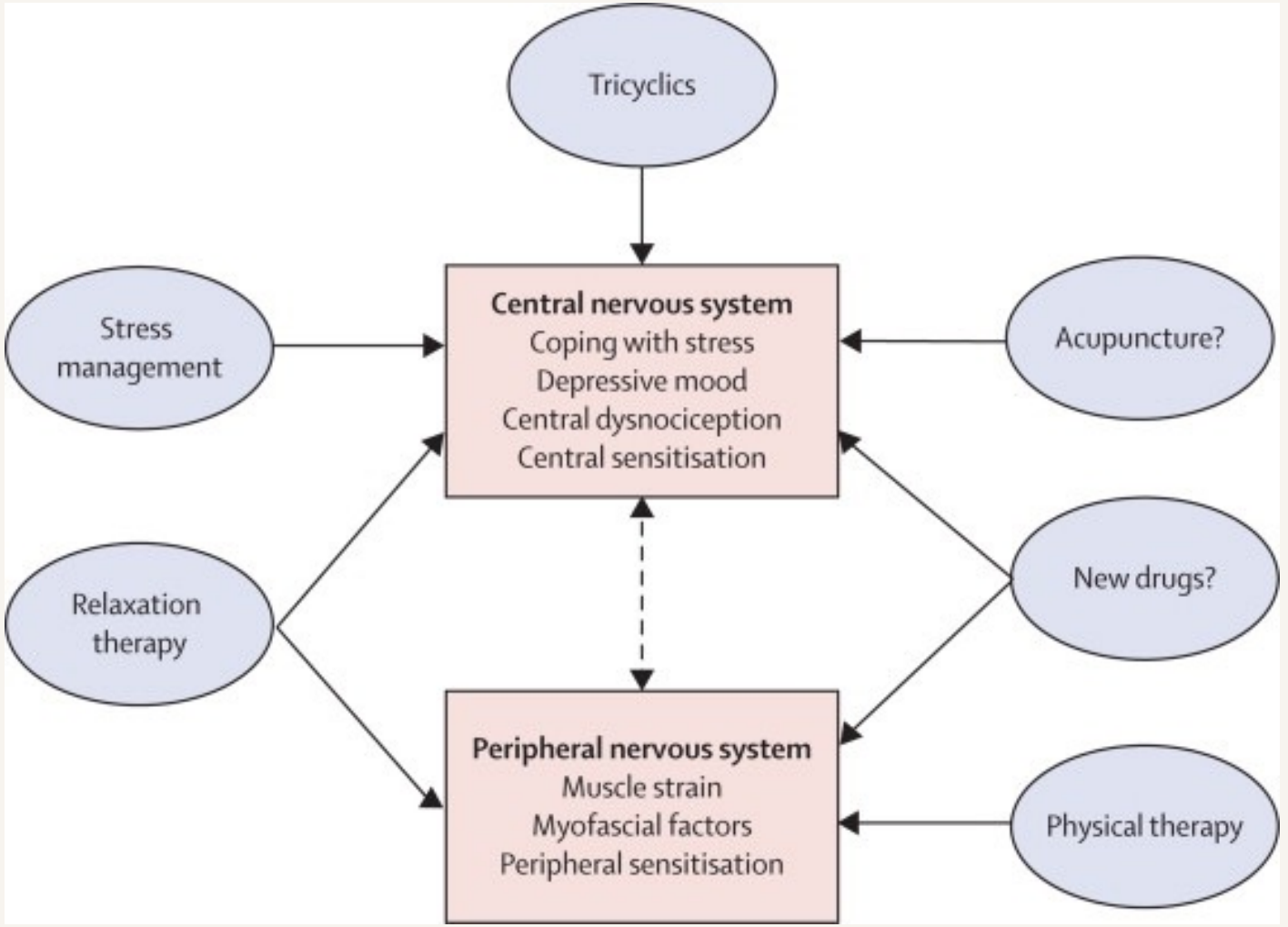
- Unrefreshing sleep
- Lack of nausea/vomiting
- Lack of phono/photophobia

Examination

- Pericranial tenderness
- Can be provoked by movements



Pathophysiology Model and potential treatment targets



Treatment of TH

Non-pharmacological

- Relaxation
- EMG biofeedback
- Physiotherapy
- Acupuncture
- Heat/Cold

Acute

- (NSAIDs)
- Paracetamol
- Caffeine

Prophylactic/Chronic

- Amitriptyline
- Mirtazipine
- Venlafaxine

1. Fumal, Arnaud et al. *Tension-type headache: current research and clinical management.* The Lancet Neurology, Volume 7, Issue 1, 70 – 83

2. Repiso-Guardeño A et a;.*Physical Therapy in Tension-Type Headache: A Systematic Review of Randomized Controlled Trials.* International Journal of Environmental Research and Public Health. 2023; 20(5):4466. https://doi.org/10.3390/ijerph20054466

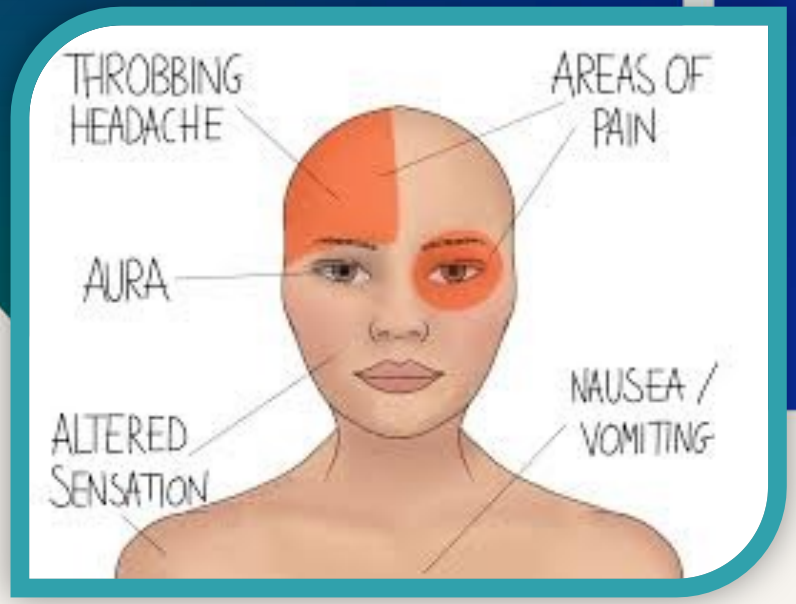
Things that don’t work

- Opioids
- Muscle relaxants
- Botox
- Occipital Nerve Blocks
- Triptans*

Bendtsen, L., Evers, S., Linde, M., Mitsikostas, D.D., Sandrini, G. and Schoenen, J. (2010), EFNS guideline on the treatment of tension-type headache – Report of an EFNS task force. European Journal of Neurology, 17: 1318-1325.

Migraine Headache

- Episodic attacks lasting 4-72hrs
- With or without Aura



- Headache features:
  - Unilateral (mostly)
  - Throbbing
  - Moderate/Severe
  - Worse with activity

- Associated with:
  - Nausea/vomiting
  - Photophobia
  - Phonophobia

Migraine with Aura

HIS Diagnostic Criteria

At least 2 attacks

1 or more fully reversible aura symptoms:

- Visual, Sensory, Speech/Language, motor, brainstem, retinal

At least 2 of the following:

- At least 1 Aura symptom spreads gradually over ≥5min, and/or 2 symptoms occur in succession.
- Each individual symptoms last 5-60min
- At least 1 aura symptom is unilateral
- The aura is accompanied, or followed within 60min, by headache

TIA has been excluded

Migraine – changes in pregnancy

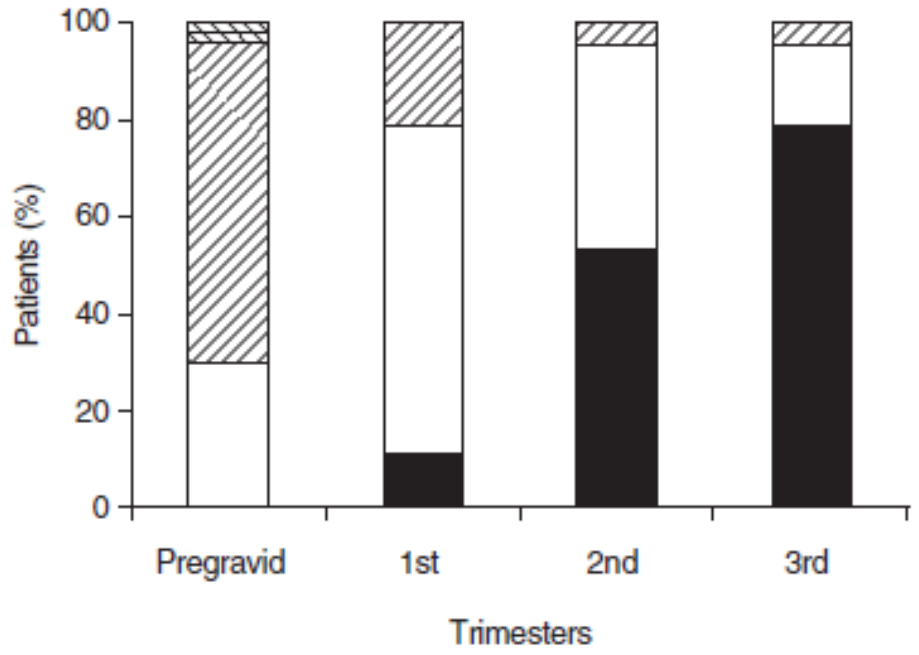


Figure 1 Attack frequency during the 3 months preceding pregnancy and during the trimesters of pregnancy in 47 women affected by migraine without aura. ■, No attacks; □, less than one attack/month; hatched, 1–3 attacks/month; double hatched, 1–3 attacks/week. First trimester vs. pregravid period, $P = 0.0001$; second vs. first trimester, $P = 0.0001$; third vs. second trimester, $P = 0.02$.

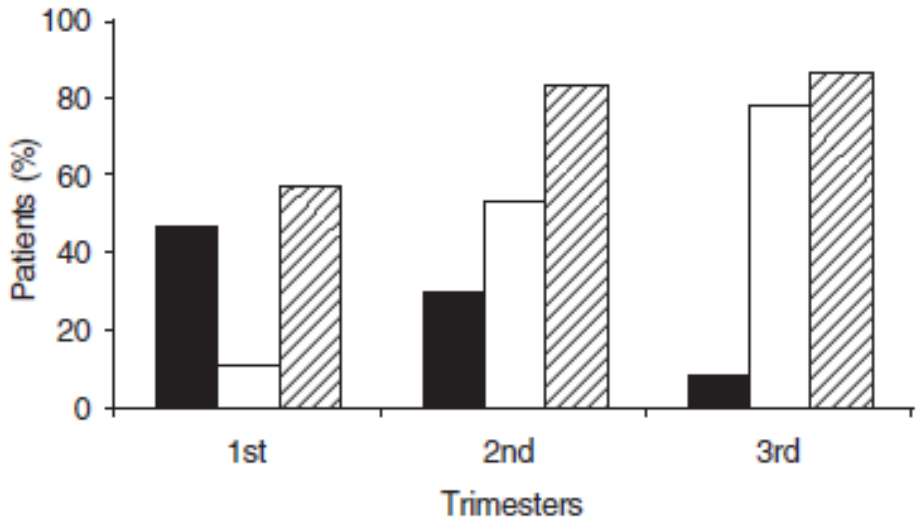


Figure 2 Course of migraine during pregnancy in 47 women affected by migraine without aura. ■, Improvement (reduction ≥50% of the attack number per trimester); □, remission (complete absence of attacks); hatched, improvement or remission. Remission: second vs. first trimester, $P = 0.0001$; third vs. second trimester, $P = 0.02$. Improvement or remission: second vs. first trimester, $P = 0.006$; third vs. second trimester, $P =$ NS.

G Sances et al *Course of migraine during pregnancy and postpartum: a prospective study,* Cephalalgia 2003; 23:17-205


RUN DARLING
THERE'S BOOZE AT THE FINISH LINE
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Migraine treatment

- Conflicting information – many women stop treatments regardless

Table.—Commonly Used Migraine Medications Listed Under the Type of Risk Associated With Their Use in Pregnancy

Category A	Category B	Category C	Category D	Category X
None	Acetaminophen	Triptans (all)	Magnesium	Dihydroergotamine (DHE)
	Caffeine	Promethazine	Benzodiazepines	
	Cyproheptadine	Narcotics	Isometheptine	
	Diphenhydramine	NSAIDs (1st and 2nd trimesters)	NSAIDS (3rd trimester)	
	Memantine	Butalbital	Butorphanol	
	Metoclopramide	Prochlorperazine	Isometheptine	
	Ondansetron	Aspirin (1st trimester)	Aspirin (2nd and 3rd trimesters)	
	Lidocaine	Methocarbamol	Valproic acid	
		Gabapentin	Topiramate	
		Zonisamide	Nortriptyline	
		Quetiapine	Imipramine	
		Propranolol	Lithium	
		Nadolol		
		Metoprolol		
		SSRI and SNRI antidepressants (except paroxetine)	Paroxetine	
		Tizanidine		
		Baclofen		
		Amitriptyline		
		Onabotulinum toxinA		

Tepper, D for the American Headache Society, *Headache Toolbox : Pregnancy and Lactation – Migraine Management*, Headache: The Journal of Head and Face Pain 2015

Acute Migraine Treatments

- Non pharmacological
  - Sleep, stress management, massage, ice packs, biofeedback, trigger avoidance
- Paracetamol
- Metoclopramide (+/- diphenhydramine)
- Low dose Aspirin
- Caffeine
- Ondansetron
- (Triptans)
- NSAIDs (not 3rd trimester)
- Botox

- Avoid opiates if possible – can trigger chronic migraine, even with intermittent use.
- Ergotamine (Caffergot) totally contraindicated

Saldanha, I.J., Cao, W., Bhuma, M.R., Konnyu, K.J., Adam, G.P., Mehta, S., Zullo, A.R., Chen, K.K., Roth, J.L. and Balk, E.M. (2021), Management of primary headaches during pregnancy, postpartum, and breastfeeding: A systematic review. Headache: The Journal of Head and Face Pain, 61: 11-43

Triptans in pregnancy

- 5-HT agonists effective in acute migraine treatment
- Specifically targeted at pathogenesis of migraines
  - Cause constriction of meningeal blood vessels and inhibit neuronal inflammation
- Sumatriptan is the oldest and most studied
- Pregnancy registry data for suma-, nara-, rizatriptan
- Norwegian Mother and Child Cohort Study
  - 1535 women exposed to triptans in pregnancy vs controls
  - 1st trimester use: no association with MCMs (OR 1)
  - 2nd/3rd trimester use: small increase in risk of atonic uterus and blood loss >500mls (OR 1.3, 1.5)
- Safe in breastfeeding

Nezvalová-Henriksen, K., Spigset, O. and Nordeng, H. (2010), 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: The Journal of Head and Face Pain, 50: 563-575.

Migraine Prophylaxis

- Indicated for frequent or very debilitating attacks
- Options:
  - Beta-blockers (Metoprolol, Propranolol)
  - Tricyclics (Amitriptyline)
  - SSRIs
  - Low dose Aspirin
  - *Calcium Channel Blockers*
  - *Riboflavin (Vitamin B2)*
- Start with low dose and increase as needed

CGRPs in pregnancy

- Very minimal data
- 1 Case series of 6 patients
- Analysis of VigiBase registry
- So far, no signs of teratogenicity or complications above population baseline.

1. Elosua-Bayes I, Alpuente A, Melgarejo L, Caronna E, Torres-Ferrús M, Pozo-Rosich P. Case series on monoclonal antibodies targeting calcitonin gene-related peptide in migraine patients during pregnancy: Enhancing safety data. Cephalalgia. 2024
2. Noseda R, Bedussi F, Gobbi C, Ceschi A, Zecca C. Safety profile of monoclonal antibodies targeting the calcitonin gene-related peptide system in pregnancy: Updated analysis in VigiBase®. Cephalalgia. 2023;43(4).


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THE
NEW YORKER
SCHWARTZ
"Hi, yeah, I actually have more of a comment than an inquisition."