CANADIAN HEADACHE CONFERENCE
COAST TO COAST

Headache and Hormones

Teshamae Monteith, MD, FAHS
Claire H. Sandoe, MD, Msc, FRCPC

Disclosures: Teshamae Monteith, MD, FAHS

Consultant/Advisory Boards: AbbVie, Teva, Axsome, Merz, Lundbeck, Pfizer

Honoraria: Medscape, Massachusetts Medical Society, American Headache Society, American Academy of Neurology, Neurodiem, Academic CME, AbbVie

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Learning Objectives

Upon completion of this activity, learners will be able to

- Describe the impact of hormones on headache over a woman's lifetime
- Understand the approach to treatment of migraine in pregnancy and lactation
- Identify considerations around migraine with aura and hormone treatments

Not covered today: Gender-affirming hormone therapy (GAHT)

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Why Do Hormones Deserve a Talk?

- Headache is more prevalent in women
- Any headache disorder: lifetime prevalence women vs men 73.3% vs 65%
- Migraine: lifetime prevalence women vs men 21% vs 11%
- Headache disorders often change when hormones change
- Treatment often modified in different life stages e.g. pregnancy, lactation

Lancet GBD 2017
Burch et al. *Headache* 2021;61(1):60-68
Stovner et al. *J Headache Pain* 2022;23(34)

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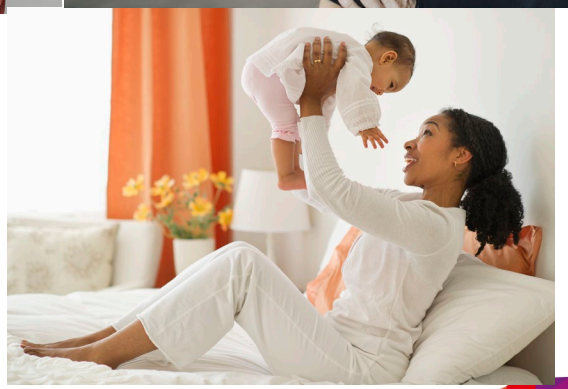
Hormone Changes to Keep in Mind

- Menarche
- Menstrual periods
- Pregnancy and lactation
- Hormonal contraceptives
- Menopause
- Hormone replacement



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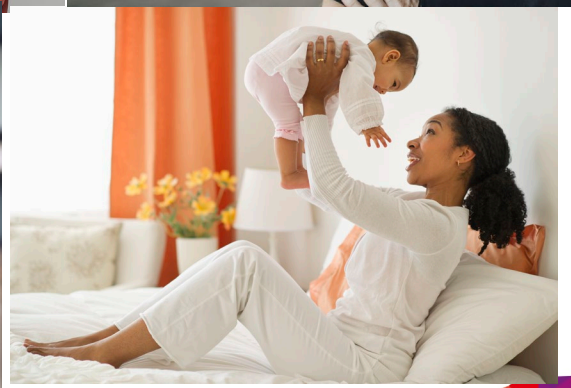

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Case: Reena, 13F

- Reena had her first menstrual periods earlier this year
- She and her mother report that she had a very bad headache after staying up late studying for an exam
- She had to leave the exam to vomit then felt better after sleeping it off
- Is this just a stress headache?

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Migraine and Menarche

- Migraine is more prevalent in boys before age 7
- Prevalence is roughly equal in girls and boys from age 8-11
- After puberty, migraine prevalence rises in girls and remains higher over the rest of the lifespan
- Reena likely has migraine!

Slater S. et al. *Cephalalgia* 2009;29:969-973
Eidlitz-Markus T and Zeharia A. *J Headache Pain* 2017;18:80

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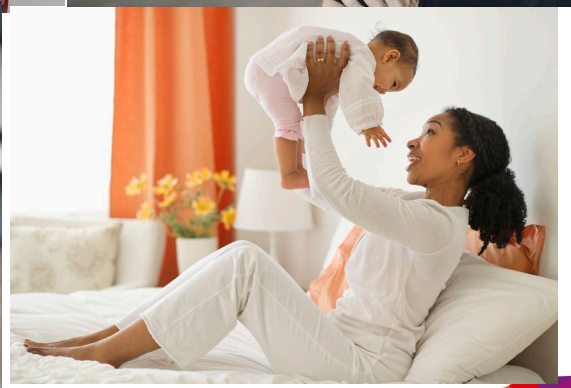

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Case: Reena, 19F

Reena reports headache starting 1 day before her menstrual periods, causing her to miss university classes, accompanied by nausea and photophobia. **Why is she having these attacks?**

a) Decreasing progesterone before periods is triggering the attacks
b) The estrogen drop before menstruation is triggering the attacks
c) Stress is the most likely cause
d) Genetics are the most likely cause

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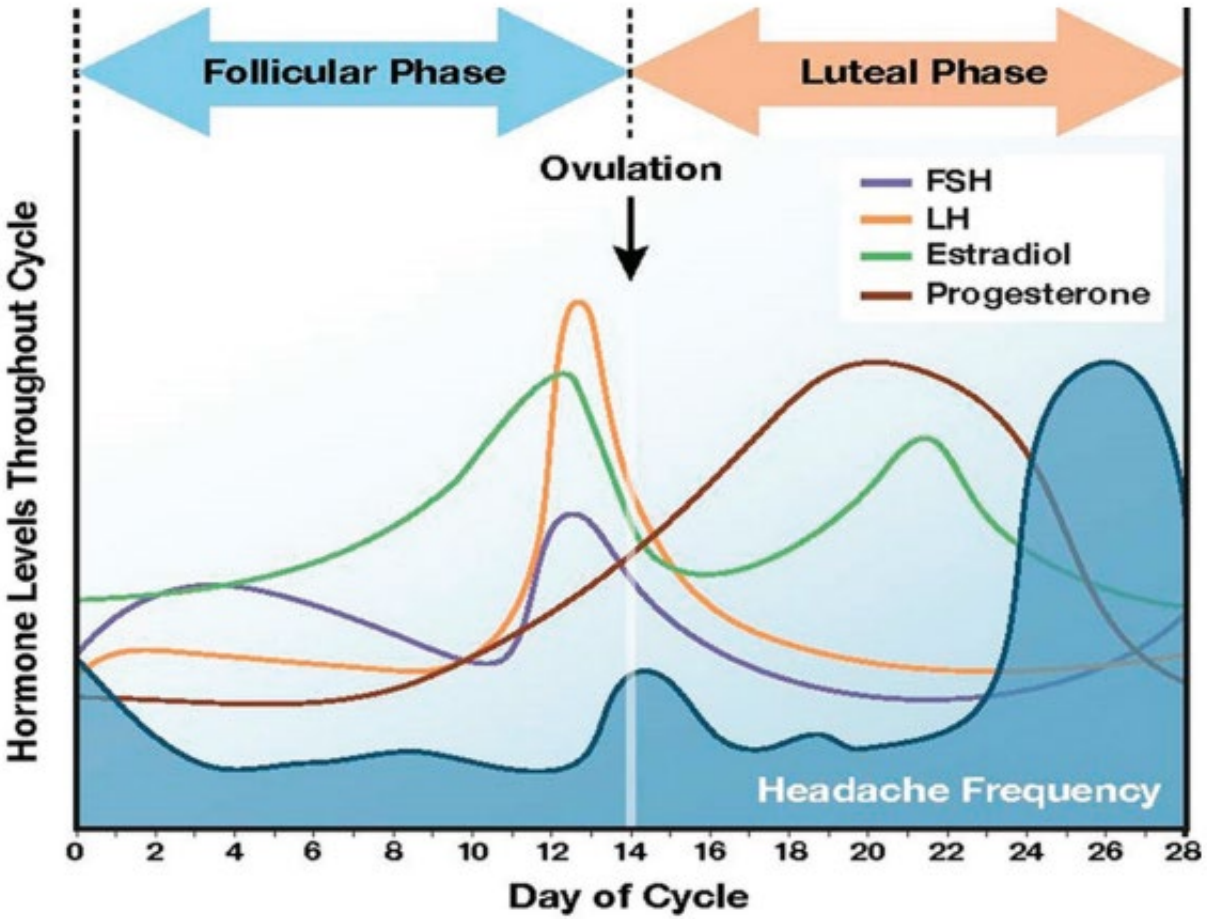
Menstrually-Related Migraine (MRM)

- Attacks occur on D-2 to D+3* of the cycle at least 2/3 of the time
- Estrogen drop thought to be trigger
- Menstrual attacks are often more severe and treatment-resistant
- Typically without aura



*There is no D0

Pavlovic J. Continuum 2021
Raffaelli B et al. *J Headache Pain* 2023;24(1):131

Menstrually-Related Migraine (MRM) Treatment

- Menstrual attacks can drive overall frequency
- Consider mini-prevention if predictable cycles and attack timing
- Even with headache at other times, improving menstrual component can improve migraine overall
- Standard migraine treatment can also still apply
- Sumatriptan-naproxen combo pill and ubrogepant have some data specifically for MRM

Pavlovic J. Continuum 2021
Martin V. *J Womens Health (Larchmt)* 2014;23(5):389-396.
MacGregor E et al. *Headache* 2023'63(8):1135-1144

Menstrually-Related Migraine (MRM) Mini-Prevention

- Time starting 1 day before expected headache, not necessarily D+1 of period
- NSAID
- Naproxen or nabumetone 500mg bid x 5-7 days
- Mefenamic acid 500mg tid x 5-7 days
- Triptan
- Naratriptan 2.5mg bid, frovatriptan 1-2.5mg bid, or zolmitriptan 2.5mg bid x 5-7 days
- Ubrogepant bid x 3-5 days (anecdotal evidence, no medication overuse risk)

Burch R. *Headache* 2020;60(1):200-216

Menstrually-Related Migraine (MRM): Other Options

- Minimize periods
- Continuous oral contraceptive
- Progesterone IUD
- Magnesium taken from ovulation until period onset
- Add-back estrogen patch (may just delay attack onset until after stopping)

Burch R. *Headache* 2020;60(1):200-216
Pavlovic J. *Continuum* 2021.

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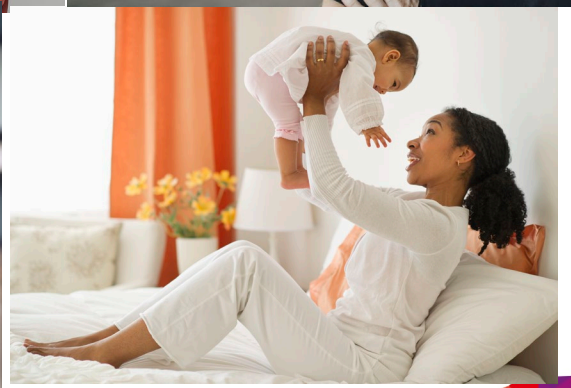

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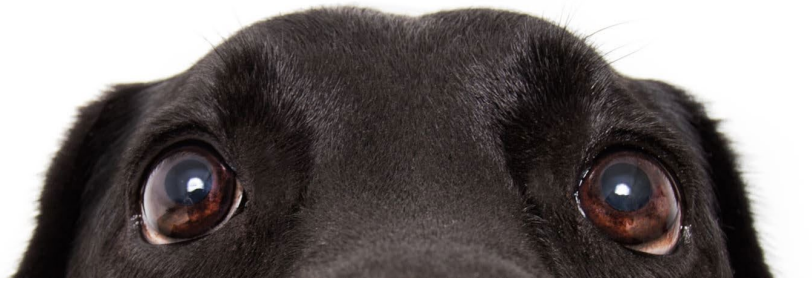
Case: Reena, 23, Pregnant at GA 8 Weeks

- Reena presents to ER with a typical migraine attack accompanied by a new visual aura lasting 20 minutes
- Headache has resolved, BP normal, neuro exam including fundi is normal

Should you scan this patient?



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Headache in Pregnancy

- Pregnancy often thought of as a red flag in SNOOP
- Prevalence of secondary headache disorders in pregnancy 25-45%*
- Post-partum, even higher at 50-75%*
- Secondary etiologies:
- Hypertensive disorders of pregnancy (preeclampsia, PRES)
- Vascular disorders (stroke, bleed, RCVS)
- Space-occupying lesions (pituitary tumor/apoplexy)
- Infections

*Among those presenting to medical attention

Sandoe C and Lay C. *Curr Neurol Neurosci Rep* 2019;19:27.

Headache Red Flags in Pregnancy (PREGNANT HA)

P roteinuria
R apid onset (thunderclap)
E levated BP or temperature
G estational age 3rd trimester
N eurological signs/symptoms
A ltered level of consciousness
N o headache hx, or hx of secondary headache disorder
T hrombocytopenia/thrombocytosis
H igh liver function tests or CRP
A gonizingly severe

Sandoe C and Lay C. *Curr Neurol Neurosci Rep* 2019;19:27.

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Case: Reena, 23, Pregnant at GA 8 Weeks

What can you counsel her about migraine trajectory in pregnancy?

a) Migraine is not usually impacted by pregnancy
b) Migraine typically worsens in pregnancy
c) Migraine typically improves in pregnancy

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Pregnancy and Migraine

- Course in T1 is variable, but hormone fluctuations can be challenging
- Migraine usually improves by T2
- 50-80% of women with migraine have improvement or cessation of migraine attacks in T2 and T3
- More common in those with history of menstrually-related migraine
- More common in those without aura
- Some patients have new aura in pregnancy (likely estrogen-related)
- Migraine is a risk factor for preeclampsia/eclampsia, reversible cerebral vasoconstriction syndrome (RCVS)

Burch R. *Headache* 2020;60(1):200-216
Pavlovic J. *Continuum 2021*

Treating Migraine in Pregnancy and Lactation

- Quality of evidence in both pregnancy and lactation is generally POOR
- Multiple forms of bias are likely at play
- True randomized, controlled studies generally do not exist
- Studies typically do not examine long-term outcomes for children
- Untreated migraine increases maternal distress, which is associated with worse fetal neurodevelopmental outcomes
- Shared decision-making is key

Wu Y et al. *Mol Psychiatry* 2024; 29(7): 2223-40.

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Pregnancy and Migraine

- Prioritize non-pharmacological strategies (e.g. lifestyle, mindfulness, yoga) when possible
- Nutraceuticals
- Magnesium, avoid high dose (high-dose IV magnesium → fetal bone demineralization)
- Vitamin D is probably good for both mom and baby
- Not great evidence for CoQ10/others in pregnancy

Burch R. *Headache* 2019;0:1-17; Pavlovic J. *Continuum 2021;* Medrea I et al. *CJNS* 2024; Puledda F et al. *Cephalalgia* 2024;44(8):3331024241252666; Puledda F et al. *Cephalalgia* 2024;44(9):3331024241269735

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Pregnancy and Migraine: Acute Treatment

- Acetaminophen +/- caffeine (especially helpful if external caffeine is limited)
- Metoclopramide
- Lidocaine nasal spray
- ?Sumatriptan: increased rate of spontaneous abortions in triptan users versus healthy controls - prioritize alternatives in T1 and while trying, if possible
- NSAIDs e.g. ibuprofen in T2
- AVOID opioids, butalbital

Marchenko A et al *Headache* 201555(4):490-501; Burch R. *Headache* 2019;0:1-17; Pavlovic J. *Continuum 2021;* Puledda F et al. *Cephalalgia* 2024;44(8):3331024241252666; Camanni M et al *Neurology 2025;104(12):e213678*

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Pregnancy and Migraine: Preventive Treatment

- Nerve blocks (lidocaine preferred in pregnancy) can be considered first-line as per IHS global practice recommendations
- Oral options
- Propranolol: IUGR if BP drops too low, stop by end T3
- Amitriptyline: stop prior to delivery to avoid neonatal withdrawal
- ?Memantine
- ?OnabotulinumtoxinA
- Published registry data and one small prospective study do not suggest harm, toxin is mechanistically unlikely to go systemic and cross placenta

Burch R. *Headache* 2019;0:1-17; Pavlovic J. *Continuum 2021;* Medrea I et al. *CJNS* 2024; Puledda F et al. *Cephalalgia* 2024;44(9):3331024241269735; Brin M et al *Neurology* 2023;101(2):e103-e113; Wong H et al *Cephalalgia* 2025;45(5):3331024251327387.

Figure 1: Non-invasive Neuromodulation Devices FDA-Cleared for Headache Therapy

A Electrical Trigeminal Neurostimulator (eTNS, CEFALY)

B Transcutaneous Electrical Nerve Stimulator (TENS, HEADATERM-2)

C Single Pulse Transcranial Magnetic Stimulator (sTMS, SAVI DUAL)

D Non-invasive Vagal Nerve Stimulator (nVNS, GAMMACORE SAPPHIRE)

E Remote Electrical Neuromodulation (REN, NERIVIO)

F Combined External Occipital-Trigeminal Neurostimulator (COT-NS, RELIVION MG)

Tepper, McAllister, Monteith, Practical Neurology, May/June 2024

Case: Reena, 23, Pregnant at GA 35 Weeks

Reena has not had any migraine attacks since GA 12 weeks. She wants to know what to expect if she chooses to breastfeed. **What do you tell her?**

a) No migraine treatments are safe in lactation
b) She will likely remain headache-free post-partum
c) Lactation can worsen migraine
d) Migraine may worsen when periods resume

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Migraine and Lactation

- Lactation can be protective especially with lactational amenorrhea
- The immediate post-partum period can be difficult as estrogen drops

Hoshiyama E et al. *Intern Med* 2012;51(22)3119-3123.
Burch R. Headache 2020;60(1):200-216
Rayhill M. Continuum 2022;28(1):72-92

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Migraine and Lactation

- Similar nonpharmacological/vitamin suggestions as before
- Riboflavin, magnesium felt safe in lactation
- Acute: acetaminophen +/- caffeine, ibuprofen, sumatriptan, eletriptan, lidocaine nasal spray, metoclopramide, ondansetron, Cefaly/Headaterm
- Preventive: amitriptyline, propranolol, verapamil, ?candesartan, nerve blocks, ?onabotulinumtoxinA

Rayhill M. *Continuum* 2022;28(1):72-92; Medrea I et al. *CJNS* 2024; Puledda F et al. *Cephalalgia* 2024;44(8):3331024241252666; Puledda F et al. *Cephalalgia* 2024;44(9):3331024241269735

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Case: Reena, 24, 10 Months Post-Partum

Reena notes that headaches worsened over the last 2 months and she is having 12 migraine days per month. She is still breastfeeding and thinks she might want to get pregnant again in the next 1-2 years. **Is a CGRP-targeted therapy safe for her?**

a) Ubrogepant is a good option in lactation
b) Atogepant is a good option in lactation
c) A CGRP monoclonal antibody is a good option in lactation
d) An oral agent would usually be tried before a CGRP-targeted option

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CGRP-Targeted Treatments in Women

- CGRP monoclonal antibodies
  - Pregnancy: Stop at least 5-6 months prior to planning pregnancy due to T ½ 1 month
  - Lactation: Not studied, not typically recommended
- Gepants
  - Pregnancy: Not recommended; given T ½, stop at least 5 days before trying
  - Lactation: Not typically recommended (but small gepant studies suggest levels in breastmilk are low)

Rayhill M. *Continuum* 2022;28(1):72-92
Baker E et al. *Breastfeed Med* 2022;17(3):277-282

Pregnancy Planning and Migraine

- 50% of pregnancies are unplanned → revisit plans and contraceptive use at each visit!
- STOP teratogenic/potentially harmful oral meds before trying
- Especially valproate, topiramate, candesartan, CGRP-targeted meds
- It may be reasonable to stop oral preventives in general before trying since most women improve in pregnancy
- Acute treatment: consider split month strategy while trying (can use less safe options such as NSAID+triptan between period and ovulation, then stop until next period)

Burch R. *Headache* 2019;0:1-17
Pavlovic J. *Continuum 2021;* Medrea I et al. *CJNS* 2024.

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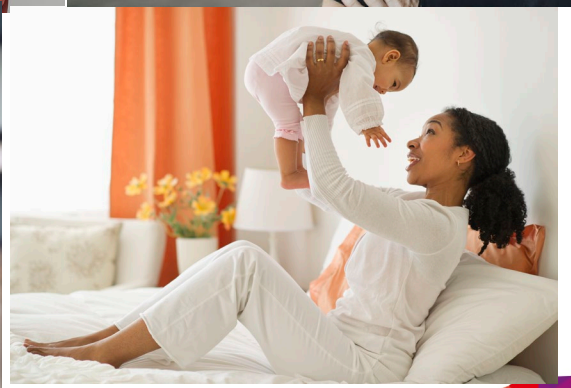

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Case: Reena, 27F

Reena reports visual aura (scintillating scotoma) lasting 45 minutes, once every few months. She has painful periods but is healthy and not a smoker.
What do you advise her about hormonal contraception?

a) A high-dose estrogen pill (50-100mcg/day) is the best option to reduce migraine attacks
b) Low-dose estrogen (20mcg/day or less) could be considered with caution
c) Progesterone-only strategies are the only hormonal option for her
d) Neither estrogen nor progesterone are safe given her auras

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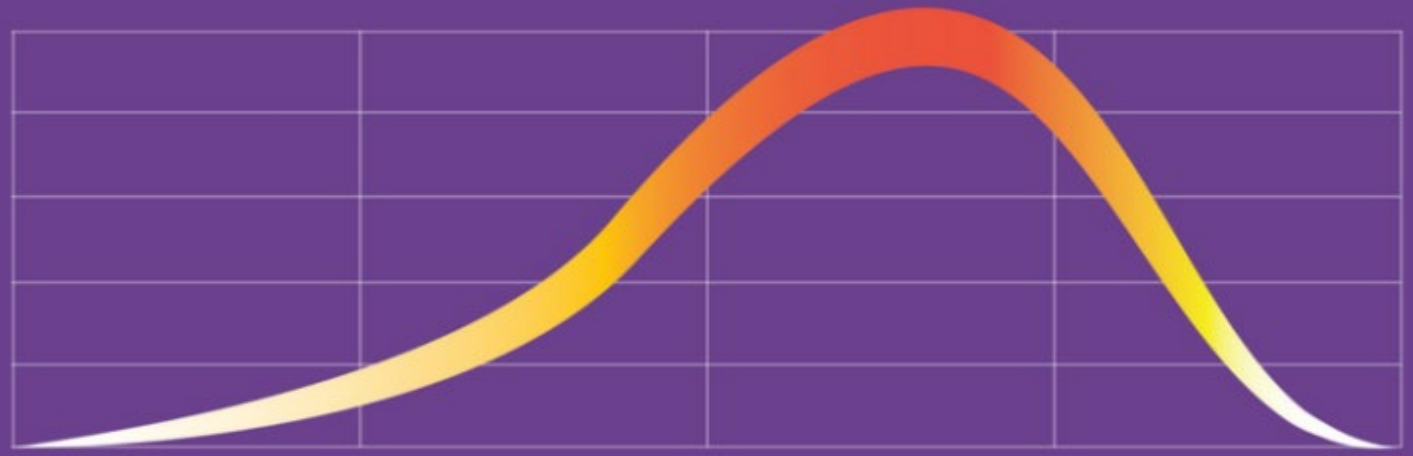
TIMELINE OF A MIGRAINE ATTACK



PRODROME
FEW HOURS TO DAYS

- IRRITABILITY
- DEPRESSION
- YAWNING
- INCREASED NEED TO URINATE
- FOOD CRAVINGS
- SENSITITIVY TO LIGHT/SOUND
- PROBLEMS IN CONCENTRATING
- FATIGUE AND MUSCLE STIFFNESS
- DIFFICULTY IN SPEAKING AND
- READING
- NAUSEA
- DIFFICULTY IN SLEEPING

AURA
5-60 MIN

- VISUAL DISTURBANCES
- TEMPORARY LOSS OF SIGHT
- NUMBENESS AND TINGLING ON PART OF THE BODY

HEADACHE
4-72 HRS

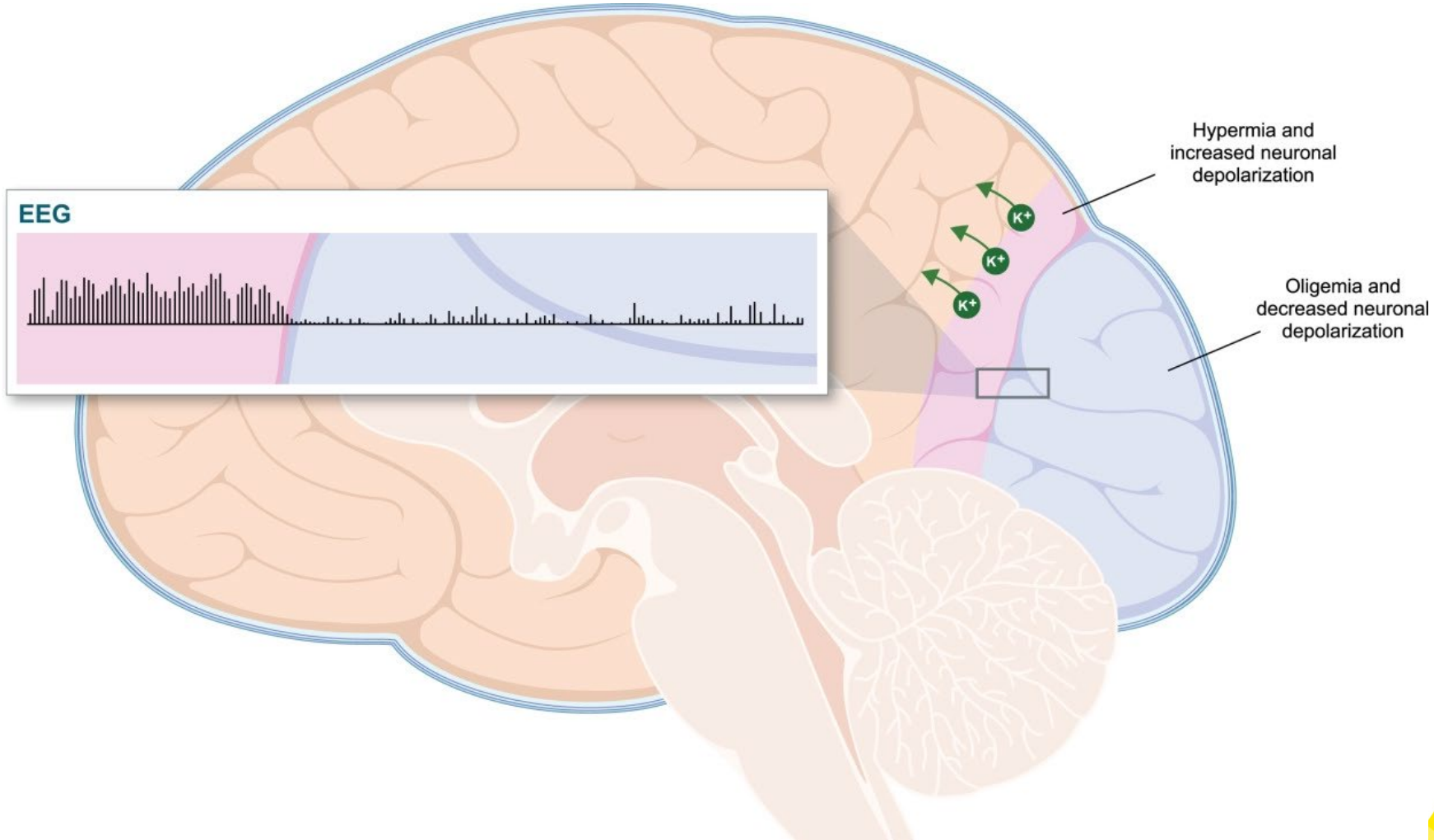
- THROBBING
- DRILLING
- ICEPICK IN THE HEAD
- BURNING
- NAUSEA
- VOMITING
- GIDDINESS
- INSOMNIA
- NASAL CONGESTION
- ANXIETY
- DEPRESSD MOOD
- SENSITIVITY TO LIGHT, SMELL, SOUND
- NECK PAIN AND STIFFNESS

POSTDROME
24-48 HRS

- INABILITY TO CONCENTRATE
- FATIQUE
- DEPRESSED MOOD
- EUPHORIC MOOD
- LACK OF COMPREHENSION

https://americanmigrainefoundation.org/resource-library/timeline-migraine-attack/

Cortical Spreading Depression and Aura



Dodick D. *Headache* 2018;58(S1):4-16.

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Migraine Diagnostic Criteria: ICHD-3 - Aura

- Cortical spreading depolarization: excitable leading wave (positive symptoms) followed by depression (negative symptoms)
- Gradual onset and spread typically lasting 5-60 minutes
- Typical: vision, sensory, speech
- NOT typical aura:
- Motor
- Brainstem (diplopia, vertigo, ataxia, decreased level of consciousness)

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Cephalalgia 2018;38(1):1-211.

Aura and Hormones

- Migraine → 2x higher risk of ischemic stroke, 1.5x higher risk of hemorrhagic stroke
- Primarily driven by migraine with aura
- Highest in those under age 45 and smokers
- Older studies suggest that combined hormonal contraceptives (CHCs) → increased stroke risk
- Recent studies: elevated risk with estrogen dose of more than 50 µg/day, likely also elevated at >30 µg/day, unclear at lower doses

Sheikh et al. *Headache* 2018;58:5-21; Batur P et al *Headache* 2023;63(6):813-821.

Aura and Hormones

- Aura characteristics impact impression of stroke risk
- Stroke risk increases with higher aura frequency (>1/month)
- Prolonged duration (>60 minutes) or more severe symptoms also likely higher risk

Calhoun et al. *Headache* 2012;52:1246-1253.
Donaghy et al. *J Neurol Neurosurg Psychiatry* 2002;73:747-750.

Aura and Hormones

- Pregnancy also carries significant health risks (although it is not a disease)
- New lower-estrogen CHCs may be safe in migraine with aura if auras are not frequent or prolonged
- One study with estrogen ring eliminated menstrually-related attacks and actually reduced aura frequency

Calhoun et al. *Headache* 2012;52:1246-1253.
Donaghy et al. *J Neurol Neurosurg Psychiatry* 2002;73:747-750.

Aura and Hormones

- Migraine without aura
- CHCs are usually fine
- Consider non-cycling or low-dose pill to minimize estrogen drop
- Monitor for new auras
- Migraine with aura
- Consider progesterone-only options
- If required and no high-risk features, low-dose estrogen with caution (20 µg/day or less preferred but avoid more than 30 µg/day), monitor for change in aura/headache

Calhoun et al. *Headache* 2012;52:1246-1253.
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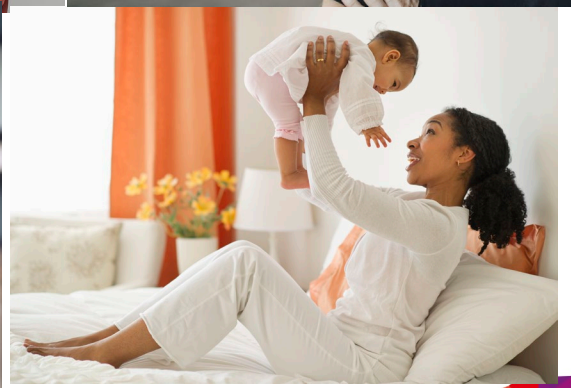

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Case: Reena, 55

Reena is having hot flashes and irregular periods, and reports worsening from previously 2 migraine days per month, to now 14 migraine days per month. **Is this normal??? Is hormone replacement recommended?**

a) She needs an urgent MRI given the pattern change
b) She is probably stressed about menopause
c) Hormone fluctuations of menopause can worsen migraine
d) Hormone replacement therapy is contraindicated given migraine history

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Menopause and Migraine

- Reena clearly has a strong hormonal influence on her migraine attacks so this is not unexpected
- Migraine brains do not like change i.e. hormone fluctuations of menopause, sleep disruption
- Menopausal transition takes 10 years on average!
- New auras may emerge in perimenopause
- Attack timing can shift, e.g., early morning or wake-up attacks
- If pattern change is significant, consider workup for secondary cause

MacGregor E. *Post Reproductive Health* 2018;24(1):11-18
Ripa P et al. *Int J Womens Health* 2015;7:773-782

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Menopause and Migraine: Hormone Replacement Therapy (HRT)

- HRT is different than contraceptive estrogen dosing – goal is physiologic replacement
- Even those with aura can often safely use HRT
- Use lowest possible dose, non-cycling, and non-oral route if possible
- If headaches/auras worsen, reduce dose and/or switch to non-oral as this may herald increased stroke risk
- Inherent risks of HRT should always be weighed
- (?increased meningioma risk with medroxyprogesterone acetate, medrogestone, promegestone)

MacGregor E. *Post Reproductive Health* 2018;24(1):11-18; Ripa P et al. *Int J Womens Health* 2015;7:773-782; MacGregor E. *Maturitas* 2020;142:24-30; Roland N et al. *BMJ* 2024;384:e078078

Menopause and Migraine

- Non-hormone options for migraine and vasomotor symptoms
- Gabapentin 300-1200mg qhs 2-3 hours before bed
- Herbal gaba
- Venlafaxine 37.5-150mg daily or duloxetine 30-60mg daily
- Fezolinetant for vasomotor symptoms

Ornello R et al. *J Clin Med* 2021;10(11):2263

Menopause and Migraine: Surgical Menopause?

- Abrupt hormone change often worsens migraine
- Not recommended in general as a migraine treatment
- Migraine may worsen (often) or improve post-hysterectomy

Ripa P et al. *Int J Womens Health* 2015;7:773-782
Ornello R. et al. *Neuropsychiatr Dis Treat* 2021;17:859-871

Menopause and Migraine: Will My Headaches Go Away After Menopause?

- Hopefully – depends a bit on your migraine path
- If the brain walks the migraine path more often, the path is easier to find and enlarges each time
- If you start off with a smaller path and let the grass grow over it between attacks, your chances are better

Take-Home Points

- Hormone changes over the lifespan can significantly impact migraine
- Safe and effective treatments can often be found in pregnancy and lactation
- Better migraine control in perimenopause better change of improving post-menopause

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THANK YOU