Women and Headache

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Objectives

- Review menstrual cycle and hormonal changes associated with menstrual migraine attacks
- Review MENSTRUAL migraine epidemiology and treatment
- Reference general migraine preventative treatments
- Evaluate child-bearing potential and medication choices/management for pregnancy and lactation

Case 1

32yo F w PMH migraine without aura since puberty. Migraines always occurred in temporal relation to her menstrual cycle. She would develop a migraine around the first day of menstruation each month and this migraine would last for days. She had recently been diagnosed with menstrual migraine by a neurologist and prescribed frovatriptan PRN. She had tried it once with mild improvement but did not continue when it the migraine persisted and was then referred to me. We discussed the importance of tracking her cycle and explained the concept of mini-prophylaxis and BID dosing with frovatriptan.

She starting using FertilityFriend app documenting first day of menstruation each month. With this she was able to start frovatriptan 2.5mg BID two days prior to expected menstruation and continue for a total of 5 days. She did very well with this plan and now follows annually only.

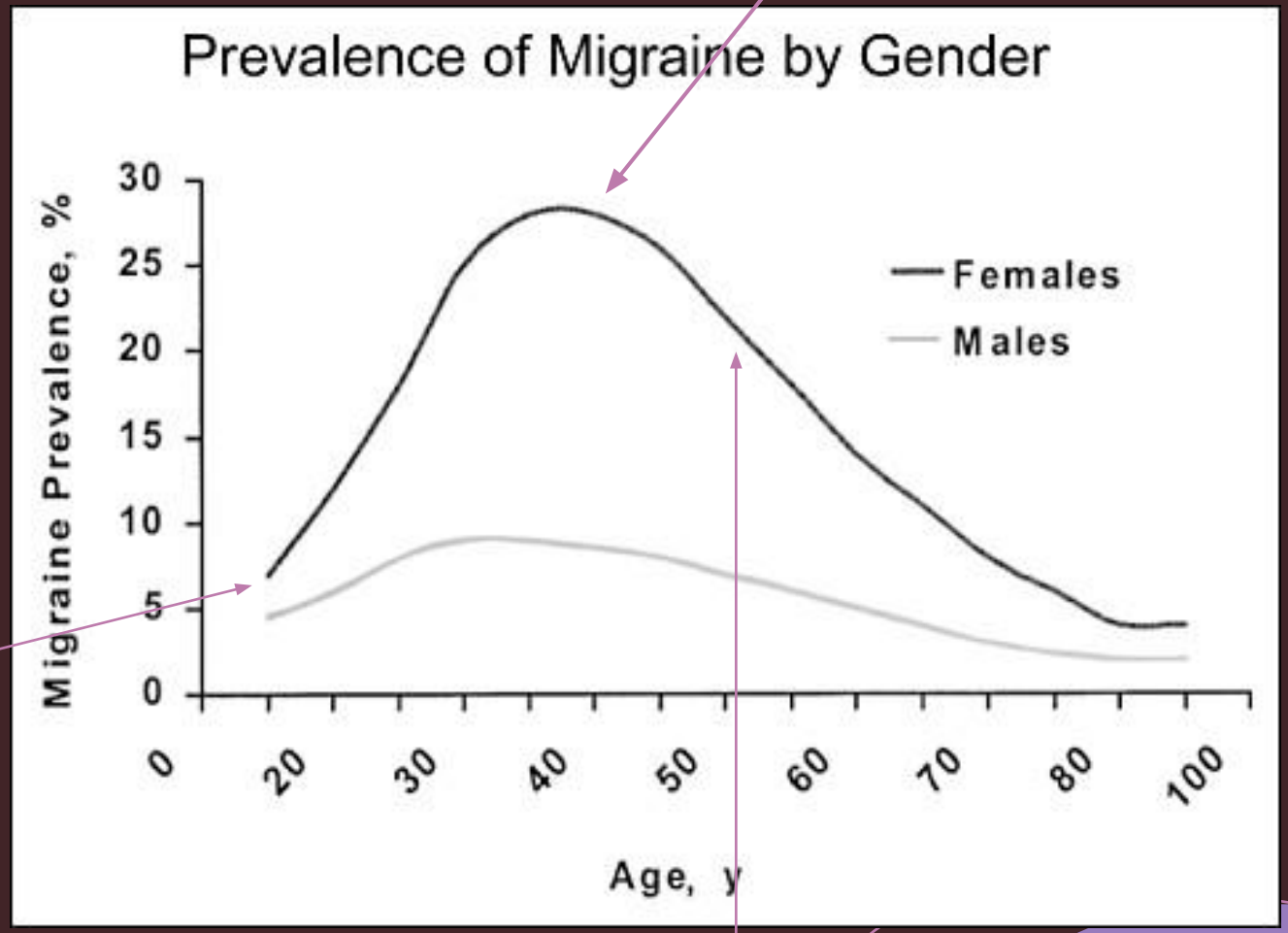
The Lifecycle and Sex

- Pre-puberty migraine prevalence: 3-10% - no gender difference
- Puberty - migraine becomes 2–3 times more common in women than in men
- After puberty -50% of female migraine attacks thought to be menstrually related
- Migraine appears to be influenced by the fluctuating hormonal status seen in menarche, menstruation, pregnancy, menopause, as well as the use of oral contraceptives and hormonal replacement therapy (HRT)
- Migraine throughout the lifespan of men appears relatively stable
- Do these findings point to ESTROGEN as the culprit?

Cairns BE et al. Maturitas 63:292-296. 2009
Silberstein SD Rev Neurol (Paris) 156(Suppl 4):4S30–4S41. 2000

Migraine Lifecycle

Migraine peaks age 35-45 for women with 25-30% of females affected vs 8% males



Boys and girls have equal rates of migraine until age 9

Stewart WF, Lipton RB, Celentan o DD,Reed ML. 1992. *JA MA* **267**:64– 69.

Migraine declines as women enter menopause

Menstrual Migraine

- Most frequently occurs in the second decade of life around the onset of menarche
- Typically without aura
- Menstrual Related Migraine (MRM): Common - occurring in 60% of women who have migraine attacks perimenstrually as well as at other times of the month
- Pure Menstrual Migraine (PMM): A much smaller percentage, 7 to 35% of women experience PMM which is defined as migraine attacks that may occur before, during, or after menstruation seen in at least two out of every three cycles with no migraine at any other time of the month
- MM prevalence also peaks around age 40, declines as menopause approaches

Todd C at al. Current Neurology and Neuroscience Reports (2018) 18: 42

ICHD3 – Menstrual Migraine

Menstrually-Related Migraine

- Attacks, in a menstruating woman, fulfilling criteria for 1.1 *Migraine without aura* and criterion B below
- Occurring on day 1 ± 2 (*ie*, days −2 to +3) of menstruation in at least two out of three menstrual cycles, and additionally at other times of the cycle.

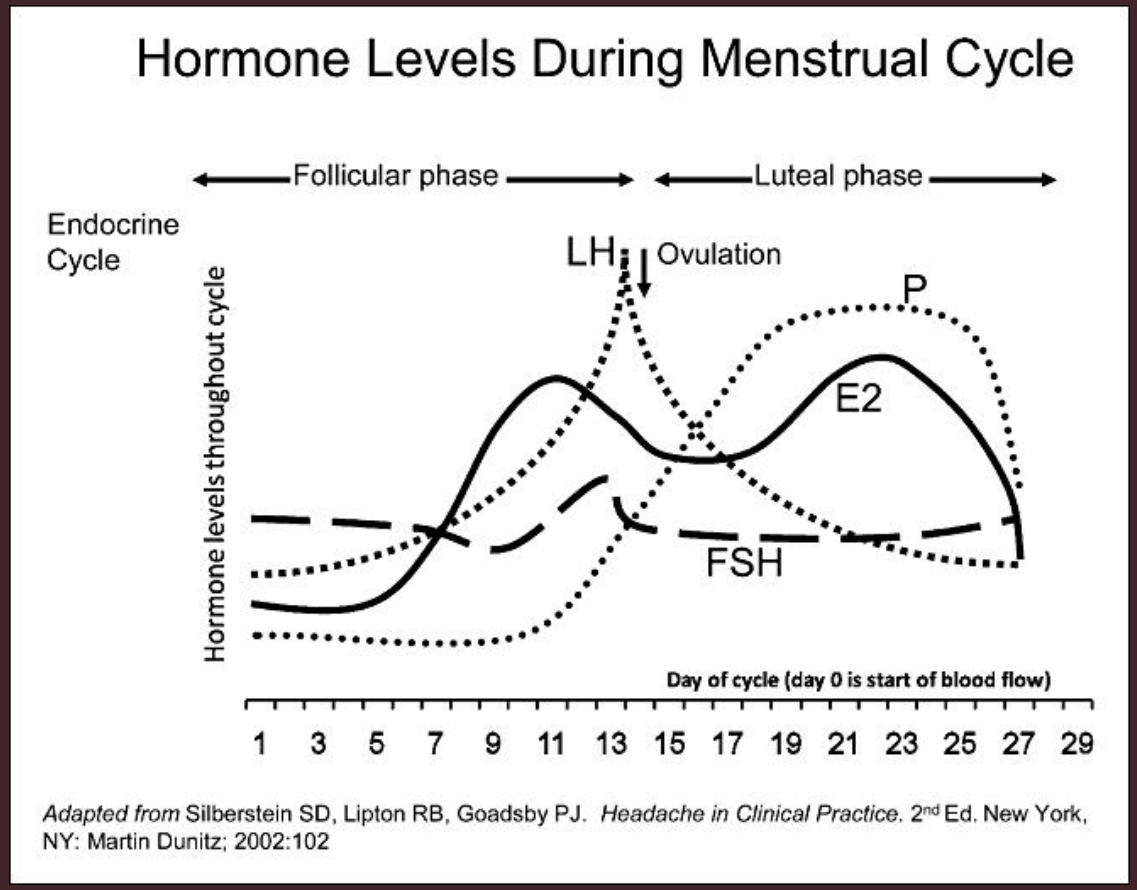
Pure Menstrual Migraine

- Attacks, in a menstruating woman, fulfilling criteria for 1.1 *Migraine without aura* and criterion B below
- Occurring exclusively on day 1 ± 2 (*ie,* days −2 to +3) of menstruation in at least two out of three menstrual cycles and at no other times of the cycle.

Estrogen Withdrawal Hypothesis

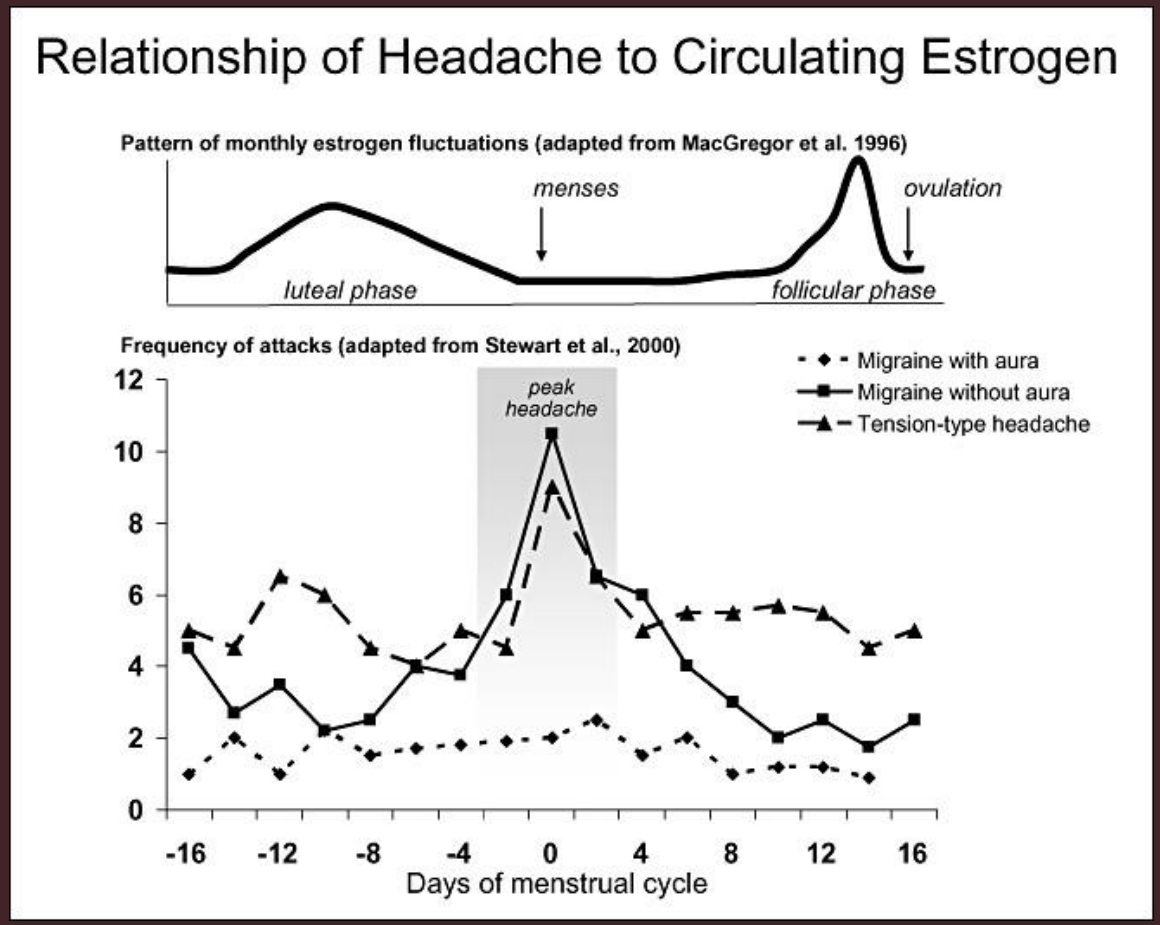
- Estrogen withdrawal hypothesis - developed by Somerville and colleagues in 1972, postulates that attacks of menstrual migraine are triggered by the decrease in estrogen levels preceding menstruation

Somerville BW. Neurology. 1972 Apr;22(4):355-65.



Martin VT(Headache 2008;48:S124-S130)

Endocrinology of the female menstrual cycle. Day 1 represents the first day of menstrual bleeding of the menstrual cycle and day 28 represents the day before the next menstrual cycle. The follicular phase includes all days prior to ovulation while the luteal phase includes all days from the day of ovulation to the last day of the cycle (adapted from Martin et al[6] and Silberstein et al[7]).



Martin VT(Headache 2008;48:S124-S130)

The graph shows the relative high occurrence of migraine without aura during the perimenstrual time of −2 to +3 of the cycle when estradiol hormone levels are low. In a population-based study, the frequency of migraine without aura and tension-type headache peaked within a few days of onset of menses. Interestingly, migraine with aura did not appear to have as strong a relationship to the hormonal fluctuations associated with onset of menses11 (adapted from Stewart et al9). Menstrual migraine appears to be triggered when serum levels fall below 45 to 50 pg/mL.8

Estrogen Withdrawal Hypothesis

Additional clinical evidence supports the role of estrogen withdrawal as a trigger for migraine. The fall in estrogen occurs with several biological conditions and is repeatedly shown to be associated with an increased risk of migraine:

- Immediately before menstruation starts when estrogen levels drop
- During the normal menstrual cycle when estrogen levels are low
- During the pill-free week in women using the combined oral contraceptive pill when estrogen is withdrawn
- After 21 days of high concentrations in women using hormone-replacement therapy
- In hysterectomized women with bilateral oophorectomies
- After birth when estrogen concentrations decline dramatically

Martin VT(Headache 2008;48:S124-S130)

Diagnosis


Perpetual calendar
January
February
March
April
May
June
July
August
September
October
November
December

Q & A

Q: Why not give everyone estrogen?

A: Regular use of exogenous hormones can be associated with an increase in frequency or new development of migraine-like or other headache.

Exogenous Estrogen Headaches

Estrogen-withdrawal Headache (ICHD-3)

- Description: Headache or migraine developing within 5 days after daily consumption of exogenous estrogen for 3 weeks or longer, which has been interrupted (usually during the pill-free interval of combined oral contraception or following a course of replacement or supplementary estrogen). It resolves spontaneously within 3 days in the absence of further consumption.
- Diagnostic criteria:
  - A. Headache or migraine fulfilling criterion C
  - B. Daily use of exogenous estrogen for ≥3 weeks, which has been interrupted
  - C. Evidence of causation demonstrated by both of the following:
    1. headache or migraine has developed within 5 days after the last use of estrogen
    2. headache or migraine has resolved within 3 days of its onset
  - D. Not better accounted for by another ICHD-3 diagnosis.

Comment: Estrogen-withdrawal following cessation of a course of exogenous estrogens (such as during the pill-free interval of combined oral contraceptives or following a course of replacement or supplementary estrogen) can induce headache and/or migraine.

Other Risks of Exogenous Estrogen

- Endometrial cancer
  - Risk of endometrial cancer increases with use of unopposed estrogens; adding progestin to estrogen therapy may reduce risk of endometrial hyperplasia, a precursor to endometrial cancer;
- Cardiovascular risks
  - Estrogens plus progestins: Women's Health Initiative (WHI) Estrogen Plus Progestin sub-study reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary embolism (PE), and deep vein thrombosis (DVT) in postmenopausal women (50-79 years) during 5.6 years of treatment with daily PO conjugated estrogens (0.625 mg) combined with medroxyprogesterone acetate (2.5 mg) in comparison with placebo
  - Estrogens alone: Sub-study of WHI study reported increased risk of stroke and DVT in postmenopausal women (50-79 years) during 6.8 years of treatment with PO conjugated estrogens (0.625 mg/day) alone in comparison with placebo
- Dementia risks
  - Women's Health Initiative Memory Study (WHIMS), sub-study of WHI study, reported increased risk of developing probable dementia in postmenopausal women 65 years and older during 4 years of treatment with daily PO conjugated estrogens (0.625 mg) combined with medroxyprogesterone acetate (2.5 mg) in comparison with placebo
  - Estrogens alone: Sub-study of WHIMS reported increased risk of developing probable dementia in postmenopausal women 65 years and older during 5.2 years of treatment with conjugated estrogens (0.625 mg/day) alone in comparison with placebo
  - Unknown whether these findings apply to younger postmenopausal women
- Breast cancer
  - The Women's Health Initiative (WHI) estrogen plus progestin sub-study also demonstrated an increased risk of invasive breast cancer; estrogens with or without progestins should be prescribed at the lowest doses and for the shortest duration
- Dose and duration
  - In the absence of comparable data, these risks should be assumed to be similar for other doses of conjugated estrogens and medroxyprogesterone acetate, as well as for other combinations and dosage forms of estrogens and progestins
  - Because of these risks, estrogens with or without progestins should be prescribed at lowest effective dose and for shortest duration consistent with treatment goals and individual risks

Should We Ever Use Estrogen?

Sacco et al. The Journal of Headache and Pain (2018) 19:76
https://doi.org/10.1186/s10194-018-0896-5

The Journal of Headache and Pain

CONSENSUS ARTICLE Open Access

Effect of exogenous estrogens and progestogens on the course of migraine during reproductive age: a consensus statement by the European Headache Federation (EHF) and the European Society of Contraception and Reproductive Health (ESCRH)

Simona Sacco[1*], Gabriele S. Merki-Feld[2], Karen Lehrmann Ægidius[3], Johannes Bitzer[4], Marianne Canonico[5], Andreas R. Gantenbein[6], Tobias Kurth[7], Christian Lampl[8,9], Øjvind Lidegaard[10], E. Anne MacGregor[11,12], Antoinette MaassenVanDenBrink[13], Dimos-Dimitrios Mitsikostas[14], Rossella Elena Nappi[15,16], George Ntaios[17], Koen Paemeleire[18], Per Morten Sandset[19], Gisela Marie Terwindt[20], Kjersti Grøtta Vetvik[21], Paolo Martelletti[22] and on behalf of the European Headache Federation (EHF), the European Society of Contraception and Reproductive Health (ESCRH)

Spoiler Alert

- The Expert Consensus is:
  1. The quality of available data is poor
  2. Further research is needed on this topic to improve the knowledge about the use of estrogens and progestogens in women with migraine.
  3. There is a need for better management of headaches related to the use of hormones or their withdrawal.

Table 5 Recommendations on the use of estrogens and progestogens in women of reproductive age with migraine considering their effect on migraine course

Treatment	Population	Recommendation	Quality of Evidence	Strength of Recommendation	Comments
21/7 combined contraceptive regimen with oral pill or patch*	Women with migraine who require hormonal contraception	Not suggested	None	Weak	Alternative contraceptive strategies are more convenient in migraineurs
Desogestrel-only 75 μg/day pill	Women with migraine, related or unrelated to menstruation, who require treatment for contraception or medical reasons	Suggested	Low	Weak	No evidence available for progestogen only-pills other than desogestrel 75 μg/day
	Women with estrogen withdrawal headache or worsening of the usual headache with combined hormonal contraceptives; women with new onset migraine with combined hormonal contraceptives	Suggested	None	Weak	
	Women with migraine, related to menstruation, who require migraine preventive treatments and who have contraindication or failure of conventional medical treatment	Suggested	None	Weak	
	Women with migraine, related to menstruation, who have not tried migraine preventive drugs and who have no need of desogestrel-only pill for contraception or medical reasons	Not suggested	None	Weak	
Combined oral contraceptives with shortened pill-free interval*	Women with migraine, related or unrelated to menstruation, who require treatment for contraception or medical reasons	Not suggested	Low	Weak	Data are too limited to support this option. No clear evidence that this may be better than conventional 21/7 regimen
	Women with estrogen withdrawal headache	Not suggested	None	Weak	
Combined oral contraceptives with oral estradiol supplementation during the pill-free interval*	Women with migraine, related or unrelated to menstruation, who require treatment for contraception or medical reasons	Not suggested	Low	Weak	Data are too limited to support this option. No clear evidence that this may be better than conventional 21/7 regimen. Alternative contraceptive strategies are more convenient in migraineurs
	Women with estrogen withdrawal headache	Not suggested	None	Weak	
Combined oral contraceptives with estradiol supplementation with patch during the pill-free interval*	Women with migraine, related or unrelated to menstruation, who require treatment for contraception or medical reasons	Not suggested	Low	Weak	Data are too limited to support this option. No clear evidence that this may be better than conventional 21/7 regimen Alternative contraceptive strategies are more convenient in migraineurs
	Women with estrogen withdrawal headache	Not suggested	None	Weak	

Table 5 Recommendations on the use of estrogens and progestogens in women of reproductive age with migraine considering their effect on migraine course *(Continued)*

Treatment	Population	Recommendation	Quality of Evidence	Strength of Recommendation	Comments
Extended regimen of combined hormonal contraceptives with pill or patches*	Women with migraine, related or unrelated to menstruation, who require treatment for contraception or medical reasons	Suggested	Low	Weak	There is no clear evidence on the preferable extended regimen (oral pill and type of pill or patch) of combined contraceptives for women with migraine Extended regimens of the contraceptive patch may be preferable over the 3 week patch + 1 patch-free week
	Women with estrogen withdrawal headache	Suggested	None	Weak	
	Women with migraine, related to menstruation, who require migraine preventive treatments and who have contraindication or failure of conventional medical treatment	Suggested	None	Weak	
	Women with migraine, related to menstruation, who have not tried migraine preventive drugs and who have no need of desogestrel-only pill for contraception or medical reasons	Not suggested	None	Weak	
Combined hormonal contraceptive vaginal ring	Women with migraine, related or unrelated to menstruation, who require treatment for contraception or medical reasons	Suggested	Low	Weak	
Transdermal estradiol supplementation with estradiol gel	Women with pure menstrual migraine	Suggested	Low	Weak	Patients should be informed that delayed migraine may occur and that treatment is potentially effective only on attacks related to menstruation
	Women with menstrually-related migraine	Suggested	Low	Weak	
	Women with estrogen-withdrawal headache	Suggested	None	Weak	
Transdermal estradiol supplementation with patch	Women with pure menstrual migraine	Not suggested	Low	Weak	
	Women with menstrually-related migraine	Not suggested	Low	Weak	
	Women with estrogen-withdrawal headache	Not suggested	Low	Weak	
Transdermal estradiol supplementation with patch in women induced in pharmacological menopause	Women with migraine	Not suggested	Low	Weak	
Subcutaneous estradiol; implant and cyclical progestogen	Women with pure menstrual migraine	Not suggested	Low	Weak	
	Women with menstrually-related migraine	Not suggested	Low	Weak	

*According to the Consensus Statement on the Safety of hormonal contraceptives in women with migraine, compounds containing estrogens are not suggested for women with migraine with aura and for women with migraine without aura and additional vascular risk factors [22]

Estrogen and Migraine with Aura

- Migraine with aura (MwA) does carry an increased risk of stroke compared to migraine without aura. This risk was demonstrated primarily in older studies with women receiving significantly higher doses of estrogen in the oral contraceptive.
- Emerging evidence from clinical practice however suggests that there is lower risk in prescribing the current low-estrogen formulations to patients with MwA assuming they have a low vascular risk profile (nonsmokers, no cardiovascular risk factors)

Sacco S, Ricci S, Degan D, Carolei A. *J Headache Pain.* 2012;13(3):177-189 de Falco FA, de Falco A. *Neurol Sci.* 2015;36 Suppl 1:57-60

Is It Only Due to The Drop in Estrogen ? Iron?

- End –menses migraines:
- In one retrospective study with 85 female patients with menstrual migraine, 35.3% reported migraine headache onset by the end of menstruation, which is days after the estrogen drop. The authors hypothesize that this type of migraine headache is not related to hormonal changes but most probably to transient anemia due to blood loss (Calhoun A, Headache. 2017 Jan;57(1):17- 20)
- A Turkish study noted an increased prevalence of iron deficiency anemia in all migraine patients (women) as compared to healthy controls and significant association between migraine and iron deficiency anemia in the menstrual migraine subgroup. There was no association between iron deficiency anemia and tension headache (Gur-Ozmen S, Karahan-Ozcan R. *Pain Med.* 2016;17(3):596-605)

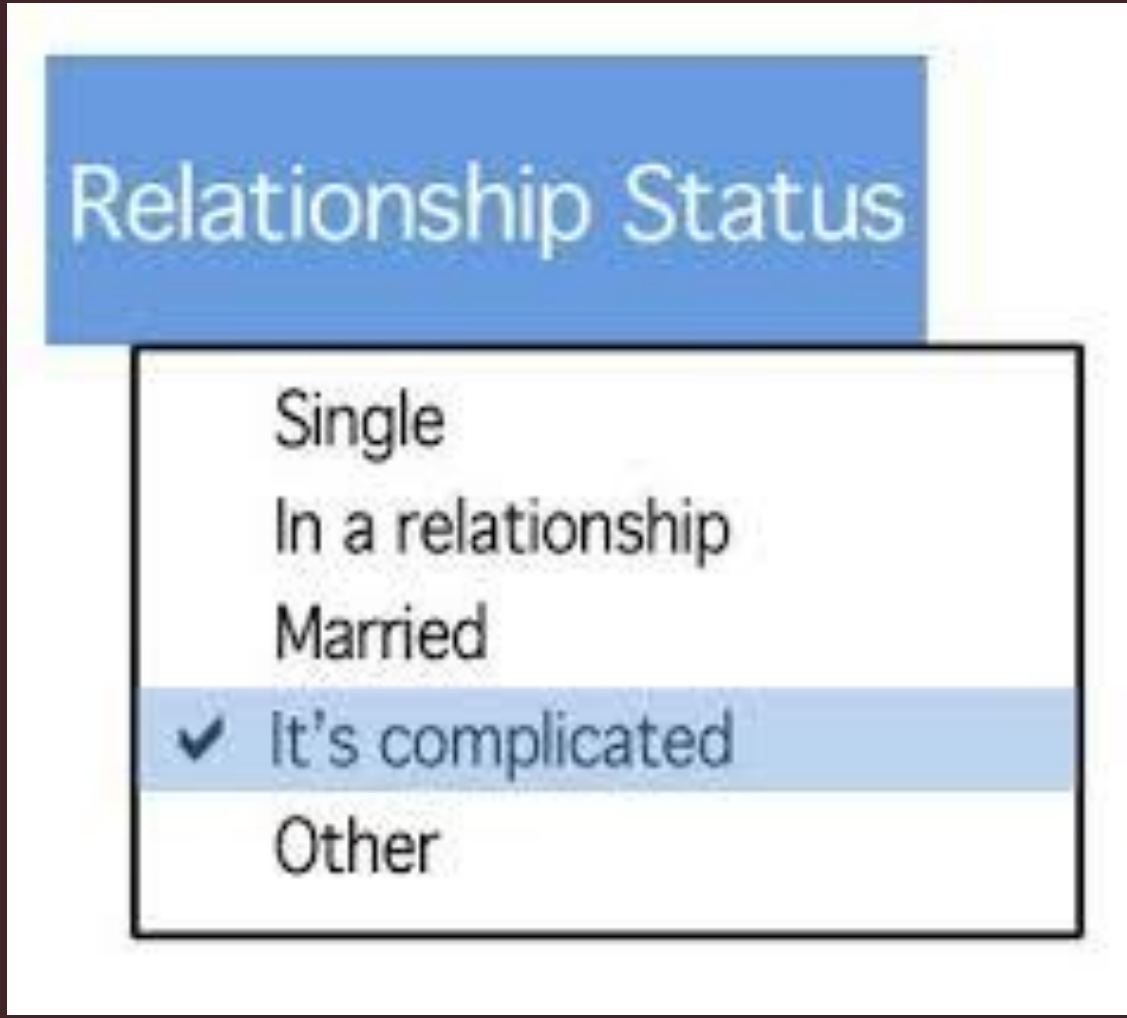
Estrogen and Pain

•Estrogen can modulate peripheral and central systems that impact our perception and ability to modulate pain

•Estrogen has been shown to impact the system response at the level of:

1. Peripheral nerves
2. Dura
3. Trigeminal ganglion
4. Trigeminal nucleus
5. Thalamus
6. Cortical systems
7. Descending modulatory systems

•There is also evidence that shows estrogen affects gray matter volumes in the brain



Estrogen and Pain

- Fluctuations in hormonal levels have been shown to influence:

1. Sensitivity to thermal pain in healthy women
2. Experimental muscle pain in women with dysmenorrhea
3. Pain intensity, unpleasantness, and functional brain activity in response to noxious stimuli

Borsook et al. Neurobiology of Disease 68 (2014) 200–214

Downstream Effects of Estrogen

- Obese women appear to have more than a two-fold risk of episodic and chronic migraine, probably due to the pathological estrogen production in adipose tissue
- Estrogen modulates serotonergic neurotransmission, by increasing the expression of the tryptophan hydroxylase and decreasing the expression of the serotonin reuptake transporter
- Estrogen also activates the endogenous opioidergic system, which has an analgesic effect on persistent, inflammatory pain
- Furthermore, estrogen induces vascular changes by modulating vasodilation and suppressing vascular inflammatory response

Horev et al.2005. Headache 45; Fava et al 2014. Eur J Neurol 21; Gupta S et al 2011. Headache 51; Warnock et al 2017.Pharmacotherapy 37; Krause DN et al 1985.J Appl Physiolo;; Miller M et al. 2008 Pharmacol Rev 60.

Treatment Options for Menstrual Migraine

1. Mini-prophylaxis: non-hormonal (preferred) vs hormonal
2. Lifestyle: hydration, sleep hygiene, caffeine intake, exercise
3. Consider Migraine Prophylactic medications if more than 4 migraine a month
4. Rescue: triptans with the possible addition of NSAIDs and/or antiemetic is a good first choice
5. Alternative Therapies: neuromodulation, biofeedback, acupuncture

Mini-Prophylaxis

Non-hormonal options:

- perimenstrual use of NSAIDs- naproxen sodium (550 mg BID) may be used effectively 2– 4 days prior to the MM and continued through day 3 of menstrual flow
- Modified triptans regimens including sumatriptan (25 mg TID), naratriptan (1 mg BID), and frovatriptan (2.5 mg BID) , started 2 days prior to the onset of MM and continued for a total of 3–5 days.
- Standard prophylactic medications may be used for 5–7 days prior to the onset of menses and continued through to the end of the vulnerable time period for migraine – this can be a transient increase in the preventive currently used.

Hormonal options:

- transdermal supplementation with estradiol gel is recommended over an estradiol patch during the week of menses

Alternative Therapies

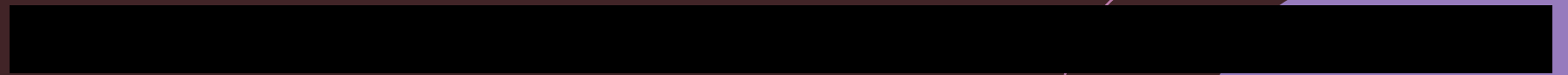
- Neuromodulation
  - Non-invasive Vagus Nerve Stimulation: One study with 56 patients (menstrual migraine, 9 %; menstrually related migraine, 91 %) concluded that non-invasive vagus nerve stimulation is an effective treatment that reduces the number of menstrual migraine/menstrually related migraine days and analgesic use without safety/tolerability concerns in subjects with menstrual migraine/menstrually related migraine. Randomized controlled studies are warranted. (Grazzi et al. 2016)
- Biofeedback
  - One study showed that biofeedback successfully reduced (>than 50%) frequency, intensity, medication use, and headache days compared to pretreatment levels in women with menstrual migraine and these effects were not transient but sustained at long-term follow-up (Gautherier et al., *Headache* 1991)
- Acupuncture
  - Systematic review published this year concluded that there is no convincing evidence to support the use of acupuncture in treating menstrual migraine. Acupuncture cannot yet be recommended to patients with menstrual migraine until more solid evidence is produced. (Yang et al. ,*BMJ Supportive & Palliative Care 2020)*

Menstrual Migraine Summary

- Menstrual migraine occurs with rapid decline in estrogen especially at the end of cycle
- Most menstrual migraine is without aura is MRM and can occur at other times of the menstrual cycle, PMM is less common.
- NSAIDS are first choice for menstrual migraine prevention
- Avoid especially high dose estrogen-containing COC's in migraine with aura to reduce CVA risk
- Estrogen can modulate peripheral and central systems that impact our perception and ability to modulate pain

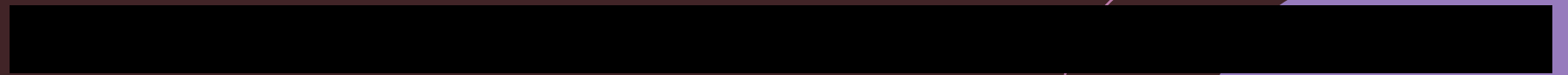
Headache and Pregnancy
Preconception Advice

- Daily folic acid supplement 0.4mg qd to reduce neural tube defects (Divalproex and Butalbital interfere with folate metabolism)
- Stop medications before attempting conception (no wash-out)
- If prophylaxis becomes necessary, use safest meds in lowest dose
- For those undergoing infertility RX, clomiphene may increase risk of migraine related CVA
- No conclusive evidence that pregnancy fetal outcomes are worse for migrainuers



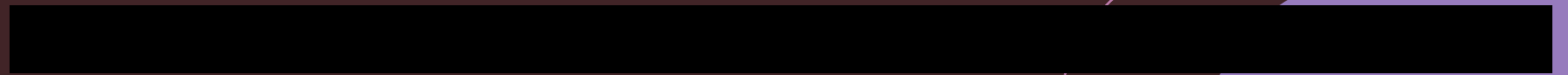
Headache and Pregnancy

- 50% of women improve by the end of the first trimester and more than 80% improve by the end of the second trimester
- Menstrual migraine/Migraines without Aura tend to improve
- First aura may occur during pregnancy or those with Migraine with Aura may have worsening of aura



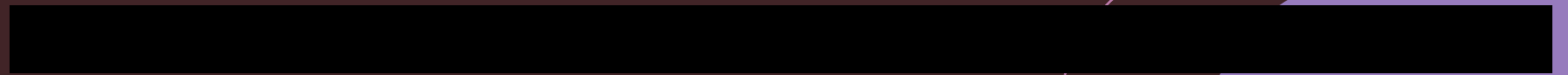
Headache and Pregnancy Complications

- Compared to women without a history of migraine, women with a history of migraine are more likely to have a secondary cause of headache including:
  - cerebral venous thrombosis
  - pregnancy-associated stroke
  - preeclampsia.



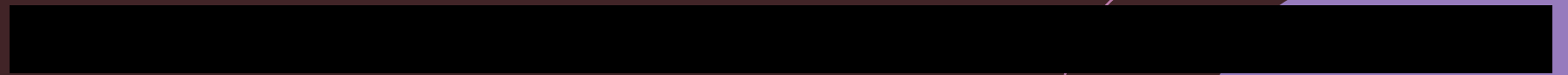
Headache and Pregnancy
Imaging?

- Sometimes necessary to exclude secondary Headache causes
- CT- ionizing radiation potential effects on fetus
- MRI – preferred; probably safe up to 3 Tesla but avoid gadolinium if possible



Nonpharmacologic Modalities

- Devices:Thermazone, Cefaly, gammaCore nVNS, eNeura sTMS
- CBT/ Mindfulness/ Biofeedback- start prior to pregnancy
- Acupuncture/Acupressure
- Massage



Reproductive Risks of Medications: Where to go for Information

FDA approved drug labeling (full prescribing information):

- Drugs@ FDA: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/
- DailyMed: http://dailymed.nlm.nih.gov/dailymed/about.cfm
- New FDA labeling as of 6.30.15 http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307.htm

Reprotox

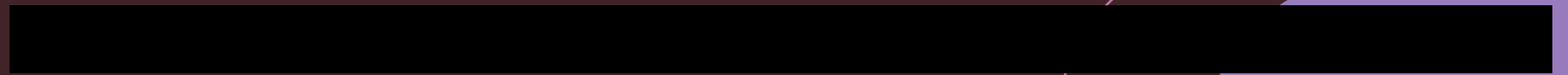
- http://va.reprotox.us/

Lactmed

- http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm

Pregnancy Registry studies (list at FDA Office of Women's Health)

- http://www.fda.gov/scienceresearch/specialtopics/womenshealthresearch/ucm134848.htm



Headache and Pregnancy
Acute Pharmacologic RX

Acute Meds	Pregnancy risk FDA	Breast-feeding risk (AAP recommends)
DHE (dihydroergotamine)	X	Not listed
Ergotamine	X	Caution
Sumatriptan	C	Compatible
Other triptans	C	Not listed
ASA	C	Caution
Barbituates	C	Caution
Acetaminophen	B	Compatible
Caffeine (moderate amount)	B	Compatible
Ibuprofen	B	Compatible
Naproxen	B	Compatible
Butorphanol	B	Compatible
Lidocaine	B	Compatible

Headache and Pregnancy Preventative Pharmacologic RX

Preventatives	Pregnancy Risks FDA	Breast-feeding (AAP recommends)
**Magnesium	B	compatible
*Propranolol, Timolol	C	compatible
Amitriptyline	C	concern
OnabotulinumtoxinA	C	caution
Atenolol	D	caution
Valproic acid	D	caution
Topiramate	X	Not listed

FDA scoring

A=no risk

B=no known risk in humans but no studies

C= risk to humans not ruled out

D= +evidence for risk to humans

X=contraindicated

(Headache) and Pregnancy/Lactation Antiemetic RX

Antiemetic Meds	Pregnancy risk FDA	Breast-feeding risk (AAP/LactMed)
*Doxylamine + vit B6	A	Compatible; small occasional dose
Emetrol	B	Not listed
Metoclopramide	B	Concern
Ondansetron	B	Caution
Prednisone	C	Compatible
Promethazine	C	Compatible

- FDA approved for nausea vomiting with pregnancy (NVP)
- Not on VA Pharmacy

CGRP mAbs and Botox preconception Counseling

- Patients taking CGRP mAbs should be advised to stop injections approximately 5 to 6 months before conception.
- Due to paucity of evidence and the lower levels of CGRP in patients with preeclampsia compared to normotensive individuals, most headache specialists believe avoidance of CGRP mAbs in pregnancy is warranted.
- There's a reduction on CGRP receptor expression in pre-eclamptic women. There's no vascular response to CGRP infusion in pre-eclamptic women. Could CGRP mAbs increase the risk of pre-eclampsia?
- The FDA's official stance is that administration of onabotulinumtoxinA is not recommended during pregnancy given the absence of well-controlled studies.
    - When pregnant mice and rats were injected intramuscularly during the period of organogenesis, the developmental no observed effect level (NOEL) was 4 U/kg. Higher doses (8 U/kg or 16 U/kg) were associated with reductions in fetal body weight or delayed ossification, or both. Rabbits apparently very sensitive to botox-FDA statement.
    - In humans, a very limited amount of data from just over 200 pregnancies reported no increased teratogenicity and no increased risk of pregnancy loss compared to the general population, but the amount of available data is insufficient to make any solid conclusions about the safety of onabotulinumtoxinA
    - wide variability exists in clinical practice on use of botox in pregnancy/pregnancy planning
    - this therapeutic option can occasionally be considered during pregnancy for women with particularly intractable and disabling chronic migraine.
    - Should probably avoid starting in botox naïve patients during pregancy

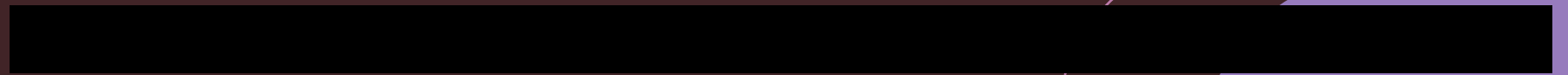
Postpartum Headache

1/4 - 1/3 of women have post-partum Headache

1/2 of migraineurs have post-partum Headache

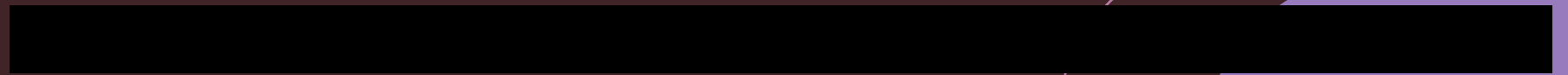
Secondary post-partum headache types:

- eclampsia/preeclampsia related
- cerebral venous thrombosis
- low pressure headache
- intracranial hemorrhage



Summary 2B-Pregnancy/Lactation

- Preconception counseling includes folic acid supplementation; start biofeedback and /or magnesium if likely needed for headache prevention
- Most migrainuers improve by end of 1st trimester
- Propranolol is first line medical prevention (failing magnesium), also compatible with lactation
- Migraine is a risk factor for pregnancy related pre/eclampsia, Hypertension, CVA
- Post-partum headaches include serious secondary causes



Acknowledgements

Menstrual Migraine
What does Estrogen Have to Do with Migraine? A deeper Dive into the Impact of Estrogen on Migraine presented at pain week 2019 by Meredith Barad, MD
Slides 3, 4, 10, 11:
American Headache Society Ambassador Series

Wolff's Headache and Other Head Pain, 8th Edition; Silberstein, Lipton, Dodick

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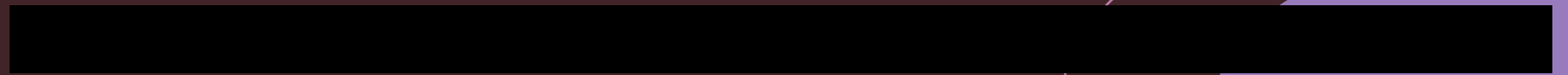

Questions?