Migraine Pearls for the Busy Practitioner

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Learning Objectives

- Diagnose migraine and recognize its impact
- Optimize the available medications when managing acute and preventive treatment of migraine

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How Common is Migraine?

- 1 billion people worldwide
- 13% prevalence in US (approx. 39 million Americans)
  - Other diseases with similar prevalence
    - Type 2 DM
    - Asthma
- 18% women; 6-7% men
- Most common neurologic disease seen in primary care
- Most common type of primary headache seen in primary care

GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. *Lancet.* 2017;390(10100):1211-1259.

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Migraine in Primary Care

- >37% of women of reproductive age in a primary care provider's waiting room have migraine
- People with episodic tension headache rarely seek medical advice
- Other primary headache disorders infrequently appear in a primary care office
- According to the United Council for Neurologic Subspecialties, there are only 636 (down from 706) certified headache specialists in the United States[1]

Couch JC, et al. *Headache*. 2003;43(5):570-571.
[1]https://www.ucns.org/Online/Diplomate_Directory/Online/Diplomate_Directory

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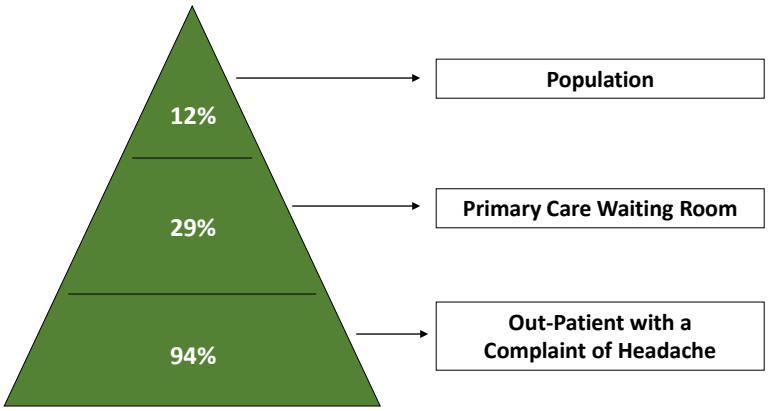
The Prevalence of Migraine in Primary Care



Lipton RB, et al. *Neurology.* 2007;68: 343-349. Couch J, et al. *Headache*. 2003;43:570-571. Tepper SJ, et al. *Headache*. 2004;44:856-864.

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Disability of Migraine

- One of leading causes of disability world-wide
  - 2nd cause of YLDs (years lived with disability)
  - #1 in women <50
- Peaks in ages 22-55 for men and women
- Affects 1 in every 4 households in US
- High socio-economic burden
  - Annual total cost (US) estimated $36 Billion
  - Annual direct + indirect costs is $9K more in patients diagnosed w/ migraine than “similar” patients w/o migraine

GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. *Lancet.* 2017;390(10100):1211-1259. Steiner TJ, et al. Migraine is the *first* cause of disability in under 50's: will health politicians now take notice? *J Headache Pain.* 2018;19(1):17. Steiner, T.J., Stovner, L.J., Jensen, R. *et al.* Migraine remains second among the world’s causes of disability, and first among young women: findings from GBD2019. *J Headache Pain* 21, 137 (2020). https://doi.org/10.1186/s10194-020-01208-0 Bonafede M, Sapra S, Shah N, Tepper S, Cappell K, Desai P. Direct and indirect healthcare resource utilization and costs among migraine patients in the United States [published online February 15, 2018]. *Headache.* doi: 10.1111/head.13275. Bonafede M et al. *Headache*. 2018;58(5):700-714.

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Diagnosis of Migraine without Aura

At least 5 attacks lasting 4-72 hours with at least 2 of the following:

1. Unilateral location
2. Pulsating quality
3. Moderate to severe pain
4. Aggravation or avoidance of physical activity

During the headache at least one of the following:

1. Nausea and/or vomiting
2. Photophobia and phonophobia
3. Not better accounted for by another ICHD-3 diagnosis

The International Classification of Headache Disorders. 3rd ed. *Cephalalgia*. 2013;33(9).

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Migraine with Aura

At least 2 attacks with 1 or more of the following fully reversible aura symptoms:

1. Visual
2. Sensory
3. Speech and/or language
4. Motor
5. Brainstem
6. Retinal

At least 3 of the following:

1. At least 1 aura symptom spreads gradually over >5 minutes
2. 2 or more occur in succession
3. Each aura symptom lasts 5-60 minutes
4. At least one aura symptom is unilateral
5. At least one aura symptom is positive
6. Aura accompanied or followed by headache within 60 minutes

The International Classification of Headache Disorders. 3rd ed. *Cephalalgia*. 2013;33(9).

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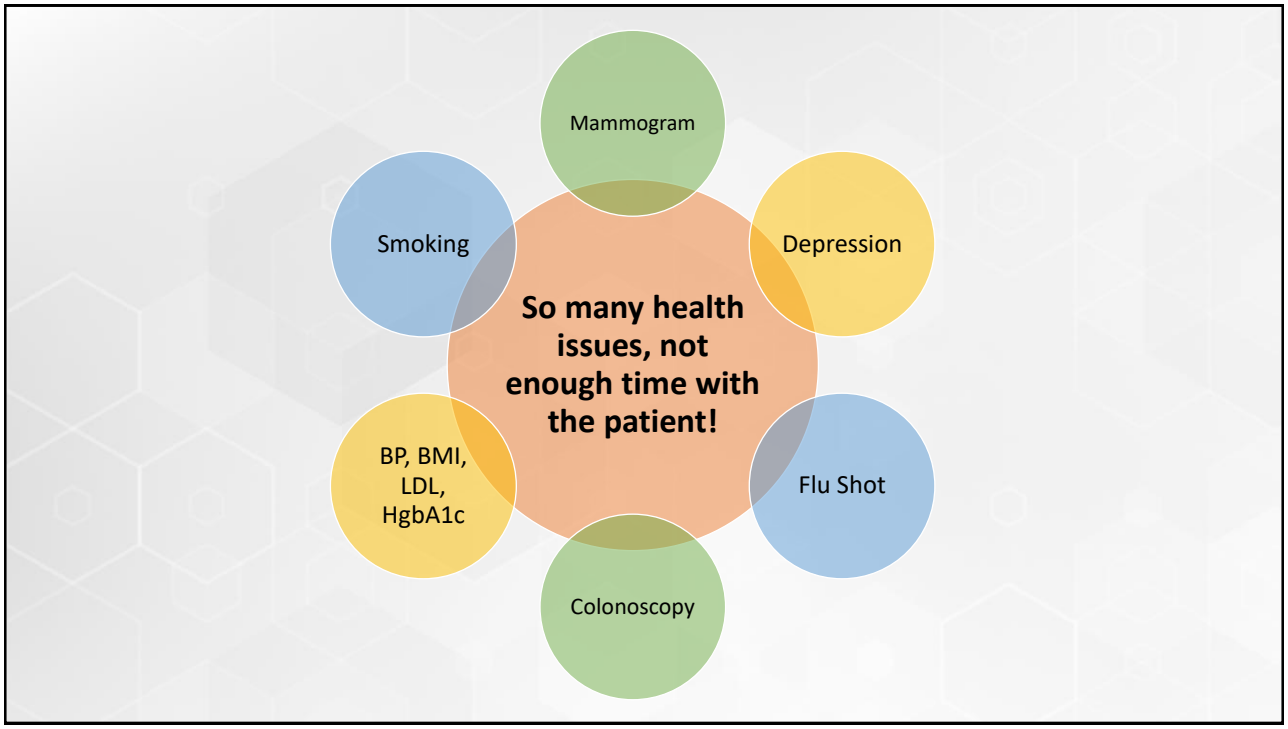

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Meet Sarah

- 28-year-old medical assistant
- History of headaches since puberty
- Has never discussed with her provider about her headaches
- Takes over the counter ibuprofen when the headache is "really bad" – sometimes doesn't work
- Has noticed her headaches are occurring more frequently over past 6 months
- Has a hard time completing her work when headache is bad because the computer light hurts her eyes
- No medication allergies, no significant PMHx
- Normal Medical Exam (including vitals, CV and neuro exam)

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Does Sarah Have Migraine?

During the last 3 months, did you have the following with your headaches?		
You felt nauseated or sick to your stomach?	❑ YES	❑ NO
Light bothered you (a lot more than when you don't have headaches)?	❑ YES	❑ NO
Your headaches limited your ability to work, study, or do what you needed to do?	❑ YES	❑ NO

- **2/3 for migraine**
- **Sensitivity: 0.81**
- **Specificity: 0.75**

Lipton, et al. *Neurology.* 2003;61:375-382.

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How Do We Treat Sarah? Goals for Acute Treatment

- Rapid relief of headache pain
- Relief of "most bothersome symptoms" (MBS) including nausea, photophobia and phonophobia
- Sustained pain freedom
- No need to rescue or take a 2nd dose
- Return to full function
- Little to no side effects from acute medication

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Acute Treatment Options for Sarah

- Triptans (5 HT-1B and 1D receptor agonists)
- Ergots/Dihydroergotamine
- NSAIDS
- Non-specific options (Analgesics, Butalbital, Narcotics) NO!!
- Non-invasive devices
- Oral CGRP receptor antagonists
- Ditan (Lasmiditan - selective 5 HT-1F receptor agonist)

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Safety Concerns: Acute Migraine Treatment Options

- Triptans and Ergots/Dihydroergotamine are all contraindicated in patients with coronary artery disease, peripheral vascular disease, uncontrolled high blood pressure and those at high risk of cardiac disease
- Triptans and Ergots/Dihydroergotamine should not be taken in the same 24-hour period due to risk of vasoconstriction
- Risk of medication overuse with triptans
- Narcotics and Butalbital are non-specific in treatment of acute migraine, can lead to medication overuse, overdose, sedation, abuse, and can cause preventives to be less effective
- NSAIDs contraindicated in many patients due to GI issues or those at risk for GI bleeding and those with certain kidney conditions
- Driving precaution with the Ditan - Lasmiditan (8 hours)

See PIs for full prescribing information.

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CGRP – The "New Kid" on the Block

- Calcitonin gene-related peptide (CGRP) – a 37 amino acid polypeptide in neurons and glial cells (universally present)
- Receptors to CGRP are located throughout the trigeminal system and multiple brain regions (as well as other locations throughout the body)
- CGRP is a vasodilator and causes neurogenic inflammation
- CGRP modulates pain signaling

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CGRP and Migraine: Where is the Evidence?

- CGRP levels are elevated during a migraine attack (measured external jugular vein)[1]
- Infusion of CGRP in migraine patients can cause migraine[2]
- Infusion of CGRP blocking medication can resolve a migraine attack in a migraine individual[3]
- New targeted CGRP blocking molecules highly effective in the acute treatment of migraine as well as prevention
  - Acute: "Gepants" small molecules
  - Preventive: large monoclonal antibodies, as well as small molecules (gepants)

1. Goadsby PJ, Edvinsson L, Ekman R. Vasoactive peptide release in the extracerebral circulation of humans during migraine headache. *Ann Neurol*. 1990;28:183-187. 2. G Lassen LH, Haderslev PA, Jacobsen VB, et al. CGRP may play a causative role in migraine. *Cephalalgia*. 2002;22:54-61.
3. Goadsby PJ, Edvinsson L. The trigeminovascular system and migraine: studies characterizing cerebrovascular and neuropeptide changes seen in humans and cats. *Ann Neurol*. 1993;33:38-56.

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Acute Medications

Medication Class	Dosing/Formulations	Prescribing Considerations
Triptans (7 available): Sumatriptan, Rizatriptan, Zolmitriptan, Almotriptan, Eletriptan, Naratriptan, Frovatriptan	Multiple dosing options Oral, nasal, injectable, breath powered formulations	Contraindicated in patients with CV disease, uncontrolled HTN, PVD Risk of medication overuse and MOH Cannot take within 24 hrs of DHE
DHE - Dihydroergotamine mesylate	0.725mg delivered via a "POD" (precision olfactory delivery)	Contraindicated in CVD, HTN, PVD Cannot take within 24 hrs of triptan
Gepants Rimegepant Ubrogepant	 75mg oral dissolvable tablet 50mg, 100mg tablet	
Ditan (Lasmiditan)	50mg, 100mg (up to 200mg)	Driving restriction 8 hours
NSAIDS (Diclofenac, Naproxen, Celecoxib)		GI, CV

DHE (Trudhesa) Data on File 2019: Impel NeuroPharma, Inc
Rimegepant (Nurtec ODT) Data on file. 2018. Biohaven Pharmaceutical
Ubrogepant (Ubrelvy) Data on file. 2018. Allergan.
Lasmiditan (Reyvow) Indianapolis, IN: Lilly USA, LLC. 1/2021; Data on File

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Non-Pharmacologic Treatment Options

- Herbal treatments
  - Magnesium 500mg (may cause diarrhea)
  - Riboflavin (vitamin B2) – dietary: 1.6-3.8 mg, supplement: 400mg
  - Co Q 10 150mg
  - Butterbur 75mg
- Acupuncture
- Biofeedback, CBT, stress-reduction
- Psychological counseling
- Yoga, exercise, meditation
- Non-invasive nerve stimulators (both acute and preventive – require Rx)
- Class IV Laser (photobiomodulation "aka cold laser") – not FDA approved for migraine but has been shown to reduce inflammation and pain in musculoskeletal and peripheral neurologic conditions – safe, non-invasive

Slavin M. *Headache*. 2019;Jun;59(S1):1-208, Abstract LB0R04.

CBT = cognitive behavioral therapy

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Recommendations for Sarah

- Lifestyle modifications
  - Sleep
  - Nutrition
  - Stress reduction
  - Modify triggers (alcohol, caffeine, etc.)
- Migraine diary
  - "Paper"
  - APP based (multiple options – migraine buddy, migraine monitor, etc.)
- Acute medication options
  - NSAIDS - (for Sarah - suboptimal in past)
  - Triptans (tend to be first line if able, most insurances require failure/contraindication)

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Sarah – 6 Months Later

- Headaches becoming more frequent
  - 4-5 migraine headache days per month (based on her diary)
- Now missing 1-2 days of work
- Has been taking oral rizatriptan MLT 10 mg for acute treatment
- Does not work well if nauseated or wakes up with severe headache as is typical when on her menses
- Tried Sumatriptan 6 mg injection but caused flushing, chest tightness, and headache seemed to get worse before it got better
- Now back to supplementing with NSAIDs

So. . . .now what?

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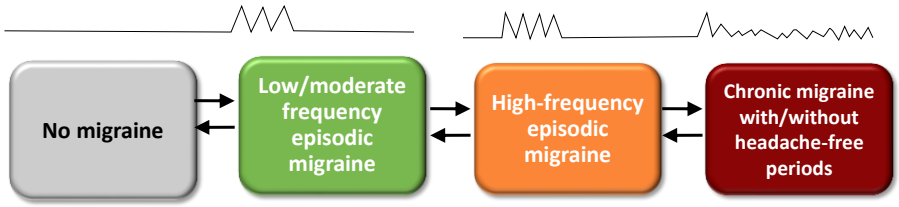
When Do We Offer Prevention for Migraine?

- Migraine Frequency
  - 4 or more migraine days (with impact) offer prevention
- Migraine Classification
  - Episodic (EM) less than 15 days per month of headache
  - Chronic (CM) 15 or more headache days per month of which 8 or more meet criteria for migraine for at least 3 months



Conversion from EM to CM at the rate of 2.5% per year

Lipton RB. *Neurology.* 2009;72(5 suppl):S3-S7.

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"Traditional" Preventive Treatments

- Anti-depressants
- Anti-epileptics
- Anti-hypertensives
- Onabotulinum Toxin A
- Non-invasive neurostimulators
- Herbal preventives
- Hormonal approaches

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FDA Approved Oral Medications for Prevention of Episodic Migraine

- Divalproex sodium
- Topiramate
- Timolol
- Propanolol

Note: Others commonly used but not FDA approved include Amitriptyline, Venlafaxine, Metoprolol, Naldolol, Atenolol, Nortriptyline, Duloxetine, Verapamil, Gabapentin, Candesartan, Fluoxetine, Escitalopram, Cyproheptadine

Short-term prevention menstrual migraine: Frovatriptan, Naratriptan, Sumatriptan, Zolmitriptan, Rizatriptan. All have shown efficacy in clinical trials but not FDA approved for prevention.

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Gepants – For Prevention

- Atogepant
  - Oral CGRP **Receptor** Antagonist for the prevention of episodic migraine
  - Dosing: 10mg, 30mg, 60mg options
- Rimegepant
  - Oral CGRP **Receptor** Antagonist for the prevention of episodic migraine
  - Dosing 75mg QOD

Atogepant (Qulipta) Data on file. 2021. Allergan Pharmaceutical
Rimegepant (Nurtec ODT) Data on file – Biohaven US-RIMODT-2100251 05/10/2021

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Anti-CGRP Monoclonal Antibodies for Migraine Prevention

- Target specific
  - Block CGRP receptor or bind the CGRP ligand
- Net effect
  - Block CGRP activity
  - Lessen the migraine cascade of inflammatory activity
  - Prevent transmission of pain signals to travel to higher order neurons
- Anti-CGRP mABs are large monoclonal antibodies and cannot cross the blood-brain barrior to any significant degree
- Anti-CGRP mABs work on the peripheral nervous system (PNS)

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Key Features – Anti-CGRP mAB's

- Work on peripheral nervous system
- No central nervous system (CNS) side-effects
- No effect on liver or kidney
- No drug-drug interactions
- Degraded by enzymatic proteolysis
- Favorable side-effect profile in clinical trials
- Approved for migraine prevention in adults **(EPISODIC AND CHRONIC)**
- No data in pregnancy and breast-feeding
- Not available in oral tablet
- Expensive to make (grown in cell cultures)
- CGRP is a vasodilator – CV considerations?
  - Stable CV in trials – no "red flags"
- Immunogenicity is possible – impact unclear
- More similar than different

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CGRP – mAB's

mAB	Dosing/Frequency	Safety Considerations
erenumab CGRP receptor blocker	70mg or 140mg SC monthly	Constipation, HTN (post-marketing), Rash, alopecia, angioedema, anaphylaxis
fremanezumab CGRP ligand blocker	225mg SC monthly or 3x225mg SC quarterly (=675mg)	Hypersensitivity reactions (rash, pruritis, urticaria)
galacnezumab* CGRP ligand blocker	120mg SC monthly (requires 240mg loading dose)	Hypersensitivity reactions (rash, urticaria, dyspnea, angioedema, anaphylaxis)
eptinezumab CGRP ligand blocker	100mg or 300mg IV infusion monthly	Hypersensitivity reactions (angioedema, urticaria, facial flushing, rash)

*Additional indication for treatment of episodic cluster headache: Dosing is 300mg (3x100mg syringes) SC At onset of cluster attach and continue monthly until cluster attack breaks.

erenumab (Aimovig) Aimovig (erenumab-aooe) prescribing information. 2018. Amgen Inc. fremanezumab (Ajovy) Fremanezumab-vfrm prescribing information. 2018. Teva Pharmaceuticals USA.
galacnezumab (Emgality) Stauffer VL, et al. Presented at: *IHC 2017*. Abstract PO-01-184. Data on file, Eli Lilly and Company
eptinezumab (Vyepti) Vyepti (Eptinezumab) prescribing information. 2020. Lundbeck Seattle BioPharmaceuticals, Inc.

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Important Points About Anti-CGRP mAB's

- No head-to-head comparator trials
- Long-term safety trials ongoing
  - To date no major "red flags" but:
  - Could there be a downside of long-term CGRP suppression?
- Insufficient data on safety during pregnancy and lactation
- All companies forming Pregnancy Registries
- Only FDA approved for 18 and over in US
  - Pediatric trials ongoing

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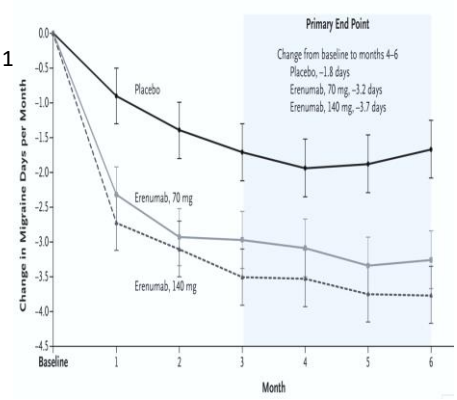
Data: No head-to-head but THEY ALL WORK!

1



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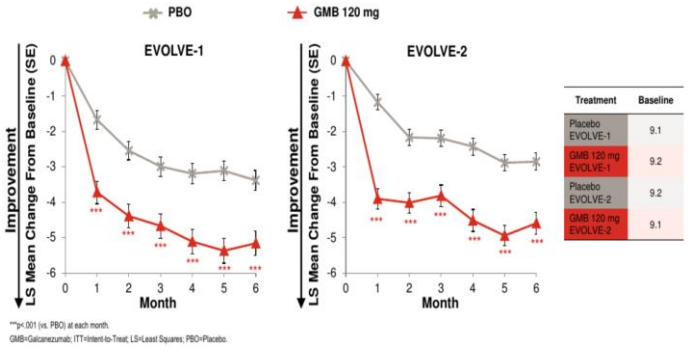

Treatment	Baseline
Placebo EVOLVE-1	9.1
GMB 120 mg EVOLVE-1	9.2
Placebo EVOLVE-2	9.2
GMB 120 mg EVOLVE-2	9.1

[1]Goadsby PJ et al. *N Engl J Med*. 2017; 377:2123-2132.

[2]*N Engl J Med*. 2017;377(22):2113-2122. Skljarevski V, et al. Efficacy and safety of galcanezumab for the prevention of episodic migraine: Results of the EVOLVE-2 Phase 3 randomized controlled clinical trial. *Cephalalgia*. 2018;38(8):1442-1454. Stauffer VL, et al. Evaluation of Galcanezumab for the Prevention of Episodic Migraine: The EVOLVE-1 Randomized Clinical Trial *JAMA Neurol*. Published online.

29

Data: No head-to-head but THEY ALL WORK!

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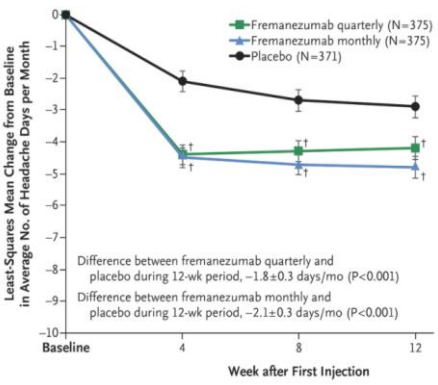

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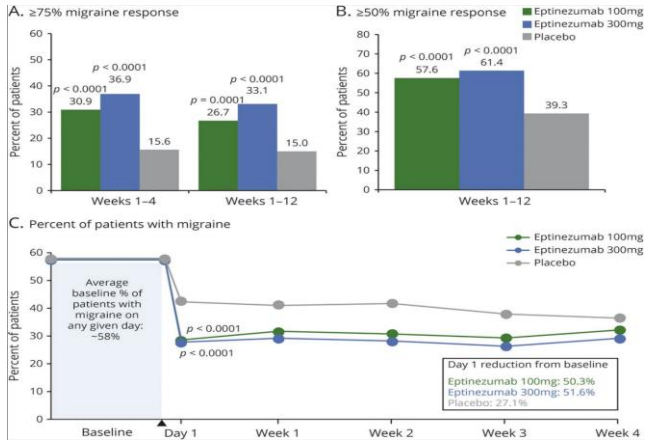

[1]Silberstein SD, et al. Fremanezumab for the Preventive Treatment of Migraine..

[2]Goadsby PJ et al. *N Engl J Med*. 2017; 377:2123-2132. Lipton RB, Goadsby PJ, Smith J, et al. Efficacy and safety of eptinezumab in patients with chronic migraine PROMISE-2. *Neurology*. Mar 2020, 94 (13) e1365-e1377.

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Who is a Candidate for an Anti-CGRP mAB?

- Adults with migraine who have 4 or more monthly migraine headache days
- Migraines are disabling
- Current or past standard preventives have either not been tolerated or have been ineffective (most insurance companies will require trial of 2 preventives prior to approval of CGRP mAB)
- If adult has chronic migraine, insurance company may require failure of 4-6 month trial with Onabotulinum Toxin A

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Onabotulinum Toxin A

- FDA approved for chronic migraine only (not EM)
- Approved protocol is 155 units injected in 31 individual sites every 12 weeks
- Sites include procerus, corrugators, frontalis, temporalis, occipitalis, upper paracervicals, and upper trapezius
- FDA approved for chronic migraine in 2010
- MOA includes inhibition of release of neuropeptides including CGRP from peripheral nervous system

Onabotulinum Toxin A (Botox)

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Adding on to Onabotulinum Toxin A?

- For chronic migraine patients not adequately controlled with Onabotulinum Toxin A . . . Can we add a mAB or a preventive gepant?
- Some retrospective data suggests benefit of Onabotulinum Toxin A with mAB

Cephalgia article 2021, Vol. 41(1) 17–32: Combined Onabotulinum Toxin A / atogepant treatment blocks activation / sensitization of high-threshold and wide-dynamic range neurons.

Onabotulinum Toxin A (Botox)

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Options for Sarah

- Acute: change her acute medication
  - "Tool Box" approach
- Prevention: meets criteria for prevention
  - 4-5 headache days per month
  - With disability (missing 1-2 days of work per month)
  - Choices/Considerations
    - Secondary gain/risk (i.e., bp control, depression, pregnancy?)
    - Insurance barriers (fail two generics before CGRP targeted therapies may be covered)

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Meet Sam

- 56-year-old white male with history of migraine
- Complains of worsening headaches over last few weeks
- Complains of scalp tenderness especially in temple region
- Has noticed some intermittent visual changes

Are his symptoms due to his migraines?

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Secondary Headaches

- Key point – migraine patients can have or develop a secondary headache
- Red flag, *"Worse headache ever"*
- SNOOP mnemonic
- Choosing wisely; blood work and brain scan are not a routine part of a headache work-up

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Worrisome Headache – "Red Flags"

'SNOOP4' – When in doubt, investigate the atypical!
Systemic symptoms (fever, weight loss); OR

- **S**econdary risk factors – underlying disease (HIV, systemic cancer)
- **N**eurologic symptoms or abnormal signs (confusion, impaired alertness, or consciousness)
- **O**nset: sudden, abrupt, or split-second (first, worst)
- **O**lder: new onset and progressive headache, especially in middle age >50 (giant cell arteritis)
- **P**attern change: first headache or different, change in type of headache
  - Postural aggravation
  - Papilledema

Dodick D. *Semin Neurol*. 2010;30:74-81.
Sadovsky D, et al. *Am J Med*. 2005:118(Suppl 1):11S-17S.

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Migraine as Risk Factor for Stroke

- Migraine is an independent risk factor for stroke in women <45 years old
- 2-fold increase in ischemic stroke compared to women without migraine
- This increase primarily driven by the subgroup of women who have migraine with aura
- Approximately 1.5 increased risk hemorrhagic stroke in women with migraine
- Other risk factors such as smoking amplify this risk

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Risk of Stroke with Use of Estrogen Containing Contraception in Women with Migraine

- Risk for both ischemic and hemorrhagic stroke higher in high dose (>50 mcg) ethinyl estradiol dose than lower dose (<50 mcg)
- OR ischemic stroke 50 mcg EE 2.9-4.8, OR 1.6-2.7 30-40 mcg EE, OR 1.7 20 mcg EE, OR .9-1 progestin only pills (data from 3 studies)
- Ischemic stroke risk higher in women **with aura** (OR 6.1) using combined oral contraception vs women without aura (OR 1.8) who used CHC's within 90 days prior to the first diagnosis of stroke

Sheikh, H., Pavlovic J., Loder, E., Burch R. Risk of Stroke Associated With Use of Estrogen Containing Contraception in Women with Migraine: A Systematic Review. *Headache.* 2018;58:5-21.

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Absolute Risk of Stroke

- 3.56 per 100,000 women reproductive age in UK population-based study
- 21.7 per 100,000 women annual stroke incidence in women with migraine with aura who use CHC's
- Increased risk of stroke in pregnancy in women with migraine (OR 7.9-30.7)

Nightingale AL, Farmer RD. Ischemic Stroke in young women: A nested case-control study using the UK general practice research database. *Stroke*. 2004;35: 1574-1578. Champaloux SW, Tepper NK, Monsour M, et al. Use of combined hormonal contraceptives among women with migraines and risk of ischemic stroke. *Am J Obstet Gynecol*. 2017;216:489.e.-489 e7. Wabnitz A, Bushnell C. Migraine, cardiovascular disease, and stroke during pregnancy: Systematic review of the literature. *Cephalalgia*. 2015;35:132-139.

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Migraine in Special Groups

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Pediatric Migraine

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Epidemiology and Key Features

- Boys and girls equal prevalence
- Pediatric (<12 years old) – migraines come on fast, resolve quicker than adults, more often associated with nausea/vomiting
- Cyclical vomiting syndrome, abdominal migraine often lead to costly GI work-ups
- Key: Look for family history and complete resolution in between attacks

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Acute Treatment

- Anti-nausea Rx (Ondansetron 4 mg every 8 hours; oral or ODT formulation)
- Acute treatment: acetaminophen vs nsaids show ibuprofen best results
- Rizatriptan oral/MLT* 5 mg (wt <88 lbs); 10 mg (wt >88 lbs)
- CGRP blockade? (ongoing trials)
- Caffeine in moderation; hydration
- Rest, avoid TV/computer screen

Am Fam Physician. 2019 Jan 1;99(1):17-24.
Am Fam Physician. 2018 Feb 15;97(4):243-251.

*MLT = orally disintegration formulation

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Preventive Treatment

- Prevention: Limited data/conflicting results
  - Propranolol
  - Topiramate
  - Cyproheptadine
  - Amitriptyline
  - Valproic acid
  - Levetiracetam
  - CGRP blockade? (on going trials – unsure of long-term effects?)

Am Fam Physician. 2019 Jan 1;99(1):17-24.
Am Fam Physician. 2018 Feb 15;97(4):243-251.

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Adolescent Migraine

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Acute Treatment Options

- NSAID's
- Anti-emetics (Ondansetron oral or ODT 4-8 mg)
- Triptans (FDA approved for ages 12-17 include Almotriptan, Rizatriptan, Sumatriptan/Naproxen combination, Zolmitriptan nasal spray)
- Non-oral triptans (nasal sprays, injectables)
- CGRP blockade? (ongoing trials)
- Caffeine in moderation
- Non-pharmacologic treatment

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Preventive Treatment Options

- Lifestyle (adequate sleep, healthy diet, stress-reduction, adequate hydration, caffeine in moderation)
- Screen for alcohol, substance abuse, depression, anxiety, issues at school/home
- Cognitive behavioral therapy (CBT)
- For females, screen for menstrual migraine and consider short-term targeted prevention during vulnerable time of cycle

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Preventive Prescription Options

- Amitriptyline, Nortriptyline – start low, increase gradually
- Escitalopram, Fluoxetine
- Propanolol
- Topiramate, Divalproex sodium
- Cyproheptadine
- Non-invasive stimulators
- CGRP blockade? (on going trials – unsure of long-term effects?)

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Pregnancy

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Migraine in Pregnancy

- Pre-conception
  - Consider discontinuing preventive medication (emphasize non pharmacologic options)
  - Consider switching medication to one with a "safer" profile in pregnancy
  - Consider ½ life . . . shorter duration preferred
  - Will need longer time for longer acting medications
    - Onibotulinum Toxin A (3-4 months)
    - mABs (5-6 months)
- During pregnancy
  - Re-evaluate throughout pregnancy as migraine often improves during pregnancy

Burch R. Headache in Pregnancy and the Puerperium. *Neurol Clin*. 2019 Feb;37(1):31-51. doi: 10.1016/j.ncl.2018.09.004. PMID: 30470274.

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Acute Treatment

- Acetaminophen
- Caffeine in moderation
- Hydration, rest
- Metoclopramide considered safe in pregnancy
- Triptans weigh risks vs benefits (observational studies - no adverse outcomes or fetal malformation 1st trimester. 2nd and 3rd trimester is associated with increased risk of uterine atony and increased blood loss during labor and delivery)
- Acupuncture, non-invasive stimulators

Briggs GG, Freeman RK. 2014. Drugs in Pregnancy and Lactation.
Burch R. Headache in Pregnancy and the Puerperium. *Neurol Clin*. 2019 Feb;37(1):31-51. doi: 10.1016/j.ncl.2018.09.004. PMID: 30470274.

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Ondansetron and Pregnancy

- Formerly thought to be safe
- One study showed an association with cleft palate
- Two studies show an association with heart defects
- At higher dosages, may increase risk of QT interval prolongation
- Used for hyperemesis but should we use for migraine?

Briggs GG, Freeman RK. 2014. Drugs in Pregnancy and Lactation.

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Preventive Options

- Nonpharmacologic options 1st (relaxation training, thermal biofeedback, electromyographic biofeedback, cognitive behavior therapy)
- Propranolol – generally considered safe
- TCA's (amitriptyline) and Verapamil 2nd line
- SSNRI's, SSRI's – weigh risk vs benefit
- Occipital nerve blocks with Bupivacaine or Lidocaine
- B-2 and Riboflavin (approx. 200 mg twice a day for each)
- Onabotulinum Toxin A in select cases if benefits outweigh risks
- NO: Valproic acid (teratogenic), topiramate, mABs, gepants (?)
- If in doubt: refer to high risk OB provider

Burch R. Headache in Pregnancy and the Puerperium. *Neurol Clin*. 2019 Feb;37(1):31-51. doi: 10.1016/j.ncl.2018.09.004. PMID: 30470274.

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Summary

- Migraine is prevalent: 30+ million adults in US
- Migraine is in our office! 94% with headache complaint
- Migraine is disabling: #1 YLD in women <50
- ID Migraine can help make a quick diagnosis
- Migraine patients need an effective acute medication
- For those patients with 4+ migraine headache days per month consider an appropriate preventive therapy
- Be on the look out for secondary headaches
- Be familiar with “special groups” (co-manage with specialist, if needed)

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