MASSACHUSETTS GENERAL HOSPITAL
NEUROSCIENCE

The Commonest Neurological Diagnosis: Migraines

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Disclosures

Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose.

Migraine Epidemiology

- **Migraine is the third most common disease in the world with an estimated global prevalence of 14.7%.**
- **Migraine affects three-times as many women as men.**
- **In the U.S., > 39 million people suffer from migraine.**
- **Total annual healthcare costs associated with migraine are estimated to be as high as $56 billion annually in the United States**
- **More than 70 % have a family history of migraine**

ICHD-3 Criteria for Chronic migraine

- Up to 4 million patients in the US have chronic migraine
- A. Headache (tension-type-like and/or migraine-like)
  on 15 days per month for >3 months and fulfilling criteria B and C
- B. Occurring in a patient who has had at least five
  attacks fulfilling criteria B-D for 1.1 Migraine without aura and/or criteria B and C for 1.2 Migraine with aura
- C. On 8 days per month for >3 months, fulfilling any
  of the following3:
  - 1. criteria C and D for 1.1 Migraine without aura
  - 2. criteria B and C for 1.2 Migraine with aura
  - 3. believed by the patient to be migraine at onset
    and relieved by a triptan or ergot derivative
- D. Not better accounted for by another ICHD-3 diagnosis.

AAN/AHS Guidelines for Migraine Prevention

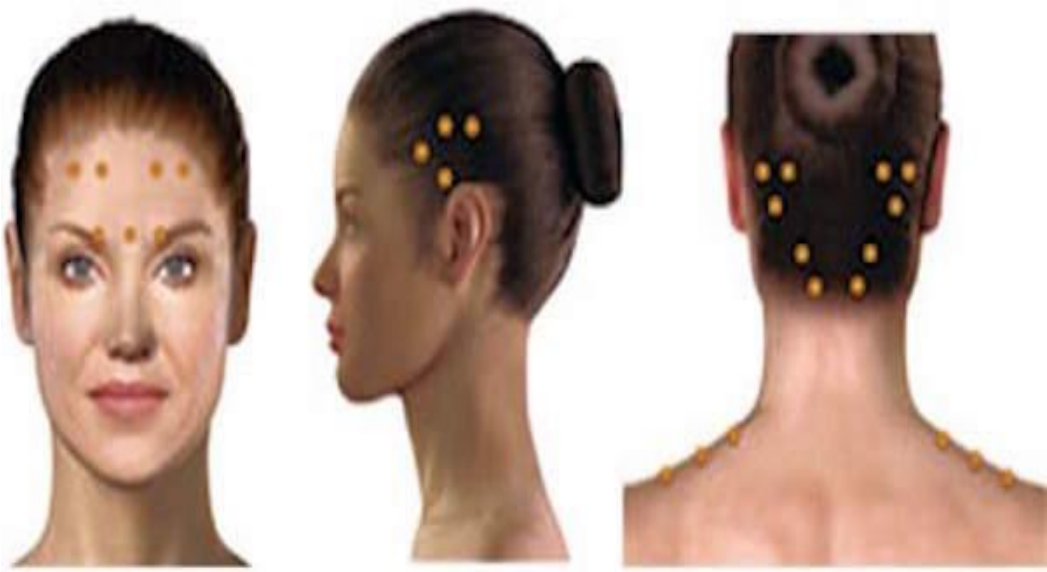
Level A: Medications with established efficacy (> 2 Class I trials) and should be offered	Level B: Medications are probably effective (one Class I or two Class II studies) and should be considered.	Level C: Medications are possibly effective (one Class II study and may be considered
Valproate Topiramate metoprolol Propranolol timolol Rizatriptan	Amitriptyline Venlafaxine Atenolol Naratriptan zolmitriptan	Lisinopril Candesartan Clonidine Guanfacine Carbamazepine cyproheptadine

OnabotulinumtoxinA (OnabotA; Botox)

- **FDA-approved in October of 2010 for chronic migraine prevention**
- **Patients 18 yo and over**
- **PREEMPT 1: no significant reduction of headache episodes after 24 wk**
- **PREEMPT 2: significant reduction of headache days, reduced disability, quality of life after 24 wk**
- **Patients who did not respond to the first treatment cycle may still respond in the second and third cycles of treatment (Silberstein et al, 2015).**

OnabotA for Chronic Migraine Treatment

- Minimum/maximum total dose per treatment cycle was 155 U into 31 sites/195 U into 39 sites
- Most insurance companies require patients having have tried at least 2 to 3 classes of preventive medications before consideration (anticonvulsants, antidepressants, or blood pressure medications).

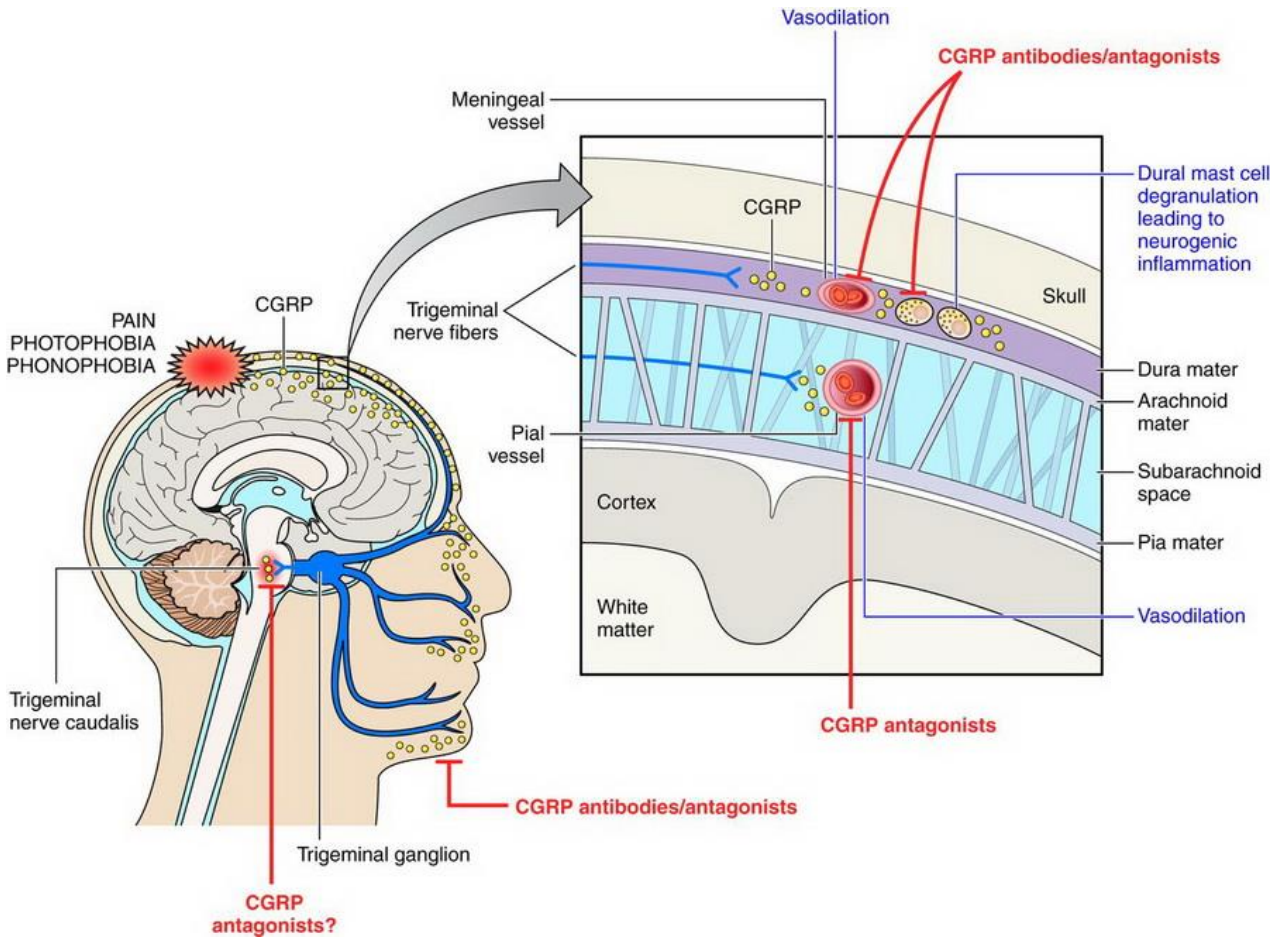


onabotulinumtoxinA (Botox) for chronic Migraine injection sites

Calcitonin Gene Related Peptide (CGRP)

- 37 –amino acid peptide, which is produced from sensory nerves that control the blood vessel activity during migraine attacks in the brain.
- Binds to CGRP receptors to cause vasodilatation and pain.
- Increase blood levels of CGRP during migraine attacks
- Triptans and Botox reduce CGRP level in migraineurs
- CGRP receptor antagonists and antibodies reduce migraine attacks

Calcitonin gene related peptide (CGRP) in migraine pathogenesis



New Treatment for Migraine Prevention- CGRP m-Antibodies

Drug	Dose	Targeting	Administration	Interval between administrations	Status
Erenumab (Aimovig)	70 or 140 mg monthly	Receptor	Subcutaneous injection	4 weeks	FDA approved
Fremanezumab (Ajovy)	Monthly 225 mg or every 3 months 225 mg x 3 injections	Ligand	Subcutaneous injection	4 or 12 weeks	FDA approved
Galcanezumab (Emgality)	240 mg for the 1st month. Then 120 mg monthly thereafter	Ligand	Subcutaneous injection	4 weeks	FDA approved

Special Considerations of anti-CGRP mAbs

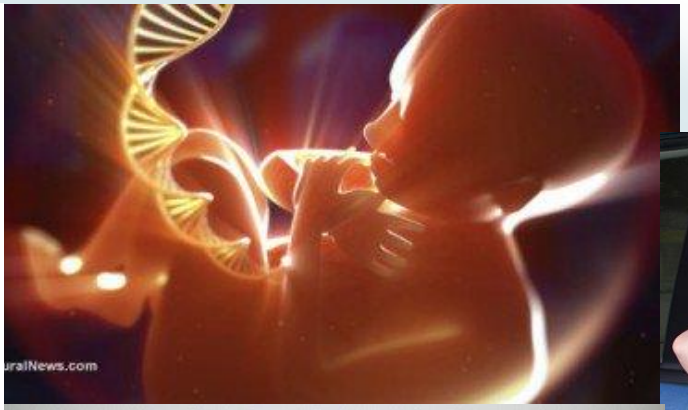
- Initial studies showed that Aimovig, Ajovy, and Emgality reduce migraine days from 1.5 to 1.9 days per month over placebo, and up to between 18.9 to 23.4% have 50% improvement over placebo.
- Pregnancy: no data in human. No adverse effects on offspring in pregnant monkeys
- Lactation: no sufficient data
- Pediatric use: under study
- Geriatric use: no sufficient data
- Neutralizing antibody: no known significance
- Latex allergy caution: Aimovig
- Autoinjector: Aimovig and Emgality

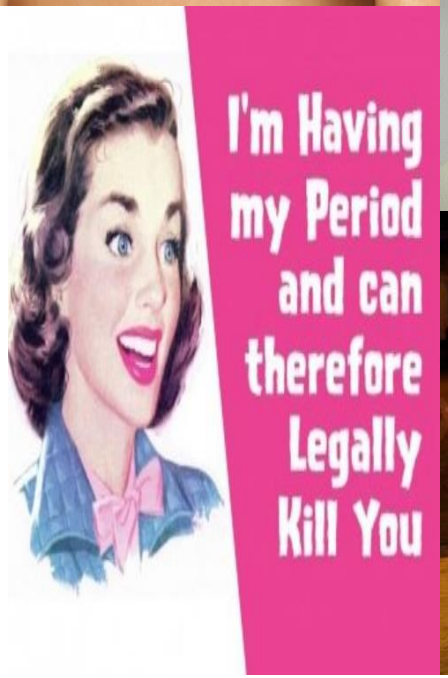
Update on Acute Migraine Treatment

Triptans	Ditan (lasmiditan or Reyvow)	Gepants (rimegepant or Nurtec, ubrogepant or Ubrelvy)
5-HT1B/D receptor agonist	5-HT_{1F} receptor agonists	Small CGRP receptor antagonists
- Can cause increased BP and coronary vasoconstriction - Avoid in patients with increased CV risk factors	- No vasoconstriction. - - Centrally acting - Side effects of Dizziness, sedation and fatigue - Fast onset - Dosing: 50, 100, or 200 mg once daily prn - No driving for 8 hrs - possible abuse potential	- No vasoconstriction; safe for patients with migraine who cannot use triptans. -Safe for CV disease, stroke or significant HTN - Slower onset but minimally side effects - Dosing: Nurtec 75 mg ODT qd prn. Ubrelvy 50, or 100 mg qd prn, max 200 mg/d. -Metabolized by CYP3A4 - Pt needs to fail 2 triptans by current guidelines

Commonly Associated Pain Conditions

- Occipital Neuralgia
- Myofascial Pain
- TMJD
- Cervicogenic Headache
- Tension Headache
- Sinus headache




I'm Having my Period and can therefore Legally Kill You

Take Home

1. Ask questions in different ways to get a complete picture ("how many HA-free days do you have per week/month").
2. Migraines are genetic. Ask about FH.
3. Migraines are comorbid with conditions like motion sensitivity and "brain freeze."
4. Migraines can present with dizziness.
5. Ask about hormonal cycles.
6. Caffeine or dietary trigger elimination can help.
7. Sinusitis or migraine?
8. Consider Botox if > 15 HA days/mo
9. Consider CGRP monoclonal antibody treatment if monthly injection is desired.

Thank You