



**Brigham and Women's Hospital**

Founding Member, Mass General Brigham

## **Advances in Diagnosis and Management of Headache**

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- Clinical focus: Headache and General Neurology
- Research focus: Migraine and Sleep



# Disclosures

- None

# Key Learning Objectives

- 1) To review advances in migraine diagnosis and clinical approach
- 2) The review advances in acute and preventive migraine treatments
- 3) To review cluster headache diagnosis, trigeminal neuralgia and treatment updates

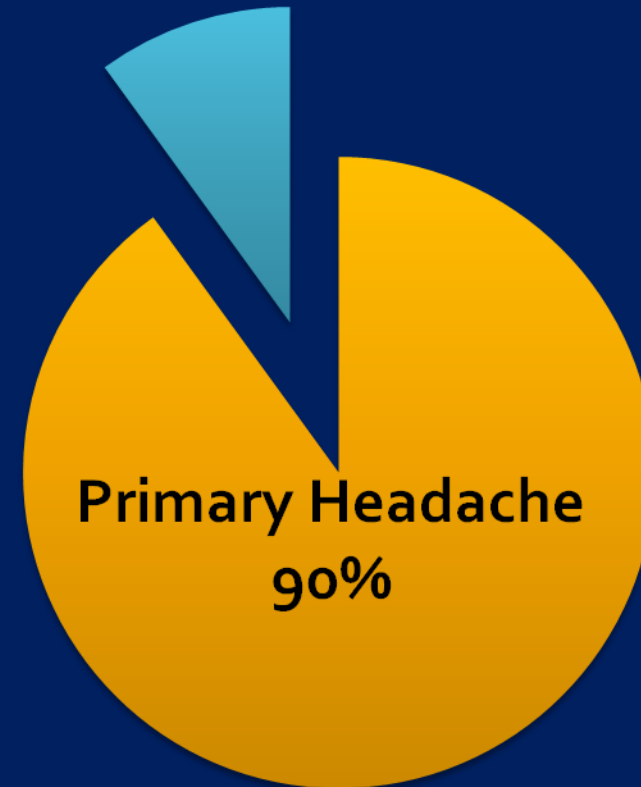
# Headache Classification and Diagnosis

- **Primary Headaches**

- Migraine
- Tension-type
- Cluster headache and TACs
- Other primary headaches

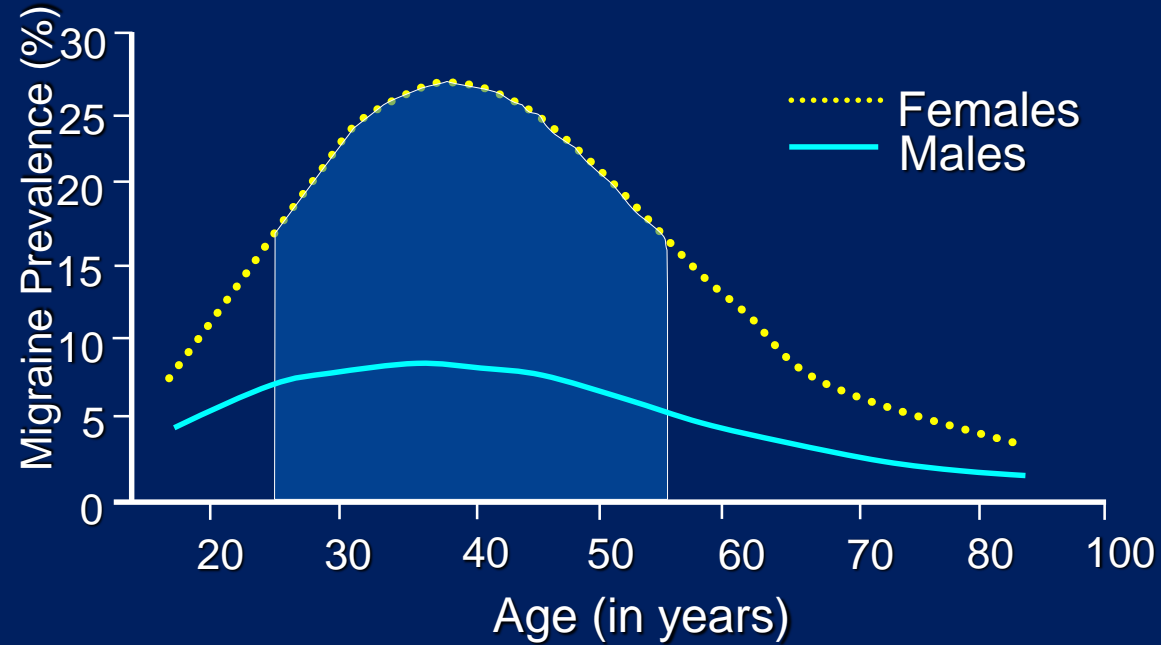
- **Secondary Headaches**

- Headaches caused by something else



# One Year Prevalence of Migraine

## Age & Sex



Approximately **1 billion people** in the world with migraine

# Migraine Associated Disability

- **#2** cause of disability overall and **#1** cause of disability in those under 50 years of age in 2016



# 2018 ICHD-3 Diagnostic Criteria for Migraine and TTH

Migraine Without Aura	Migraine with Aura	Tension type headache
5+ attacks	2+ attacks	10+ attacks
4 to 72 hours (untreated)	---	30 minutes to 7 days
Two of the following <ul style="list-style-type: none"> <li>- Unilateral location</li> <li>- Pulsating quality</li> <li>- Moderate or severe intensity</li> <li>- Aggravation by or causes avoidance of routine physical activity</li> </ul>	1+ fully reversible aura symptoms: <ul style="list-style-type: none"> <li>- Typical: Visual (hemianopia), Sensory, Speech and/or language</li> <li>- Motor</li> <li>- Brainstem</li> <li>- Retinal (monocular)</li> </ul>	Two of the following <ul style="list-style-type: none"> <li>- Pressing/tightening quality</li> <li>- Bilateral location</li> <li>- Mild to moderate intensity</li> <li>- No aggravation by routine physical activity</li> </ul>
At least one of the following: <ul style="list-style-type: none"> <li>- Nausea and/or vomiting</li> <li>- Photophobia and phonophobia</li> </ul>	Three of six: <ul style="list-style-type: none"> <li>- spreads gradually over <math>\geq 5</math> minutes</li> <li>- lasts 5–60 minutes</li> <li>- two or more aura symptoms occur in succession</li> <li>- Unilateral</li> <li>- Positive</li> <li>- the aura is accompanied, or followed within 60 minutes, by headache</li> </ul>	Both: <ul style="list-style-type: none"> <li>- No nausea or vomiting</li> <li>- No more than one of photophobia or phonophobia (ie, you can have either one and still be diagnosed with TTH)</li> </ul>



# Migraine aura subtypes

## Subtypes

- Typical:
  - Visual
  - Sensory
  - Speech and/or language
- Brainstem aura
  - At least two: Dysarthria, Vertigo, Tinnitus, Hypacusis, Diplopia, ataxia not attributable to sensory deficit, decreased level of consciousness (GCS  $\leq 13$ )
- Hemiplegic
  - Fully reversible motor weakness\* + fully reversible typical aura
  - \*weakness generally lasts <72 hours, but may persist for longer
- Retinal (monocular) – extremely rare



Chronic migraine defined as **migraine or strongly suspected migraine** on  $\geq 15$ d/mo

*ICHD3 1.3 Chronic Migraine*

A. **Headache on  $\geq 15$  d/mo** for >3 mo

B. In a patient who has had  $\geq 5$  attacks fulfilling criteria for  
1.1 *Migraine without aura* or 1.2 *Migraine with aura*

C. **On  $\geq 8$  d/mo** for >3 mo fulfilling any of the following:

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

## 2022 ACR Appropriateness Criteria:

migraine or tension type headache w/ normal neurologic exam

- Initial imaging = Usually Not Appropriate

# 2020 AHS Imaging guidelines for migraine

- Systematic review of CT, MRI >40 years (23 studies)
- Common abnormalities:
  - chronic ischemia (CT)
  - non-specific white matter lesions (MRI)
- No need for neuroimaging in patients with migraine with normal neurological exam, with no atypical features or red flags
  - Red flags include fever, immunosuppression, papilledema, pregnancy

# 2021 European Headache Federation Imaging guidelines for migraine

- Only role is to confirm/exclude causes of secondary headache suspected on basis of red flags
- Imaging can be harmful (exposure to radiation)
- MRI preferred to CT, but can reveal insignificant abnormalities which can alarm the patient and lead to further unnecessary testing

# 2022 ACR Appropriateness Criteria: Conditions where imaging is Usually Appropriate

Headache/condition	Imaging
Cluster headache	MRI with and without contrast
Headache with features of IIH	MRI head w or w/o contrast, CT head w/o contrast
Headache with features of hypotension	MRI head with and w/o contrast
New headache/pattern during pregnancy or peripartum	MRV w/o IV contrast, CTV
Headache with “red flags”	MRI w and w/o contrast, MRI w/o contrast, CT w/o contrast

# Migraine comorbidities and disease progression/treatment

- Episodic migraine associated with: Insomnia, Anxiety/Depression, Gastric Ulcers/GI bleeding, Epilepsy
- Comorbidity associated with future risk of chronic migraine
- High frequency/chronic migraine patients more likely to have severe disability, chronic pain, arthritis, high cholesterol, ulcers and depression
- Addressing comorbidities (CBT for mood or insomnia) reduces headache days significantly

# Migraine and CV risk

- Epidemiologic studies report that migraine with aura is a risk factor for MI and stroke (~2x – 6 vs 2.5 events/100,000 people)
- Association is stronger for women, women <45, those who smoke and those on estrogen containing OCPs (6x – 15 events/100K people)
- Recommended that women with aura avoid combined OCPs
  - Contraindicated by WHO and ACOG
  - Use caution/consider other risks (age >35, smoking status, HTN) by International Headache Society and Amer Headache Society
  - Lack of good quality studies with low dose estrogen use

Oie et al. 2020 Migraine and risk of stroke. *Journal of Neurology, Neurosurgery and Oncology*.

Sheikh et al 2017. Risk of Stroke Associated With Use of EstrogenContaining Contraceptives in Women With Migraine:A Systematic Review. *Headache*



# Migraine and CV risk

- 2021 European Society for Cardiology Guidelines recommend migraine with aura should be considered in CVD risk assessment (Class IIA)
- Not currently in AHA or USPHS guidelines
- One recent model added migraine with aura in a risk prediction algorithm for women – showed it did not improve risk stratification (likely due to low prevalence of MA with other CV risk factors at the population level)
- May warrant discussion for intermediate risk patients

Visseren et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. European Heart Journal 2021.

Rist et al. Contribution of Migraine to Cardiovascular Disease Risk Prediction. Journal of American College of Cardiology. 2023

# Acute Migraine Treatments

# Selected Therapies for Acute Migraine (pre-2020)

Class	Mechanism of action	Medications	Select side effects
Acetaminophen*		At 1000 mg, may be effective for nonincapacitating migraine attacks	Hepatotoxicity at higher doses
NSAIDs*		Aspirin, Diclofenac, Ibuprofen, Naproxen*	GI upset, bleeding, may increase risk of MI or stroke with increased duration of use
Triptans*	5-HT <sub>1b/d</sub> agonists	Short acting: Suma- (PO/SQ/NS), Zolmi- (PO/NS), Ele-, Almo-, Riza- Long acting: Frovatriptan and naratriptan	Contraindicated in those with CAD (cause vasoconstriction), Chest or facial muscle tightness
Ergotamines	5-HT <sub>1b/1d/1f</sub> agonist; 5-HT <sub>1a/2a</sub>	Dihydroergotamine nasal spray* (also IV/IM/SQ)	Contraindicated in those with CAD or PVD. FDA black box warning with CYP3A4 inhibitors
Antiemetic agents	Anti-dopaminergics	Chlorpromazine, metoclopramide, prochlorperazine (PO/suppository)	Sedation, restlessness (akathisia), dystonic reactions

\*These have a strong level of evidence (Level A) by the American Headache Society to support their use in an acute migraine attack, although for tylenol this is only true for non-incapacitating attacks. Modified from Charles A. N Engl J Med 2017;377:553-561 and Ailani J. Continuum June 2021; 597-612

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Ditans	5-HT <sub>1f</sub> agonists (no vasoconstriction)	Lamiditan	FDA warning – no driving for 8 hours after. Schedule V controlled substance
Gepants	CGRP-receptor antagonists	Ubrogepant, Rimegepant	Nausea

# Selected triptans, doses for adults:

		Typical Dose (mg)	T1/2 (h)	Least side effects	Headache Freedom at 2 h/24h
Faster acting oral	Rizatriptan	5 or 10 mg	2-3		Second best
	Sumatriptan	50 or 100 mg	2.5		x
	Zolmitriptan	1.25 or 2.5 mg	3		Third best
	Almotriptan	12.5 mg	3-4	X	x
	Eletriptan	20 or 40 mg	4		Best (68%)/ Best(54%) of all
Longer-acting oral	Frovatriptan	2.5 mg	26	X	x/unknown
	Naratriptan	2.5 mg	6	X	x/same as placebo
Subcutaneous	Sumatriptan	4 or 6 mg			x
Intranasal	Sumatriptan	10 or 20			x
	Zolmitriptan	2.5 or 5 mg			x

# Safety warnings of triptans (5HT-1B/D agonists) - updates

- Contraindicated in those with CAD/Angina or at high risk (uncontrolled HTN)
  - *<2 vascular risk factors, risk of vascular event was 4/100,000 treated attacks*
  - History of stroke, TIA or hemiplegic or basilar migraine
- Serotonin syndrome with coadministration of SSRIs/SNRIs is found to be exceedingly rare (0.6 cases/10,000 person-years) and about 25% of patients on triptans are coprescribed a SSRI/SNRI (continues to have FDA advisory warning)

Ref: Sumatriptan - FDA approved labeling text, November 2013, Martin VT, Goldstein JA. Evaluating the safety and tolerability profile of acute treatments for migraine. *Am J Med.* 2005; 188 (Suppl 1): 36s-44s

Orlova Y, Rizzoli P, Loder E. Association of Triptan Antimigraine Drugs and Selective Serotonin Reuptake Inhibitor or Selective Norepinephrine Reuptake Inhibitor Antidepressants With Serotonin Syndrome. *JAMA Neurol.* 2018 May.

# Newer Acute Migraine Treatments

- Lasmiditan (Reyvow) (5HT-1F agonist)
  - FDA approval October 2019
  - No coronary artery vasoconstriction
  - Side effects: dizziness, sedation, driving impairment (for 8 hours)
- Gepants (CGRP-receptor antagonist)
  - FDA approval December 2019
  - Ubrogepant 50 or 100 mg (Ubrelvy)
  - Rimegepant 75 mg (Nurtec) – fast acting oral disintegrating (both acute and preventive)
  - Side effects: nausea, somnolence, dry mouth

Consider in patients with contraindications to triptans or failed to respond to at least 2 oral triptans

(American Headache Society Consensus Statement)

# Acute treatments for migraine that are discouraged

- Bultalbutal containing medications (ie, butalbital, Tylenol, caffeine +/-codeine)
  - High overuse potential and risk for medication overuse headache
  - Sudden cessation in habitual users can result in seizures/coma
- Opiates and benzodiazepines
  - Rarely prescribed and should never be first line
  - Contrary to guidance, 37% currently use or keep on hand opioid medications to treat headaches (contrary to guidance) (CaMEO study, representative of US population)

Hutchinson S, Lipton RB, Ailani J, Reed ML, Fanning KM, Manack Adams A, Buse DC. Characterization of Acute Prescription Migraine Medication Use: Results From the CaMEO Study. Mayo Clin Proc. 2020 Apr; 95(4):709-718  
Lipton RB, Buse DC, Friedman BW, Feder L, Adams AM, Fanning KM, Reed ML, Schwedt TJ



## ED treatment of migraine

- Should offer (level B)
  - IV metoclopramide and prochlorperazine
  - SC sumatriptan
  - Dexamethasone to prevent recurrence
- May avoid (level C)
  - Injectable morphine and hydromorphone and hydromorphone should be avoided as first line

## Treatment of status migrainosus (>72 hours)

- Dihydroergotamine IV infusions
  - Raskin protocol, q8h, contraindicated in those with CAD/Angina
- Others
  - Valproic acid 500 mg IV, Magnesium Infusion, IV lidocaine, more frequent dosing of IV acute medications

Orr SL, Friedman BW, Christie S, Minen MT, Bamford C, Kelley NE, Tepper D. Management of Adults with Acute Migraine in the Emergency Department: The American Headache Society Evidence Assessment of Parenteral Pharmacotherapies. *Headache*. 2016; 56:911-940

# Preventive Treatments

# When to initiate a preventive

- Attacks significantly interfere with daily routine despite acute treatment
- Frequent attacks (also consider disability)
  - SHOULD offer for 3 HA Days/Month with severe disability; 4 with some disability and 6 with no disability)
- Acute migraine treatment is ineffective or contraindicated
- Medication-overuse headache is present
- Patient preference

TABLE 4 Criteria for identifying patients for preventive treatment<sup>a</sup>

Prevention should be ...	Headache days/month	Degree of disability required <sup>a</sup>
Offered	6 or more	None
	4 or more	Some
	3 or more	Severe
Considered	4 or 5	None
	3	Some
	2	Severe

<sup>a</sup>As can be measured by the Migraine Disability Assessment Scale, Migraine Physical Function Impact Diary, or Headache Impact Test.

Ailani et al. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache*. 2021; 61:1021-1039.

# Medication overuse headache



- Headache occurring on  $\geq 15$  days/month in a patient with a pre-existing headache disorder (*typically chronic migraine and you code for both*)
- Regular overuse for  $> 3$  months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache
  - Ergotamine  $> 10$  days/month
  - Triptan  $> 10$  days/month
  - Acetaminophen  $> 15$  days/month
  - NSAID  $> 15$  days/month
  - Opioid  $> 10$  days/month
  - Combo analgesic  $> 10$  days/month
- Not better accounted for by another ICHD-3 diagnosis.

# Classes of Treatments for Migraine Prevention

Class	
Antiepileptics	Divalproex sodium*, topiramate*, gabapentin
Antidepressant drugs	Amitriptyline and other tricyclic antidepressants, venlafaxine and other serotonin norepinephrine reuptake inhibitors (SNRIs)
Beta-blockers	Propranolol*, metoprolol, timolol*
Other antihypertensive drugs	Verapamil, lisinopril, candesartan
Neurotoxins	OnabotulinumtoxinA* (chronic migraine only)
Calcitonin gene-related peptide monoclonal antibodies	Erenumab (SQ)*, fremanezumab (SQ)*, galcanezumab (SQ)*, eptinezumab (IV)
Other	Memantine, cyproheptadine
Herbal and nutritional supplements	Magnesium, vitamin B2 (riboflavin), feverfew, coenzyme q10 and melatonin

\*FDA approved for migraine

# Migraine treatment - Preventive

Drug	Level of Evidence	Migraine Dose	Side effects/clinical notes
Topiramate	A	100 mg daily	modest weight loss, slightly increases risk of kidney stones and acute angle closure glaucoma, avoid in pregnancy
Propranolol and Metoprolol	A	60 mg daily	bradycardia, exercise intolerance, asthma exacerbation May help with comorbid anxiety
Divalproex sodium	A	500-1000 mg daily	Neural tube defects, typically avoided in women of reproductive age
Amitriptyline	B	10-50mg nightly	constipation, dry-mouth, weight gain, can prolong QT Lower doses than what is used for depression, may help with sleep initiation
OnabotulinumtoxinA (chronic migraine)	A	155 units q3 months	Lack of systemic side effects, may cause focal weakness, do not use in those with neuromuscular disease

Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology* 2012;78(17): 1337-1345.

# Which preventive to choose?

Clinical situation	Contraindicated/Avoid	Consider
Hypotension	Anihypertensive drugs	
Nephrolithiasis	Topiramate, zonisamide	
Possibility of pregnancy	Valproate, topiramate, lisinopril, candesartan, feverfew	Propranolol first line; amitriptyline, verapamil, coenzyme Q10 second line
Glaucoma	Topiramate (narrow-angle glaucoma), amitriptyline	
<i>Obesity</i>	<i>Valproate, amitriptyline</i>	<i>Topiramate</i>
<i>Anxiety</i>	<i>Topiramate</i>	<i>Beta-blockers</i>
<i>Insomnia</i>	<i>Memantine</i>	<i>Amitriptyline</i>
<i>Fatigue/exercise intolerance</i>	<i>Beta-blockers</i>	<i>Topiramate, venlafaxine</i>
<i>Frequent aura</i>		<i>Verapamil, valproate, magnesium topiramate</i>

# Newer Treatments for Migraine Prevention (since 2018) – CGRP m-Ab and some gepants

- Erenumab
  - 70 or 140 mg SQ monthly
  - Constipation, hypertension, hypersensitivity
- Fremanezumab
  - 225 mg SQ monthly (most common) or 675 mg SQ q3months
- Galcanezumab
  - 240 mg SQ loading dose, then 120 mg SQ monthly
- Eptinezumab
  - 100-300 mg IV infusion every 3 months
- Rimegepant 75 mg every other day; Atogepant 60 mg daily

MABs Contraindicated in pregnancy and breastfeeding. Should be stopped prior to attempting pregnancy.



# AHS 2024 position statement on CGRP tx

- The evidence for the efficacy, tolerability, and safety of CGRP-targeting migraine preventive therapies (the monoclonal antibodies: erenumab, fremanezumab, galcanezumab, and eptinezumab, and the gepants: rimegepant and atogepant) is substantial, and vastly exceeds that for any other preventive treatment approach...and that serious adverse events associated with CGRP-targeting therapies are rare.
- "CGRP-targeting therapies should be considered as a first-line approach for migraine prevention along with previous first-line treatments without a requirement for prior failure of other classes of migraine preventive treatment."

# Treating migraine in pregnancy: preventive meds

Medication	Safety	Effectiveness
<b>Propranolol</b>	<b>More</b>	<b>Most</b>
Memantine		Moderate
Magnesium, CoQ10		Least
<b>Botox, amitriptyline/nortriptyline</b>	Moderate	Most
Venlafaxine		Moderate
Riboflavin, Verapamil, Gabapentin		Least
CGRP (mAb and gepants), Topiramate, VPA	Least	Most
Lisinopril/Candesartan		Moderate

# Treating migraine in pregnancy: acute meds

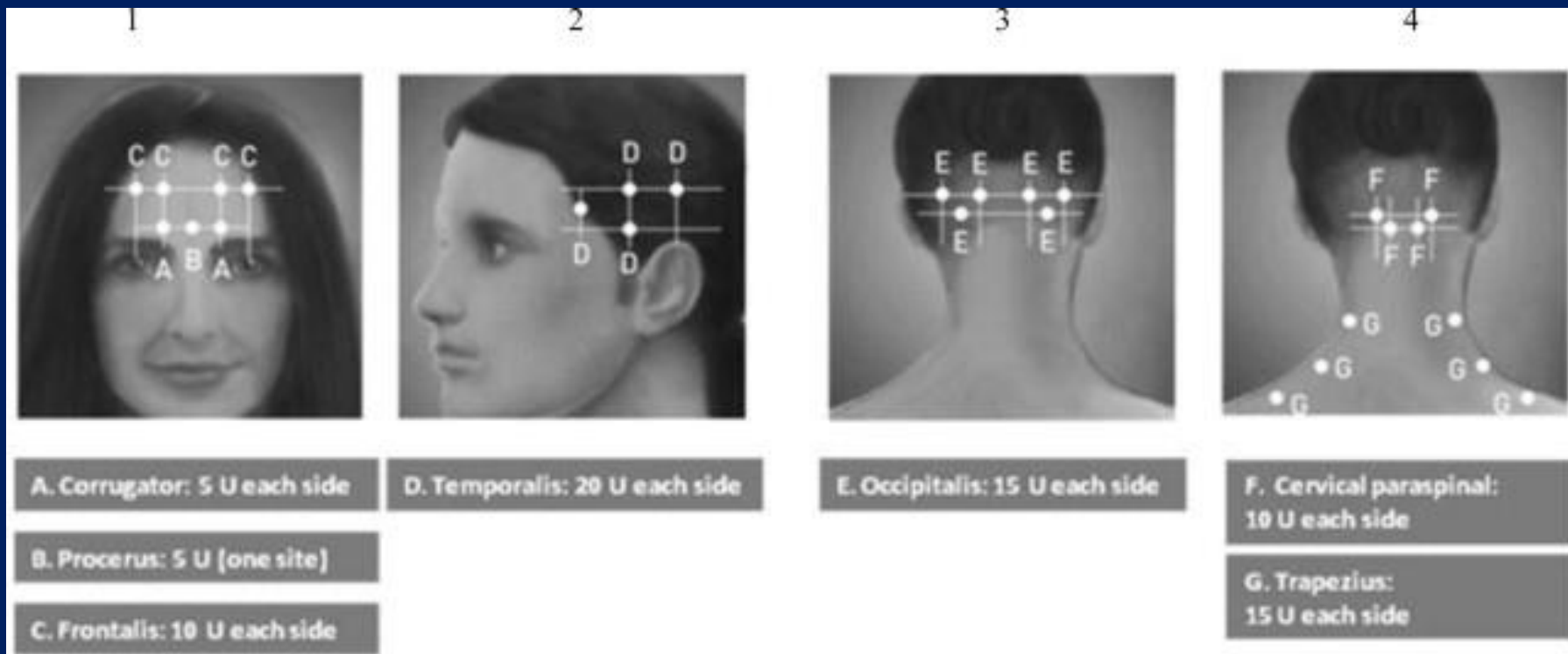
Medication	Safety	Effectiveness
Metoclopramide, Lidocaine (SQ), Acetaminophen, Cyclobenzaprine,	More	Moderate
Ondansetron (nausea adj), Triptans	b/w safest and moderate	Most
Ibuprofen (2 <sup>nd</sup> trimester only), Prednisone, Prochlorperazine	Moderate	Moderate
Oxycodone, Butalbital (gen not recc for migraine)	Moderate	Least
Lasmiditan, Gepants, Magnesium (IV), Ergots	Least	Least

# FDA cleared neuromodulation devices for migraine

- Applied externally for intermittent use
- Hand-held vagal nerve stimulator (gammaCore)
  - acute and preventive, also for cluster
  - Blocks connections from vagus n to trigeminal n
- Supraorbital stimulation (Cefaly)
  - Acute and preventive
  - Stimulates A-beta fibers to mask C fibers
- Transcranial magnetic stimulation (SpringTMS)
  - May block cortical spreading depression
- Remote electrical stimulation (Nerivio)
- Very few side effects (paresthesia, vasovagal syncope for gammaCore, contraindicated with implanted devices for gammaCore and SpringTMS)

# Migraine treatment (preventive, cont'd)

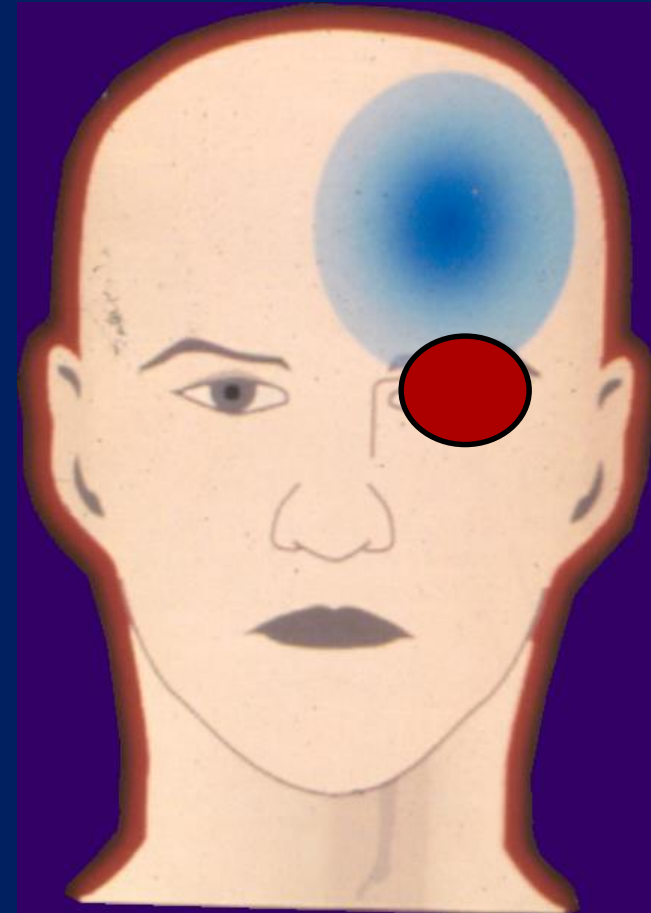
- Chronic migraine only (>15 days per month)
  - Botulinum toxin (FDA approved protocol, 31 injections, every 3 months)



Cluster headache and the trigeminal  
autonomic cephalalgias

# ICHD3 Diagnostic Criteria For Cluster Headache

- Attack duration: 15 minutes to 3 hours; once daily to 8 per day
- Episodic cluster period= 7 days to 1 year, pain free remission of at least 3 months
- Unilateral orbital/ supraorbital/ temporal location; severe or very severe
- One of these ipsilateral autonomic signs/symptoms
  - Rhinorrhea, conjunctival injection/ tearing, meiosis, ptosis, eyelid edema/ facial swelling
  - Or general restlessness



# Cluster Headache

## Clinical features:

- “the worse pain known”
- Seasonal/diurnal patterns
- More common in men (M:F 3:1)
- Onset: 20s-40s
- Risks: smoking, excessive alcohol intake
- Often misdiagnosed as migraine
- Patients are at high risk of depression, increased risk of suicide



Wei & Goadsby. Cluster headache pathophysiology – insights from current and emerging treatments. *Nature Reviews Neurology*. 17, 308-324 (2021)

Edvardsson B. Symptomatic cluster headache: a review of 63 cases. *Springerplus*. 2014 Feb 3, 3:64




# Cluster Headache/TACs/TN - Workup

- American College of Radiology 2019 criteria: Should be investigated with MRI of the brain, contrast recommended
  - r/u prolactinoma, carotid dissection and AVM
  - Recent data shows that it does not have to be a dedicated pituitary MRI

# Hemicrania Continua

- Unilateral, side-locked, continuous pain of moderate intensity with periods of severe exacerbation
- Ipsilateral autonomic features, including conjunctival injection, tearing, nasal congestion, even ptosis, are reported.



Indomethacin  
responsive headache  
(75 mg TID x2 weeks  
= adequate trial)

# Other Trigeminal Autonomic Cephalalgias and Paroxysmal Hemicrania Continua

Name	Location	Duration	Attack frequency/day	Associated Features	Treatment
<b>Cluster</b>	Unilateral Orbital	15-180 min	1-8	Lacrimation, conjunctival injection, rhinorrhea	Verapamil, inhaled oxygen 15 L/min
<b>Paroxysmal Hemicrania</b>	V1, ophthalmic division	2-30 min	>5	Lacrimation, conjunctival injection, rhinorrhea	Indomethacin – with complete control
<b>SUNCT</b>	Unilateral orbital to temporal region	15 s to 4 min	3-200	Conjunctival injection AND lacrimation	Lamotrigine, IV lidocaine
<b>SUNA</b>	Unilateral orbital to temporal region	15 s to 4 min	3-200	Conjunctival injection OR lacrimation + rhinorrhea/nasal congestion	Lamotrigine, IV lidocaine

SUNCT = short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing

SUNA = short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms

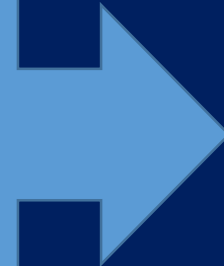
# Cluster headache – treatment basics

- Abortive

- 100% oxygen – nonrebreather mask for 15 minutes (10-15L)
- Sumatriptan SQ injection (given brevity of attacks)

- Bridge

- Steroids tapers –initiated at the beginning of a cluster cycle.
- +/- greater occipital nerve blocks (lidocaine+steroid)



- Preventive

- Verapamil (high doses, watch for PR interval)
- Lithium
- **Galcanezumab 300 mg qmonthly until cluster cycle ends**
- Less evidence for: valproate, gabapentin, topiramate, **neuromodulatory devices**



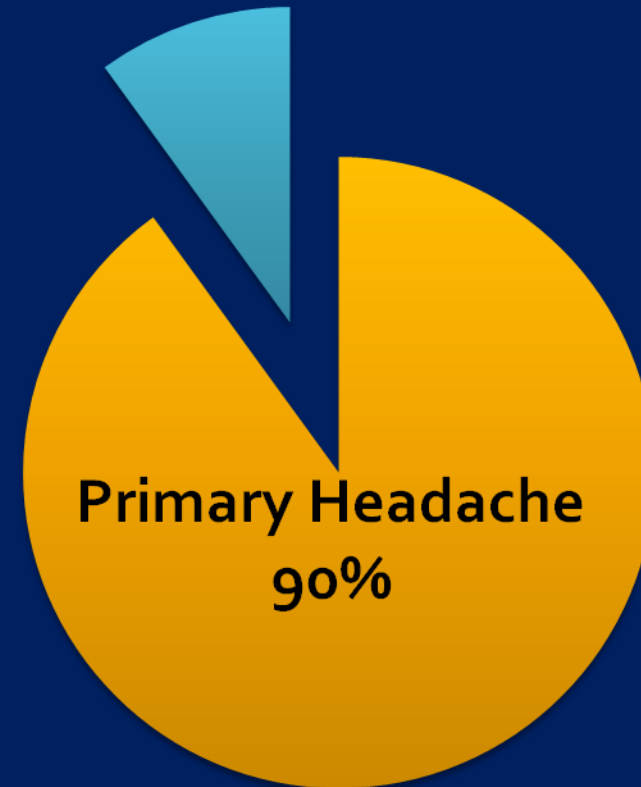
# Trigeminal neuralgia (“tic douloureux”)

- Brief (second to <2 minutes) recurrent paroxysms of severe neuropathic unilateral facial pain in the distribution of one or more divisions of the trigeminal nerve
- Electric shock-like, shooting, stabbing or sharp in quality
- Women: men (3:1)
- May be precipitated by innocuous stimuli (eg, chewing, talking)

Differentiated from cluster by:  
lack of autonomic symptoms, no radiation  
beyond divisions of trigeminal nerve and  
short attack duration

# Headache Classification and Diagnosis

- **Primary Headaches**
  - Migraine
  - Tension-type
  - Cluster headache and TACs
  - Other primary headaches
- **Secondary Headaches**
  - Headaches caused by something else
- **Neuropathies & Facial Pains**



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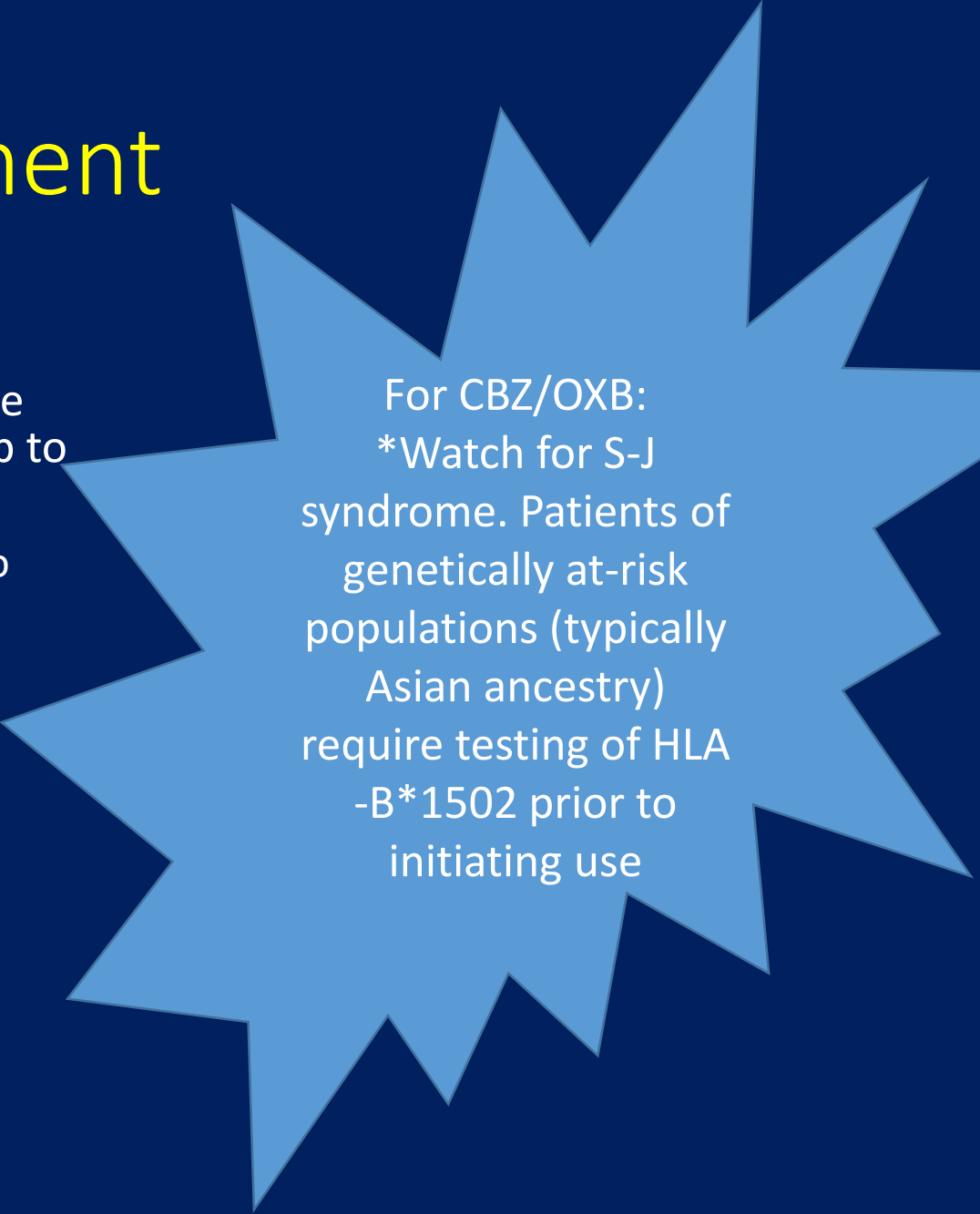
# Trigeminal neuralgia subtypes

- Classical
  - Neurovascular compression of the trigeminal nerve (demonstrated during surgery or MRI with atrophy/dislocation at the root)
- Secondary
  - Etiologies include MS plaques (rare bilateral symptoms), tumors in the cerebellopontine angle, and AV malformations
- Idiopathic
  - Rare, 11% of patients, includes neurovascular *contact* with trigeminal nerve root (no compression)



# Trigeminal neuralgia treatment

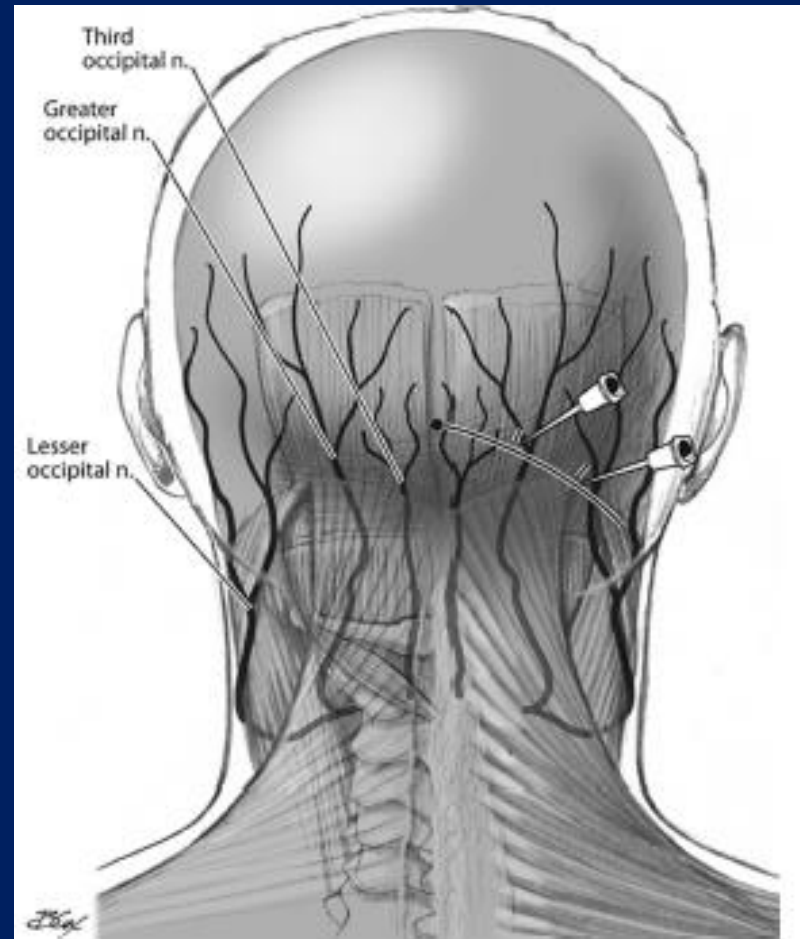
- First line:
  - Carbamazepine (200-1200 mg/day) or oxcarbazepine (600-1800 mg/day) in BID dosing - reduces pain in up to 90% of patients.
    - CBZ auto-induces its metabolism, so typically need to increase dose at 2-3 weeks
- Second line:
  - Lamotrigine, baclofen, pregabalin or gabapentin, topiramate, valproate
- Surgery (microvascular decompression):
  - If refractory to medical treatment



For CBZ/OXB:  
\*Watch for S-J syndrome. Patients of genetically at-risk populations (typically Asian ancestry) require testing of HLA -B\*1502 prior to initiating use

# Occipital Neuralgia

- Paroxysmal shooting/stabbing pain in dermatomal distribution of the GON, LON or 3rdON
- Pain typically radiates forward
- Associated with dysesthesia during stimulation of the scalp, tenderness over the emergence of the nerve
- Temporarily improved by local anesthetic block
- Patients with migraine also have may have tenderness over posterior skull base, and sometimes respond well to nerve blocks
- Secondary causes very rare



**FIGURE 7-3**

Location of greater occipital, lesser occipital, and third occipital nerves with location of greater and lesser occipital nerve blocks.

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# Occipital neuralgia treatment

- Physical therapy
- Tricyclic antidepressants, antiepileptics
- Nerve blocks (pain relief for a few weeks or months)
- Rare: pulsed radiofrequency treatment, Botox

# Less common neuralgias

Neuralgia	Features	Nerve	Distribution	Comments
Glossopharyngeal <sup>37</sup>	Sharp, stabbing, severe	CN IX and X	Side of the throat, tonsillar area, base of tongue	First desc in 1920. Mostly idiopathic, rarely symptomatic
Supraorbital	long-lasting attacks of moderate to severe frontal pain	SON (see Fig 1)	Frontal and SO region	Tenderness over the SO notch
Supratrochlear <sup>38</sup>	Long-lasting or episodic pain and sensory disturbance	STN	Medial forehead	Tenderness in the SO rim medially over the nerve. Distinguish from SON
N. Intermedius	Paroxysmal brief shock-like	Sensory branch of VII	Deep auditory canal	
Auriculotemporal Neuralgia	Paroxysmal, brief shock-like	ATN (see Fig 1)	Anterior to the tragus	

# Summary Points

- Migraine is a clinical diagnosis, imaging is only recommended for atypical features or red flags
- Address comorbidities in all migraine patients and cardiovascular risk in patients with migraine with aura.
- New classes of migraine medications (ditan, gepants, CGRP mAb) and devices expand preventive and abortive options
- Better understanding of safer medications to use for migraine in pregnancy
- Cluster headache requires imaging to r/o secondary conditions, some evidence to support Galcanezumab (CGRP mAb) or consider neuromodulatory device

# Key References

- International Classification of Headache Disorders – 3: [www.ichd-3.org](http://www.ichd-3.org)
- Evans RW et al. Neuroimaging for Migraine: The American Headache Society Systematic Review and Evidence-Based Guideline . *Headache* 2020; 60; 318-336
- Charles A. N Engl J Med 2017;377:553-561 and Ailani J. Continuum June 2021; 597-612
- Do, T.P., Guo, S. & Ashina, M. Therapeutic novelties in migraine: new drugs, new hope? J Headache Pain (2019) 20: 37.
- AHS Consensus Statement. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. *Headache*. 2019; 59:1-18
- Hutchinson S, Lipton RB, Ailani J, Reed ML, Fanning KM, Manack Adams A, Buse DC. Characterization of Acute Prescription Migraine Medication Use: Results From the CaMEO Study. *Mayo Clin Proc*. 2020 Apr; 95(4):709-718
- Burch, R. Preventive Migraine Treatment. *Continuum (Minneap Minn)*. 2021; 27(3, Headache):613-632
- Orr SL, Friedman BW, Christie S, Minen MT, Bamford C, Kelley NE, Tepper D. Management of Adults with Acute Migraine in the Emergency Department: The American Headache Society Evidence Assessment of Parenteral Pharmacotherapies. *Headache*. 2016; 56:911-940
- Ailani et al. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache*. 2021; 61:1021-1039.
- Rayhill, M. CONTINUUM: Lifelong Learning in Neurology 28(1):72-92, February 2022
- Suri et al. Cluster Headache: A Review and Update in Treatment. *Curr Neurol Neurosci Rep*. 2021



Thank you

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