


## OVERVIEW OF HEADACHES FOR THE PRIMARY CARE PROVIDER

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October 25<sup>th</sup>, 2024



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## Disclosures

- ☐ No financial disclosures
- ☐ Will mention use of off label drugs



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## Objectives

- ☐ How to approach patients with headaches
- ☐ Common headache syndromes
- ☐ Uncommon headache syndromes
- ☐ Primary vs Secondary headache syndromes
- ☐ Update on migraine treatment

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## Headache History

- ☐ Open ended questions
- ☐ Timing
  - Age of onset
  - How often
  - Length (without meds)
  - How often are you headache free
- ☐ Quality/characteristics
  - Type of pain
  - Activity
  - Location - always same location?
  - Positional
  - Severity
- ☐ How many type of headaches
- ☐ Associated symptoms
  - Nausea, vomiting, photo or phonophobia
- ☐ “take me through a typical headache”
- ☐ Relationship to menarche, menses, pregnancy
- ☐ Over time
  - Character, duration, frequency, intensity
- ☐ Warning/aura and/or prodrome
  - Aura precedes or occurs during a headache
  - Can be without pain
  - 30% of migraines
- ☐ Triggers
- ☐ What do you do during a headache?
- ☐ Family history
  - 80% of children have a family hx

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## Headache Tracking

Diary apps		
Migraine Buddy	migrainebuddy.com	Migraine tracking app
Manage My Pain Pro	managemypainapp.com	Tracks headaches and other chronic pain
Migraine Mentor	bontriage-headache-tracker-ios.soft112.com	Uses artificial intelligence to provide patient feedback
iHeadache	iheadache.com	Detailed headache tracking
Migraine Insight	migraineinsight.com	Migraine tracking app

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## Exam

- ☐ Vital signs
- ☐ General neuro exam
- ☐ Fundoscopic exam
  - Optometry/ophthalmology
- ☐ Palpation of nerves and temporal vessels
- ☐ Mallampati

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## When to Image?

- ❑ Not recommended for the standard headache patient
- ❑ Consider when:
  - s/s concerning for secondary headache
  - New onset headache over age 50
  - Abnormal neuro exam
  - Change in characteristics of the headache
- ❑ MRI preferred

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## Primary vs Secondary

- ❑ Primary headache
  - Migraine, tension, cluster.....
  - Majority of headaches (migraine)
  - Rely in ICHD-3 classification
- ❑ Secondary headache
  - Underlying pathological condition
    - Infection, mass lesion, CSF leak.....
  - History and exam can help identify red flags

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## Red Flags

TABLE 1-2	SNNOOPIQ List of Headache Red Flags*
1) Onset pattern	Primary (secondary headaches listed in ICHD-3 categories)
2) Systemic symptoms including fever <sup>†</sup>	Headache attributed to infection or nonvascular intracranial disorders, carotid or pheochromocytoma
3) Headset in history	Neoplasms of the brain, metastasis
4) Neurologic deficit or dysfunction (including decreased consciousness)	Headaches attributed to vascular, nonvascular intracranial disorders, brain abscess and other infections
5) Onset of headache is sudden or abrupt	Subarachnoid hemorrhage and other headaches attributed to cranial or cervical vascular disorders
6) Older age (50 years)	Giant cell arteritis and other headache attributed to cranial or cervical vascular disorders
7) Pattern change or recent onset of headache	Neoplasms, headaches attributed to vascular, nonvascular intracranial disorders
8) Positional headache	Intracranial hypertension or hypotension
9) Precipitated by sneezing, coughing, or exertion	Posterior fossa malformations, Chiari malformation
10) Papilloedema	Neoplasms and other nonvascular intracranial disorders, intracranial hypertension
11) Progressive headache and atypical presentations	Neoplasms and other nonvascular intracranial disorders
12) Pregnancy or puerperium	Headaches attributed to cranial or cervical vascular disorders, postural puncture headache, hypertension-related disorders (eg, eclampsia), cerebral venous sinus thrombosis, hypophysitis, anemia, diabetes
13) Painful eye with autonomic features	Pathology in posterior fossa, pituitary region, or cavernous sinus; Tolosa-Hunt syndrome; sphenoidal causes
14) Posttraumatic onset of headache	Acute and chronic posttraumatic headache, subdural hematoma and other headache attributed to traumatic disorders
15) Pathology of the immune system such as HIV	Opportunistic infections
16) Rapidly escalating or new drug at onset of headache	Medication-overuse headache, drug incompatibility

\* ICHD-3 = International Classification of Headache Disorders, Third Edition.  
 † Reported with permission from Dr. TP, et al, Neurology, © 2019 American Academy of Neurology.  
 \* Change flag for assessment.

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## Diagnostic Work Up

- ❑ Exam
  - Scalp tenderness, febrile, papilledema (bedside vs optometry), focal deficits....
- ❑ Imaging
  - CT brain vs MRI
    - With or without contrast
  - MRV vs CTV
  - CTA vs MRA
- ❑ Lumbar puncture
  - Infection, opening pressure, malignancy
- ❑ Labs
  - ESR, CRP, CBC, infectious eval

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## Thunderclap Headache

- ❑ Starts at peak intensity
- ❑ Concerning for secondary
  - Some can be primary – diagnosis of exclusion
- ❑ Primary concerns:
  - RCVS
  - SAH
  - Meningitis
  - Spontaneous intracranial hypotension

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## Nocturnal Headaches

- ❑ Awake from sleep or waking up for other reasons and noticing headache
- ❑ Possible secondary headaches
  - Medication overuse
  - OSA
  - Nocturnal hypertension
  - Intracranial hypertension
- ❑ Common in primary headache disorders
  - Most common time for migraines is early hours of morning
- ❑ Hypnic Headache – headache in older individual occurring exclusively during sleep (1-3 am).
  - Bilateral lasting 15-30 minutes without autonomic findings
  - Wakes patients up
  - "alarm clock"
  - Need to r/o secondary causes
  - Typically responds to nighttime caffeine or melatonin

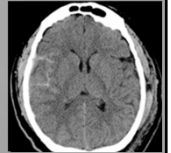
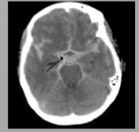
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## COMMON TYPES OF SECONDARY HEADACHES

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## Subarachnoid Hemorrhage

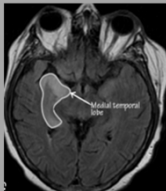
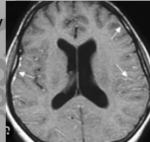
- ▣ Sudden, severe, thunderclap headache
  - "worst headache of my life"
  - Photo/phonophobia, nausea, neck pain/stiffness
- ▣ Aneurysmal rupture
- ▣ Urgent imaging
  - CT/CTA
  - LP
- ▣ Medical emergency



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## Meningitis/Encephalitis

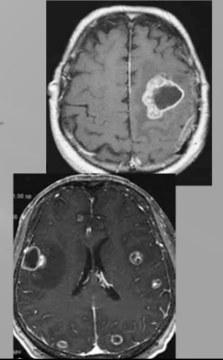
- ▣ Headache with fever, neck stiffness, altered consciousness.
  - Fever, white count.....
- ▣ Can lead to focal deficits and seizures
- ▣ Precipitating factors (mosquito bites)
- ▣ Brain imaging followed by LP
- ▣ Empiric antibiotic/antiviral therapy



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## Intracranial Mass

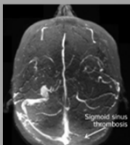
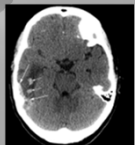
- ▣ Progressive headache
- ▣ Worse in the morning
- ▣ Associated with neurological deficits.
- ▣ High suspicion if known malignancy
  - 50-70% of brain tumors are metastatic
- ▣ Edema may respond rapidly to steroids



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## Venous Sinus Thrombosis

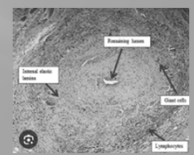
- ▣ Headache most common symptom
  - can be positional (increased pressure)
- ▣ Can worsen to focal symptoms, encephalopathy, brain hemorrhage, seizures...
  - Visual disturbances are common
- ▣ Papilledema important clue
- ▣ Risk factors
  - Pregnancy, post partum, malignancy, OCP
  - Sinus or ear infection.
- ▣ Diagnose with MRI brain/MRV or CTV



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## Giant Cell Arteritis

- ▣ Vasculitis effecting large-medium sized arteries
- ▣ New-onset headache in patients over 50
  - Associated with fevers, chills, jaw claudication, vision changes
  - Muscle stiffness c/w PMR
  - Arm claudication
- ▣ Headache type and location variable
  - Frequently over temple
- ▣ Eval:
  - Imaging
  - CBC, ESR, CRP
  - Temporal artery biopsy
- ▣ Can cause permanent vision loss and stroke
- ▣ Steroid treatment during work up



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### Arterial Dissection

- ▣ Tear or flap in the intra/extra cranial vessels.
  - Blood flow between layers of vessels
- ▣ Damage to adjacent neurogenic structures
- ▣ Symptoms
  - Unilateral headache or neck pain
  - Horner syndrome
  - TIA/Stroke like symptoms
- ▣ Trauma vs spontaneous
  - CTD is a common risk factor
- ▣ Noninvasive vascular imaging
  - CTA/MRA

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### Reversible Cerebral Vasoconstrictive Syndrome

- ▣ Thunderclap headache
  - Can be recurrent
  - Mimics SAH
- ▣ Reversible cerebral vasoconstriction
  - Days to weeks
- ▣ Triggered by meds/activities
  - Sex, exertion, Valsalva
  - Vasoactive drugs (decongestants, SSR, cannabis...)
- ▣ Can be associated with stroke-like symptoms
- ▣ MRI with MRA/CTA
- ▣ Benign and self limiting
  - Avoid offending agents
  - CCBs

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### IIH

- ▣ No secondary cause of intracranial HTN
- ▣ Recent onset of headache or change in pattern of chronic headache
- ▣ Headache types vary
- ▣ More common in obese, childbearing age, females
- ▣ Transient visual obscurations
- ▣ Pulsative tinnitus
- ▣ Worse in AM (prolonged recumbence)
- ▣ Provoking meds
  - Tetracycline meds, Lithium, Vit A and retinoids.

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### Spontaneous Intracranial Hypotension

- ▣ Spinal CSF leak
  - Idiopathic or relatively mild trauma
- ▣ Sudden headache or clear pattern change
- ▣ Orthostatic headache
  - At least in beginning
  - Brought on by Valsalva
  - Progressive
  - Can be post traumatic
  - Coat hanger location
  - Worsen as day progresses
- ▣ Cause of NDPH
- ▣ More common if joint hypermobility
- ▣ MRI brain w/w.o. Spin imaging.

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## Less Common Primary Headache Disorders

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## Cluster Headaches

- ☐ Exquisitely painful
  - High rates of suicide
- ☐ Unilateral (typically side locked)
- ☐ Ipsilateral autonomic features
  - Lacrimation
  - Conjunctival injection
  - Orbital edema
  - ptosis, miosis
  - Nasal congestion or rhinorrhea
- ☐ Restless, agitated
- ☐ 2-4:1 male to female ratio
- ☐ Peaks in 20's
- ☐ Circadian pattern
  - Average 1-2 attacks per day, lasting 1-2 hours, 1-2 times per year, lasting 6-12 weeks, same time daily (2 am most common).
  - Spring and fall most common
- ☐ Predictable triggers such as alcohol

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## Cluster

**ICHD-3 Diagnostic Criteria for Cluster Headache, Episodic Cluster Headache, and Chronic Cluster Headache\***

**Cluster headache**

A At least five attacks fulfilling criteria B-D

B Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes when untreated<sup>a</sup>

C Either or both of the following

1 At least one of the following symptoms or signs, ipsilateral to the headache

- a Conjunctival injection and/or lacrimation
- b Nasal congestion and/or rhinorrhea
- c Eyelid edema
- d Forehead and facial sweating
- e Miosis and/or ptosis

2 A sense of restlessness or agitation

D Occurring with a frequency between one every other day and eight per day<sup>b</sup>

E Not better accounted for by another ICHD-3 diagnosis

**Episodic cluster headache**

A Attacks fulfilling criteria for cluster headache and occurring in bouts (cluster periods)

B At least two cluster periods lasting from seven days to one year (when untreated) and separated by pain-free remission periods of ≥3 months

**Chronic cluster headache**

A Attacks fulfilling criteria for cluster headache and criterion B below

B Occurring without a remission period, or with remissions lasting <3 months, for at least one year

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## Paroxysmal Hemicrania

- ☐ Unilateral paroxysms of pain
  - Side locked
- ☐ Very frequent short attacks
  - 2-30 minutes
  - Median of 9 per day
- ☐ Ipsilateral cranial autonomic symptoms
- ☐ Clear and typically absolute response to Indomethacin
  - 25 mg three times daily titrated upward
  - GI protection

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## Paroxysmal Hemicrania

**ICHD-3 Diagnostic Criteria for Paroxysmal Hemicrania\***

A At least 20 attacks fulfilling criteria B-E

B Severe unilateral orbital, supraorbital and/or temporal pain lasting 2 to 30 minutes

C Either or both of the following

1 At least one of the following symptoms or signs, ipsilateral to the headache

- a Conjunctival injection and/or lacrimation
- b Nasal congestion and/or rhinorrhea
- c Eyelid edema
- d Forehead and facial sweating
- e Miosis and/or ptosis

2 A sense of restlessness or agitation

D Occurring with a frequency of ≥5 per day<sup>a</sup>

E Prevented absolutely by therapeutic doses of indomethacin<sup>b</sup>

F Not better accounted for by another ICHD-3 diagnosis

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## Hemicrania Continua

- ☐ Persistent unilateral pain
  - Side locked
  - Wave/wane
- ☐ Ipsilateral autonomic symptoms
- ☐ Clear and typically absolute response to Indomethacin

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## Hemicrania Continua

**ICHD-3 Diagnostic Criteria for Hemicrania Continua\***

A Unilateral headache fulfilling criteria B-D  
 B Present for >3 months, with exacerbations of moderate or greater intensity  
 C Either or both of the following  
 1 At least one of the following symptoms or signs, ipsilateral to the headache  
 a Conjunctival injection and/or lacrimation  
 b Nasal congestion and/or rhinorrhoea  
 c Eyelid oedema  
 d Forehead and facial sweating  
 e Miosis and/or ptosis  
 2 A sense of restlessness or agitation, or aggravation of the pain by movement  
 D Responds absolutely to therapeutic doses of indomethacin<sup>†</sup>  
 E Not better accounted for by another ICHD-3 diagnosis

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## New Daily Persistent Headache

- ☐ Abrupt continuous headache lasting 3+ months
  - Migraine or tension pathway
  - No hx of headaches
- ☐ Distinctly remembered onset
  - Exact day of onset
- ☐ Frequency associated with viral illness (Covid-19)
  - Stressful event
- ☐ Imaging required – need to r/o secondary headache

**ICHD-3 Diagnostic Criteria for New Daily Persistent Headache\***

A Persistent headache fulfilling criteria B and C  
 B Distinct and clearly remembered onset, with pain becoming continuous and unremitting within 24 hours  
 C Present for >3 months  
 D Not better accounted for by another ICHD-3 diagnosis<sup>††</sup>

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## Trigeminal Neuralgia

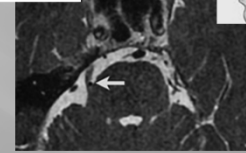
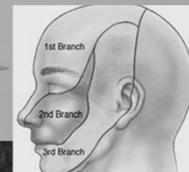
- ☐ Recurrent unilateral pain
- ☐ Brief shock like pain
  - Quick on/off
- ☐ Limited to trigeminal nerve distribution
  - 1 or more typically V2 or V3
- ☐ Triggered by innocuous stimuli
- ☐ Average 6<sup>th</sup> decade of life
- ☐ Pathological spontaneous firing of nerve
- ☐ Idiopathic vs neurovascular injury
- ☐ Imaging recommended
  - MRI brain with posterior fossa sequences

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## Trigeminal Neuralgia

**ICHD-3 Diagnostic Criteria for Trigeminal Neuralgia\***

A Recurrent paroxysms of unilateral facial pain in the distribution(s) of one or more divisions of the trigeminal nerve, with no radiation beyond,<sup>†</sup> and fulfilling criteria B and C  
 B Pain has all of the following characteristics  
 1 Lasting from a fraction of a second to 2 minutes<sup>†</sup>  
 2 Severe intensity<sup>†</sup>  
 3 Electric shocklike, shooting, stabbing, or sharp in quality  
 C Precipitated by innocuous stimuli within the affected trigeminal distribution<sup>†</sup>  
 D Not better accounted for by another ICHD-3 diagnosis



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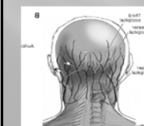
## Nummular Headache

- ☐ “coin shaped”
  - Small well circumscribed are on the scalp
  - Non radiating
  - Tenderness or numbness in the region
- ☐ Parietal or temporal locations most commonly
- ☐ Persistent or episodic
- ☐ Imaging to r/o bony lesions

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## Occipital Neuralgia

- ☐ Frequently associated with migraine
- ☐ Unilateral or bilateral occipital pain
- ☐ Sharp lancinating pain triggered by pressure/compression
  - Positive Tinel sign
- ☐ Associated with cervical disc disease
  - C2-3 foraminal narrowing



**ICHD-3 Diagnostic Criteria for Occipital Neuralgia\***

A Unilateral or bilateral pain in the distribution(s) of the greater, lesser and/or third occipital nerves and fulfilling criteria B-D  
 B Pain has at least two of the following three characteristics  
 1 Recurring in paroxysmal attacks lasting from a few seconds to minutes  
 2 Severe in intensity  
 3 Shooting, stabbing, or sharp in quality  
 C Pain is associated with both of the following  
 1 Dysesthesia and/or allodynia apparent during innocuous stimulation of the scalp and/or hair  
 2 Either or both of the following  
 a Tenderness over the affected nerve branches  
 b Trigger points at the emergence of the greater occipital nerve or in the distribution of C2  
 D Pain is eased temporarily by local anesthetic block of the affected nerve(s)  
 E Not better accounted for by another ICHD-3 diagnosis

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### Migraine Prevention

- ▣ Decrease frequency and severity of attacks
- ▣ 4+ headache days per month
- ▣ Give adequate trial (2-3 months)
  - Goal of 50% reduction
- ▣ Combination therapy
- ▣ Nonspecific: antihypertensives, antidepressants, antiseizure
  - Selection based on comorbidities or side effect profile
  - Slow titration upward
  - Prone to side effects
  - Failure of two classes would be indication to move upwards in therapy
- ▣ Specific: CGRP antagonists
  - Start at optimal dose
  - More rapidly effective
  - Well tolerated
  - More caution when using Erenumab
  - OnabotulinumtoxinA
  - Chronic migraine only

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### Migraine Prevention

**Antidepressant**

- ◆ Amitriptyline (tricyclic)
- ◆ Venlafaxine (SNRI)

**Antihypertensive**

- ◆ Atenolol
- ◆ Candesartan
- ◆ Lisinopril
- ◆ Metoprolol
- ◆ Nadolol
- ◆ Propranolol
- ◆ Timolol

**Antiseizure**

- ◆ Divalproex sodium
- ◆ Sodium valproate
- ◆ Topiramate

**CGRP pathway targeted treatments**

- ◆ Atogepant (small-molecule CGRP-receptor antagonist)
- ◆ Eptinezumab (monoclonal antibody to CGRP)
- ◆ Erenumab (monoclonal antibody to the canonical CGRP receptor)
- ◆ Fremanezumab (monoclonal antibody to CGRP)
- ◆ Galcanezumab (monoclonal antibody to CGRP)
- ◆ Rimegepant (small-molecule CGRP-receptor antagonist)

**NMDA antagonist**

- ◆ Memantine

**OnabotulinumtoxinA\***

**Triptans used for short-term prevention of menstrually related migraine:**

- ◆ Frovatriptan
- ◆ Naratriptan
- ◆ Zolmitriptan

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### CGRP Antagonists

Evidence-based Recommendations for the CGRP-targeted Monoclonal Antibodies in the Preventive Treatment of Migraine\*

Recommendation	Agent	Dosing	Evidence of efficacy*
The CGRP monoclonal antibodies are effective for preventive treatment of episodic migraine	Eptinezumab	100 mg or 300 mg every 12 weeks	High
	Erenumab	70 mg or 140 mg every 4 weeks	High
	Fremanezumab	275 mg every 4 weeks	High
	Fremanezumab	475 mg every 12 weeks	High
The CGRP monoclonal antibodies are effective for preventive treatment of chronic migraine	Galcanezumab	240 mg loading, 120 mg every 4 weeks	High
	Eptinezumab	100 mg or 300 mg every 12 weeks	High
	Erenumab	70 mg every 4 weeks	High
	Fremanezumab	275 mg every 4 weeks	Moderate
	Fremanezumab	475 mg every 12 weeks	High
	Fremanezumab	475 mg every 12 weeks	High
	Galcanezumab	240 mg loading, 120 mg every 4 weeks	High

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### Preventative Devices

Device	Study	Effectiveness
rTMS	Multiple/ Celsly	YES
tTMS	Multiple/ eNeura	YES

**Multiple/ Celsly:** Acute and preventive treatment of migraine in adults age 18 and up

**eNeura:** Acute and preventive treatment in adults and adolescents > age 12 years

**Multiple/ Celsly:** Active stimulation (20 minutes daily for 3 months) reduced mean number of headache days/months; the 50% responder rate for active vs sham treatment was 38.1% vs 12.1%. In prospective open-label study, 1 hour of treatment within 3 hours of treatment reduced pain by 52.1%, 2 hours of treatment reduced pain by 52.8%, and only 34.6% used rescue medication for following 24 hours.

**eNeura:** In pivotal trial, 39% given active stimulation had pain relief vs 22% with sham stimulation; at 24 and 48 hours, 29% and 27% of people who had active stimulation, respectively, had continued relief vs 16% and 13% with sham stimulation. Active stimulation using a preventive protocol resulted in 2.75 fewer mean headache days per month.

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### Abortive Treatment

- ▣ Complete pain relief at 2 hours
- ▣ Treat early
  - Carry meds with you
- ▣ Different meds for different headaches
- ▣ Start/use higher doses
- ▣ May need non-oral formulation
- ▣ Combined treatments
  - Stratified approach
  - NSAIDs, acetaminophen, triptans, gepants
- ▣ Treat accompanying symptoms (nausea)
  - Nausea effects absorption
  - Metoclopramide and promethazine independently treat headaches
  - Suppositories are available
  - Ondansetron
- ▣ Treat at time of aura?

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**Evidence-based Options for Acute Treatment of Migraine**

Treatment	AHRQ strength of evidence <sup>10,11</sup>
<b>Established as effective<sup>10</sup></b>	
Triptans (all doses, all formulations)	Moderate to high
Dihydroergotamine nasal spray	Moderate to high
Calcitonin gene-related peptide receptor antagonists (gepants)	Low to high
Lasmiditan	High
Over-the-counter nonsteroidal anti-inflammatory drugs (NSAIDs): aspirin, ibuprofen, naproxen	Moderate
Prescription NSAIDs: celecoxib oral solution, diclofenac	Moderate
<b>Probably effective<sup>10</sup></b>	
NSAIDs: ketoprofen, IV and IM ketorolac	NA
IV magnesium (for migraine with aura)	Insufficient to low
Opioid-containing combinations: codeine/acetaminophen, tramadol/acetaminophen	Low
Ergotamine/caffeine	Moderate
Antiemetics: prochlorperazine, promethazine, droperidol, chlorpromazine, metoclopramide	Low
Acetaminophen	Moderate

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## Triptans

- ▣ Mainstay migraine specific acute treatment
- ▣ Nasal sprays and subcutaneous injections are faster acting
  - ODTs are also available
- ▣ Triptan sensation
  - Flushing, heat, pressure, anxious
- ▣ Avoided with cardio and cerebrovascular disease
  - Poorly controlled HTN
- ▣ Serotonin syndrome treatment
  - Use with SSRI/SNRI
  - Extremely low risk
  - Appropriate to prescribe while providing patient with information
- ▣ Meta-analysis showed pain free at 2 hours of 37-50%.

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## Triptans

TABLE 3-1 Migraine-specific Acute Treatments

Medication	Dose and route of administration	Maximum daily dose	Important Interactions
<b>Triptans<sup>a</sup></b>			
Almotriptan	12.5 mg orally; may repeat after 2 hours	25 mg	MAO-A inhibitors; CYP3A4 inhibitors such as telotristate
Eletriptan	20 mg, 40 mg orally; may repeat after 2 hours	80 mg	CYP3A4 inhibitors such as telotristate, erythromycin, and verapamil
Frovatriptan	2.5 mg orally; may repeat after 4 hours	7.5 mg	
Naratriptan	1 mg, 2.5 mg orally; may repeat after 4 hours	5 mg	
Risatriptan	5 mg, 10 mg orally and orally disintegrating tablets; may repeat after 2 hours	30 mg, 15 mg if taking propranolol	MAO-A inhibitors
Sumatriptan oral	25 mg, 50 mg, 100 mg orally; may repeat after 2 hours	200 mg orally	MAO-A inhibitors
Sumatriptan/naproxen oral	85 mg sumatriptan/500 mg naproxen; may repeat once after 2 hours	2 tablets per 24 hours	MAO-A inhibitors
Sumatriptan nasal	5 mg, 10 mg, 20 mg nasal spray; 22 mg orally disintegrated powder; may repeat after 2 hours	40 mg nasal spray, 44 mg oral powder	MAO-A inhibitors
Sumatriptan subcutaneous injection	3 mg, 4 mg, 6 mg subcutaneous injection; may repeat after 1 hour	12 mg SQ injection	MAO-A inhibitors
Zolmitriptan	2.5, 5 mg orally; orally disintegrating tablet; nasal spray; may repeat after 2 hours	10 mg	MAO-A inhibitors, omeprazole

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## Lasmiditan

- ▣ 5HT1f receptor agonist
  - Similar to triptan but without vasoconstriction
- ▣ Efficacy
  - 31% pain freedom at 2 hours
  - 44% freedom of most bothersome symptom
- ▣ Side effect burden
  - Dizziness, nausea, paresthesia
  - Somnolence
  - Driving safety
    - ▣ No driving or other alertness requiring activity for 8 hours

Lasmiditan	50 mg, 100 mg, 200 mg orally; repeat dose is not recommended	One dose	SSRIs, SNRIs and other serotonergic medications; P-glycoprotein or breast cancer resistance protein substrates
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## Gepants

- ▣ Small molecule CGRP antagonists
- ▣ Ubrogепant
  - Dose repeated in 2 hours
- ▣ Rimegepant
  - 1 dose per day
- ▣ 37% relief of most bothersome symptoms
- ▣ 21% pain freedom at 2 hours
- ▣ Very well tolerated
  - < 4% dry mouth, nausea, somnolence
- ▣ Causation with Ubrogепant if taking CYP3A4 inhibitors
- ▣ No risk of vasoconstriction
- ▣ No risk for MOH

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## Gepants

Rimegepant	75 mg orally dissolving tablet; repeat dose is not recommended	75 mg	Strong CYP3A4 inhibitors (avoid use); moderate CYP3A4 inhibitors including verapamil
Ubrogепant	50 mg, 100 mg orally; may repeat after 2 hours	200 mg	Strong CYP3A4 inhibitors (avoid use); moderate CYP3A4 inhibitors including verapamil (limit dose to 50 mg per 24 hours)

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TABLE 3-4  
**Neuromodulation Devices for Acute Treatment of Migraine**

Device	Frequency and duration of use	Effectiveness	Adverse effects
<b>Superoorbital trigeminal nerve stimulation<sup>15</sup></b>	60-minute stimulation as needed	Mean change in pain intensity after 1 hour on 0-10 visual analogue scale: -3.46 versus -1.78 with sham	Paresthesia
<b>Noninvasive vagus nerve stimulation<sup>16</sup></b>	Bilateral 100-second stimulations to the right and left sides of the neck within 20 minutes of migraine onset; allowed to repeat once after 15 minutes if pain not improved	Pain freedom at 2 hours not statistically different from placebo, but pain relief at 2 hours and pain freedom at 30 and 60 minutes were better than placebo	Discomfort at site of contact with skin
<b>Remote electrical neuromodulation<sup>17</sup></b>	Stimulation of upper arm for 45 minutes, starting within 1 hour of attack onset	Pain freedom at 2 hours in 37.4% of the active group versus 18.4% in the sham group	Paresthesia, redness, warmth in area of device contact with skin
<b>Single-pulse transcranial magnetic stimulation<sup>18</sup></b>	Two pulses at aura onset	Pain freedom at 2 hours 39% with active treatment versus 22% with sham	Headache, migraine, sinusitis
<b>External combined occipital and trigeminal neurostimulation<sup>19</sup></b>	30-60 minute stimulation within 30 minutes of headache onset	Pain freedom at 2 hours 46% with active treatment versus 2% with sham	Migraine, pain, unpleasant sensation during treatment, numbness or tingling

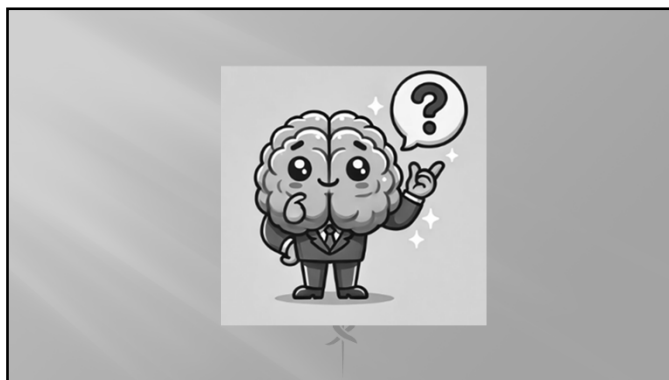


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