Pharmacotherapeutic Management of Headaches in Primary and Urgent Care

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Disclosures

- Speaker Bureau:
  - Sanofi-Pasteur, Merck, Moderna, Seqirus, and Pfizer: Vaccines
  - Exact Sciences: Colorectal caner
  - AstraZeneca: COPD and Asthma
  - AbbVie and Pfizer: Migraines
  - Axsome: Depression and Migraines
- Consultant:
  - Sanofi-Pasteur, Pfizer, Merck, Seqirus, and Moderna: Vaccines
  - AstraZeneca: COPD and Asthma
  - GSK: OA/Pain
  - AbbVie and Pfizer: Migraines
  - Axsome: Depression and Migraines

No experimental or investigational use of drugs or devices will be presented.
Off-label use will be identified as such if discussed.

All relevant financial relationships have been mitigated

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Objectives

- Upon completion, the participant will be able to:

1. Discuss current research regarding the etiology of primary and secondary headaches
2. Identify the signs and symptoms of primary and secondary headaches, including medication overuse
3. Discuss the various pharmacologic and non-pharmacologic treatments available for individuals with primary headaches

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Headaches

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Case Study: JJ

- 17-year-old female with a 5–7-year history of headaches
  - Headaches occur 1–2 ×/week; last 24 hours
  - Pain always starts in "my sinus;" (Frontal-either side)
  - Occurs whenever the "weather changes"
  - **8** on 1–10 scale, pulsating; associated with nausea, photophobia; relieved by sleep and ibuprofen (Advil®) 800 mg × 2 doses
  - Presents for a "sinus evaluation"

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Case Study: JJ

Physical Exam

- VSS
- General Appearance
  - Affect – Variable, appropriate
  - Dress/grooming – Normal
  - Posture, facial expressions, manner, attention span – Normal
  - Speech – Spontaneous, smooth, articulate
  - Judgment – Intact
  - Mini-mental state examination (MMSE) – 29
- Skin
- HEENT – Normal
- Lungs – Clear
- Heart – S_1, S_2: RRR
- Peripheral Vascular System: Dorsalis pedis and posterior tibialis: 2+ bilaterally

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Case Study: JJ

Physical Exam – *Neuro*

- CN's intact
- Gait smooth and coordinated
- Heel/toe – Intact
- Strength – 5+/5+
- Pronator drift – Negative
- Reflexes – 2+ bilaterally and equal
- Negative Babinski
- Sensory intact
- Equilibrium/coordination – Intact
  - Negative Romberg

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Migraine Prevalence (American Migraine Study II)

- There are currently 28 million migraine sufferers ages 12+ years in the United States.
  - 21 million females: Approximately 18.2% of women
  - 7 million males: Approximately 6.5% of men
- Migraine prevalence peaks in the 25–55 age range.
  - These are the most productive years of the lifespan.
- One in 4 households has at least 1 migraine sufferer.

Source: Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*. 2001 Jul-Aug;41(7):646-57. doi: 10.1046/j.1526-4610.2001.041007646.x. PMID: 11554952.

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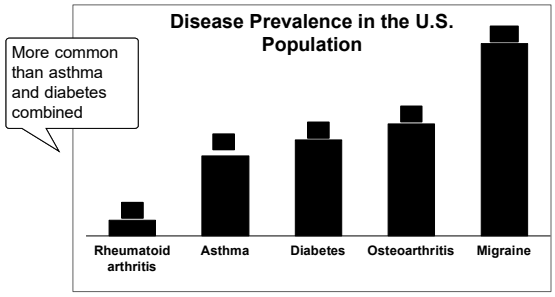
Migraine Prevalence



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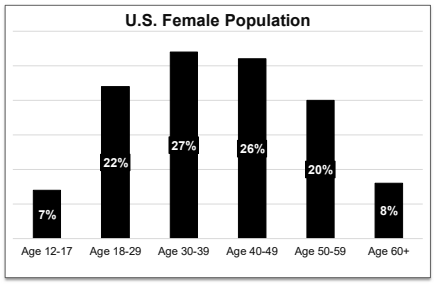
Migraine Prevalence



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Headache Diagnosis: Primary vs. Secondary Headache

Evaluate for Signs or Symptoms of Secondary Headache

Secondary Headache → Diagnose, Treat and/or Refer

Primary Headache → Diagnose, Treat

Image source: https://www.shutterstock.com/image-photo/young-woman-suffering-headache-against-dark-718238359

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Secondary Headaches: Prevalence

- 1% of office HA presentations
- 3.8% of ED HA presentations

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Headache Diagnosis: Primary Headache Types

- Tension-type headache
- Migraine
  - Migraine without aura
  - Migraine with aura
  - Chronic migraine (complication of migraine)

- Cluster headache
- Other primary headaches
  - Cough headache
  - Exertional headache
  - Sexual activity headache
  - Hemicrania continua

Olesen J et al. *Cephalalgia*. 2004;24(suppl 1):1-151.

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Headache Diagnosis: History

- Medical history
- Headache history
  - For each headache type
    - Onset
    - Location
    - Quality
    - Intensity
    - Duration
    - Frequency
    - Associated symptoms
- Impact on routine physical activity

Image source: https://www.shutterstock.com/image-photo/young-woman-suffering-headache-against-dark-718238359

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Headache Diagnosis: Examinations

- Physical exam including:
  - Vital signs
  - Head
  - Neck

- Neurological exam including:
  - Mental state examination (attention, consciousness, language)
  - Cranial nerve function with fundoscopy
  - Nuchal rigidity
  - Focal neurological deficits
  - Coordination and gait

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Features Suggestive of Secondary Headache: SNOOP

- **S**ystemic symptoms or signs of systemic disease
  - Fever, myalgias, weight loss
  - Malignancy, acquired immunodeficiency syndrome
- **N**eurological symptoms or signs
- **O**nset sudden (thunderclap headache)
- **O**nset before age 5 years or after age 50 years
- **P**attern change
  - Progressive headache with loss of headache-free periods
  - Change in type of headache

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Red Flags for Secondary Headache

Indications for HA workup

- First/worst HA
- Abrupt-onset HA
- Head trauma
- Progression or fundamental change in pattern
- New HA in ages <5 yo or >50 yo
- New HA with cancer, immunosuppression

- HA with syncope or seizure
- HA triggered by exertion/Valsalva/sex
- Neurologic symptoms >1-hour in duration
- Abnormal general or neurologic examination

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Secondary Headache

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Case Study: JD

- 1-week history of blurred vision and worsening headache in a 46-year-old male.
  - Headache is 5 on 1–10 scale.
    - Now associated with vomiting and blurred vision
  - Seen 3 days ago, diagnosed tension headache
  - No improvement despite medications
  - Had been feeling well until this began; no other symptoms

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Case Study: JD

Physical Exam

- PE – VSS
- Head – Normocephalic (N/C); no abnormalities
- Ears – Canals/TM's normal; hearing intact
- Nose – Turb/mucosa normal; no discharge, abnormalities

- Mouth – Mucosa moist; tongue midline; gag intact
- Nodes – Nonpalpable, nontender
- Lungs – Clear bilaterally; no crackles, wheezes, or rubs

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Case Study: JD

- CN II – XII intact; exceptions noted
  - Papilledema
  - Conversant but slow responses to questions
  - Neat and clean
  - Seems to stare at examiner
  - Tries to smile at times; not always appropriate for the situation

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Papilledema

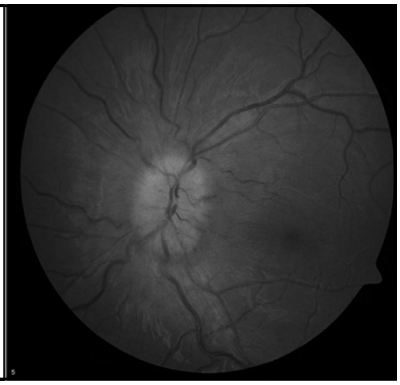

Image source: Shutterstock

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Diagnostics

- CT with contrast ordered stat
  - MRI is the most sensitive test, particularly when gadolinium (contrast) is used.
- Stat CT scan confirmed a large glioblastoma in the frontal region.
  - Within 4 hours, underwent a debulking procedure
  - Pathology confirmed and experimental chemotherapy was initiated.
  - Unfortunately, tumor was fatal with 3 – 4 months of presentation.

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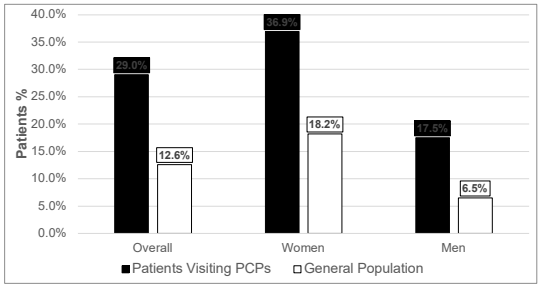
Waiting Room Study:
Results Compared with General Population



Source: https://pubmed.ncbi.nlm.nih.gov/12943491/

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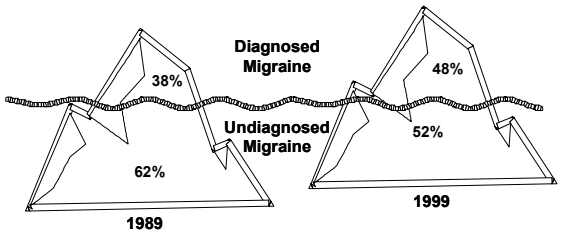
The Diagnosis of Migraine Has Increased Modestly
(Using IHS Criteria)



14.6 million migraine sufferers remain undiagnosed

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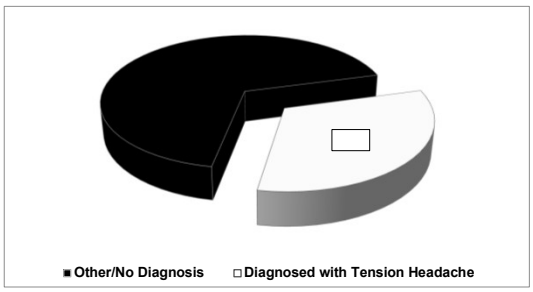
Undiagnosed migraine sufferers often report receiving a diagnosis of tension headache.



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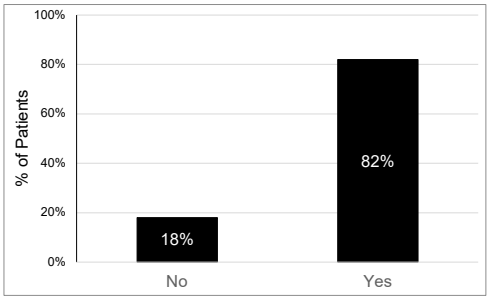
In the presence of neck pain, tension headache is frequently diagnosed.



Source: https://pubmed.ncbi.nlm.nih.gov/12011269/

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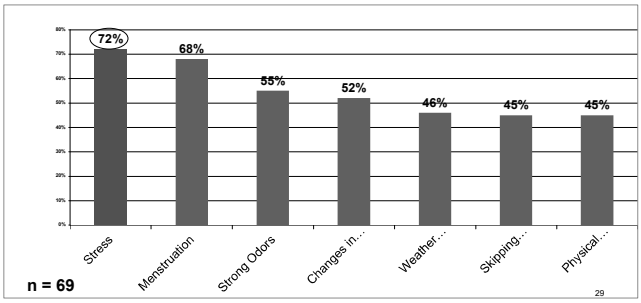
Stress is the most frequently reported trigger of migraine.



n = 69

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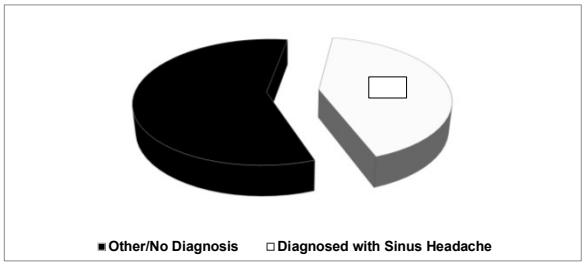
Undiagnosed patients often report receiving a diagnosis of sinus headache.



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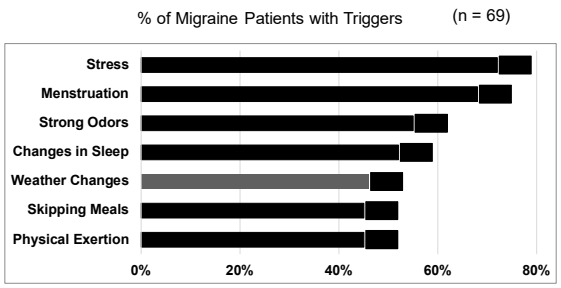
Migraine can be triggered by weather.



Source: https://pubmed.ncbi.nlm.nih.gov/7758098/

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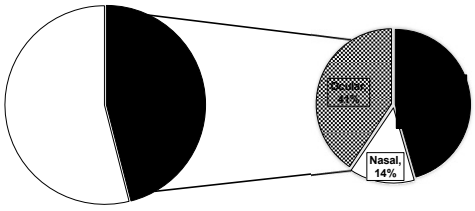
Like sinus headache, migraine may present with autonomic symptoms.



46% of patients had at least 1 autonomic symptom during migraine attacks.

Of these,
- 14% had only nasal symptoms.
- 41% had only ocular symptoms.
- 46% had both nasal and ocular symptoms.

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Summary of Clinical Data

- Most patients with self-described "sinus" headache:
  - May actually have migraine and migrainous headache as defined by IHS criteria (90%)
  - Experience sinus pain and pressure, nasal symptoms, ocular symptoms and weather as a trigger.
  - Are disabled by their headaches
  - Are dissatisfied with Rx and OTC medications they are using to treat these headaches

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Female Life Events that Influence Migraine

- Menarche
- Menses
- Oral contraception
- Pregnancy
- Lactation
- Menopause
- Hormone therapy

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Migraine and Menarche

- Females suffer from migraine at a 3:1 ratio to males.
- Beginning with puberty, migraine is more common in girls.

- Menstrually-associated migraine begins at menarche in 33% of women.
- 60–70% of female sufferers experience migraine in association with menses.

Sources:
https://pubmed.ncbi.nlm.nih.gov/35015948/#:~:text=Pure%20menstrual%20migraine%20is%20defined,cycle%2C%20not%20just%20around%20menstruation.
Semin Neurol 2017; 37(06): 601-610. DOI: 10.1055/s-0037-1607393

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Menstrual Migraine: Definitions

- Menstrually-associated migraine (MAM):
  - Women who experience attacks that occur both perimenstrual and at other times of the month
  - 60–70% of female migraineurs report a menstrual relationship to their headaches.

- Menstrual migraine (MM):
  - Women who experience attacks that occur only perimenstrually
  - True menstrual migraine occurs in only 7–14% of female migraineurs.

Benedetto C et al. *Cephalalgia*. 1997;20:32-34

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Characteristics of Menstrually-Associated Migraine (MAM) Attacks

- Longer in duration than non-MAM attacks
- Perceived by some to be more difficult to treat than non-MAM attacks

- Predictable in some women
- Influence of co-existing premenstrual dysphoric disorder (PMDD)

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Migraine Vulnerability During the Menstrual Cycle

- Can occur before, during, and after menstruation
  - Migraine may be part of premenstrual syndrome (PMS), now a part of the DSM-IV criteria for premenstrual dysphoric disorder (PMDD)
  - Greatest likelihood of menstrual migraine on Day **-**1 to Day **+**4, but can vary
  - Decrease in estrogen levels in the late luteal phase is likely trigger for migraine
- **Although migraine may be related to PMDD, it is important to treat migraine as an individual disorder with migraine-specific treatment.**

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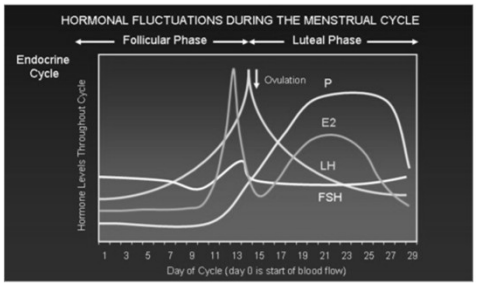
Hormonal Levels During Menstrual Cycle



Adapted from Hatcher RA, Trussell J, Stewart, F. *Contraceptive Technology. 17th Revised Ed.* New York, NY. Ardent Media, Inc. 1998: Appendix, Figure 2.

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Impact of Hormones on Migraine

Progesterone given during the menstrual cycle will postpone bleeding but not the headache.

Estrogen given during the menstrual cycle will postpone the headache but not the bleeding.

Constant levels of estrogen can prevent the migraine attack.

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New Insights into Migraine Pathophysiology

A Scientific Hypothesis for the "Tension-Like" and "Sinus Like" Presentation of Migraine

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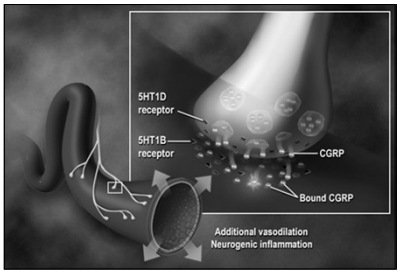
The Migraine Process:
Activation of Nerves and Blood Vessels



Source: New Trends in Headache and Migraine Treatment, Kathie Teta, RN, CPNP, PANDA Neurology, Atlanta, GA. https://slideplayer.com/slide/5278897/
Or Global Journal of Otolaryngology https://juniperpublishers.com/gjo/pdf/GJO.MS.ID.555646.pdf.
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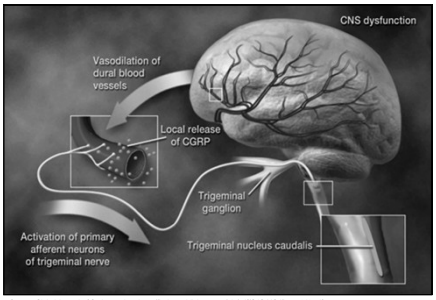
The Migraine Process:
Activation of the Trigeminal Nucleus Caudalis (TNC)



Source: Global Journal of Otolaryngology https://juniperpublishers.com/gjo/pdf/GJO.MS.ID.555646.pdf
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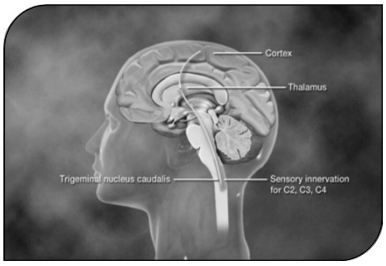
Trigeminal Nucleus Caudalis (TNC):
Processing and Relaying Migraine Pain

Activation of the TNC can result in referred pain.



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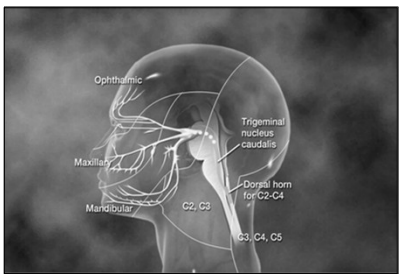
Activation of the TNC may result in referred pain that could be perceived anywhere along the trigeminocervical network.



Source: Global Journal of Otolaryngology https://juniperpublishers.com/gjo/pdf/GJO.MS.ID.555646.pdf
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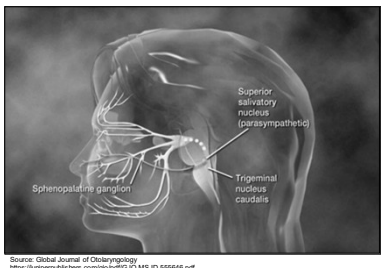
Activation of the TNC may result in reflex activation of cranial parasympathetic nerves extending into sinus cavities and tear ducts.



Source: Global Journal of Otolaryngology
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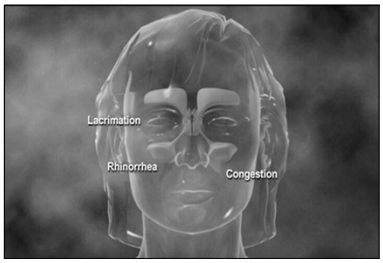
Cranial parasympathetic activation may explain "sinus-like" symptoms in migraine.



Source: Global Journal of Otolaryngology
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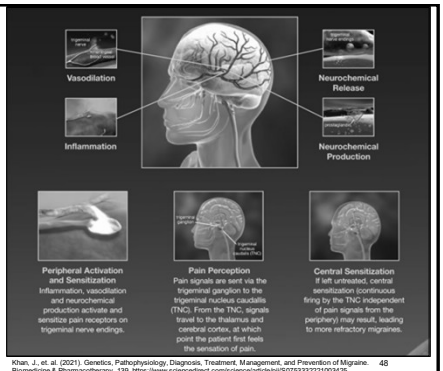
Pathophysiology of migraine is no longer just neurovascular.

Multiple mechanisms of migraine exist.



Khan, J., et. al. (2021). Genetics, Pathophysiology, Diagnosis, Treatment, Management, and Prevention of Migraine. Biomedicine & Pharmacotherapy. 139. https://www.sciencedirect.com/science/article/pii/S0753332221003425

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Episodic Migraine Without Aura: Diagnostic Criteria
At Least 5 Attacks Fulfilling the Criteria Below

- ☑ Headache attack lasting 4 to 72 hours (untreated or unsuccessfully treated)

AND

- ☑ Not attributable to another disorder

Description of Headache	***AND***	***Associated Symptoms***
☑ Two of the following:		☑ One of the following
❑ Unilateral location		❑ Nausea and/or vomiting
❑ Pulsating quality		❑ Photophobia and phonophobia
❑ Moderate or severe intensity (inhibits or prohibits daily activities)		
❑ Aggravated by or causing avoidance of routine physical activity (e.g., walking or climbing up stairs)		

https://medicalcriteria.com/web/migraine/ 49

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Episodic Migraine Aura: Diagnostic Criteria
At Least 2 Attacks Fulfilling the Criteria Below

- ☑ Meets the IHS criteria for migraine without aura

AND

- ☑ Not attributable to another disorder

- ☑ Three of the following:
- ❑ Recurrent one or more fully reversible visual, sensory, and/or speech symptoms (focal neurological symptoms)
- ❑ **At least 1 aura symptom develops gradually over ≥5 minutes, or different symptoms occur in succession over ≥5 minutes**.
- ❑ Each aura symptom lasts ≥5 minutes and ≤60 minutes.
- ❑ Migraine headache begins during or within 60 minutes of aura.

https://medicalcriteria.com/web/migraine/

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Episodic Tension-Type Headache: Diagnostic Criteria
At Least 10 Episodes Occurring <1 Day/Mo

- ☑ Headache lasting 30 minutes to 7 days

AND

- ☑ Not attributable to another disorder

Description of Headache	***AND***	***Associated Symptoms***
☑ Two of the following:		☑ Both of the following
❑ Pressing/tightening quality (nonpulsating)		❑ No nausea or vomiting (anorexia may occur)
❑ Mild or moderate intensity (may inhibit, does not prohibit activities)		❑ Either photophobia or phonophobia
❑ Bilateral location		
❑ Not aggravated by physical activity such as walking or climbing stairs		

https://medicalcriteria.com/web/migraine/ 51

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Episodic Cluster Headache: Diagnostic Criteria
At Least 5 Attacks Fulfilling the Criteria Below

- ☑ Frequency of attacks: 1 every other day to 8 per day

AND

- ☑ Not attributable to another disorder

Description of Headache	AND	***Associated Symptoms***
☑ All of the following:		☑ One of the following present on the pain side:
❑ Severe or very severe		❑ Conjunctival injection and/or lacrimation
❑ Unilateral orbital, supraorbital, and/or temporal pain		❑ Nasal congestion or rhinorrhea
❑ Lasts 15 to 180 minutes (untreated)		❑ Eyelid edema
		❑ Forehead and facial sweating
		❑ Miosis or ptosis
		❑ A sense of restlessness or agitation

https://medicalcriteria.com/web/migraine/

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AHS Guidelines: Acute Treatment for Migraine

- **Established Efficacy**
  - Triptans
  - Ergots
    - Dihydroergotamine nasal spray/inhaler
  - NSAIDs
    - Diclofenac, aspirin, naproxen, ibuprofen
  - Acetaminophen 1000 mg

- **Combinations**
  - Acetaminophen/aspirin/caffeine 500/500/130 mg
  - Sumatriptan/naproxen 85/500mg
- **Butorphanol nasal spray 1 mg**
- **Gepants**
  - Ubrogepant
  - Rimegepant

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AHS Guidelines: Acute Treatment for Migraine

Probably Effective

- Antiemetics
  - Metoclopramide IV, prochlorperazine IV/IM
- Antidopamine
  - Chlorpromazine IV, droperidol IV

- Ergots
  - Dihydroergotamine IV/IM/SC, ergotamine/caffeine
- NSAIDs
  - Flurbiprofen, ketoprofen, ketorolac IV/IM

- Others
  - $MgSO_4$ IV, isometheptene
- Combinations: Codeine/ acetaminophen, tramadol/ acetaminophen
  - Although opioids are probably effective, they are not recommended for regular use.

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5 $HT_{1B/1D}$ Antagonists

- Sumatriptan (Imitrex®)
  - Acute migraine and acute cluster headache
  - SC, nasal spray and tablet **(Injection: Ages 6 years and older)
- Zolmitriptan (Zomig®)
  - Acute migraine and menstrual migraine prophylaxis
  - Tablet (2.5 and 5.0 mg tablets); MLT, nasal spray

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5 $HT_{1B/1D}$ Antagonists

- Naratriptan (Amerge®)
  - Acute migraine and menstrual migraine prophylaxis
  - Tablet (1 mg and 2.5 mg)
- Frovatriptan (Frova®)
  - Acute migraine and menstrual migraine prophylaxis
  - Tablet (2.5 mg)

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5 $HT_{1B/1D}$ Antagonists

- Rizatriptan (Maxalt®) (acute migraine headache)
  - Tablet and ODT (5 and 10 mg) **6 years of age and older
- Almotriptan (Axert®) (acute migraine headache)
  - Tablet (6.25 mg and 12.5 mg) **12 years of age and older
- Eletriptan (Relpax®) (acute migraine headache)
  - Tablet (20 mg and 40 mg)

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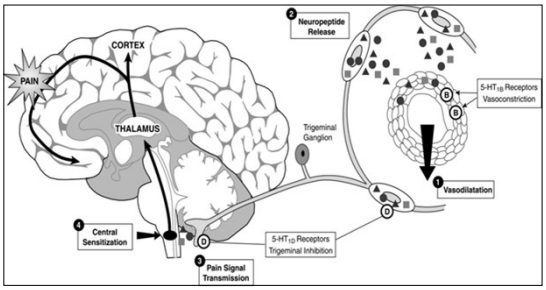
Migraine-Specific Therapy: The Mechanism of Action



https://americanheadachesociety.org/wp-content/uploads/2018/05/NAP_for_Web_-_Acute_Treatment_of_Migraine-1.pdf&tbnid=NCcUsNnjqjFSRM&vet=1&docid=U6YpNyjlOYZq8M&w=670&h=306&source=sh/x/im

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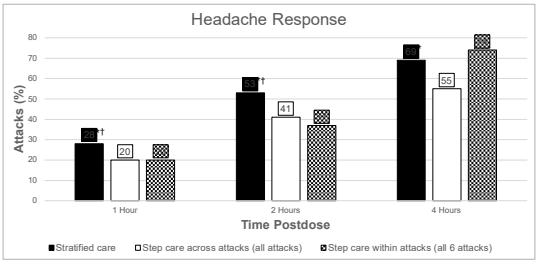
Stratified Care vs. Step Care



*P <0.001 for stratified care vs. step care across attacks.
†P <0.001 for stratified care vs. step care within attacks.

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What else can I do?

- Add NSAID to triptan.
- Provide ondansetron or similar for nausea.
- Encourage nonpharmacologic adjuncts to treatment.
- Do I need to avoid in individuals on an SSRI?

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Additional Non-Pharmacologic Options

- Transcranial magnetic stimulator (TMS) technology (Cerena™ device)
  - Placed at the back of the neck with first symptoms of migraines
- Transcutaneous electrical nerve stimulation (TENS) device (Cerafly®)
  - Prophylactic option
  - Looks like a headband worn around forehead
  - Use for 20 minutes. Transmits electrical stimulation to the trigeminal nerves

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Newer Options

CGRP antagonists/inhibitors
- Ubrogepant (Ubrelvy®)
- Rimegepant (Nurtec® ODT)

- Acute treatment of migraine in adults with and without aura
- Multiple targets to treat acute migraine
- Can use in individuals with stable cardiovascular/ cerebrovascular disease

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New Medications for Acute Treatment of Migraine

	Gepants		Ditan
	Rimegepant	**Ubrogepant**	**Lasmiditan**
Approved indication	Acute treatment of migraine with/without aura in adults		
Route of administration	Orally disintegrating tablet	Oral tablet	Oral tablet
Frequency	As needed; No more than 1-dose/24 h	As needed; a 2nd dose may be taken ≥2 h after 1st dose; No more than 200 mg/24 h	As needed; No more than 1 dose/24 h
Dose strength	75 mg	50 mg, 100 mg	50 mg, 100 mg

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Zavegepant (Zavzpret™)

- **Name: Zavegepant**
- Class: gepant (CGRP antagonist)
- Indication
  - Adults with acute migraine with and without aura
- Dose
  - 10 mg via a single spray into one nostril at the onset of migraine (Maximum dose in 24-hour period is 10 mg.)

https://www.pfizermedicalinformation.com/patient/zavegepant/patient-package-insert

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Zavegepant (Zavzpret™)

- Efficacy
  - Two, double-blind, placebo-controlled trials
  - Study 1
    - N=623 (drug) and N=624 (placebo)
    - Pain free at two hours: 23.6% vs. 14.9% (p<0.001)
    - Most bothersome symptom free at 2 hours: 39.6% vs. 31.1% (p 0.001)
- Similar findings in Study 2
- Also looked at return to normal function, pain relief, sustained pain freedom at 48 hours

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Zavegepant (Zavzpret™)

- Adverse events (drug vs. placebo)
  - Taste disorders (18% vs. 4%)
  - Nausea (4% vs. 1%)
  - Nasal discomfort (3% vs. 1%)
  - Vomiting (2% vs. <1%)

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Zavegepant (Zavzpret™)

Drug Interactions

- Zavegepant is a 3A4 substrate but no significant interactions with 3A4 inhibitors or were inducers seen.
- OATP1B3 inhibitors
  - Coadministration with rifampin
    - Strong OATP1B3 inhibitor ***and***
    - 3A inducer resulted in an increase in AUC of Zavegepant 2.3-fold.

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Zavegepant (Zavzpret™)

Drug Interactions

- OATP1B3 inducers
  - Has not been studied however, may decrease AUC of Zavegepant
- Intranasal decongestants
  - May decrease the efficacy of Zavegepant
  - If absolutely needed, use 1-hour or more after Zavegepant.

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Zavegepant (Zavzpret™)

- Precautions/contraindications
  - Avoid use in pregnancy and lactation.
    - Animal models did not demonstrate any issues, but inadequate safety data.
  - No indication in children
  - Avoid use in patients with severe hepatic impairment (no studies).
  - Avoid use in patients with creatinine clearance of <30 mL/min.
- Cost
  - $1,168.00 for 6 sprays (devices) per drugs.com

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Early Treatment:

Abortive Medications

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Headache experts agree that the optimal treatment strategy is to treat early, before central sensitization occurs.

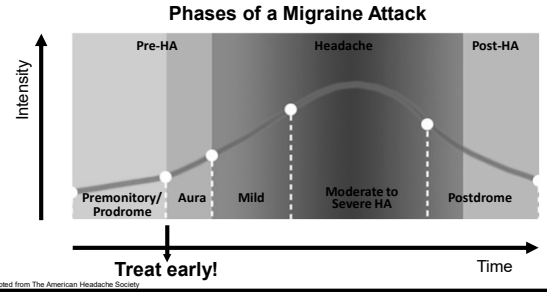

Image adapted from The American Headache Society

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Too Much of a Good Thing…

Use of products more than 2–3 times per week will result in medical overuse headache (MOH).

- Medication overuse headache
  - Worsening of head pain caused by frequent and excessive use of immediate relief medications
  - Bilateral, diffuse headache
  - Waxes and wanes
  - Associated with fatigue, n/v, restlessness
  - Will never get better on any medications until rebounding is eliminated

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When is migraine prophylactic medication warranted?

- Any or all of the following:
  - 3 or more migraine headache days per month
  - Attacks which interfere with daily routines despite acute treatment
  - Contraindication to or failure of abortive treatments
  - Acute treatments lead to adverse events, including medication overuse

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AHS/AAN Migraine Prevention Guidelines

https://headachejournal.onlinelibrary.wiley.com/action/doSearch?AllField=Migraine+Prevention+Guidelines

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AHS Guidelines: Preventive Treatment for Migraine

Established efficacy

- Anticonvulsants
  - Divalproex sodium, valproate sodium, topiramate
- Beta-blockers
  - Metoprolol, propranolol, timolol

- Triptans
- OnabotulinumtoxinA

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AHS Guidelines: Preventive Treatment for Migraine

Probably effective

- Antidepressants
  - Amitriptyline, venlafaxine
- Beta-blockers
  - Atenolol, nadolol

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AHS Guidelines: Preventive Treatment for Migraine

Possibly effective

- ACE inhibitors
  - Lisinopril
- Alpha-agonists
  - Clonidine
  - Guanfacine
- Anticonvulsants
  - Carbamazepine
- Beta-blockers
  - Nebivolol, pindolol
- Antihistamines
  - Cyproheptadine
- Angiotensin receptor blockers
  - Candesartan

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Calcitonin gene-related peptide (CGRP) Inhibitors: Prophylaxis

- Atogepant (Qulipta™)
  - Indicated for migraine headache prophylaxis
  - 10, 30, and 60 mg dose
  - 10–60 mg once daily
  - Adults only
  - CGRP substrate
- Rimegepant
  - Also indicated for migraine headache prophylaxis
  - 75 mg ODT
  - Dosed once every other day
  - CGRP substrate

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New Medication Class

- CGRP-inhibitor (Large molecules)
- Monoclonal antibody
- Adults only for the prevention of migraine

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New Medication Class

- Four products
  - Erenumab (Aimovig®)
    - 70–140 mg SC monthly
  - Fremanezumab (Ajovy®)
    - 225 mg SC monthly or 675 mg SC every 3 months
    - 225 mg SC indicated 6 – 17 years > 45 kg
  - Galcanezumab (Emgality®)
    - 240 mg SC × one then 120 mg monthly
    - Also approved for cluster headache: 300 mg SC monthly at start of cluster cycle
  - Eptinezumab (Vyepti®)
    - 100 mg or 300 mg IV infusion every 3 months

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What about cluster headaches?

- Oxygen – 7L via mask (high flow oxygen)
- Abortive therapies
  - Avoid medications such as opioids.
- Prophylaxis
  - Lithium: Best studied prophylactic medication
  - Galcanezumab (newest approved medication)

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Chronic Daily Headache: Pathway to Diagnosis

Headache 15 days or more per month

Exclude secondary headache

Classify based upon duration

Short:	Long:
Cluster	Chronic migraine
Trigeminal neuralgia	Hemicrania continua
Paroxysmal hemicranias	New persistent daily

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Prevalence of CDH

4.1% OF 13,000 General Public (~50% chronic migraine)

30% - 80% Headache Clinic Population

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Proposed Pathophysiology

Migraine Cycles

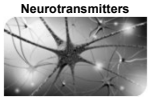
Medication Overuse

Stress

Infections Trauma

Hyperexcitability of pain systems

Neurotransmitters



Genetic Factors

Sinus, Oral, Dental Pathology

Cervical Spine

Image sources: Shutterstock

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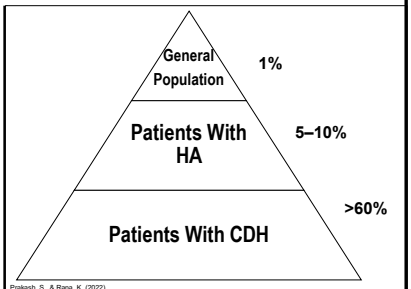
Common Pitfalls in Migraine Diagnosis: Importance of Medication Overuse

- MOH is common, but widely unrecognized.
- MOH is almost always transformed migraine
- Ask patients about all pain medication use!



Prakash, S., & Rana, K. (2022). Pitfalls in the Diagnosis of Migraine, Chronic Migraine, and Medication Overuse Headaches. *Pitfalls in the Diagnosis of Neurological Disorders*. 75.

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MOH Diagnosis

- Patients typically overuse multiple medications simultaneously.
  - Mean tablets/day = 5.2
  - Most commonly overused drugs are:
    - Butalbital combinations (48%)
    - Acetaminophen (46%)
    - Opioids (33%)
    - ASA (32%)
    - Triptans (18%)

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When do we see medication overuse?

- Ergotamine, triptans, opioids, butalbital (any formulation)
  - ≥10 days per month or more
- Analgesic overuse
  - >15 days per month

- Total exposure ≥15 days per month
- Triptan overuse more likely to increase migraine frequency

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Chronic Migraine: Diagnostic Criteria
Migraine Fulfilling the Criteria Below

☑ Meets the IHS criteria for migraine without aura

AND

☑ Not attributable to another disorder

- ❑ Occurs ≥15 days per month for ≥3 months
- ❑ Usually begins as migraine without aura and progresses
- ❑ As chronicity develops, headache tends to lose its attack-like presentation.
- ❑ When medication overuse is present, it is the likely cause of the chronic symptoms. (Medication overuse headache [MOH])

https://medicalcriteria.com/web/migraine/

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Chronic Daily Headache

- Requires multimodal approach to the treatment of their pain
  - Treat underlying comorbidities.
  - Set limits on abortive medications (<2 days per week).
  - Use adjunctive therapies: Acupuncture, pressure, other nonpharmacologic options.

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Long-Term Headache: Oral Options

- Long-term: Prednisone
  - 0.5 – 1.0 mg/kg/day
  - 21-day taper
  - Slowly withdraw other abortive medications.
  - Ramp up prophylactic medication at same time.
  - Protect stomach.

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Other Principles

- Ramp up preventative medication while pulling away abortive

- Reduce amount used by 10–25% weekly.
  - i.e., 60 butalbital pills per month means 15 pills per week
  - Each week: Go down by 10% or 1–2 tablets.
  - Will take 3 months to remove overused drug
  - If rapid withdrawal needed – Phenobarbital

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Abortive Medications

- Avoid medications that patient is overusing.
  - Opioids, barbiturates, ergotamines

- Use ones that patient has not been using.
  - Hydroxyzine
  - Metoclopramide
  - NSAIDs

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Additional Therapy for Chronic Migraine

- OnabotulinumtoxinA (Botox®)
  - Chronic migraine: Recommended total dose 155 units, as 0.1 mL (5 units) injections per each site divided across 7 head/neck muscles

- AbobotulinumtoxinA (Dysport®)

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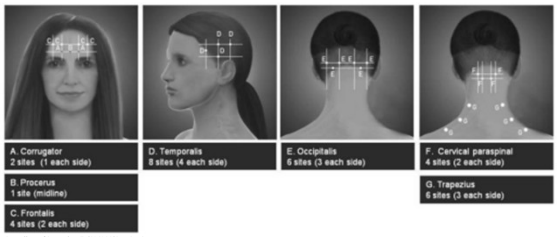
Additional Therapy for Chronic Migraine



https://www.fda.gov/media/124201/download

https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/103000s5236lbl.pdf

https://cdn.amegroups.cn/journals/pbpc/files/journals/8/articles/53057/public/53057-PB6-7383-R2.pdf

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My Medication Doesn't Work…

- Prednisone
  - 60, 40, 20 mg/day

or

- Ketorolac
  - 30–60 mg IM

- Antiemetic
  - Ondansetron or similar
- IV fluids

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Office Based Abortive Treatment

- Treatment with injectable anti-nausea medication
  - Dopamine antagonist, if sedation is not an issue (e.g., prochlorperazine 5–10 mg IM)
  - Ondansetron, if sedation is to be avoided (e.g., 8 mg ODT)

- Treatment with a migraine specific therapy
  - Subcutaneous sumatriptan (usually 4–6 mg SQ)
  - Dihydroergotamine (usual dose 1 mg SQ or IM)

- Treatment with injectable NSAID especially if allodynia is present (e.g., ketorolac 60 mg IM)

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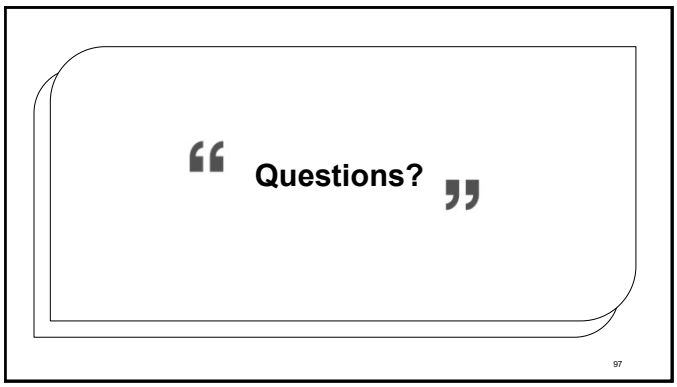
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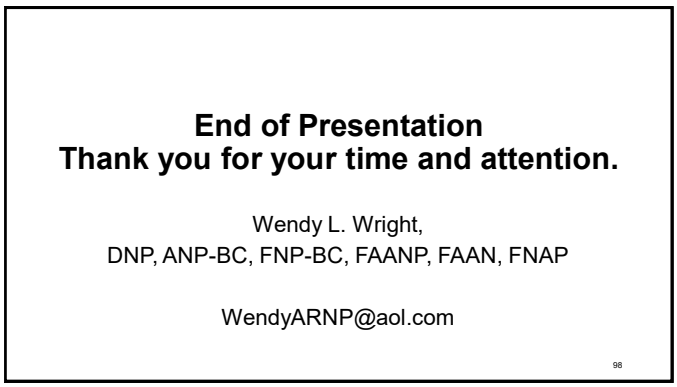
End of Presentation
Thank you for your time and attention.
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