TREATMENT AND PREVENTION OF PEDIATRIC MIGRAINE

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LEARNING OBJECTIVES

- Diagnose common presentations of pediatric headache
- Identify the red flag symptoms and signs in patients with secondary headache
- Discuss lifestyle modification and headache hygiene with patients and families
- Recognize which pediatric headache patients should be referred for imaging +/- specialist
- Develop a comprehensive headache action plan utilizing acute and preventive treatments

DISCLOSURES

- No financial or relationship disclosures

- discussing several therapies for the treatment of headache disorders in children. Even when these therapies have a labeled use for migraine in adults, the majority of them are unlabeled/investigational in children.

MIGRAINE PATHOPHYSIOLOGY

MIGRAINE PATHOPHYSIOLOGY

- Highly complex, inherited disorder of sensory processing
- Recurrent headaches and associated symptoms with neurologic dysfunction also in interictal phase
- Same process as adults, some different symptoms

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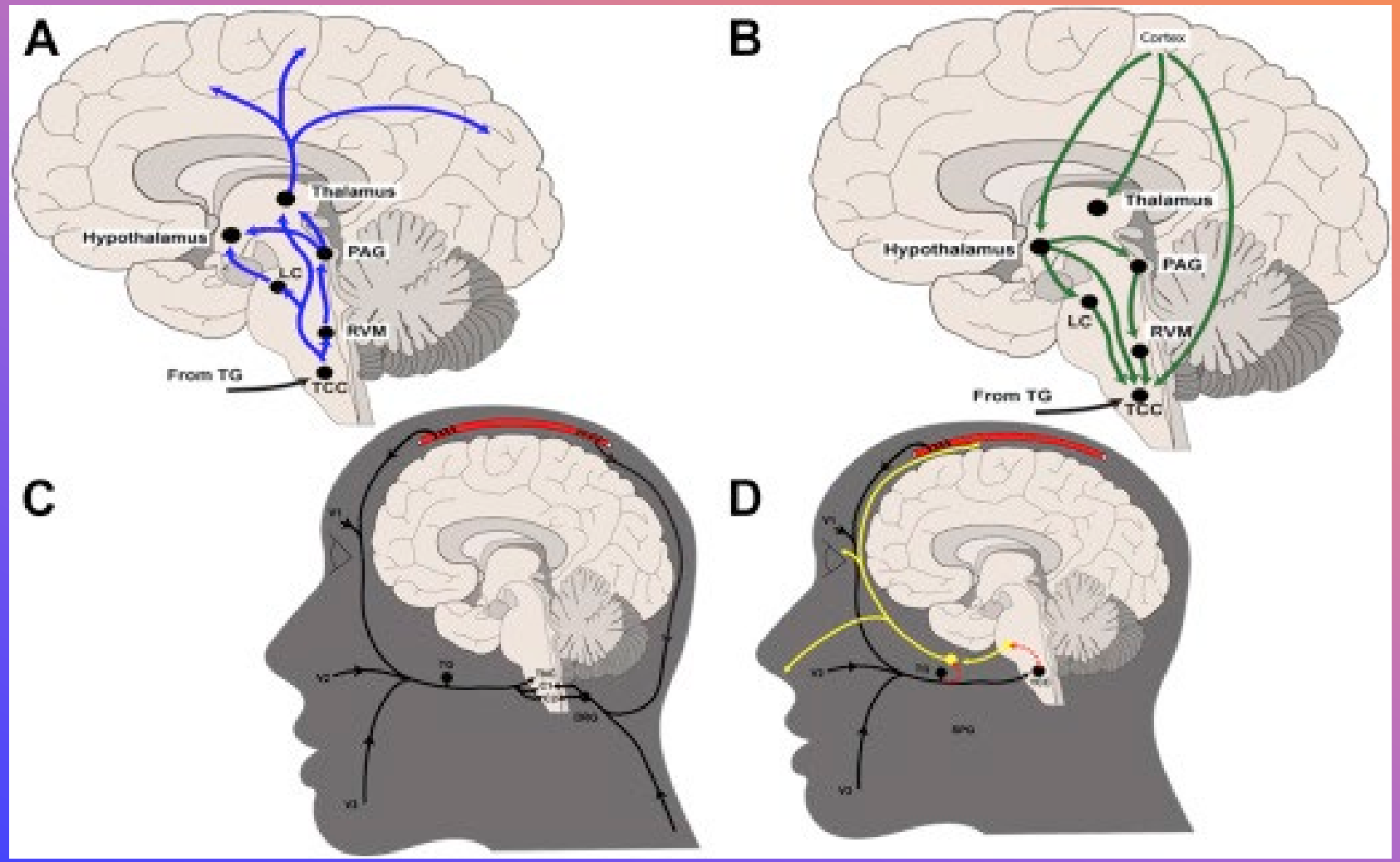

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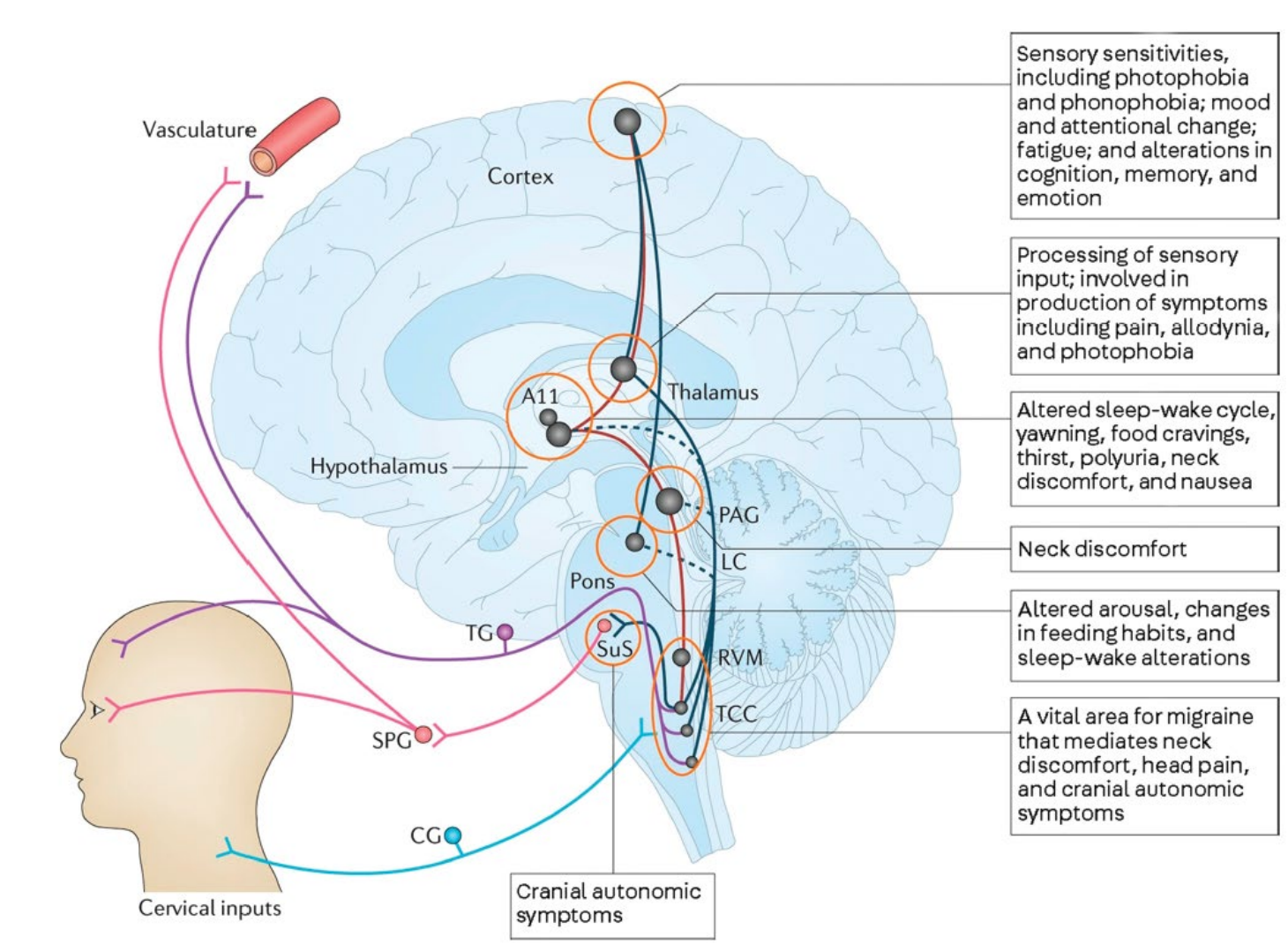
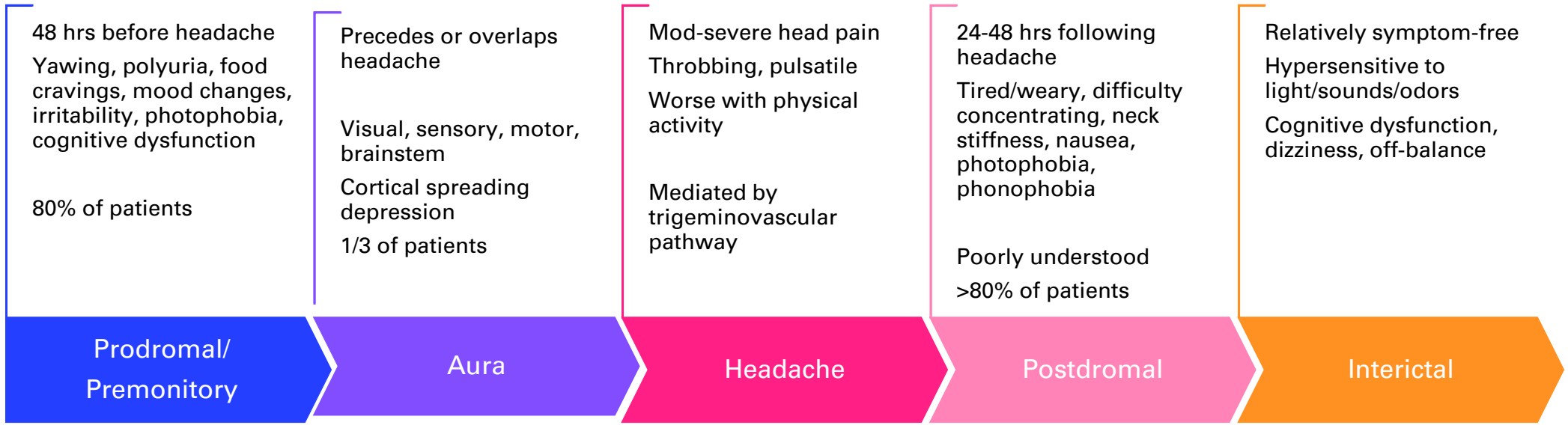


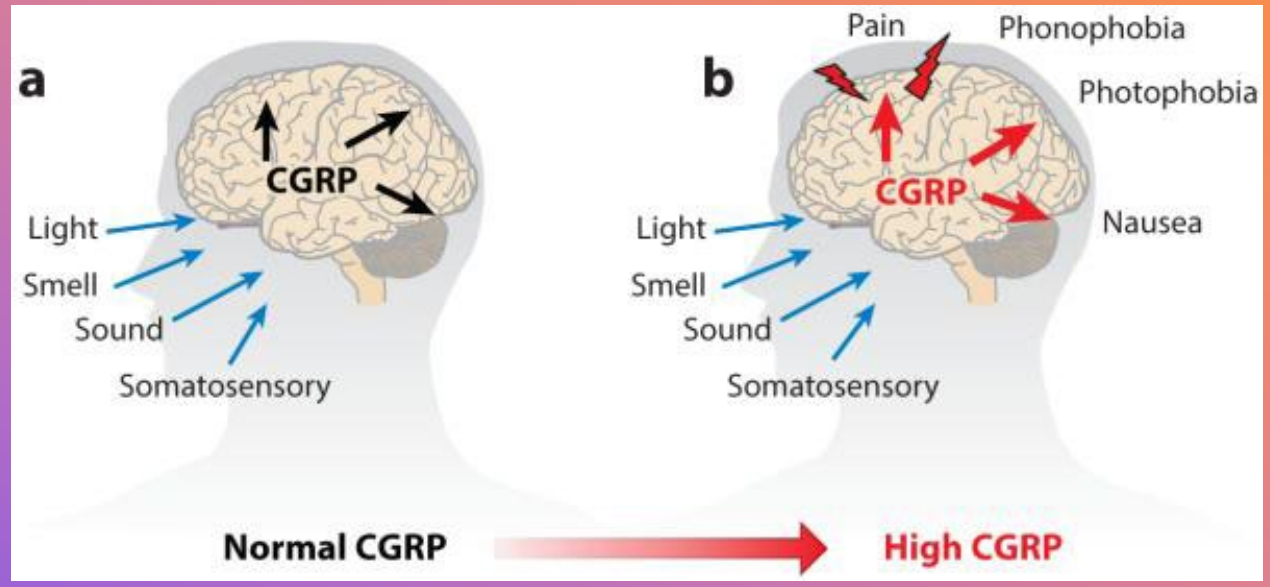
5 phases of migraine



- Phases may overlap or vary

CGRP

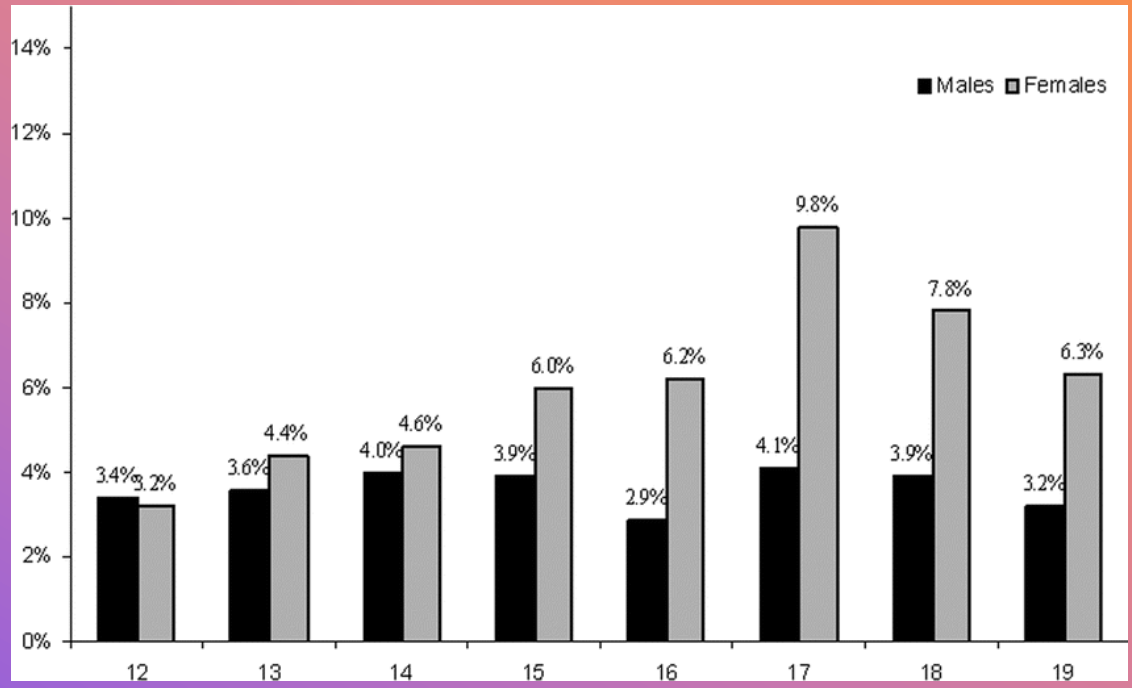
- Ubiquitous peptide found in brain, gut, vasculature, etc.
- Causes arterial vasodilation, neurogenic inflammation, activation of meningeal nociceptors
- Enhances synaptic transmission through glutamate transmission -> peripheral and central sensitization
- Bidirectional model between CGRP and CSD



PREVALENCE

- 60% of children/adolescents with significant headache
- 7-9% with migraine, more when including probable dx
- Age 10: 5% boys and girls
- Age 15: 5% boys and 7% girls
- Age 20: 6% boys and 10% girls

- ¾ managed by PCP, ¼ by neurology



PROGNOSIS

- Migraine is the leading cause of disability for children and adolescents worldwide
- ¾ of children will continue to have symptoms as adults

- HOWEVER:

- 2/3 of children respond to current therapies
- Children who respond to preventive treatment have better headache control as adults

Table 4. Headache Severity at Initial Diagnosis and Follow-up*

Headache Severity	1983	1993	2003
No headache	0	15 (25)	16 (27)
Mild	20 (33)	16 (27)	9 (15)
Moderate or severe	40 (67)	29 (48)	35 (58)
Total	**60 (100)**	**60 (100)**	**60 (100)**

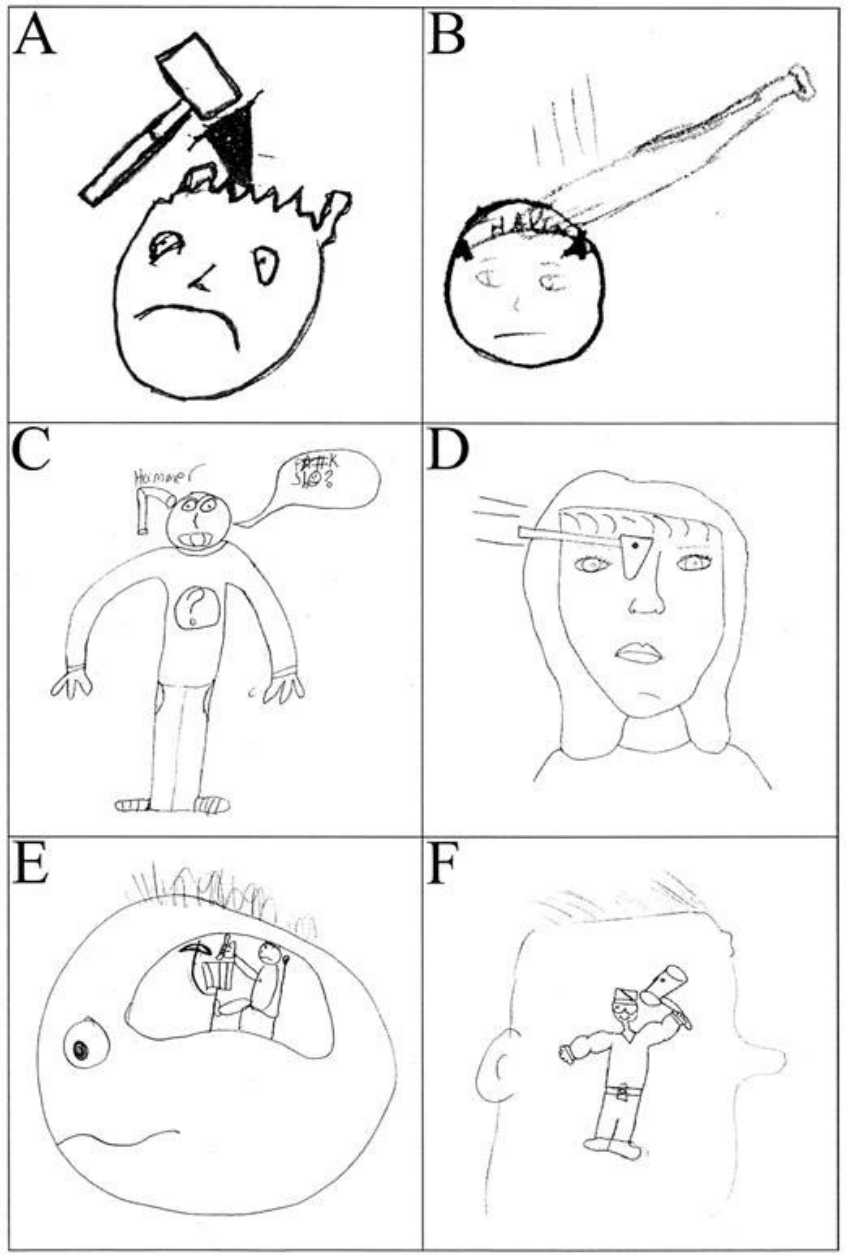
*Data are given as number (percentage) of patients.

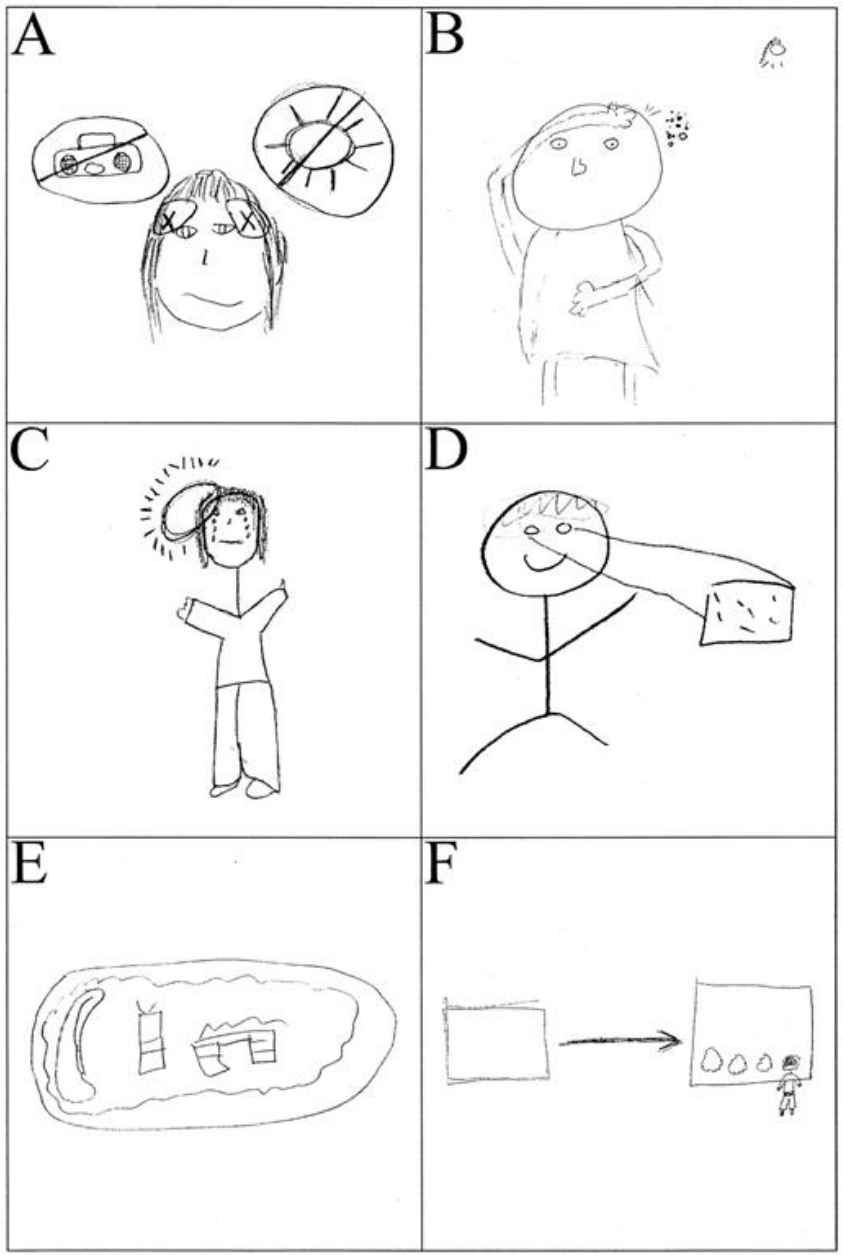
HISTORY

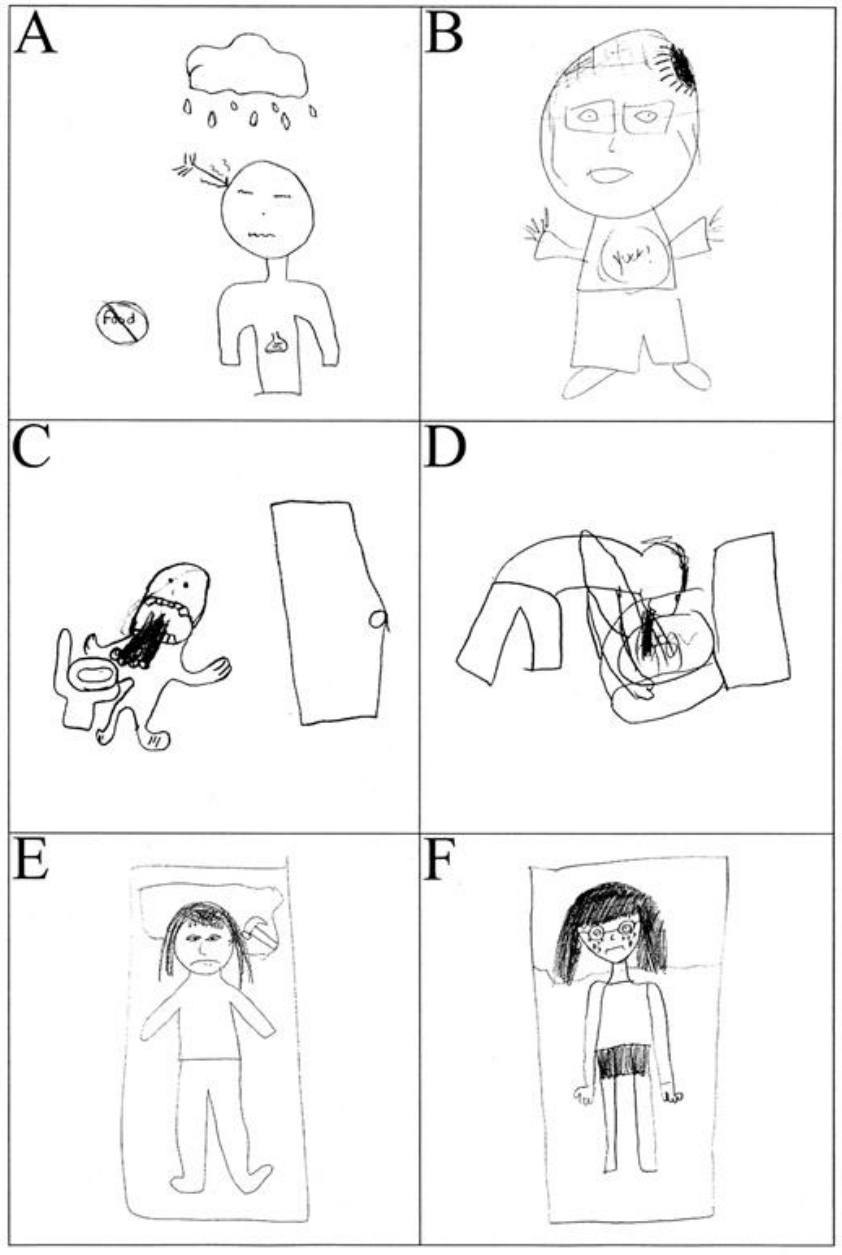
- Include patient and parent
- Consider allowing patient to draw migraine

Key components:

- Monthly headache frequency (# of days in last 30 days counting both small and big headaches)
- Pattern: intermittent/stable vs escalating
- Location: point to pain
- Pain quality: squeezing your head, knocking on head, head exploding, throbbing, stabbing, pressure
- Pain scale: 1-10 or small-medium-big







POUNDING PAIN

VISUAL AURAS

NAUSEA

ASSOCIATED FEATURES

- Premonitory/prodrome: facial pallor, fatigue, mood changes, yawning (1/3 young children, 2/3 teens)
- Aura: visual (spots, lines, etc) , sensory (numbness/tingling), speech, motor symptoms, generalized feeling of weakness, focal weakness
- Photophobia and/or phonophobia
- Pallor, anorexia (young); difficulty thinking, lightheadedness, fatigue, osmophobia (teens)
- Cranial autonomic symptoms
- Postdrome: fatigue, cognitive difficulties, and nausea often persist for hours after the pain has resolved. >80% of children develop new symptoms (thirst, somnolence, visual disturbances, and food cravings) after the pain has resolved

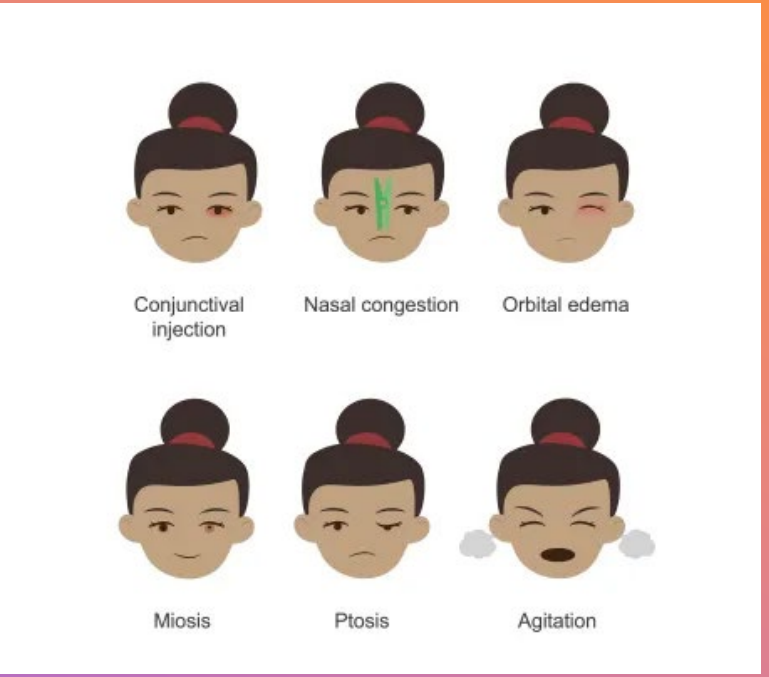
AURAS

- Visual most common: seeing extra spots, lines, or lights, loss of vision. NOT INCLUDING ORTHOSTATIC CHANGES
- Sensory: numbness or tingling
- Weakness: all-over muscle fatigue vs numbness leading to clumsiness vs true paresis (familial hemiplegic migraine)
- Brainstem: vertigo, dysarthria, diplopia, tinnitus, impaired hearing, lack of coordination, confusion, and sometimes loss of consciousness

CRANIAL AUTONOMIC SYMPTOMS

- Eyes: Conjunctival injection, lacrimation, ptosis
- Nose: nasal congestion or rhinorrhea
- Face: facial flushing
- Ears: ear pressure

- BILATERAL SYMPTOMS ARE COMMON IN MIGRAINE
- Unilateral symptoms also possible with migraine but may suggest trigeminal autonomic cephalalgia



HEADACHE RELATED DISABILITY: PEDMIDAS

- tested and validated for ages 4 -18, covers last 3 months
- mirrors the use of the adult MIDAS developed for adults age 20-50

1) How many days of school missed in last month 2/2 HA:
   - A) Full days
   - B) Half days
   - C) function <50% ability

2) Days you could not do home activities (chores, homework) 2/2 HA
3) Days you could not participate in activities (sports, going out) 2/2 HA
   a) days you participated but at <50% of usual ability 2/2 HA

HEADACHE RELATED DISABILITY: PEDMIDAS

Results scored on 50 point scale

Can be followed over time to assess response to treatment

PedMIDAS Score Range	Disability Grade
0 to 10	Little to none
11 to 30	Mild
31 to 50	Moderate
Greater than 50	Severe

RELATED SYNDROMES

- **Cyclical vomiting:** episodes of recurrent emesis
- **Abdominal migraine:** disabling abdominal pain w/wo HA

- Benign paroxysmal torticollis: intermittent head tilt with malaise, pallor, irritability, ataxia, and nausea/vomiting
- Benign paroxysmal vertigo: "drunk gait" or trouble standing up w/wo nystagmus
- Colic: excessive crying as baby

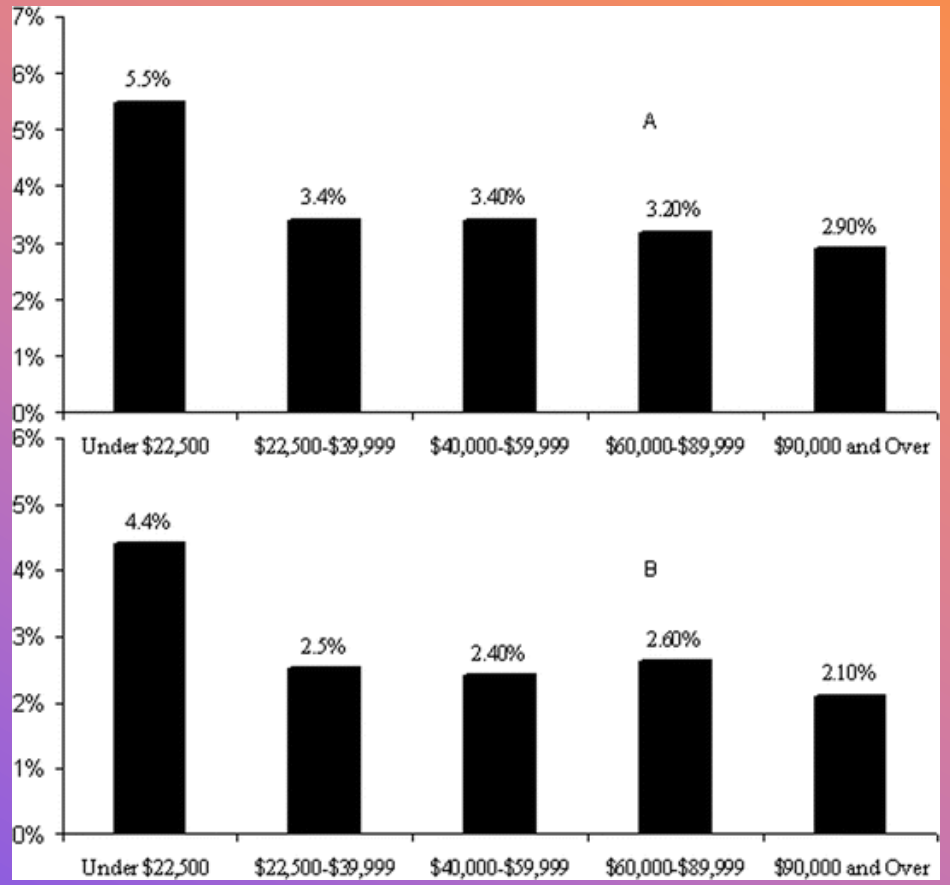
- Childhood periodic syndromes usually younger age
- CV and AM persists in teens
- Respond to migraine meds

COMORBIDITY

- **Obesity:** Higher BMI -> higher frequency/disability
- **Epilepsy:** increased rate of migraine
- **Atopic:** allergic rhinitis or conjunctivitis with increased migraine
- **Anxiety/depression:** higher disability even when controlling for frequency
- **ADHD:** associated with migraine, also causes stress, use of stimulants
- **Sleep:** higher with narcolepsy and restless leg syndrome

INFLUENCES

- **Parental history of migraine:** onset 10-11 years before parents, 2-3 years earlier than patients without fam hx
- **Early onset:** presenting before age 6 -> more likely to need prevention
- **Lower household income:** Higher migraine without fam hx
- **Early menarche (<12):** Increased odds of migraine/HA



SOCIAL

- Adverse childhood events (physical/emotional/sexual abuse, financial stress, parental divorce, recent death, mental illness, addiction) have been shown to predispose to headache in childhood and later

- Consider HEADS exam for teenagers

Table 3. Logistic Regression Models Examining the Association Between Number of ACEs and History of Frequent or Severe Headaches (Including Migraine) in Children Ages 3-17 Years

ACE Score for a Child	Unadjusted OR (95% CI)	Adjusted OR (95% CI) †, †
No ACE	Ref	Ref
1 ACE	1.65 (1.31, 2.07)	1.34 (1.07, 1.68)
2 ACE	2.74 (2.12, 3.54)	2.15 (1.66, 2.80)
3 ACE	2.93 (2.20, 3.90)	1.89 (1.40, 2.53)
4 or more ACE	5.26 (4.10, 6.75)	3.4 (2.61, 4.43)

† Adjusted OR: adjusted for age, sex, race, ethnicity, depression, anxiety, epilepsy, brain injury, average sleep, and weight concern.

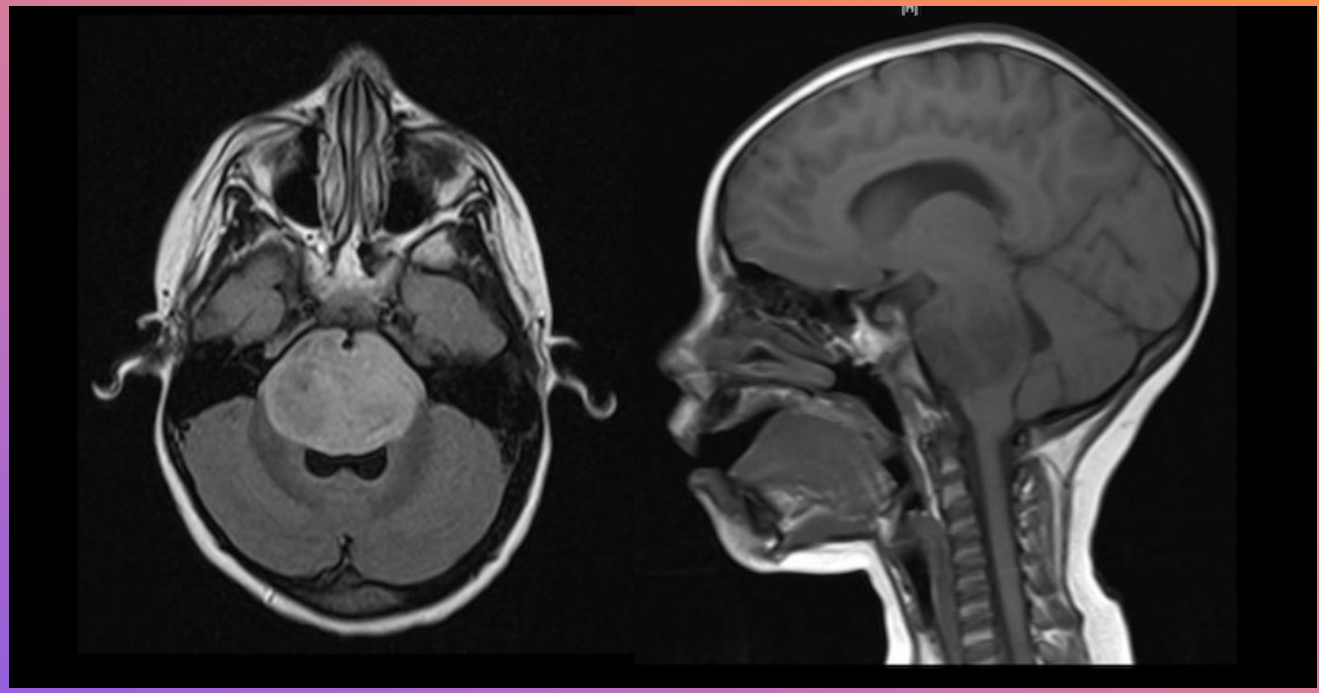
PHYSICAL EXAM

- Rule out: Facial asymmetry, visual/eye abnormalities, papilledema, motor asymmetry
- Vitals: hypertension, tachycardia, serial HCs
- Neck: limitations or pain with motion
- Sinuses: palpate for tenderness
- Jaw: Assess for TMJ (pain, clicking)
- Allodynia: rub forehead and scalp, palpate occipital nerves
- Continuous/positional headache: orthostatic vitals

RED FLAGS

Headache is due to life threatening causes (e.g. brain tumor) in:

- 2-3% of children presenting to EC
- 1% of children in primary care setting



SNOOP4Y

Red Flag	Significance
Systemic signs/symptoms	
Fever, acute symptoms	Infections ranging from minor to serious[35] are the most common cause of headache in children in the emergency department
Head trauma	Relatively common cause for headache in the emergency department
Vomiting	Consistent with migraine[38] but also a risk factor for brain tumors[39]
Weight loss	Can be a symptom of malignancy
Comorbidities	Many systemic illnesses, including rheumatologic, oncologic, vascular, and hematologic conditions; genetic syndromes; and abnormalities of the immune system predispose to other serious causes for headache
Medications	Headache can be a medication side effect[40]
Neurologic signs/ symptoms	Abnormal gait, ataxia, papilledema, changes in personality/behavior/cognition, visual disturbances/eye movement abnormalities, and seizure[39] are red flags for serious secondary headache

LP

SNOOP4Y

Onset sudden	Thunderclap onset of headache in which pain peaks instantly is rare in children but can signal serious causes such as cerebral hemorrhage or reversible cerebral vasoconstriction syndrome; the full range of differential diagnosis from adults with thunderclap headache should be considered, and imaging should be pursued
Onset in sleep/early morning	Headache causing a child to awaken from sleep or occurring early in the morning has been associated with intracranial lesions[41] and can be suggestive of sleep apnea and other sleep disorders[42]; however, this diurnal pattern is also common in primary headache disorders[43]
Positional exacerbation	
Worse upright	Headache that resolves when supine and worsens immediately upon standing or slowly throughout the day can suggest spontaneous intracranial hypotension or postural tachycardia syndrome[33]
Worse supine	Consider increased intracranial pressure from tumor or idiopathic intracranial hypertension

SNOOPPPPY

Precipitated by Valsalva	Brief headaches triggered by Valsalva maneuvers can signal intracranial abnormalities; headache triggered by cough along with signs/symptoms of brainstem/cerebellum/cervical spinal cord dysfunction[38] may suggest Chiari malformation (although Chiari malformation may be found incidentally with other headaches and is of varying significance)
Parents (lack of family history)	Several studies have found that lack of family history of headaches is associated with higher odds of having a serious cause of headache in children[39]; most children with migraine have a family history of migraine, although the parent(s)/guardian(s) may not be aware of the diagnosis
Progressive or new	Significant change in the headache pattern, new headache, or progressively escalating headache raises the level of concern for secondary cause[44]; however, many new-onset headaches are not caused by structural brain abnormalities[44] and may be attributed to relatively benign causes such as viral infections; furthermore, studies have used different cutoff points from days to months[45] when trying to determine when a "recent-onset" headache is worrisome, so the newness of the headache must be interpreted with the presence or absence of other headache features
Young age	Some studies have found that children of younger age (defined as either ≤5 years[45,46] or ≤7 years[39]) were more likely to be diagnosed with a life-threatening headache, whereas other studies have refuted that concern[44]

WHEN NOT TO IMAGE

- Stable frequency of headaches
- Absence of red flags
- Normal neuro exam

Unnecessary imaging -> increased costs

Recommendations

1. Obtaining a neuroimaging study on a routine basis is not indicated in children with recurrent headaches and a normal neurologic examination (Level B; class II and class III evidence).
2. Neuroimaging should be considered in children with an abnormal neurologic examination (e.g., focal findings, signs of increased intracranial pressure, significant alteration of consciousness), the coexistence of seizures, or both (Level B; class II and class III evidence).
3. Neuroimaging should be considered in children in whom there are historical features to suggest the recent onset of severe headache, change in the type of headache, or if there are associated features that suggest neurologic dysfunction (Level B; class II and class III evidence).

LABS

- No general recommendations, send based on clinical picture

Basic headache labs to consider:
CBC (anemia)
CMP (electrolyte imbalance, liver/kidney dysfunction)
Iron panel (iron deficiency with or without anemia)
TSH (hypo and hyper can lead to headache)
ESR/CRP (inflammation, confirm iron studies)

PRIMARY HEADACHE DISORDERS

- Migraine: ~7-9%
- Tension headache: ~10-24%
- Trigeminal autonomic cephalgias: RARE (cluster in teens <0.1%)
- Primary stabbing headache: RARE

Table 3 Comparison between the headache population younger than 6 years of age and 100 consecutive school headache patients older than 6 years of age selected in 2003

Headache type	Headache children younger than 6 years	Headache children older than 6 years
Migraine, %	35.2	57.0
Episodic tension headache, %	18.1	17.0
Chronic daily headache, %	4.8	13.0
Idiopathic stabbing headache, %	12.4	3.0
Post-traumatic headache, %	17.1	8.0
Other secondary headaches, %	9.5	2.0

EPISODIC MIGRAINE

- In children and adolescents, migraine duration may last 2-72 hours
- Migraine is more often bilateral
- Migraine headache is often frontotemporal
- Subset of patients have facial pain – still grouped under migraine
- Episodic: 1-14 days per month
- High frequency episodic: 8-14 days per month

Diagnostic criteria:

A. At least five attacks[1] fulfilling criteria B-D

B. Headache attacks lasting 4-72 hr (untreated or unsuccessfully treated)[2;3]

C. Headache has at least two of the following four characteristics:

1. unilateral location
2. pulsating quality
3. moderate or severe pain intensity
4. aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)

D. During headache at least one of the following:

1. nausea and/or vomiting
2. photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis.

MIGRAINE WITH AURA

Visual aura is most common (90% of aura)
Common patient mistakes:
- incorrect lateralization
- sudden vs. gradual onset
- monocular (retinal migraine) instead of homonymous visual disturbances
- mistaking sensory disturbance for weakness
- aura duration

A. At least two attacks fulfilling criteria B and C
B. One or more of the following fully reversible aura symptoms:

1. visual
2. sensory
3. speech and/or language
4. motor
5. brainstem
6. retinal

C. At least three of the following six characteristics:

1. at least one aura symptom spreads gradually over ≥5 minutes
2. two or more aura symptoms occur in succession
3. each individual aura symptom lasts 5-60 minutes[1]
4. at least one aura symptom is unilateral[2]
5. at least one aura symptom is positive[3]
6. the aura is accompanied, or followed within 60 minutes, by headache

D. Not better accounted for by another ICHD-3 diagnosis.

CHRONIC MIGRAINE

Headache occurring on 15 or more days per month for greater than 3 months, with migrainous features on more than 8 days per month

A. Headache (migraine-like or tension-type-like[1]) on ≥15 days/month for >3 months, and fulfilling criteria B and C

B. Occurring in a patient who has had at least five attacks fulfilling criteria B-D for 1.1 *Migraine without aura* and/or criteria B and C for 1.2 *Migraine with aura*

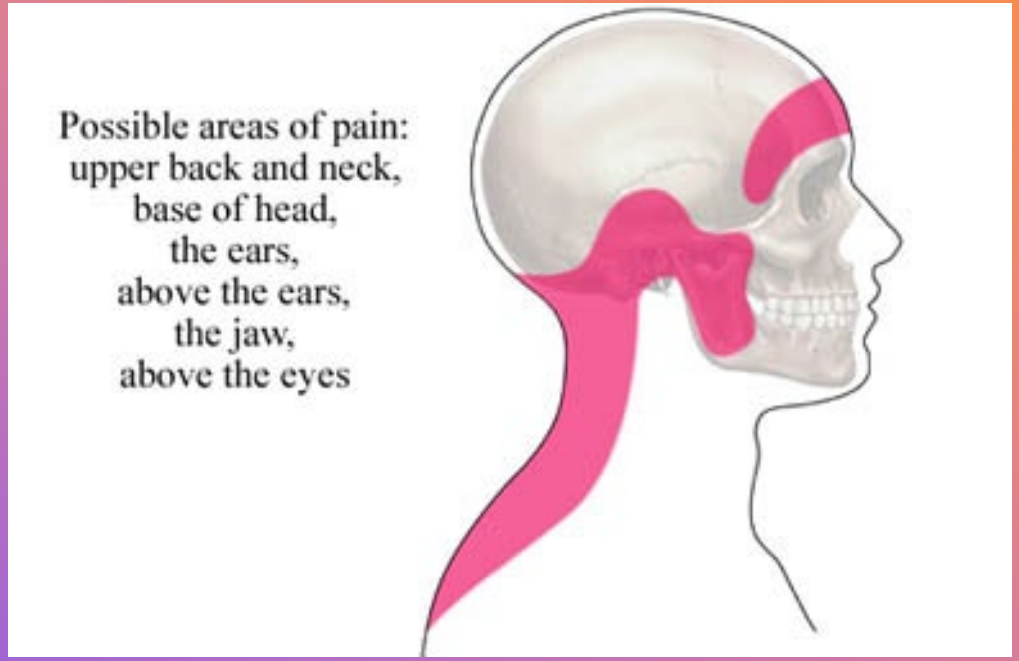
C. On ≥8 days/month for >3 months, fulfilling any of the following[2]:

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[3;4;5].

TENSION HEADACHE

- Mild-moderate, non-disabling head pain
- Lack of associated symptoms such as nausea/vomiting
- Occurs in 10-24% of children and adolescents
- But may do not seek care due to mild attacks
- Treat with NSAIDs/Tylenol



TRIGEMINAL AUTONOMIC CEPHALGIAS

Rare in children

- Cluster headache
- Paroxysmal hemicrania
- Hemicrania continua
- short-lasting unilateral neuralgiform headache attacks

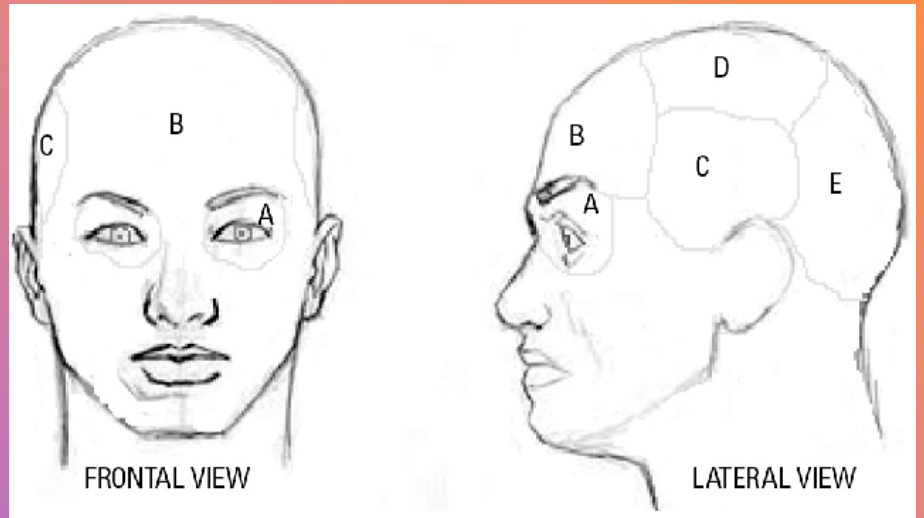
- unilateral headache +/- prominent cranial parasympathetic autonomic features, lateralized and ipsilateral to the headache.
- Restlessness present, may be less pronounced in childhood

TRIGEMINAL AUTONOMIC CEPHALGIAS

Syndrome	Pain location	Attack duration	Autonomic features	Migrainous features	Exacerbants
Trigeminal autonomic cephalalgias					
Cluster	Unilateral frontal/ temporal/periorbital	Minutes to hours	Always	Sometimes	Alcohol, sleep
Paroxysmal hemicrania	Unilateral frontal/ temporal/periorbital	Minutes	Always	Sometimes	Neck turning
Short-lasting unilateral neuralgiform headache attack syndromes (SUNHA)	Unilateral V1	Seconds to minutes	Always	Rarely	Cutaneous, thermal, mechanical
Hemicrania continua	Unilateral	Minutes or hours superimposed on baseline pain	Always	Often	Variable

PRIMARY STABBING HEADACHE

- Very brief episodes of stabbing pain, can be severe
- NO autonomic features
- Usually only require treatment if frequent
- Overlap with migraine

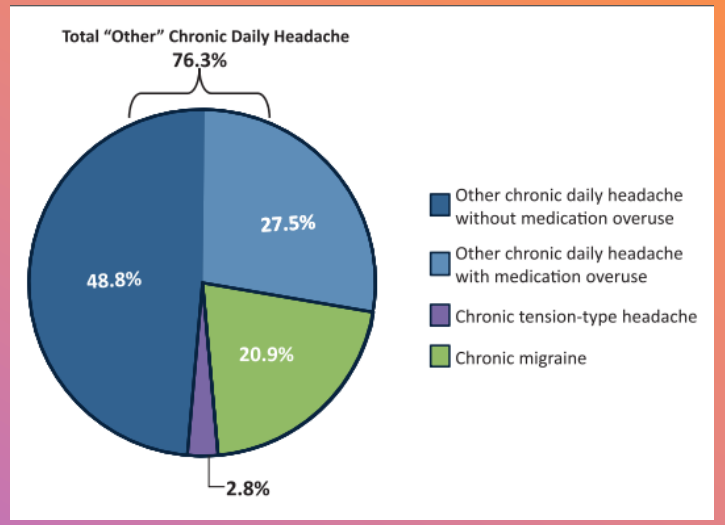


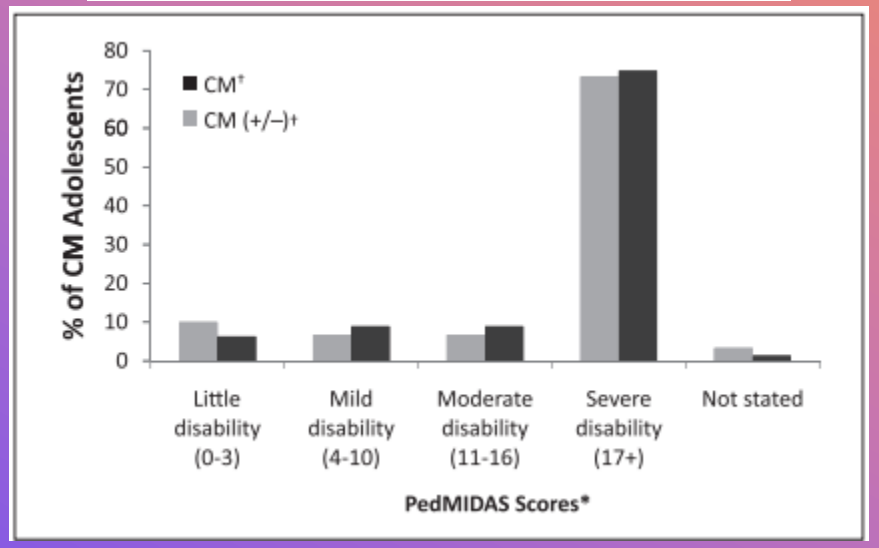
Place	n	%
Orbital	1	3.3
Frontal	1	3.3
Temporal	16	53.3
Parietal	4	13.3
Occipital	8	26.7
Total	30	100

Fig 2. Distribution of the Jabs.

FREQUENT/DAILY HAS

- 1.5% of children: several times weekly or daily headaches
- More common in female, increasing with age
- Chronic migraine: >=15 headache days, 8 or more migraine
- High rates of disability in teens with chronic migraine





DAILY HEADACHES

- Physical/sexual abuse more common in these patients
- Majority have anxiety related to school
- Subset with significant psych disease / school phobia (may contribute to seasonal pattern)
- Acute family financial stress more common
- Depression and anxiety -> worse disability
- Poor sleep -> poor response to therapy

Table 3. MANOVA analysis of differences between adolescents with and without a lifetime psychiatric comorbidity.

	Psychiatric comorbidity (*n* = 42)	No psychiatric comorbidity (*n* = 51)		
	Mean (SD)	Mean (SD)	F	*P*
PedMIDAS Total Score	71.12 (35.05)	53.94 (27.23)	7.07	.009*
PedsQL Child/Teen Report	68.11 (16.13)	75.83 (12.36)	6.82	.010*
PedsQL Parent Report	69.95 (14.90)	77.02 (15.93)	4.80	.031*

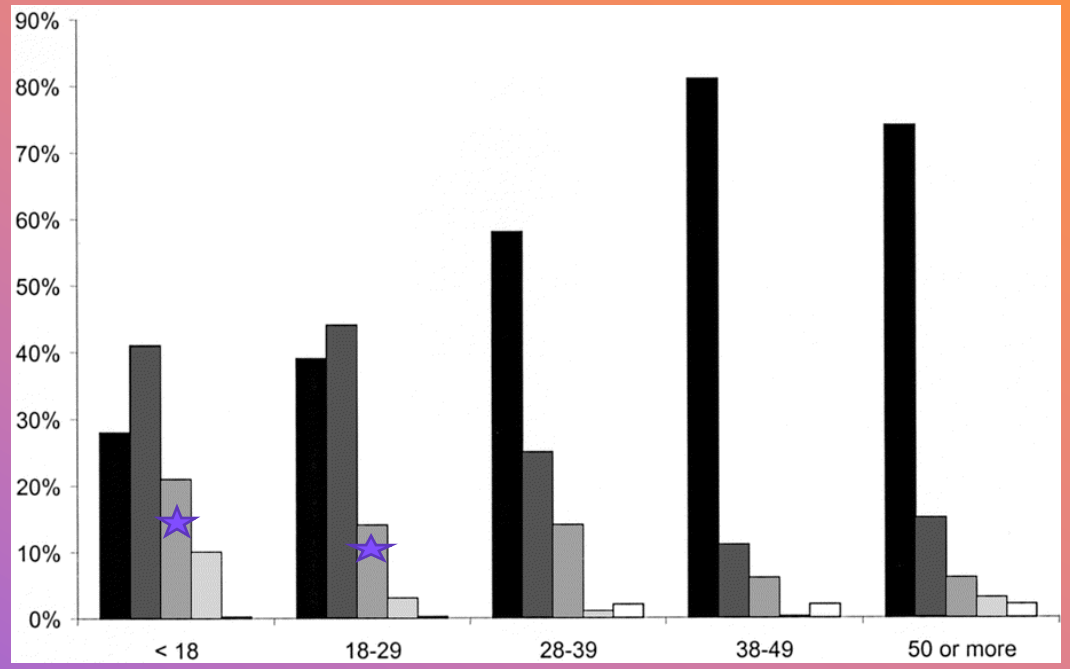
*Statistically significant at.05. MANOVA: multivariate analysis of variance; PedMIDAS: Pediatric Migraine Disability Assessment; PedsQL: The Pediatric Quality of Life Inventory.

	History of Abuse (n = 8)		No History of Abuse (n = 114)	
Variable	**Mean**	**SD**	**Mean**	**SD**
Headache frequency (0–28)	24.57	6.02	20.78	5.47
Pain intensity (VAS)	6.10	0.72	5.56	1.69
CDI (0–54)	13.63	10.19	7.62	6.42
PedMIDAS total score (0–540)	62.63	29.59	65.25	35.56

NEW DAILY PERSISTENT HEADACHE

- No history of significant headache
- Distinct onset, present ever since for 3+ months
- May continue years or decades
- 1/5 of all pediatric patients with ‘chronic daily headache’

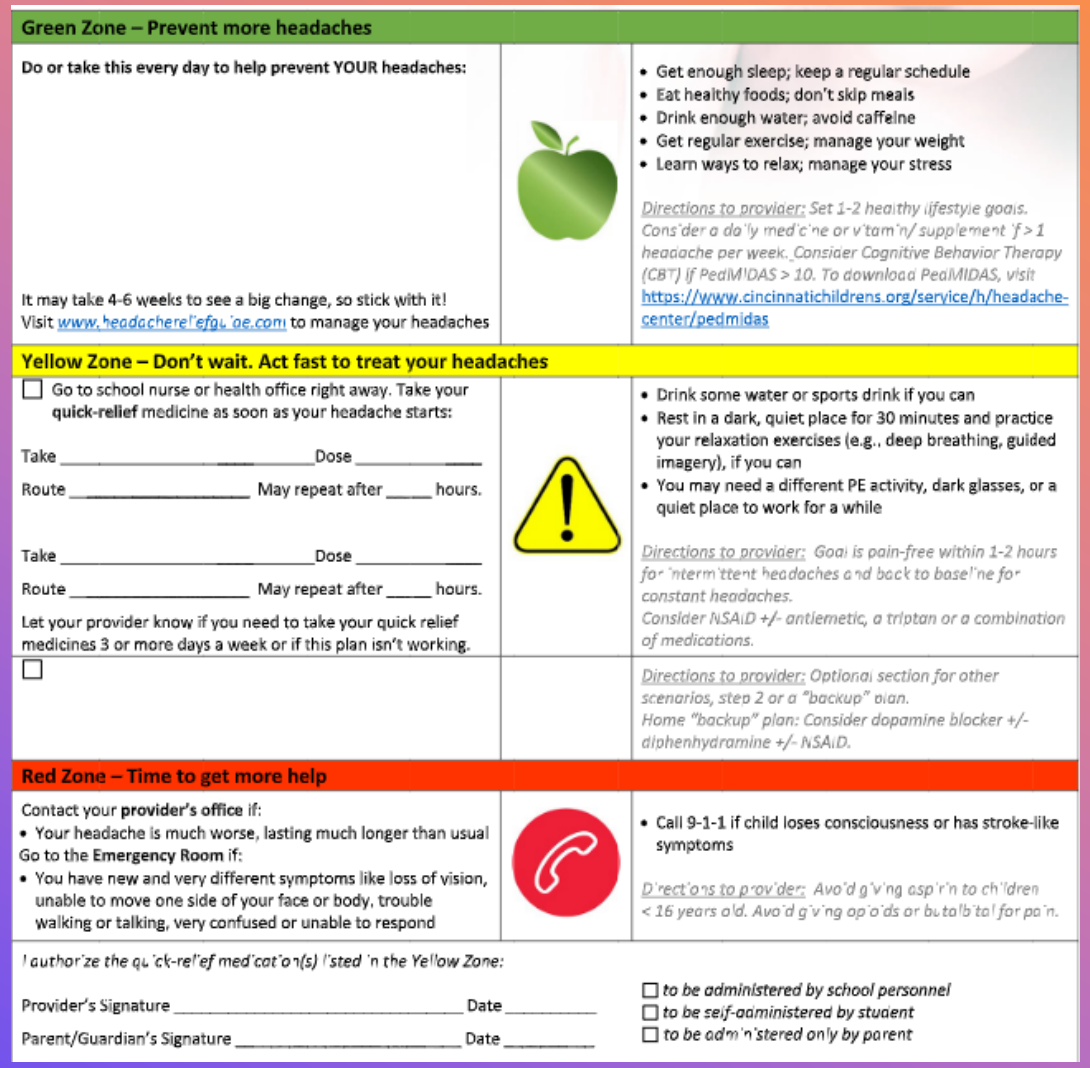
- MOST TREATMENT RESISTENT HEADACHE TYPE, REFER ASAP



ACUTE ACTION PLAN

- All patients with migraine should be given an acute treatment plan for headache
- school note to excuse at symptom onset so patient can hydrate, take acute med, and rest

- https://headachejournal.onlinelibrary.wiley.com/doi/epdf/10.1111/head.13681



Green Zone – Prevent more headaches

Do or take this every day to help prevent YOUR headaches:

- Get enough sleep; keep a regular schedule
- Eat healthy foods; don't skip meals
- Drink enough water; avoid caffeine
- Get regular exercise; manage your weight
- Learn ways to relax; manage your stress

Directions to provider: Set 1-2 healthy lifestyle goals. Consider a daily medicine or vitamin/ supplement if > 1 headache per week. Consider Cognitive Behavior Therapy (CBT) if PedMIDAS > 10. To download PedMIDAS, visit https://www.cincinnatichildrens.org/service/h/headache-center/pedmidas

It may take 4-6 weeks to see a big change, so stick with it!
Visit www.headachereferguide.com to manage your headaches

Yellow Zone – Don't wait. Act fast to treat your headaches

☐ Go to school nurse or health office right away. Take your **quick-relief** medicine as soon as your headache starts:

Take _____ Dose _____
Route _____ May repeat after ____ hours.

Take _____ Dose _____
Route _____ May repeat after ____ hours.

Let your provider know if you need to take your quick relief medicines 3 or more days a week or if this plan isn't working.

- Drink some water or sports drink if you can
- Rest in a dark, quiet place for 30 minutes and practice your relaxation exercises (e.g., deep breathing, guided imagery), if you can
- You may need a different PE activity, dark glasses, or a quiet place to work for a while

Directions to provider: Goal is pain-free within 1-2 hours for intermittent headaches and back to baseline for constant headaches.
Consider NSAID +/- antiemetic, a triptan or a combination of medications.

☐

Directions to provider: Optional section for other scenarios, step 2 or a "backup" plan.
Home "backup" plan: Consider dopamine blocker +/- diphenhydramine +/- NSAID.

Red Zone – Time to get more help

Contact your **provider's office** if:
- Your headache is much worse, lasting much longer than usual

Go to the **Emergency Room** if:
- You have new and very different symptoms like loss of vision, unable to move one side of your face or body, trouble walking or talking, very confused or unable to respond

- Call 9-1-1 if child loses consciousness or has stroke-like symptoms

Directions to provider: Avoid giving aspirin to children < 16 years old. Avoid giving opioids or butalbital for pain.

I authorize the quick-relief medication(s) listed in the Yellow Zone:

Provider's Signature _____ Date _____
Parent/Guardian's Signature _____ Date _____

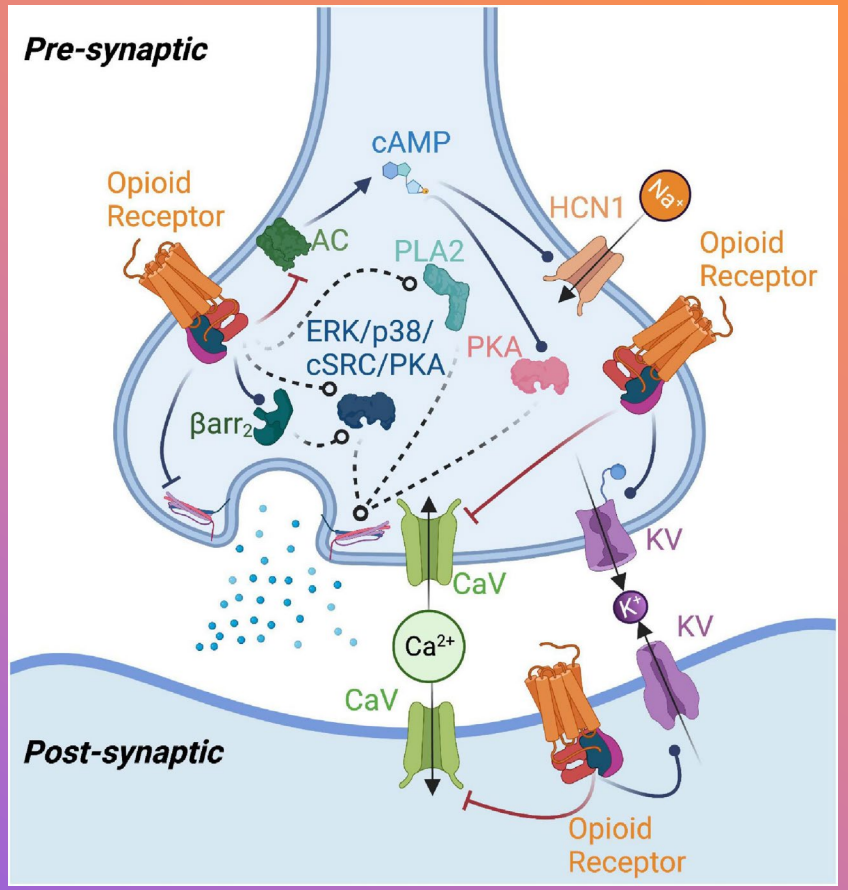
☐ *to be administered by school personnel*
☐ *to be self-administered by student*
☐ *to be administered only by parent*

FIRST STEP

- **Ibuprofen** 7.5-**10mg/kg/dose, given every 4-6 hrs prn migraine**
  - Ibuprofen has nearly 3x odds of efficacy as placebo (OR 2.9, 95% CI 1.0-8.1), and 2x odds as acetaminophen (OR 2.2, 95% CI 1.1-4.0)
- Alternative: naproxen 5-6mg/kg/dose given q8h prn migraine
- Avoiding NSAIDs?: acetaminophen 15mg/kg/dose q4-6hrs
- Avoiding all meds? devices

WHY NOT OPIOIDS?

- Opioids should not be used routinely for migraine therapy!
- Opioid use → pain receptor changes → less responsive to other migraine medication → escalation of opioid use → medication overuse headache
- A national practice variation study has found that pediatric migraineurs leaving pediatric ER received opioids 5.4% of time but triptans only 1% of time



MEDICATION OVERUSE

- Simple analgesics (NSAIDs/Tylenol): limit to 14 days or less per month
- Triptans: limit to 9 days or less per month
- Combo analgesics (with caffeine): limit to 9 days or less per month

DEVICES

- External trigeminal nerve stimulator (Cefaly): no prescription, acute and preventive mode, available online, FDA approved 12+

- Remote electrical neuromodulation (Nerivio): acute and preventive, online prescription needed, FDA approved 12+

TRIPTANS

- Should be considered if first line ineffective

Recommended triptans for adolescents (12+):

- Sumatriptan/naproxen tab
- Rizatriptan tab or ODT
- Almotriptan tab
- Nasal spray sumatriptan
- Nasal spray zolmitriptan

Younger children (6-11): rizatriptan 5mg tab or ODT

	Time to onset (hrs)	Half Life (hrs)	Preparations and Dosing
Fast Active Triptans			
Sumatriptan	1.5	2-2.5	Tab: 1mg/kg/dose, 25mg (<50kg), 50mg (>50kg), 100mg Nasal Spray: 5mg (<50kg, <9yrs), 10mg (>10-11 yrs), 20mg (>50kg, >12yrs)
Zolmitriptan*	2	2.5-3	Regular/ZMT: 2.5mg (<12yrs), 5mg (>12 yrs) Nasal Spray: 5mg (>12 yrs)
Rizatriptan*	1.2-2.5	2-3	Regular ODT: 5mg (<40kg), 10mg (>40kg)
Almotriptan*	1.4-3.8	3.2-3.7	Tab: 6.25mg or 12.5mg or 25mg (>50kg)
Eletriptan	1-2	4-7	Tab: 20mg or 40mg (>50kg)
Slow Active Triptans			
Naratriptan	2-3	5-6	Tab: 1mg, 2.5mg
Frovatriptan	2-4	24-30	Tab: 2.5mg

**FDA approved medication for children*

TRIPTANS

- Triptans are serotonin 5HT31B,1D receptor agonists – block release of vasoactive peptides at trigeminal nucleus caudalis
- Most effective if taken when pain is still mild, which tends to be earlier in attack (does not shorten aura duration)
- But… only 1/3 of patients pain free at 2 hours
- And… 1/4 of migraineurs do not respond to triptans

TRIPTAN TRIALS

- Novel trial designs to reduce placebo effect -> showed efficacy and safety
- Straight randomization -> safety but not efficacy
- Much of current practice is based on adult or non-ED evidence
- Kids are different than adults – in migraine presentation (shorter duration) and responses
- More difficult to obtain precise data in kids – compounded by polypharmacy prior to presentation
- … AND a high placebo response rate (can be as high as 60% range)
-

TRIPTAN DATA

Name	Dosing	FDA approval	# of pediatric trials
*almotriptan PO	6.25mg or 12.5mg	Yes, 12-17 year olds	1 (positive)
*rizatriptan MLT	5mg MLT 20-39kg 10mg MLT ≥ 40kg	Yes, 6-17 year olds	2 (both positive)
zolmitriptan PO	2.5mg, 5mg, or 10mg	No	2 → 1 high placebo response; 1 similar efficacy (at 2.5mg) as ibuprofen
*zolmitriptan NS	2.5mg or 5mg NS	Yes, 12-17 year olds	2 (all positive, 1 with placebo challenge)
sumatriptan NS	5mg, 10mg (if <40kg) or 20mg NS	No (AAN parameter only)	3 (all positive)
sumatriptan injectible	3mg (<30kg), 6kg (>30kg), or 0.06mg/kg	No	2 (1990's, open label)
sumatriptan PO	50mg or 100mg	No	1 (not more effective than placebo)
*sumatriptan/naproxen PO	Suma 10mg/ naproxen 60mg (can increase to 85mg/500mg)	Yes, 12-17 year olds	2 (both positive)
* FDA approved			

TRIPTAN CONTRAINDICATIONS

- Avoid in patients with a history of cardiovascular disease, including stroke, transient ischemic attacks, myocardial infarction, severe peripheral vascular disease, ischemic bowel disease, and coronary vasospasm, including Prinzmetal angina

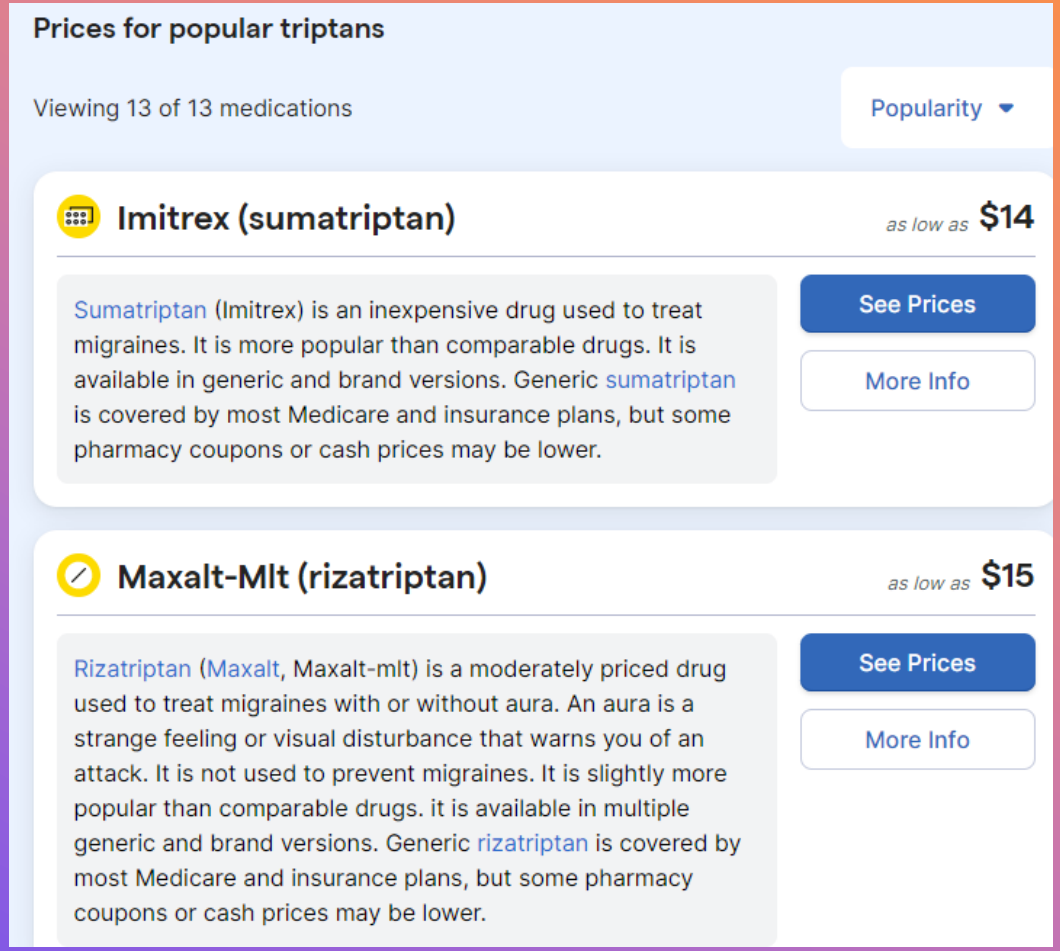
- Avoid in patients with cardiac accessory conduction pathway disorders, including Wolff-Parkinson-White syndrome

- Based on known pharmacology and effects on vascular muscle in triptans rather than absolute contraindications
- less common in pediatric patients but should be considered

- Per FDA, triptans are contraindicated in those with a history of hemiplegic aura or migraine with brainstem aura. This contraindication was based on a view of migraine pathophysiology that is no longer considered current.

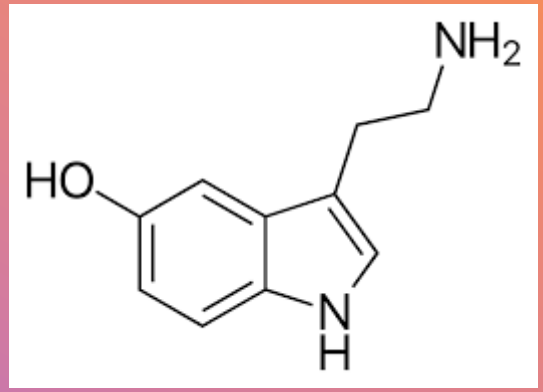
TRIPTAN OPTIONS

- 6-11yo: rizatriptan 5mg tab or ODT
- Unable to swallow pills: rizatriptan ODT, sumatriptan NS, zolmitriptan NS
- Rapid escalation or significant nausea: sumatriptan NS and zolmitriptan NS
- Terrible insurance: sumatriptan tabs ($6), rizatriptan ($4)
- Side effects -> use triptans with slower onset (naratriptan, frovatriptan)



SEROTONIN SYNDROME

- In 2006, FDA warned about risk of serotonin syndrome in patients taking triptans concurrently with SSRI or SNRIs
- Triptans do not interact with the 5HT2 receptor
- Therefore not pharmacologically plausible that triptan use could precipitate serotonin syndrome in someone on an SSRI or SNRI
- American Headache Society position paper:
- "With only Class IV evidence available in the literature and available through the FDA registration of adverse events, inadequate data are available to determine the risk of serotonin syndrome with the addition of a triptan to SSRIs/SNRIs or with triptan monotherapy."



ANTI-NAUSEA MEDS

- Consider adding as third step if significant nausea/vomiting
- Data limited in peds
- Can consider DRAs which can help both nausea and migraine pain:
- Prochlorperazine 5-10mg q8h prn, metoclopramide 5-10mg q8h prn
- BUT must take with dose of Benadryl (12.5-25mg) to prevent extrapyramidal side effects
- Ondansetron also an option but frequent use could worsen HA

SMART LIFESTYLE

Factor	Advice
Sleep: consistent and sufficient	
Bedtime and wake-up time	Maintain a consistent bedtime routine and avoid daytime napping to prevent disruptions to the sleep-wake cycle[99]; children 3-5 years of age should sleep 10-13 hours per day (including naps), children 6-12 years of age should sleep 9-12 hours per day, and teenagers should sleep 8-10 hours per day[100]
Problems falling asleep	Use bed only for sleep, turn off screens at least 1-2 hours before bed to limit blue light exposure[101]
Problems staying asleep	Consider causes such as sleep apnea, depression
Daytime somnolence	Consider causes such as sleep apnea, depression

SMART LIFESTYLE

Meals and hydration: consistent and sufficient	
Missed meals	Recognize that fasting can be a trigger
Well-balanced diet	Eat a variety of fruits and vegetables, protein, and dairy (or another source of vitamin D)
Access problems or limited time	Address time limitations and food insecurity with individualized solutions; consider social work consult
Water consumption	≥8 cups per day for children older than 9 years of age (more for teenage boys and extra at times of high exertion)[102]
Other beverage consumption	Limit to avoid weight gain as obesity is associated with worsened migraine frequency and disability[21]
Caffeine consumption	High caffeine consumption is associated with increased odds of headache in adolescents,[95] probably because of caffeine withdrawal[103]
Activity: consistent and sufficient	
Address inactivity	Inactivity in adolescents is associated with higher odds of migraine[95]; weight loss in overweight teenagers can contribute to headache improvement[21]
Exercise	Meta-analyses in adults have concluded that exercise may be a beneficial and safe treatment for migraine[104]

SMART LIFESTYLE

Relaxation: cope with stress and prevent migraines	
Sources of stress	Home-related stressors (eg, arguments with siblings, observing parental disagreements) or school-related stressors (eg, difficulty in school, fear of doing poorly) can be triggers for headache
Help cope with stressors	Validate the normalcy and commonality of stressors and discuss coping strategies
Relaxation strategies	Cognitive-behavioral therapy can help migraine in children[105]; mindfulness-based stress reduction looks promising[106]
Triggers: avoidance/management	
Weather	Changes in weather patterns are commonly reported as headache triggers; use of long-acting triptans may help to prevent migraine attacks around storms[107]
Specific foods	Little evidence shows that foods other than alcohol and caffeine are consistent headache triggers, although many patients report avoiding specific foods
Menses	Refer to the section on menstrual migraine

HEADACHE DIARY

- Total number of days with any headache
- Number of headache days considered bad/severe
- Focus on days not pain scale

Essential to track response to treatment

Many apps available or can print a blank calendar

- **Most educational migraine tracker:** Migraine Buddy
- **Most comprehensive pain tracker:** Manage My Pain Pro
- **Most simple migraine tracker to use:** Headache Log
- **Best app for managing blue light exposure:** Blue Light Filter & Night Mode
- **Best to manage sleeplessness and anxiety:** BetterSleep Relax and Sleep
- **Best migraine tracker for sharing with your doctor:** Health Log
- **Most detailed record keeping:** N1 Headache
- **Best for community:** Bezzy Migraine

PREVENTION

- Consider with frequent headaches (4/month) or significant disability with attacks
- Many prescription preventives have not shown efficacy over placebo in pediatric trials
- Placebo response may be beneficial if no harm done, so at minimum should consider nutraceuticals with little/no s/e

- May take 6-8 weeks to see improvement
- Goal for improvement: headache frequency cut in half
- Can stop after at least 6 months of headache stability

NUTRACEUTICALS

- Preliminary data supports use of magnesium and Coq10 for pediatric prevention
- Safety shown with vitamin D and riboflavin, mixed data for efficacy
- Once daily dosing better for adherence
- Take these every single day regardless of headache
- Unable to swallow pills: gummies, chewable tabs, liquid drops

Nutraceuticals[114]			
Riboflavin	50-400 mg/d either once daily or divided into two doses	Urine discoloration	Limited studies
Magnesium	Elemental magnesium 9 mg/kg/d with food (magnesium oxide divided 3 times a day; others used)	Diarrhea	Limited studies, some positive
Coenzyme Q10	1-3 mg/kg/d in the morning with food	Insomnia, gastrointestinal upset	Limited studies, some positive
Vitamin D	Studies have used 400 IU/d for children with normal blood level of Vitamin D; 800 IU/d for mild and 5000 IU/d for moderate Vitamin D deficiency	Well tolerated	Limited studies
Melatonin[115]	2-3 mg every day at bedtime	Sedation	Limited studies, some positive

BARRIERS

- 5-40% adolescents with chronic headache had not seen any provider in past year
- Delayed referral to specialist -> higher 10 yr risk of chronic migraine
- Underdiagnosed: ~17% migraine, ~36% “headache”, ~45% no headache diagnosis
- Correct diagnosis of migraine leads to better treatment outcomes

BARRIERS

- Of patients awaiting neurology referral from PCP:
- 5% of those who would qualify for preventive treatment received prevention
- NONE received a triptan
- 17% seen within 4mo

In our study group, 46.6% (395/849) of children were referred to the neurology department for more than a year after the onset of migraine. About 19% of patients consulted with a neurologist between 6 and 12 months (161/849), 9.2% (78/849) were evaluated by a neurologist between 4 and 6 months, and only in 17.5% (149/849) of cases, it was a consultation obtained in less than 4 months. With 7.5% (63/849) of patients, it was unknown how long it took to access a child neurologist after the onset of migraine as the parents and children could not recall the onset of symptoms. The time to see a headache specialist was not separately analyzed.

BARRIERS

- General neurologists: 28.7% triptan usage, 63% nutraceuticals, 37% prescription prevention
- Headache specialists: 56.7% triptan usage, 38.7% nutraceuticals, 66% prescription prevention
- No statistically significant difference in treatment outcomes but different patient populations

Table 2.—Comparison of Management Practices Between Headache Specialist and Non-Headache Specialists N = 469

Treatment Variable	Headache Specialist (N = 135)	General Neurologist (N = 334)	*P*-Value	95% CI for the Difference in Proportion
Imaging	93 (68.9%)	248 (74.2%)	.238	(−15.0%, 4.3%)
Triptan use	76 (56.7%)	96 (28.7%)	<.001	(18.1%, 38.5%)
Use of natural supplement for prophylaxis	52 (38.7%)	212 (63.7%)	<.001	(−35.4%, −15%)
Use of prescription drugs for prophylaxis	90 (66.7%)	125 (37.4%)	<.001	(19.2%, 39.3%)
Short-term outcome of treatment				
No significant improvement	36 (26.7%)	74 (22.2%)	.483	(−4.7%, 13.7%)
Mild to moderate improvement	63 (46.7%)	150 (44.7%)		
Significant improvement	36 (26.3%)	108 (32.3%)		

BARRIERS: CGRP INHIBITORS

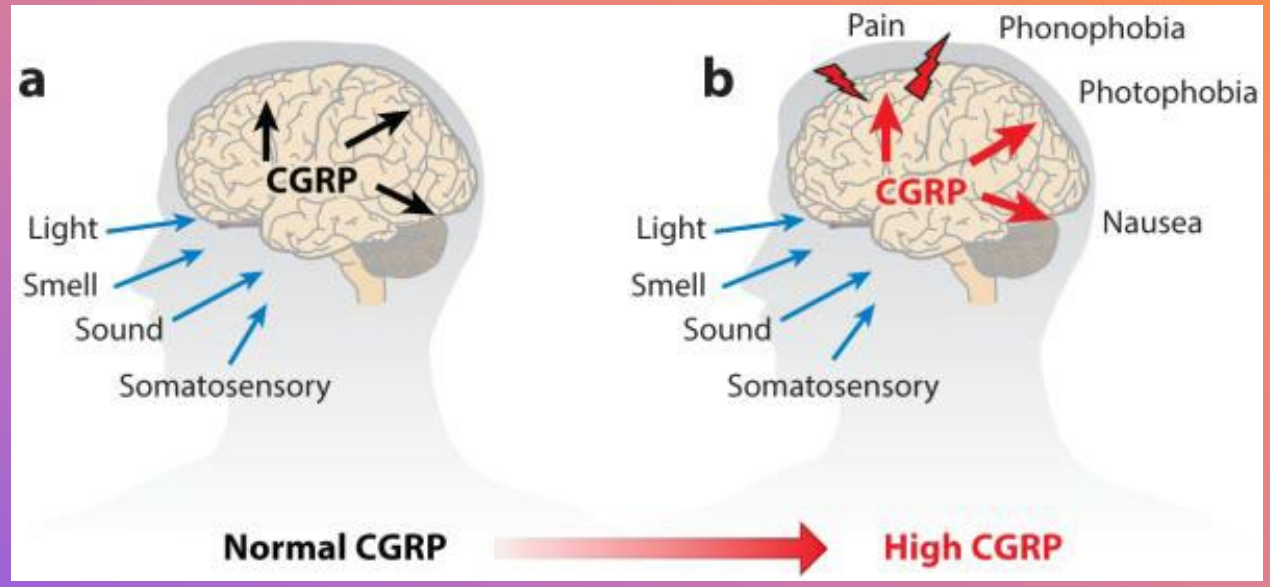
- Insurance coverage for postpubertal teens with intractable migraine is poor
- Similar issues for botox coverage

- CGRP monoclonal antibodies (MABs) (migraine prevention):
- Erenumab (Aimovig)
- Fremanezumab (Ajovy)
- Galcanezumab (Emgality)
- Eptinezumab (Vyepti)

- CGRP receptor antagonists (gepants)(abortive and/or preventive)
- Rimegepant (Nurtec): Acute or preventive
- Ubrogepant (Ubrelvy): Acute treatment
- Atogepant (Qulipta): Preventive treatment
- Zavegepant (Zavzpret): Acute treatment

CGRP

- **<u>Ubiquitous peptide found in brain, gut, vasculature, etc.</u>**
- Causes arterial vasodilation, neurogenic inflammation, activation of meningeal nociceptors
- Enhances synaptic transmission through glutamate transmission -> peripheral and central sensitization
- Bidirectional model between CGRP and CSD



CGRP INHIBITORS IN TEENS

- 16 clinical trials evaluating the safety and efficacy of CGRP inhibitors in pediatric patients. Data unavailable for several years
- Few retrospective reports of CGRP inhibitor safety, Benefits noted in two

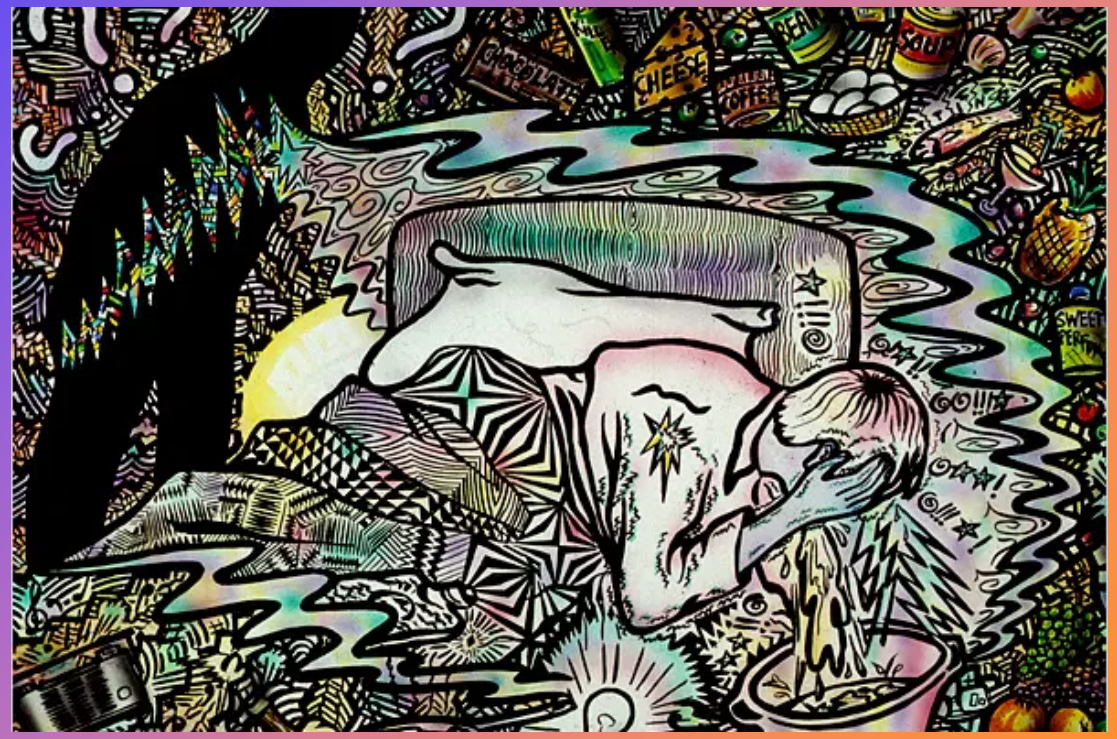
- Pediatric & Adolescent Headache Special Interest Group of the AHS issued recommendations of using anti-CGRP mAbs in select adolescents

Eligible candidates:
- postpubertal
- >=8 headache days per month
- PedMIDAS) score ≥30
- failure of >=2 preventive therapies

SPECIFIC QUESTIONS

Can email me at gage.Rodriguez@ochsner.org for more questions

If able to access E-consults for pediatric neurology at Ochsner can send E-consult and it will route to my inbox



Summary

- Migraine is underdiagnosed and undertreated in the pediatric population
- Patients should receive a headache diagnosis, treatment action plan, education on lifestyle goals, and prompt referral when indicated
- Action plans should utilize OTC meds and triptan if these are ineffective
- Consider prevention in patients with frequent (>4/30) or disabling headaches

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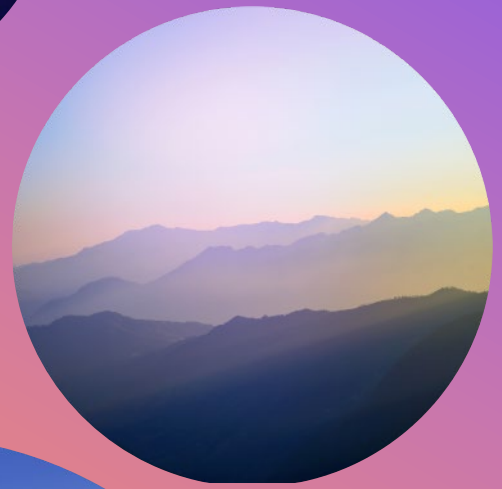

THANK YOU

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