

Headaches in Children: Clinical Pearls and Recent Advances

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Conflict of Interest : None



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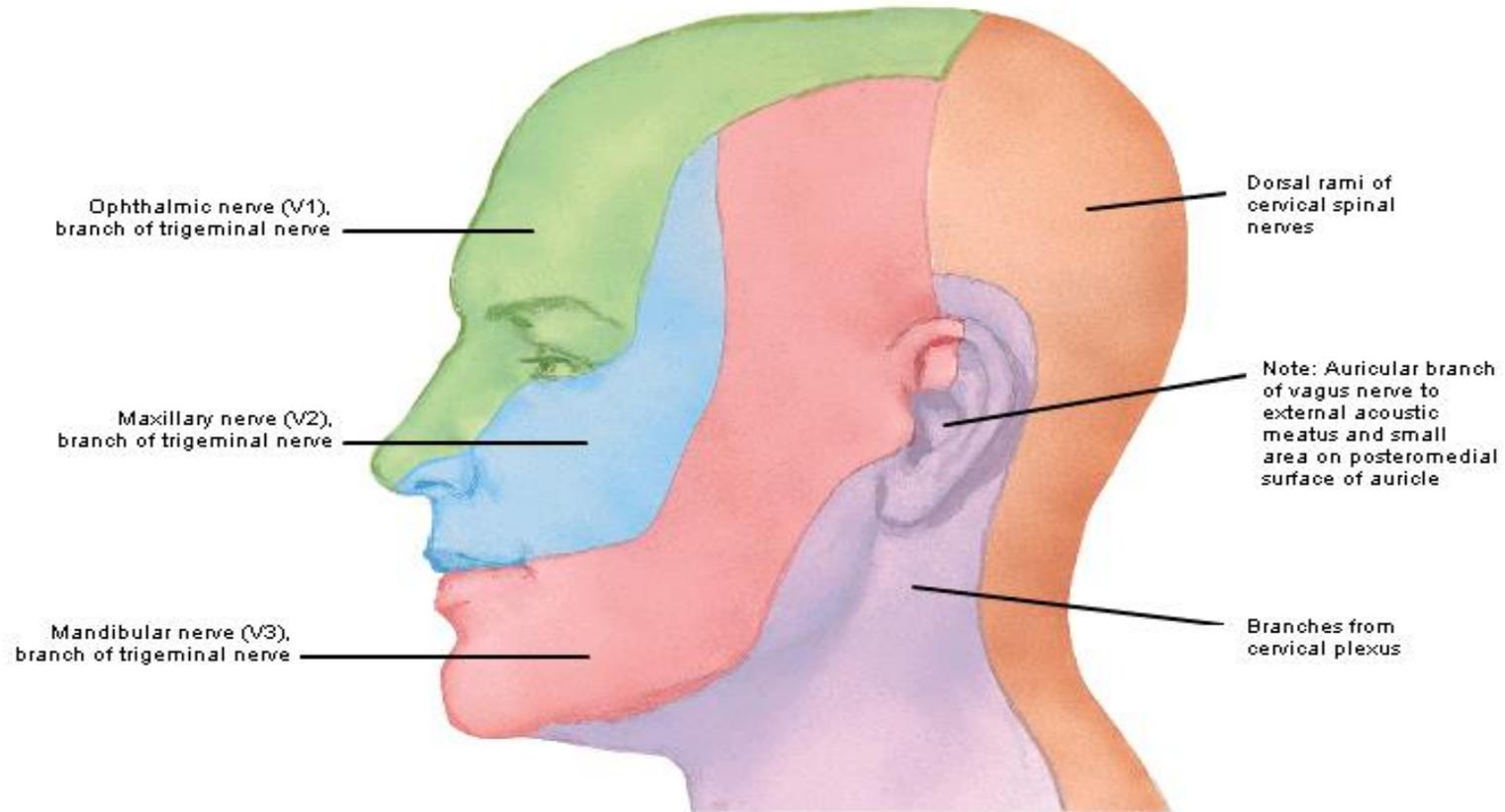
Question: How many patients with headaches have you seen in the last one month ?

- A. 0-5 patients
- B. 5-10 patients
- C. 10-20 patients
- D. More than 20 patients

Objectives

- Discuss the epidemiology of headaches in children
- Discuss the types of headaches especially primary and secondary causes
- Approach to pediatric patients of different ages with headaches
- Delineate how to differentiate secondary headaches
- Common modes of treatment: abortive vs preventative
- Treatment of comorbidities
- Alternative treatments
- Recent advances in the treatment of pediatric headaches

Dermatomes of Head and Neck



Introduction

- Headaches: common symptom experienced by 95% of individuals at some time
- Primary headaches: spontaneous, unrelated to known cause or antecedent event
 - ❖ Major types: **migraine, tension type** and cluster
 - ❖ Recurrent headaches: significant disruption of quality of life or loss of productivity
- Secondary headache: identifiable underlying cause
 - ❖ Potentially dangerous cause; treatment depends on the cause

Introduction(cont)

- One of the most common complaint coming to PCP or neurologist
- First task as clinician: separate primary from dangerous underlying secondary causes
- Common cause of quality of life lost
- Common reasons for absence from school and decreased performance
- Relative challenge of getting a complete history of headache
- More challenging if they become chronic daily headache

Migraine and School Performance

Table 2 School achievement and absenteeism as a function of headache diagnosis

School performance	Below average		On average		Above average		Relative risk (95% CI) ^a	p Value ^b
	No.	%	No.	%	No.	%		
No headache	257	23.2	499	45.0	352	31.8	Reference	Reference
Episodic tension-type headache	165	23.8	271	39.2	256	37.0	1.09 (0.97-1.2)	NS
Probable migraine	269	28.5	387	41.0	287	30.4	1.52 (1.33-1.74)	<0.001
Episodic migraine	158	32.5	170	35.0	158	32.5	1.32 (1.12-1.6)	0.001
Chronic migraine	13	37.1	12	34.3	10	28.6	1.6 (1.02-2.5)	0.05 ^c
School days missed	Never		1 day		2 days or more		Relative risk (95% CI) ^a	p Value ^b
	No.	%	No.	%	No.	%		
Tension-type headache ^a	548	80.5	83	12.2	50	7.3	Reference	Reference
Probable migraine	694	74.1	146	15.6	96	10.3	At least 1 day 1.1 (1.02-1.2); 2 days or more 1.04 (1.0-1.1)	0.03 ^c 0.03 ^c
Episodic migraine	328	68.2	69	14.3	84	17.50	At least 1 day 1.2 (1.1-1.3); 2 days or more 1.15 (1.1-1.2)	<0.001 <0.001
Chronic migraine	23	65.7	2	5.7	10	28.6	At least 1 day 1.2 (1.0-1.6); 2 days or more 1.3 (1.1-1.7)	0.04 ^c <0.001

Migraine and migraine subtypes in preadolescent children

Association with school performance

Table 3 Multivariate analyses of determinants of school performance and of school absenteeism in children with migraine

	Wald χ^2 value	p Value	Odds ratio for predictors	95% CI	
				Lower	Upper
School performance					
Gender (female vs male)	0.558	0.016	1.748	1.108	2.757
SDQ scores (abnormal vs normal)	1.305	<0.001	3.689	2.228	6.109
Duration of attacks	1.129	<0.001	3.092	1.878	5.091
Frequency of attacks	0.989	0.014	2.688	1.221	5.918
Severity of headaches	1.853	0.000	6.379	3.202	12.708
Nausea	1.208	0.000	3.346	2.046	5.473
Use of analgesics	0.801	0.001	2.228	1.403	3.539
School absenteeism					
Duration of attacks	0.936	0.004	2.550	1.351	4.812
Severity of headaches	1.655	0.001	5.232	2.008	13.630
Use of analgesics	1.129	0.000	3.093	1.694	5.650
Nausea	1.741	0.000	5.703	2.622	12.405

Abbreviations: CI = confidence interval; SDQ = Strengths and Difficulties Questionnaire.

Tool to Assess Severity: Pediatric Migraine Disability Score

PedMIDAS

Development of a questionnaire to assess disability of migraines in children

A.D. Hershey, MD, PhD; S.W. Powers, PhD; A.-L.B. Vockell, RN, MSN, CPNP;
S. LeCates, RN, MSN, CFNP; M.A. Kabbouche, MD; and M.K. Maynard, BS

Headache Disability.

The following questions try to assess how much the headaches are affecting day-to-day activity. Your answers should be based on the last three months. There are no “right” or “wrong” answers so please put down your best guess.

1. How many full school days of school were missed in the last 3 months due to headaches? _____

2. How many partial days of school were missed in the last 3 months due to headaches (do not include full days counted in the first question)? _____

3. How many days in the last 3 months did you function at less than half your ability in school because of a headache (do not include days counted in the first two questions)? _____

4. How many days were you not able to do things at home (i.e., chores, homework, etc.) due to a headache? _____

5. How many days did you not participate in other activities due to headaches (i.e., play, go out, sports, etc.)? _____

6. How many days did you participate in these activities, but functioned at less than half your ability (do not include days counted in the 5th question)? _____

Total PedMIDAS Score _____

Headache Frequency _____

Headache Severity _____

Epidemiology

- Prevalence varies based on age with frequency increasing with age
- Migraine frequency averages 5% less than 10 years and higher in adolescents
- Prior to puberty, equal in boys and girls
- By late adolescence, girls outnumber boys 3:1
- Chronic migraine: common in children 5-12 years(0.6%) and adolescents(0.8-1.8%)
- Low socioeconomic status: 4 times more likely to have chronic migraine



Migraine prevalence by age and sex in the United States: A life-span study

TW Victor¹, X Hu¹, JC Campbell¹, DC Buse² and RB Lipton²

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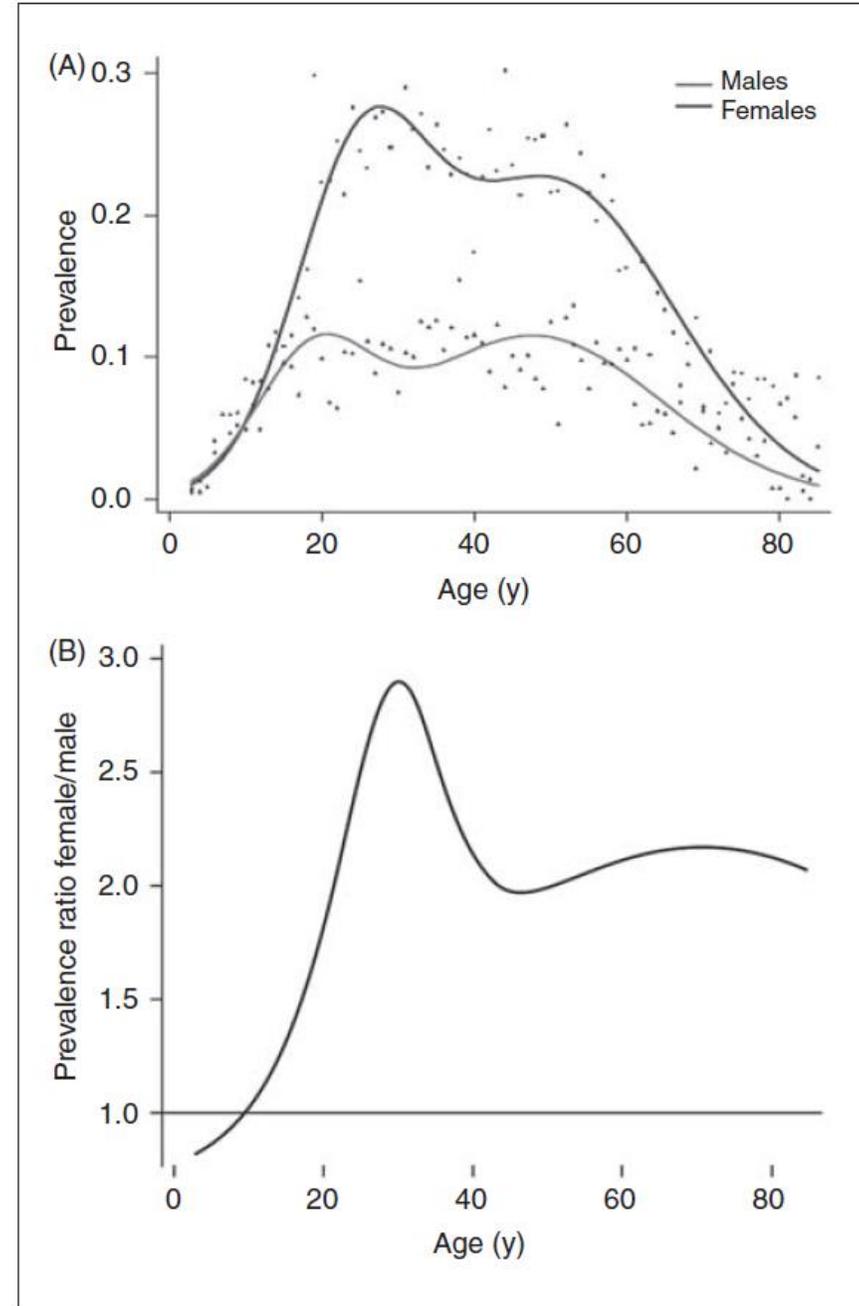


Figure 2. (A) Age-specific, 1-year period prevalence of self-reported, physician-diagnosed migraine. (B) Prevalence ratio female/male

Classification of headaches

- Primary headaches
 - OR Idiopathic headaches
 - THE HEADACHE IS ITSELF THE DISEASE
 - NO ORGANIC LESION IN THE BEACKGROUND
 - **TREAT THE HEADACHE!**
- Secondary headaches
 - OR Symptomatic headaches
 - THE HEADACHE IS ONLY A SYMPTOM OF AN OTHER UNDERLYING DISEASE
 - **TREAT THE UNDERLYING DISEASE!**

The differentiation between 1° and 2° is critical as it dictates diagnostic approach and guides treatment and prognosis.



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Headache Classification Committee of the International Headache Society (IHS)

**The International Classification of Headache Disorders,
3rd edition (beta version)**

Classification of Headache

Classification of headache 1. Primary headache (from IHS 2003)

(must have characteristic or benign features without abnormal neurological signs)

1. Migraine
2. Tension-type headache
3. Cluster headache and other trigeminal autonomic cephalgias
4. Other headache not associated with structural lesion

Classification of headache 2. Secondary headache (from IHS 2003)

5. Head or neck trauma
6. Cranial or cervical vascular disorders
7. Non-vascular intracranial disorders
8. Substances or their withdrawal
9. Infection
10. Disorder of homeostasis
11. Eye, ENT, orofacial, or cervical disorders
12. Psychiatric disorder
13. Cranial neuralgias and central causes of facial pain
14. Headache not classifiable

Migraine and its Pathophysiology

- Headache syndrome due to combination of inherited genetic susceptibility and environmental factors(e.g. foods, stress, hormones, fatigue, sleep)
- Abnormalities in ion channels (CACNA1A, ATP1A2 and SCN1A)
 - Messenger molecules **nitric oxide (NO)**, **serotonin (5-hydroxytryptamine; 5-HT)** and **calcitonin gene-related peptide (CGRP)**
- Two current theories
 - ❖ Vasogenic theory and Neurovascular theory
 - Caffeine exposure: Temporarily vaso-constrictive; frequent exposure leads to vasodilation

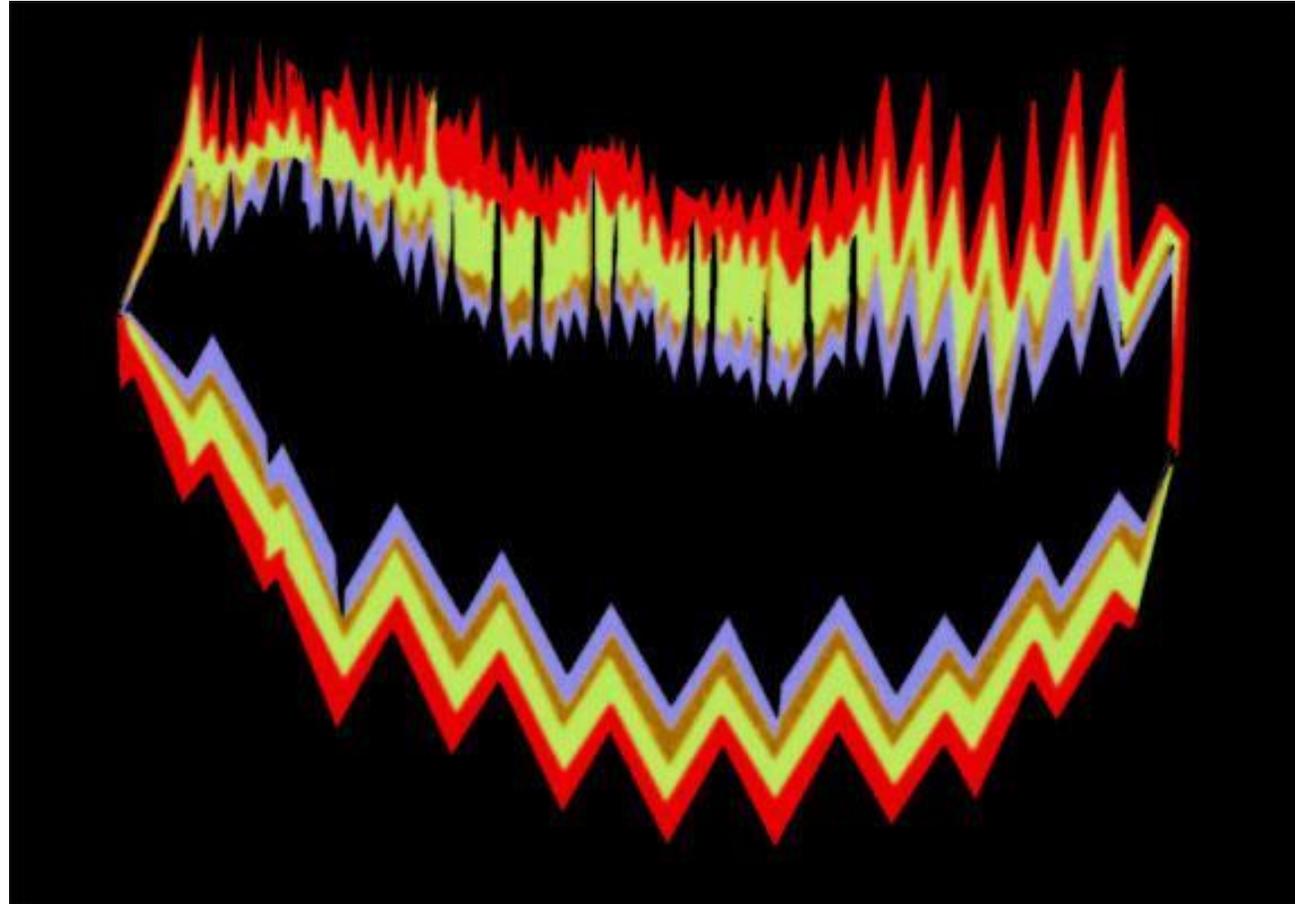
Migraine without aura: Diagnostic Criteria

- A. At least five attacks¹ fulfilling criteria B–D
- B. Headache attacks lasting 4-72 hours (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 (e.g. 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: Diagnostic Criteria

- 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 two of the following four characteristics:
 - 1. at least one aura symptom spreads gradually over ≥ 5 minutes, and/or two or more symptoms occur in succession
 - 2. each individual aura symptom lasts 5-60 minutes¹
 - 3. at least one aura symptom is unilateral²
 - 4. the aura is accompanied, or followed within 60 minutes, by headache
- D. Not better accounted for by another ICHD-3 diagnosis, and transient ischaemic attack has been excluded.

Visual aura in Migraine



Visual Aura in Migraine



Periodic Syndromes in Children Probably Associated with Migraine (Migraine Variants)

- Cyclic vomiting syndrome:
 - ❖ Elementary school children with periodic attacks of frequent vomiting
 - ❖ Abdominal discomfort, and anorexia
- Abdominal migraine
 - ❖ Recurrent attacks of abdominal pain with diffuse in location and dull in quality.
 - ❖ Additional features: pallor, anorexia, nausea and vomiting
 - ❖ Treatment: anti-emetics, triptans

Approach to a Child with Headache

History and Physical exam: Important points to consider

- Depends on age: less than 6, preadolescent and adolescent
- Children's good headache historians
- Child sits closest to the clinician
- Set expectation at the outset
- Good headache history is 'taken not given'

What are the common clinical presentations of headache ?

Presentation	Usual location of presentation
Recurrent headaches	Clinic
Sudden severe headache(first time) for hours	Emergency department
Chronic daily headache	Emergency department and clinic
Headache more than 72 hours with history of prior headaches (status migrainosus)	Emergency Department or clinic

History and Physical Exam(cont.)

- mnemonic SMART—sleep, meals, activity, relaxation, and trigger
- Developed at Seattle Children's Hospital; helpful in guiding the history
- Chronology: first time or recurrent ; if recurrent whether progressive or not
- Medications including supplements, OTC and OCP and recent change or discontinuation of medications
- Lifestyle: sleep, water intake, skipping of meals, caffeine and exercise

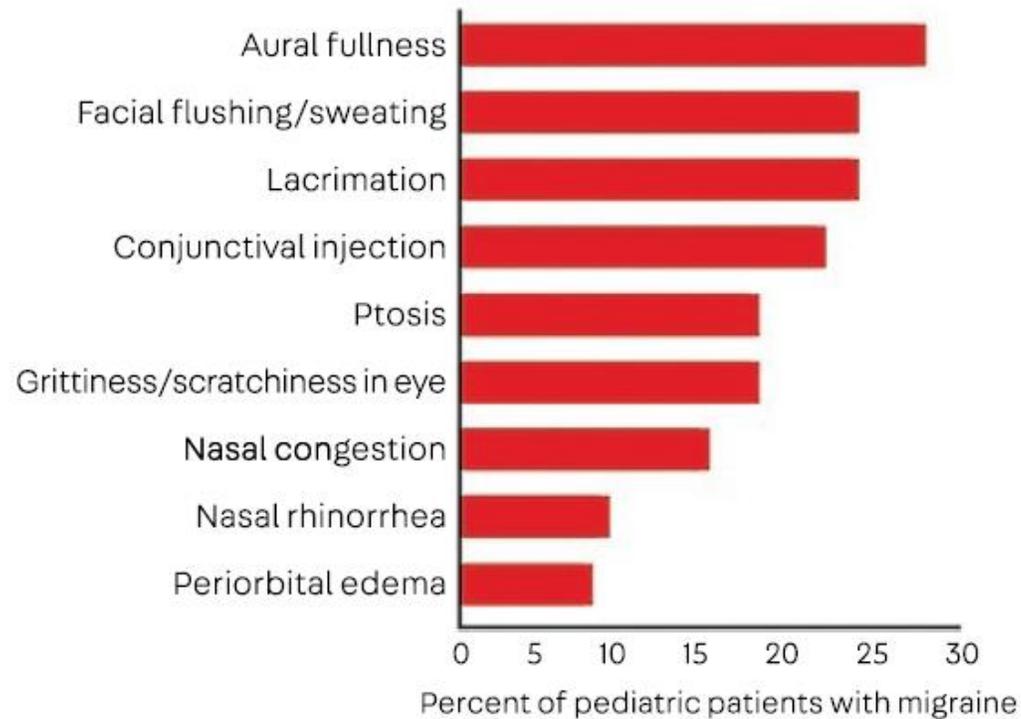
Red flags for Secondary Headaches in Children and Adolescents

- Headache worsening with supine posture or Valsalva maneuver, cough and exercise
- Recurrent thunderclap headaches
- New onset headaches with accompanying concerning features
- Visual changes not characteristics of migraine
- Focal neurological findings
- Immunocompromised children
- Headaches with visual field defects, diplopia, decreased visual acuity and transient visual obscurations

The following are not red flags in children!

- Headache worsening with upright posture(except post-LP headache)
- Headache accompanied by nasal congestion, itchy eyes and ear fullness
 - Sinus headache: most common misdiagnoses
 - Cranial autonomic symptoms common

Autonomic Symptoms in Children with Migraine



Consideration of Neuroimaging in Headache

- Atypical headache presentation (vertigo, intractable vomiting and waking up with headache)
- Headache onset < 6 months
- Children < 6 years
- No family history of migraine
- Change in headache type
- Subacute headache and progressive severity
- First and worst headache
- Systemic signs and symptoms
- Headache accompanied by confusion, seizure, altered mental status and focal neurologic complaint

Question: Which one of the following may be seen in normal individuals as well as children with pseudo-tumor cerebri?

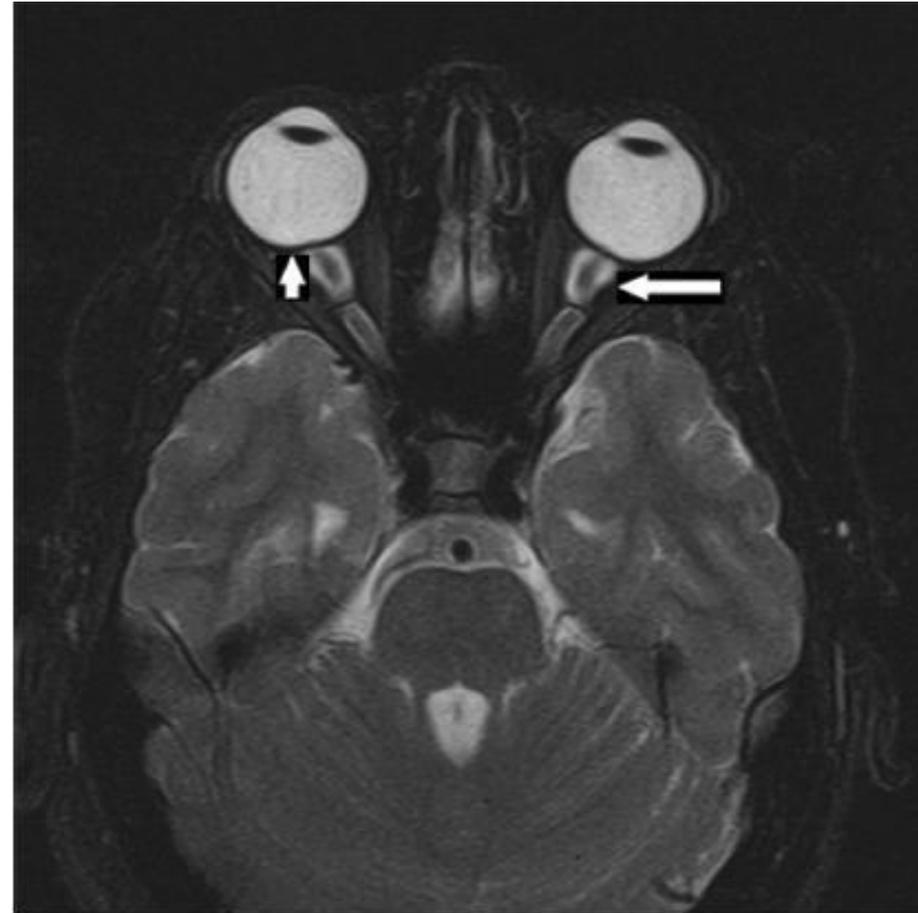
- A. Absence of venous pulsation on fundoscopy
- B. Retinal hemorrhages
- C. Opening pressure of CSF more than 25 cm of water
- D. Lateral rectus palsy

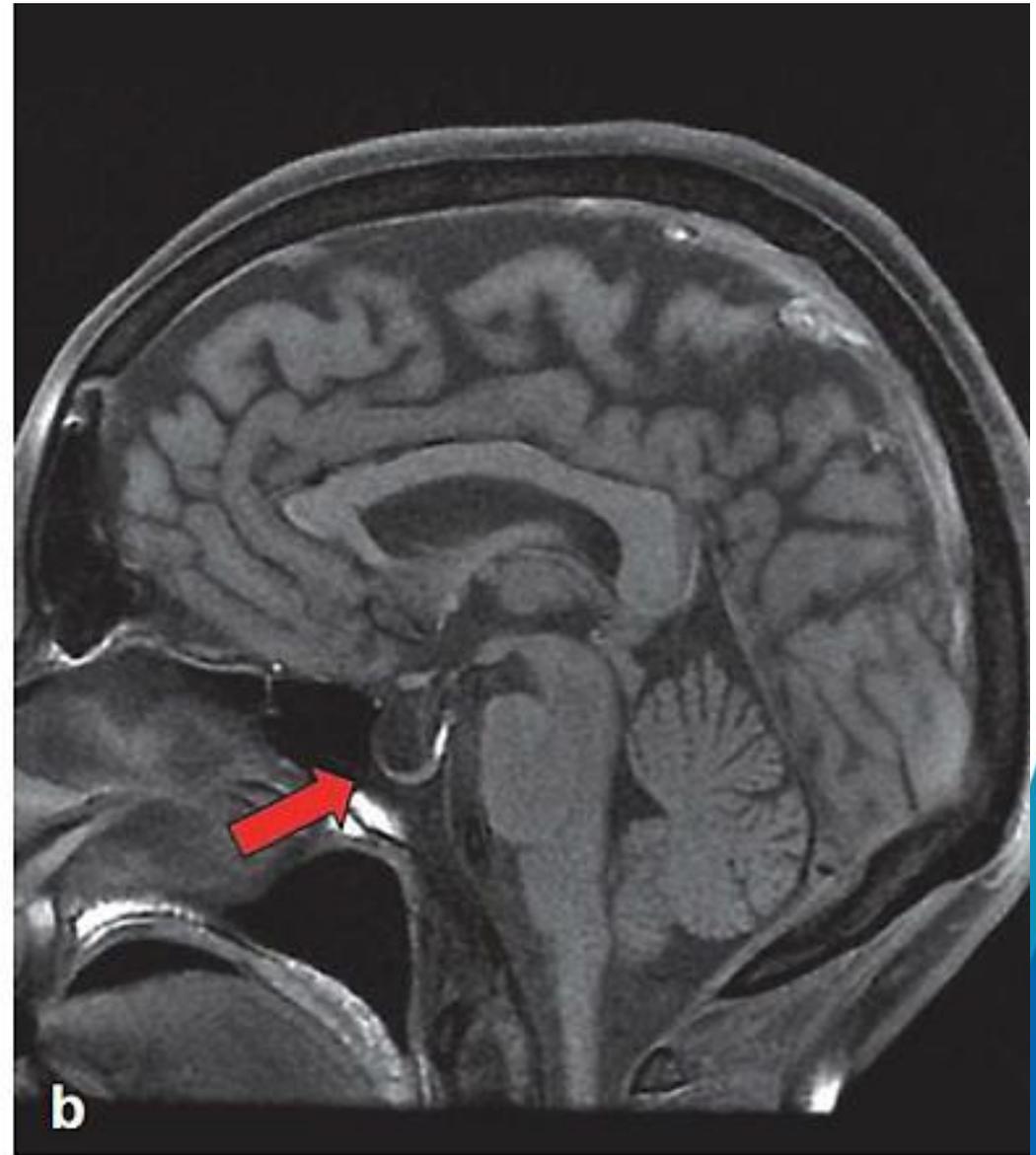
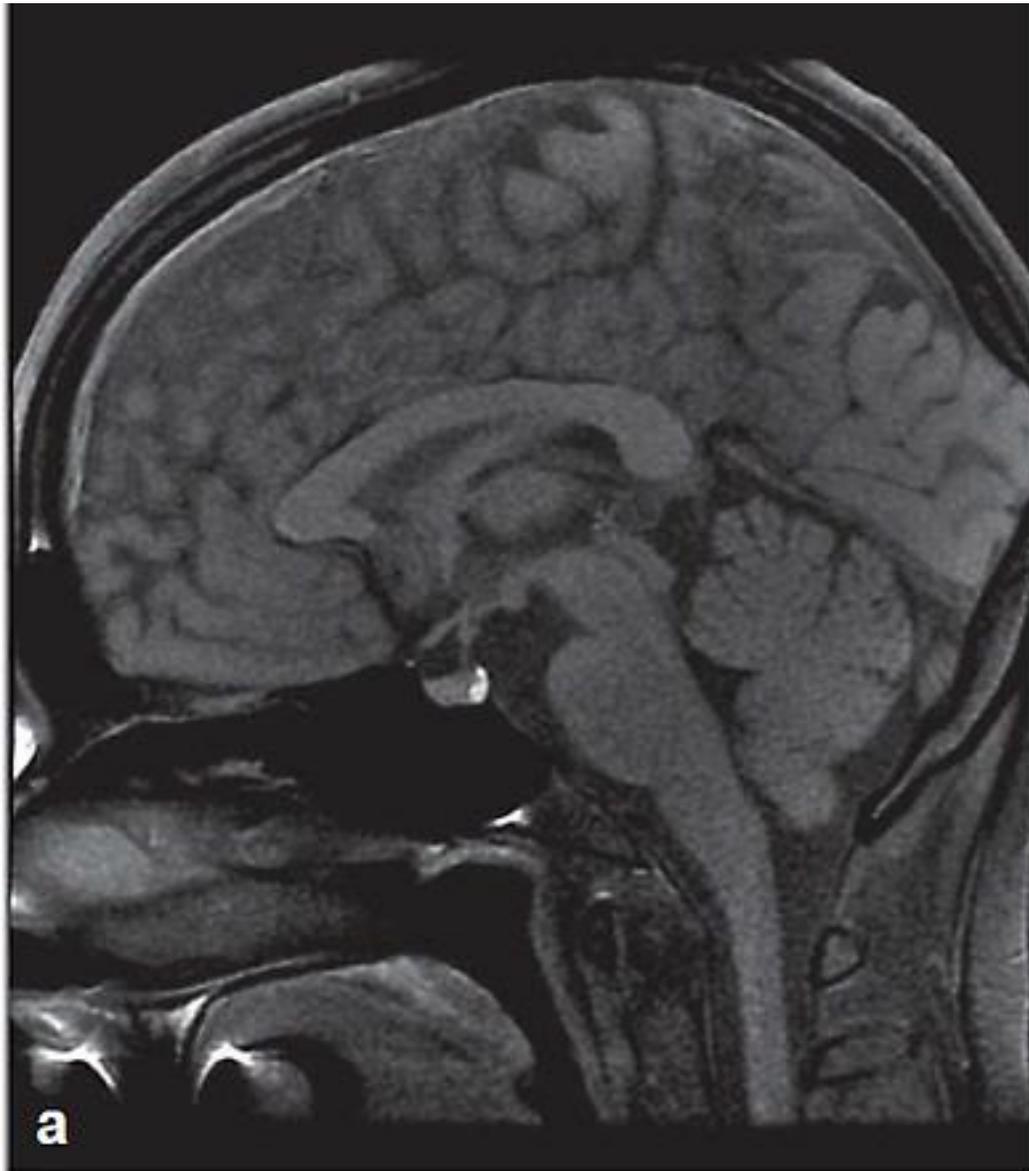
Pseudotumor cerebri (Normal, Stage I-V)



Pseudotumor Cerebri

- Dilatation of optic nerve sheaths
- Flattening of posterior globes
- Empty Sella syndrome





 **Ba** Figure 1: Cerebral MRI scan of normal sella turcica with regular pituitary gland (a) and empty sella (b)

Secondary Causes of Intracranial Hypertension

- Medications

Doxycycline, minocycline

Lithium, growth hormone, oral contraceptives

Vitamins D deficiency, Vitamin A excess or deficiency

Steroid withdrawal

- Cerebral sinus venous thrombosis
- Endocrine causes: hypoparathyroidism

Principles of Management of Primary Headaches

- Multidisciplinary team of providers
- Acute or abortive treatment
- Treatment of status migrainosus
- Pharmacologic preventive treatment
- Behavioral preventive treatment
- Management of comorbidities

Which one of the following triptans is approved by FDA to be used in children 6 years and older?

- A. Rizatriptan
- B. Sumatriptan
- C. Naratriptan
- D. Almotriptan

Acute therapy or Outpatient Abortive Therapy

- NSAIDS: acetaminophen, ibuprofen. Shown efficacy in controlled trials
- Consider to avoid overuse: medication overuse headache
- Triptans:

FDA approved

- ❖ Almotriptan(oral), zolmitriptan(nasal spray), rizatriptan(melt) and sumatriptan/naproxen(oral):12-17 years
- ❖ Rizatriptan(melt): children 6 years and older

ER management and Treatment of Status Migrainosus

- Acute migraine attack lasting more than 72 hours
- Admission to ER or inpatient floor to break the headache
- Medication choices:
 - ❖ antidopaminergic (prochlorperazine and metoclopramide)
 - ❖ NSAIDS (IV ketorolac)
 - ❖ Triptans
 - ❖ Antiepileptic (valproic acid)
 - ❖ Dihydroergotamine

Management of Status Migrainosus

- Combination regimen: every 6-8 hours

Ketorolac: 0.5 mg/kg maximum

Prochlorperazine: 0.15 mg/kg maximum 10 mg

Diphenhydramine: 12.5-25 mg

- Combination regimen with prochlorperazine: response rate of 93%
- Valproic acid IV 15-20 mg/kg IV (can be followed by PO)

Brief Communication

Inpatient Treatment of Status Migraine With Dihydroergotamine in Children and Adolescents

Marielle A. Kabbouche, MD; Scott W. Powers, PhD; Ann Segers, RN, BSN; Susan LeCates, MSN, CNP;
Paula Manning, RN; Shannon Biederman, MSN, CNP; Polly Vaughan, MS, CNP; Danny Burdine, RA;
Andrew D. Hershey, MD, PhD

- 74.4 % patients seizure free
- Dose 1 mg for more than 25 mg or >9 years every 8 hours
- Half dose if <25 kg or <9 years
- Pregnancy test in female
- Premedicated with prochlorperazine or metoclopramide for 3 doses followed by ondansetron as needed.

Status epilepticus response with doses of DHE

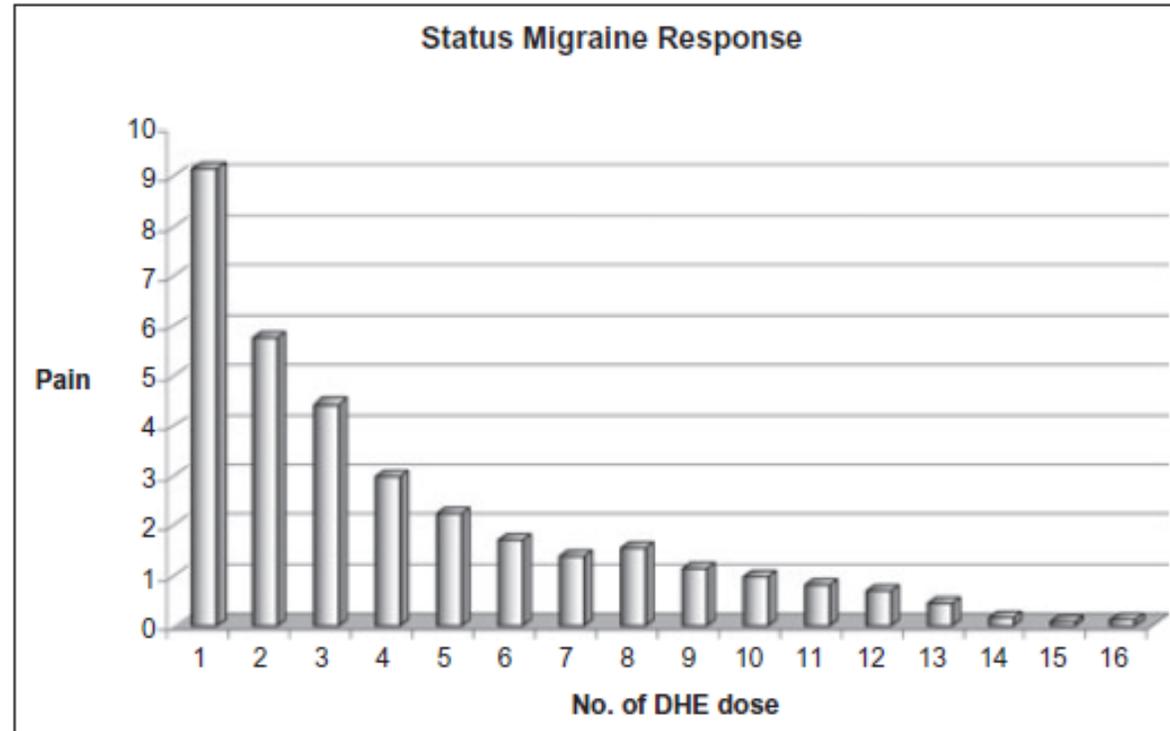


Figure.—Status migraine response to DHE. Gradual improvement of the pain from headache with multiple doses of DHE given every 8 hours. As noticed on the chart, there is a steep response by dose no. 5 followed by another remarkable response by dose nos. 12-13. DHE = dihydroergotamine.

Preventive Treatment of Migraine

Broad categories

- Anti seizure medications
- Antidepressant medications
- Antihypertensive medications
- Antihistamines (cyproheptadine)
- Supplements
 - ❖ Melatonin: thought to be as effective as amitriptyline
 - ❖ Riboflavin, Magnesium, CoQ10 etc.
 - ❖ Butterbur (herbal)

Anti-seizure Medications for Migraine Prophylaxis

	Dose	Side effects /comments
Topiramate	1-2 mg/kg	paresthesia, decreased sweating, memory problems, kidney stones, anorexia
Valproic Acid	15-30mg/kg	weight gain, alopecia, thrombocytopenia
Gabapentin	300-1200 mg	sedation, ataxia, weight gain, peripheral edema
Lamotrigine	100-200 mg	rash Needs slow titration
Levetiracetam	500-1500 mg	behavioral problems, sleepiness
Zonisamide	100-200 mg	kidney stones, cognitive problems

Medications for Prevention of Migraine

	Dose	Side effects/Comments
Antidepressant		
Amitriptyline	0.1-1 mg/kg/day QHS	Sedation, dizziness,
Nortriptyline	10-75 mg/day QHS	Sedation, QT prolongation
Antihypertensive		
Propranolol	2-4 mg/kg/day	Fatigue, dizziness, exercise induced asthma
Verapamil	4-10 mg/kg/day div TID	Constipation, dizziness
Flunarizine	5-10 mg qhs	Sedation, weight gain

Cyproheptadine

- Used in young children less than 6 years
- Dose: 0.2-0.4 mg/kg/day at bed time
- Antihistamine and serotonin antagonist with anticholinergic and calcium channel blocking properties.
- Single dose at bedtime helps to avoid daytime sleepiness
- Common side effect: appetite stimulation and weight gain, sleepiness
- Somnolence occurs; administered only at night.
- Anticholinergic toxicity is rare.

Randomized controlled Trial on Amitriptyline, Topiramate and Placebo

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Trial of Amitriptyline, Topiramate, and Placebo for Pediatric Migraine

Scott W. Powers, Ph.D., Christopher S. Coffey, Ph.D., Leigh A. Chamberlin, R.D., M.Ed.,
Dixie J. Ecklund, R.N., M.S.N., Elizabeth A. Klingner, M.S., Jon W. Yankey, M.S., Leslie L. Korbee, B.S.,
Linda L. Porter, Ph.D., and Andrew D. Hershey, M.D., Ph.D., for the CHAMP Investigators*

Tension type headache

- Definition: Recurrent headaches with at least 10 episodes in the past year, lasting 30 minutes to 7 days, with two of the following four headache features:
 - ❖ non-pulsatile, diffuse in location, not worsened or aggravated by physical activity, and mild to moderate in severity.
- Prevalence variable(5-11% to 29-58%) owing to rarity to clinic
- Equal distribution in boys and girls
- Less disabling, less likely to miss school and have below average performance
- Nausea and vomiting unlikely

Treatment of Tension Type Headaches

- No randomized controlled trials for TTH treatment in children
- Not all require preventive treatment
- Physical therapy
- Counselling by therapist
- Supplements
 - ❖ Riboflavin
 - ❖ Magnesium
 - ❖ Melatonin

Lifestyle Modification in Headache Management

- Sleep

American Academy of Sleep Medicine Recommendations for Sleep in Children and Adolescents

Age (years)	Recommended Hours of Sleep
3-5	10-13 hours per 24 hours including naps
6-12	9-12 hours
13-18	8-10 hours

- Regular pattern of sleep
- Particularly difficult in teens: physiologic sleep phase delay
- Sleep disorders including obstructive sleep apnea

Lifestyle Management of Migraine

- Avoidance of dehydration
 - Avoiding to skip meals
 - Avoidance of caffeinated drinks
 - Avoidance of migraine triggers
- Chocolate typically not a trigger!
- Regular physical activity

Cognitive Behavioral Therapy(CBT) in Migraine

- CBT plus preventive medication better than preventive medication plus lifestyle modification(study done in children 10-17 years)
- Course of therapy relatively short
- Improved adherence to lifestyle and medications may be part of mechanism
- Access to CBT may be a challenge
- Stigma around anything called “therapy” and insurance coverage

Biofeedback and Relaxation techniques

- Biofeedback: uses monitors to measure the physiologic effects as patients undergo relaxation self-therapies.
- Effectiveness of biofeedback probably related to patients feeling that they have control over their pain.
- Relaxation techniques include distraction, guided imagery, breathing exercises, and self-hypnosis
- Alternatives: yoga classes and meditation classes

Other Methods of Migraine Treatment(adults)

- Botulinum toxin(FDA approved in chronic migraine in adults)
- External Trigeminal Nerve Stimulation Device (e-TNS ; Cefaly)
- Noninvasive Vagal Nerve Stimulator(VNS)

Calcitonin Gene-Related Peptide (CGRP) receptors blocker

- Eremunab: First CGRP receptor blocker
- Others in pipeline: fremanezumab and galcanezumab
- One a month subcutaneous injection
- Long term efficacy unknown
- Costly treatment(average annual cost \$5000)
- Not approved in children

Chronic Daily Headache

- Four groups: chronic migraine(CDH), chronic tension type headache(CTTH), hemicranias continua and new daily persistent headache
- CDH and CTTH start as episodic forms
- Small but significant proportion of children
- Intractable
- Frequent arrival to neurology clinic and as inpatient
- Treatment options limited but similar in all forms

Treatment of Chronic Daily Headache

- First and most important: discontinue the current use of analgesics
- Continuation of analgesics: revert back to episodic in about $\frac{3}{4}$
- Inclusion of non-pharmacologic forms of treatment
- Initiation of prophylactic medications
- Establish a plan to rotate abortive treatment
- ❖ Long acting analgesics or triptans are preferred
- May remain refractory despite above plan
- Botulinum toxin for chronic migraine form of CDH in adults

Comorbidities Associated with Headache

- Incorporation of multidisciplinary team to help manage comorbidities
 - ❖ Physical therapy, psychiatry, psychologist, dietician
- Common comorbidities
 - ❖ Sleep related: sleep apnea and insomnia
 - ❖ Obesity
 - ❖ Asthma and allergies
 - ❖ Epilepsy
 - ❖ Depression and anxiety

Questions???

Thanks!

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