Headaches in Children

- **Acute** - trauma, infection
- **Acute, recurrent** - migraine or equivalents in younger children
- **Chronic, progressive** - increased intracranial pressure, degenerative disease, vascular, hydrocephalus
- **Chronic, stable** - tension, medication overuse, new daily persistent headaches (NDPH), transformed migraine, pseudotumor cerebri


Headaches - Red Flags!

- Focal neurologic signs or symptoms, papilledema, stiff neck, unequal pupils, ataxia
- Changes in vision
- Presence of seizures (higher in migraineurs)
- Diagnosis of tuberous sclerosis, neurofibromatosis, other neurocutaneous disorders
- Nocturnal, early morning headaches with emesis
- Chronic, progressive headaches, especially in young children

Pediatric Migraine - IHS II Criteria

Recurrent headaches lasting 1-72 hours with associated nausea/emesis and/or photophobia and phonophobia, aggravated by physical activity.
Often bilateral frontotemporal rather than unilateral, moderate to severe pain, often pulsating
At least 5 “attacks” with headache-free intervals

PEDIATRIC MIGRAINE “EQUIVALENTS”
- Benign paroxysmal torticollis
- Benign paroxysmal vertigo
- Cyclic vomiting
- Abdominal migraine
- Acephalic migraine (mostly auras alone)
- Acute confusional migraine
- Recurrent Limb Pain (RLP) - upper > lower
- Above total about 10% of pediatric migraneurs
- First three more common in younger children


Migraine Genetics
- I often have to yell at parents (Moms) to get a positive family history, but am usually successful
- Migraine is a strongly genetic disease, often progressive over time.
- Most (< 80%) people who claim to have episodic “sinus”, “allergy” or “stress” headaches in fact have migraine!
- Specific genes for specific migraine phenotypes are being identified (FHM).


Pathophysiology of Migraine
- Genetic influences cause a hyperexcitable cortex, similar to epileptics
- It’s now felt that migraine is a channelopathy
- Disturbances of neuronal ion channels have a lower threshold for external and internal signals
- These stimuli cause neuronal hyperexcitation followed by spreading depression and vasodilatation/inflammation, mediated by CGRP and substance P. This activates trigeminal meningeal afferents, causing pain, maybe.....


Pathophysiology (Cont.)
- Central sensitization plays a major role. Jury is still out on peripheral sensitization.
- Primary meningeal afferent neurons become activated by previously innocuous stimuli.
- These sensitize second–order neurons in trigeminal brainstem and cervical regions. This can lead to allodynia during and between attacks. Second–order sensitization may lead to involvement at third– and higher–order brainstem and brain levels.


Cortesi EM. Pathophysiology of Migraine. Semin Neurol. 2010;30:120-130

Migraine Phases
- Prodrome- occurs 2-48 hours before the aura, less well studied in pediatrics; overall, in 75% teens, 65% of 6-12 years, 33% <6 years; most common symptoms are facial pallor or shadows, fatigue, irritability
- Aura- uncommon (only 33%) in children; 5% aura only
- Headache- bifrontal or diffuse
- Postdrome- not well studied, presumed same as adults (related or fatigued/exhausted, cognitive ‘fog’, can last for days)

**Headache Comorbidities**

- Anxiety (#1)
- Depression
- Sleep disorders
- Other pain conditions (IBS, musculoskeletal)
- Functional disruption and disability often more determined by these than the pain!
- Overall, psychopathology is three times more likely than teens without headaches


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**Teens with Migraines**

- Are at a significantly greater risk for suicide
- Teens who have migraines with aura are 6 times more likely to have a high suicide risk than those without aura.
- Are 3.5 times more likely to have a psychiatric disorder than those without migraine
- Have at least a 50% chance of having at least one psychiatric disorder if their headaches are daily. About 20% have major depression and/or panic and anxiety disorders.
- Have a higher frequency of previous physical abuse (30%)
- Often not diagnosed and treated for many years!


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**Pain Scales**

**HATE ‘EM!!!**

**Additional Pain Quality of Life Scale**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Stay in bed all day. Feel hopeless and helpless about life</td>
</tr>
<tr>
<td>1</td>
<td>Stay in bed at least half the day. Have no contact with peers or friends</td>
</tr>
<tr>
<td>2</td>
<td>Get out of bed but don’t get dressed. Remain at home all day</td>
</tr>
<tr>
<td>3</td>
<td>Get up and at least minimal activities at home. Feel anxious/hopeless</td>
</tr>
<tr>
<td>4</td>
<td>Do simple chores at home. No outside activities</td>
</tr>
<tr>
<td>5</td>
<td>More frequent and broad range of activities. Limited outside activities (1 day per week)</td>
</tr>
<tr>
<td>6</td>
<td>Amputated off limited home/limited social activities on weekdays</td>
</tr>
<tr>
<td>7</td>
<td>Amputated on a few hours per day. Unable at least 5 hours per day. More frequent and broad range of activities</td>
</tr>
<tr>
<td>8</td>
<td>Amputated at home limited days Action on weekends</td>
</tr>
<tr>
<td>9</td>
<td>In a school or at work. Feel less a day. Participate in something mildly stressful</td>
</tr>
<tr>
<td>10</td>
<td>Participated at least twice and stressful, normal work and school</td>
</tr>
</tbody>
</table>

Source: Liang, MD, PhD
Menstrual Migraine (MM)

1. Pure Menstrual Migraine – usually migraine without aura that occurs only from days -2 to +3 of the menstrual period (about 15% of female migraineurs, 3% teens)
2. Menstrually-Related Migraine - occurs during menses but at other times as well (about 50% of female migraineurs). May be related to elevated prostaglandins.


MM Treatment

- Acute - usual OTC meds, triptans, DHE nasal spray
- Short-term preventive - magnesium 400mg/day beginning at day 14 of cycle; naproxen 500mg BID from days -5 to +5 of menses; triptans, especially frovatriptan/naratriptan/eletriptan BID from days -3 to +3; if on daily preventive Rx, increase doses during vulnerable time
- Long-term preventive - usual meds but watch for teratogenic risks; hormonal therapy also used


Effects of Pregnancy

- Migraine with aura less likely to improve than migraine without aura
- Higher risk of pre-eclampsia
- No significantly increased pregnancy outcome risks
- If taking valproate, must take high doses of folate
- Triptans - rated pregnancy category C (risk of teratogenicity not excluded), probably safe
- I’m often told that Moms stopped having migraines after pregnancy, or had a few only during pregnancies


Tension Headaches

- Episodic tension-type headaches (ETTH) and chronic tension-type headaches (CTTH). Episodic defined as 8 or less per month, chronic 15 days/month or more.
- Unlike migraine, no major sex difference
- Most common worldwide headache, ETTH up to 78%, CTTH 2-3%
- Lots of other somatic complaints - myalgias, poor sleep, nausea, fatigue, poor memory and concentration and memory issues.

Unsalp A, Dirik E, Kurul S. Prevalence and clinical findings of migraine and tension-type headache in adolescents. Pediatrics Int. 2007;49:943-949

Chronic Tension-Type Headaches

- Prevalence of 10-24% of children, female predominance only above 12 years
- Usually described as tightening, band-like, mild to moderate in severity, bilateral, not worsened by physical activity, few if any autonomic features
- Strong family history of migraine
- Pain varies from mild to severe
- Most teens don’t recognize that their “tension” or milder headaches are, in fact, migraines!
Chronic Tension Headaches (Cont.)

- **Acute Treatment**: NSAIDs, Excedrin Migraine, triptans less effective unless have co-existent migraines
- **Preventive Treatment**: amitriptyline, nortriptyline, venlafaxine, duloxetine, topiramate, valproate, SSRIs, tizanidine; ? BOTOX
- **Lifestyle Changes**: exercise (stretching and postural relaxation), regimented diet and sleep schedules, reduce alcohol, behavioral therapy: these unfortunately are more effective in children 6 years and younger than in teens


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Post-Traumatic Headaches

- In 2008, more than 55,000 high school football players suffered a concussion
- During 2008, nearly 50,000 high school boys and girls soccer players suffered a concussion.
- Nearly 40% of these returned to action prematurely (before they were asymptomatic and medically cleared)
- Concussion during sports were second only to motor vehicle accidents as the leading cause of brain injury in persons aged 15-24 years.
- Headache prevalence and duration is greater in those with mild head injury compared to those with more severe trauma. Similarly, post-concussion syndrome more likely after mild trauma.

Post-Traumatic Headaches (Cont.)

- Headaches may be migraine-like, tension-type or mixed
- MOH may perpetuate these headaches
- I often find that mild trauma triggers a migraine disorder in teens genetically susceptible to develop migraine and other headaches.
- Treatment similar to other chronic headaches: tricyclics, propranolol, valproate; nonmedical
- Return to contact sports only after patient is not having any neurologic symptoms or sequelae


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Occipital Neuralgia

- Pain is felt in the distribution of the greater or lesser occipital nerves which are tender to palpation (allodynia)
- One type related to migraine. Severe, often unilateral, lasts 2-36 hours. May have a visual aura, typically has associated nausea and emesis
- Can be sustained muscle contraction associated with neck soreness and stiffness. Pain may spread laterally to the forehead and orbits (“ram’s horn”). Allodynia often present. Pain reproducible by pressing on nerves.
- Often responds to usual headache preventive medications
- Diagnosis can be confirmed, temporarily treated, by occipital nerve block

**Headache Chronification**

- Transition from episodic to chronic headaches is not well understood; estimated that adults with episodic migraine develop CDH at 3%/year
- For many, a progressive disease
- Often associated with other chronic pain conditions, especially musculoskeletal (neck, back), traumatic life events (emotional and physical); anxiety, depression; genetics
- Central sensitization of brainstem neurons can trigger allodynia, often an easy and early clinical sign of chronification, or central sensitization


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**Chronification (Cont.)**

- Some factors are non-modifiable (age, head injury history, low socioeconomic status)
- “Modifiables” - weight, stress (?), sleep, caffeine, depression, analgesic overuse (MOH)
- Must screen for anxiety and depression; MOH; allodynia; other chronic pain conditions such as fibromyalgia, IBS; poor sleep
- Treatment - aggressive and early! I tell my patients I want them to have no more than 2 migraines per month; behavioral management of comorbid psychopathology; lifestyle changes; stop MOH! Focus on restorative sleep.


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**Central Sensitization**

- People with a variety of chronic pain conditions tend to develop changes in brain and spinal cord which amplify pain transmission, decrease inhibition
- The ascending pain pathways get facilitated, the descending inhibitory pathways are impaired
- Pain thresholds are first decreased via peripheral sensitization (maybe), then trigeminal neurons sensitized, then up the “chain of command” – brainstem, thalamus, amygdala, other limbic centers


Medication Overuse Headaches (MOH)

• Defined as headaches occurring at least 15 days per month in patients who overuse acute pain medications.
• Formerly called “rebound” headaches
• Prevalence in general population >1%, in patients with CDH >33%, in some clinics >80%
• Thought to take 2-3 months to evolve, hard to know if MOH causes CDH or CDH causes MOH.

MOH (Cont.)

• MOH patients who take daily pain medications for non-headache reasons may develop CDH only if they have migraines.
• Some patients with CDH will revert to episodic migraines if they stop daily pain medications.
• Medications most implicated in MOH: opioids, barbiturates; also ergots, caffeine, maybe triptans
• MOH less common from NSAIDs, acetaminophen, triptans if headaches less than 10/month
• MOH more common in patients with anxiety, depression, substance abuse

MOH Treatment

• Withdrawal symptoms can last 2-10 days
• Can try bridge outpatient pulse of steroids, naproxen, topiramate, valproate, antiemetics
• Inpatient detox more likely required in patients who have been taking narcotics, tranquilizers
• Inpatient protocols include: IV DHE, hydration, IV steroids, triptans, IV valproate, behavioral
• Unfortunately, relapse rates >40% in adults

New Daily Persistent Headache (NDPH)

• A form of chronic daily headaches (CDH), with abrupt onset, often with distinct tension and migraine features, becoming more common
• Defined as: onset within 3 days of initial headache and remains daily for at least 3 months
• Prevalence: 4-5% adults, 1% teenagers (females > 2:1), probably much more common in teens than CTTH
• Etiologies: Past history of migraine, febrile illness, mild-moderate trauma, anxiety/depression

NDPH Treatment

• Very similar to CDH:
  1. Amitriptyline, start 0.5-1mg/kg @ bedtime (25mg maximum), increase to 1-3mg/kg
  2. Topiramate, start 0.5mg/kg @ bedtime (25mg maximum), increase to 50-100mg
  3. Propranolol, start 1mg/kg divided BID
  4. “Alternatives”- riboflavin, Coenzyme Q10, magnesium, butterbur, massage, Vit. D
  5. Inpatient IV medications if needed
  6. Bio-behavioral, relaxation, imaging, SLEEP!
Chronic Daily Headache (CDH)

- Often reflects “chronification” of episodic migraine.
- Definition: Headaches which occur on at least 15 days/month for > 3 months in the absence of organic pathology.
- Prevalence: < 4% girls/women, < 2% boys/men; in preadolescents 1.7% (girls 2.2%, boys 1.1%).
- Typically, patients have episodic migraine-like headaches plus continuous, less intense migranous or tension headaches.
- More common when parent(s) have CDH.

Chronic Daily Headaches (ICHD-2)

- Chronic (transformed) migraine (CM): Headache progressing from less than 15 days/month to ≥15 days/month for >3 months.
- Chronic tension-type headache (CTTH): Low-grade daily or almost-daily chronic headache without migranous features.
- New daily persistent headache (NDPH): Abrupt onset of unrelenting new CDH, may be complicated by drug overuse; no history of evolved migraine or ETTH.
- Hemicrania continua (HC): rare, indomethacin-responsive headache disorder; continuous, unilateral, fluctuating, moderate-severe pain; can alternate sides; intermittent or continuous subtypes.

CDH Risk Factors (Adults)

- Obesity
- History of frequent headaches (>1/week)
- Caffeine usage
- Analgesic medication overuse
- Anxiety and mood disorders, stress
- Sleep disturbance

CDH/NDPH Risk Factors- Peds

- Medication Overuse less common
- Genetic and Environmental Influences
- Sleep disturbances
- Stressful life events, physical and/or emotional
- Minor head trauma 23%
- EBV infection 21%
- Others- hypothyroidism, hypertension, excess caffeine
- None in 1/2 to 2/3

CDH (Cont.)

- Many children have had their headaches without treatment for years before being referred and treated.
- Common morbidities: sleep disturbances (>50%), psychiatric disorders (50%), dizziness/POTS (30%), medication overuse (20%).
- In a study I presented last year, a large number of CDH teens had musculoskeletal pain, disturbed sleep, IBS, fatigue and other pain conditions; attendance at school was another issue for many.
CDH Work-up

- Neuroimaging (CT, MRI) unlikely to yield any “surgically relevant” findings in the absence of clinically significant abnormalities on neurologic exam or presence of seizures.
- Routine labs also unlikely to yield significant results in the absence of relevant clinical signs or symptoms. I usually check magnesium and vitamin D levels; sometimes thyroid, lupus
- Lumbar puncture should be done if clinically indicated- obese, presence of papilledema, abnormal vision, early morning headaches; “disabled” patient

Hershey AD. Recent developments in pediatric headache. Curr Opin Neurol. 2010;23:249-253

CDH/Migraine Treatments

- Urgency and aggressiveness depends on whether child is going to school, participating in normal activities of daily living.
- May need inpatient admission for IV meds if has been in “status migrainosus”, to ED many times. Unfortunately, a common occurrence.
- Often a mixture of acute, abortive and preventive medications and non-medical treatments is the most successful regimen.
- Long-term headache freedom rate: 30%, many CDH patients return to being episodic migraneurs


CDH/Migraine Treatments (Cont.)

- Acutely, typical over-the counter meds in high doses can be initially tried, such as ibuprofen, naproxen, acetaminophen/aspirin/caffeine. Oral metoclopramide, prochlorperazine, baclofen may be tried. Can combine with triptans. Push fluids! Treat early!
- Triptans such as sumatriptan, rizatriptan, almotriptan and zolmitriptan in oral, dissolving or spray forms have been found to be effective, even in young children. In teenagers, I have found DHE nasal spray to be useful when triptans have failed.

Bigal ME, Borucho S, Serrano D, Lipton RB. The acute treatment of episodic and chronic migraine in the USA. Cephalalgia, 2009; 29:891-897

CDH/Migraine- ED Treatments

- In the emergency department setting, intravenous medications are often tried. Most commonly used in children and teens are ketorolac for pain; promethazine, prochlorperazine, metoclopramide and ondansetron for nausea and vomiting.
- Sometimes, headaches are terminated after this approach, sometimes only temporarily, and sometimes not at all.
- If the above are not successful, admission is usually necessary.


CDH Treatment (Cont.)

Very similar to NDPH:
1. Amitriptyline, start 0.5-1mg/kg @ bedtime (25mg maximum), increase to 1-3mg/kg
2. Topiramate, start 0.5mg/kg @ bedtime (25mg maximum), increase to 50-100mg
3. Propranolol, start 1mg/kg divided BID
4. Consider valproate, gabapentin, clonazepam, venlafaxine, duloxetine, BOTOX, fluoxetine
5. “Alternatives”, riboflavin. Coenzyme Q10, magnesium, butterbur, massage
6. Inpatient IV medications if needed
7. Biobehavioral, relaxation, imaging, SLEEP!

**INPATIENT JUSTIFICATIONS**

- Symptoms are severe and refractory to outpatient management
- Headaches associated with MOH, chronic opioids, drug toxicity
- Compounding behavioral, social, psychiatric co-morbidities render outpatient treatment ineffective; cannot sort out factors
- Patient has had multiple ED visits
- Patient is clinically desperate, DISABLED!!

**INPATIENT TREATMENTS**

- Interrupt daily headache with parenteral protocols, 24 hours a day
- Initiate rehab strategies- out of bed, PT and OT
- Stop offending analgesics if MOH is present
- Implement preventive pharmacotherapy
- Identify effective abortive therapy
- Treat behavioral and psychiatric co-morbidities (mood and personality disorders)
- Education, discharge and outpatient planning

**CDH Conclusions**

- Chronic daily headache is a common disorder
- It is one of the most disabling of the primary headache conditions
- Sufferers frequently are affected by daily pain, experience neuropsychiatric co-morbidities, behavioral disturbances, and drug overuse dilemmas
- Treatment requires complex medication regimens, detoxification, sleep and behavioral management
- Advanced and severe cases may require inpatient care

**CDH Outcomes**

- 2/3 report some reduction in headache intensity or frequency
- 12% have residual CDH, although many still have migraine headaches 4-5 days/month
- CTTH becomes much less over time
- Early onset of CDH portends longer duration
- Baseline presence of major depression does not predict long-term outcome


**Product Pipeline (?)**

- **Acute Rx**: diclofenac with potassium bicarbonate, CGRP receptor antagonists, serotonin receptor agonists (triptans and others)
- **Chronic Rx trials**: topiramate, propranolol, implantable occipital nerve stimulators, tonabersat, BOTOX, “alternative” approaches, transcranial stimulation, vagal nerve stimulators
Chronic Pain Treatment Impediments

- Catastrophization
- Hypervigilance
- Focusing only on pain severity and reduction
- Focusing only on mediation treatment (will manage 50-60% of pain at best)
- Not focusing on function!!!
- Not emphasizing that restoration of normal function almost always precedes pain reduction, not the other way round
- For some patients, accepting that they may always have pain will actually result in less pain (ACT)

Pain-Associated Disability Syndrome (PADS)

- Described in 1998 as “a spiral of increasing pain-related disruption of function” in children
- Seen in all types of pediatric chronic pain disorders, head, visceral, musculoskeletal, etc.
- Preventing or addressing this should be the primary goal of pediatric pain management


PADS Prevention

- Must assess functional limitations at home, school, etc., not just focus on pain as the only dimension
- Sole treatment focus on medications often does not result in functional restoration
- Best treatment program is multimodal with emphasis on non-medical therapies, including cognitive/behavioral

Clinic Name: Dayton Children’s Clinical Trials (DCCT)
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