The “Chronification” of Migraine

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The “Horrification” of Migraine

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Overview

- Define chronic migraine
- Pathophysiology
- Risk factors
- “Pearls” for chronic headache management
ICHD – 2R
Chronic Migraine

A. Headache $\geq 15$ days/month for $\geq 3$ months

B. Patient had $\geq 5$ attacks fulfilling ICHD-2 Migraine with/without aura

C. On $\geq 8$ days/month for $\geq 3$ months headache fulfills criteria for migraine and/or obtains relief with triptan or ergot

D. No medication overuse and not attributed to another disorder
Chronic Daily Headache

- 2.4% - 4.7% worldwide
- 1.3% - 2.4% chronic migraine
Chronic Headache in Preadolescent Children

Persistent Myth

- The difference between episodic migraine and chronic migraine is purely because of psychological influences.
## Psychiatric Co-morbidities

<table>
<thead>
<tr>
<th></th>
<th>Episodic Migraine</th>
<th>Chronic Migraine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>14%</td>
<td>28%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>48%</td>
<td>66%</td>
</tr>
</tbody>
</table>

Psychiatric Co-Morbidities in Adolescent Chronic Daily Headache

- 21% Major Depression
- 19% Panic Disorder
- 20% Current High Suicide Risk
- Most correlated to migraine with aura

Psychiatric influences are not specific to migraine

- Bidirectional relationship to depression and anxiety in other neurological conditions as well
Epilepsy and Depression

- History of depression:
  - Four to Seven fold higher risk of developing epilepsy
  - Two fold less likely to be seizure-free with AED after 5 years
  - Seven fold less likely to be seizure-free after anterior temporal lobectomy for refractory epilepsy
  - 9-22% individuals with epilepsy have depression

Kanner. Epilepsy Currents 2011
Harden. Neurology 2002
Association between major depression and the development of medical and neurological disorders.

Depression and epilepsy: Epidemiologic and neurobiologic perspectives that may explain their high comorbid occurrence
Perhaps not all chronic migraineurs are crazy after all…but how did this myth become so pervasive?

- No objective findings
- Considered a benign condition
- People in pain are unpleasant
- Lack of education in neurology training
- Excluded from most headache trials
- Little research funding
### Impact of Chronic Migraine

<table>
<thead>
<tr>
<th>5 days over past 3 months…</th>
<th>Episodic Migraine</th>
<th>Chronic Migraine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missed work/school</td>
<td>2.2%</td>
<td>8.2%</td>
</tr>
<tr>
<td>Missed household chores</td>
<td>24.3%</td>
<td>57.4%</td>
</tr>
<tr>
<td>Missed family activities</td>
<td>9.5%</td>
<td>36.9%</td>
</tr>
</tbody>
</table>

Pediatric headache disability similar to disability scores in cancer and rheumatological diseases

Remission of chronic migraine significantly decreases disability scores

Manack A et al. Neurology 2011;76:711-718
American Migraine Prevalence and Prevention Study (AMPP)

- In 2004: US survey of 120,000 households
- 162,576 responders: 30,721 reported at least one severe headache in previous year
- Phase 2: 24,000 randomly selected for 5 year follow up study
One year prognosis of migraine in the population
Natural History in Migraine

Migraine

- Remission
  - Evolution to symptom free over prolonged period of time
- Persistence
  - Relative clinical stability and no markers of progression
- Progression
  - Clinical
    - Evolution to chronic migraine
  - Functional
    - Functional changes in the PAG
    - Central sensitization
  - Anatomical
    - Lesions in the brain
    - Lesions outside the brain

Bigal M E, Lipton R B Neurology 2008;71:848-855
Neurovascular Theory

- Cortical Spreading Depression
- Reactive blood vessel changes
- Increased plasma protein leakage
- Subsequent activation of trigeminal nucleus with central sensitization (allodynia)
CSD Stimulates Trigeminal Sensory Fibers

Trigeminal nerve fibers in the meningeal vessels
Release of CGRP, substance P & Inflammatory Cytokines
Activation of Nociceptors

The inflammation and edema activate peripheral meningeal nociceptors

Nociceptors transmit signals to the trigeminal ganglion and the TNC
Central sensitization: sensitization of second-order neurons in the trigeminal nucleus caudalis mediates cutaneous allodynia.
Symptoms of Central Sensitization

Patients often avoid 1 or more of the following activities because of cutaneous allodynia

- Combing hair
- Pulling hair back (ponytail)
- Shaving
- Wearing eyeglasses
- Wearing contact lenses
- Wearing jewelry
- Wearing snug clothing
- Using a heavy blanket in bed

- Allowing shower water to hit the face (“it feels like pins and needles”)
- Resting the face on the pillow on the migraine side
- Rubbing back of neck
- Cooking (“the heat is too much”)
- Breathing through the nose on cold days (“it burns”)

Cutaneous allodynia most prevalent in chronic migraine

![Bar chart showing prevalence of cutaneous allodynia in different headache conditions.](chart_image.png)
Functional Imaging in Migraine vs Controls: Increased cortical thickness in migraine
Structural and Functional Changes Evident in High Frequency Migraine vs Low Frequency Migraine
Cerebellar infarct-like lesions: the CAMERA study.

Periaqueductal Gray Matter Dysfunction in Migraine: Cause or the Burden of Illness?
Frequent Pain Aggregates in Families

A. Mother with no headaches
D. Mother with CDH
Risk factors
Un-modifiable

- Age (declines after 50)
- White race
- Low education/socioeconomic status
- Head injury
Modifiable Risk Factors

- Attack Frequency
- Medication overuse
- Stressful life events
- Caffeine Overuse
- Obesity
- Unhealthy lifestyle
- Snoring
- Other pain syndromes
Attack Frequency

- Risk of developing CM increasing in a nonlinear manner with baseline headache frequency
- Elevated risk begins at 3 or more headaches a month

Headache frequency predicts progression to CDH
Estimates were calculated using multinomial logistic regression (p < 0.005).
Current theories on Medication Overuse Headache
Not “rebound headaches”

- Increase in headaches occur with repeated exposure to certain abortive medicines, not because of withdrawal.
- Term “rebound” increases misguided belief that long acting narcotics won’t increase headaches.
The abortive medicine used matters

- Doubled risk of transformation to chronic migraine at one year:
  - Barbiturate compounds 5 days/month
  - Opiates 8 days/month (risk higher in men)
  - Triptans 10 days/month
  - NSAIDS 14 days/month

Medication Overuse
Risk factor or headache diagnosis?

- Complete wean off overused abortives does not always resolve headaches
- Overuse of abortives does not always lead to chronic migraines
- Consider conceptualizing as risk factor for lowering headache thresholds which may increase headache frequency and decrease response to preventative treatments
Frustrations in Treating Chronic Headaches
Pain Scale

“11/10”

Eleven is One louder
Pain Scale

- Don’t debate.
- Believe pain.
- Chronic pain does not look like acute pain
Frustration and Anger

- “Why can’t anyone tell me why I have headaches?”
- “Why doesn’t anything work for me?”
- “No one can help me.”
Blame Congress!
Disability Adjusted Life Years

2007 NIH Funding per DALY

<table>
<thead>
<tr>
<th>Condition</th>
<th>Funding (US Dollars)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine</td>
<td>29</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>739</td>
</tr>
<tr>
<td>Asthma</td>
<td>426</td>
</tr>
<tr>
<td>Diabetes</td>
<td>810</td>
</tr>
<tr>
<td>Ovarian Cancer</td>
<td>746</td>
</tr>
<tr>
<td>Stroke</td>
<td>232</td>
</tr>
<tr>
<td>Arthritis</td>
<td>330</td>
</tr>
<tr>
<td>MS</td>
<td>933</td>
</tr>
<tr>
<td>Parkinson's</td>
<td>823</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1421</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>775</td>
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</table>
“Can’t you give me anything for the pain?”
Request for immediate pain relief.

- Focus on prevention – abortives will fail in chronic migraine. (leading to frequent phone calls)
- Educate patient that opiates increase production of CGRP which is implicated in migraine
“No, stress doesn’t affect my headaches at all.”
Befriend a pain psychologist.