Headache Management in Primary Care

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Mayo Clinic
Rochester, MN
7th Annual Lloyd Hayes Symposium
Greenville, SC
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Disclosures

- I have no relevant financial relationships to disclose at this time.
- Many medications used to treat migraine and other primary headache disorders do not have an FDA-approved indication for these purposes.
Goals/Objectives

At the end of this talk you should be able to:

■ Explain the pathophysiology of common headache types

■ Develop exam skills relevant to the evaluation of patients with headache

■ Describe the basic approach to the management of common headache types
Note

- Will focus on treatments that are widely available at the current time
- Will try to be practical and tell you exactly what I do (for better or worse)
Outline

- Migraine
- Tension-type headache
- Cluster headache
Patient 1

- 26-year-old female with ten year hx headache
- Frequency two per month, each headache lasts 24 hours
- Bilateral temporal pain
- Throbbing, 9/10
- Associated with nausea, photophobia, phonophobia, osmophobia
- No vomiting or aura
- Often goes into a dark room and “sleeps it off”

- Using stairs worsens headache
- Triggered by missing meal, sleeping longer on weekend, alcohol
- Menses does not clearly trigger
- Acetaminophen does not help
- Misses 1 day of work per month
- Minimal alcohol, no tobacco, six cups coffee per day
- Mother had migraine
- Exam normal
History and Physical Exam

- First goal is to determine if patient has a secondary headache disorder (<10% of headaches)

- Second goal is to classify primary headache disorder once you have determined that no secondary disorder exists (>90% of headaches)
Secondary Headaches
SNOOP₄ Headache Red Flags

- **Systemic symptoms** (fever, weight loss) or **Systemic disease** (malignancy, HIV)
- **Neurologic symptoms or signs** (confusion, impaired alertness or consciousness)
- **Onset sudden** (acute or thunderclap headache)
- **Onset after age 50 years**
- **Previous headache history** (new or different—change in attack frequency, severity, or clinical features)
- **Progressive and/or persistent** (daily)
- **Precipitation by Valsalva** (cough, bend)
- **Postural**
- **Headache** (single or particular headache)

History must be taken, not just accepted

<table>
<thead>
<tr>
<th>Thunderclap headache</th>
<th><img src="image" alt="Graph" /></th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine</td>
<td><img src="image" alt="Graph" /></td>
</tr>
<tr>
<td>Chronic tension-type headache</td>
<td><img src="image" alt="Graph" /></td>
</tr>
<tr>
<td>Transformed migraine</td>
<td><img src="image" alt="Graph" /></td>
</tr>
<tr>
<td>Cluster headache</td>
<td><img src="image" alt="Graph" /></td>
</tr>
<tr>
<td>Intracranial lesion</td>
<td><img src="image" alt="Graph" /></td>
</tr>
</tbody>
</table>

**FIGURE 4.1** Temporal patterns of headache; see Chapter 11 for a discussion of primary daily headache types.
5-minute Examination of Headache Patient

■ Vitals

■ Head and neck
  - Palpate (skull base, TMJs, temporal arteries, upper cervical facets, pericranial muscles, paranasal sinuses)
  - Listen (auscultate the head, orbits, and neck)

■ Focused neurological examination
  - Talk to patient (mental status), watch them walk
  - Cranial nerves (fundus, visual fields, ocular motility, facial symmetry, palate/tongue)
  - Upper motor neuron exam (arm extensor and leg flexor strength, DTRs, plantar responses)
Migraine without aura
International Headache Society
2013 Diagnostic Criteria

- At least five attacks fulfilling criteria below
- Headache lasting 4-72 hours (untreated or unsuccessfully treated)
- During headache has at least one of the following:
  - nausea and/or vomiting
  - photophobia and phonophobia
- Headache has at least two of the following characteristics
  - unilateral
  - pulsating quality
  - moderate or severe intensity
  - aggravation by or causing avoidance of routine physical activity (walking or climbing stairs)
- Headache not attributed to another disorder
Migraine pathophysiology

- Genetically induced hyper-excitable brain
- If a genetically primed neuron is triggered by change in the external or internal environment, it may activate and induce the brain pathways that normally conduct head pain to awaken and produce the symptoms of migraine
- Neurovascular headache
- Car alarm misfire

Rothrock, Headache, 2008
Migraine is misdiagnosed as:

- Tension-type headache 44%
- Sinus headache 43%
- Cluster headache 18%

Why Is Migraine Frequently Mistaken for Tension-Type Headache?

- Neck pain is common during migraine (75%)
- Migraine headache is often bilateral (40%)
- Stress is a common migraine trigger
- Comorbid depression and anxiety obscure diagnosis
Why Is Migraine Frequently Mistaken for Sinus Headache?

- Pain is often located over the sinuses
- Sinus medication may provide relief
- Migraine frequently triggered by weather changes
- Tearing and nasal congestion common during migraine attacks
Tension-type Headache is Common in Population but RARE as a Chief Complaint in the Office

General Population
- Migraine: 16%
- Tension-type Headache: 78%
- Other: 6%

Primary Care Practice
- Migrainous: 76%
- Tension-type Headache: 3%
- Other: 18%

Simple, Accurate, Fast Screener for Migraine

- Strongest predictors of migraine diagnosis
  - **Photophobia**
    - *Does light bother you when you have a headache?*
  - **Impairment (Disability)**
    - *Has a headache limited your activities for a day or more in the last 3 months?*
  - **Nausea**
    - *Are you nauseated or sick to your stomach when you have a headache?*

- 2 out of 3 symptoms: 93% PPV
- 3 out of 3 symptoms: 98% PPV

*PIN the diagnosis*

Which clues from the history help you separate migraine aura from TIA?
Migraine with aura

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 minutes
   3. at least one aura symptom is unilateral
   4. the aura is accompanied, or followed within 60 minutes, by headache

D. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded
# Migraine Aura vs. TIA

<table>
<thead>
<tr>
<th>Migraine</th>
<th>TIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive visual symptoms</td>
<td>Visual loss</td>
</tr>
<tr>
<td>Gradual onset/evolution</td>
<td>Abrupt</td>
</tr>
<tr>
<td>Sequential progression</td>
<td>Simultaneous occurrence</td>
</tr>
<tr>
<td>Repetitive attacks of identical nature</td>
<td>Repetitive attacks of identical nature (15%)</td>
</tr>
<tr>
<td>Flurry of attacks mid-life</td>
<td>Duration &lt; 15 minutes</td>
</tr>
<tr>
<td>Duration up to 60 minutes</td>
<td>Headache uncommon</td>
</tr>
<tr>
<td>Headache follows ~ 50%</td>
<td></td>
</tr>
</tbody>
</table>

Fisher CM. *Stroke* 1986;17:1033-1042
Aura

- Tissot (18th century Swiss physician) quoting a patient:

- “It begins in the eyes; when I least expect it my sight becomes suddenly disordered, but more on one side than the other, like that of a person who has looked at the sun. This lasts about ten minutes; afterwards an arm and a leg of the same side, one time one side and one another, go to sleep. I feel a tingling as if ants were on them; I have the same feeling in the mouth and tongue, and further, during this period, I have the greatest difficulty in speaking. This lasts about half a quarter of an hour; afterwards, the pains in the head commence, but only in the temples, where they persist with great severity during seven or eight hours. When I can be sick, I get relief.”
“Dependence on mental anxiety, bodily exhaustion, overwork to the eyes, gastric derangement, want of exercise.

Origin from a small spot near the centre of vision.

Orderly outward spread from the original spot.

Blindness to boundaries, but not to general impressions of light and colour.

Luminosity in the dark.

Bright bastioned margin, with gleams of various colours.

Tremor and ‘boiling.’

Gradual occupation of one (lateral) half of the field of view.

Gradual recovery of clear vision in rear of the outward-spreading cloud.

Disappearance of the phenomenon in about half an hour.

Sequelae: headache and nausea, and sometimes affection of speech and hearing, and even an approach to hemiplegia.”
Goals of acute treatment

■ Immediate
  – Minimize pain
  – Treat associated symptoms
  – Minimize disability
  – Ultimate goal is freedom from pain within 2 hours, no headache recurrence or rescue meds within 24 hours, and no adverse events

■ Long-term
  – Avoid overuse
  – Minimize phone calls, urgent care, ED visits
Acute migraine treatment principles

- Treat early
- Limit to 2 days per week (with exceptions)
- Use correct dose and formulation
- Use non-oral meds if:
  - early or severe nausea and vomiting, or
  - wakes up with migraine, or
  - severe migraine develops rapidly
- Assess patient’s side effect propensity
- Some patients respond to one drug and not another, try drug with 2 headaches before moving on
Tip

- Treat early at mild, but not too often
  - Some migraineurs have more than 10 headache days per month and are at risk for acute headache medication overuse
  - Those patients must ration their acute therapies to 10 days per month (or about 2 days per week)
  - One approach in this circumstance is to have the patient treat first with an NSAID, then if headache not better at 1 hour move to a triptan

Taylor and Kaniecki, Curr Treat Options Neurol, 2011
Acute treatment options

- **Nonspecific**
  - NSAIDs
  - simple analgesics
  - combination analgesics
  - antiemetics/neuroleptics
  - isomethoptene combo
  - opioids

- **Specific**
  - ergotamine/DHE
  - triptans
AAN practice guideline: acute medications

- Use migraine-specific agents (triptans, DHE) in patients with moderate or severe migraine or whose mild-to-moderate headaches respond poorly to NSAIDs or combinations such as aspirin plus acetaminophen plus caffeine (Excedrin)

- Specific treatments are preferred because of efficacy and lack of dependence, habituation, and addiction

www.aan.com/go/practice/guidelines; Silberstein, Neurology, 2000
Acute treatment: the evidence

- Triptans (Class A)
- DHE-45 (Class A)
- Acetaminophen + aspirin + caffeine (Class A – studied in non-disabling attacks)
- Aspirin (Class A)
- Naproxen sodium (Class A)
- Ibuprofen (Class A)
- Butorphanol Intranasal (Class A)
- Sumatriptan/naproxen sodium (Class A)
- Diclofenac potassium (Class A)
- Prochlorperazine IV (Class A)

Updated American Academy of Neurology Guidelines; in progress
### CHS recommendations acute migraine treatment

<table>
<thead>
<tr>
<th>Drug and route</th>
<th>Recommendation</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended for use in episodic migraine (Use) (HA &lt;15D/M)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Triptans and other migraine specific-medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Almotriptan PO</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>Eletriptan PO</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>Frovatriptan PO</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>Naratriptan PO</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>Rizatriptan PO</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>Sumatriptan SC, PO, IN</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>Zolmitriptan PO, IN</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>DHE IN, SC</td>
<td>Weak</td>
<td>Moderate</td>
</tr>
<tr>
<td>Ergotamine PO</td>
<td>Weak (not recommended for routine use)</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

Worthington et al. Can J Neurol Sci 2013
<table>
<thead>
<tr>
<th>Drug and route</th>
<th>Recommendation</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended for use in episodic migraine (Use) (HA &lt;15D/M)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ASA/NSAIDs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA PO</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>Diclofenac potassium PO</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>Ibuprofen PO</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td>Naproxen sodium PO</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetaminophen PO</td>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td><strong>Opioids and Tramadol (not recommended for routine use)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioid (i.e. codeine)-containing medications PO</td>
<td>Weak</td>
<td>Low</td>
</tr>
<tr>
<td>Tramadol-containing medications PO</td>
<td>Weak</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>Anti-emetics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Domperidone PO</td>
<td>Strong</td>
<td>Low</td>
</tr>
<tr>
<td>Metoclopramide PO</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>Drug and route</td>
<td>Recommendation</td>
<td>Quality of evidence</td>
</tr>
<tr>
<td>---------------</td>
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<td>-------------------</td>
</tr>
<tr>
<td><strong>NOT recommended for use in episodic migraine (Do not use, except under exceptional circumstances) (HA &lt;15D/M)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Butalbital-containing medications PO</td>
<td>Strong</td>
<td>Low</td>
</tr>
<tr>
<td>Butorphanol IN</td>
<td>Strong</td>
<td>Low</td>
</tr>
</tbody>
</table>

Worthington et al. Can J Neurol Sci 2013
Trigeminovascular Anti-migraine Targets

- Cortex
- Phonophobia, Photophobia
- Thalamus
- Trigeminal ganglion
- Autonomic activation: Nausea, Emesis
- Trigeminal nucleus caudalis
- Intracranial blood vessels

<table>
<thead>
<tr>
<th>TRIPITAN</th>
<th>Typical Dose</th>
<th>May Repeat In</th>
<th>Maximal Dose/day</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sumatriptan</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tabs 25,50,100 mg</td>
<td>100 mg</td>
<td>2 hrs</td>
<td>200 mg</td>
</tr>
<tr>
<td>NS 5,20 mg</td>
<td>20 mg</td>
<td>2 hrs</td>
<td>40 mg</td>
</tr>
<tr>
<td>SC 4,6 mg</td>
<td>6 mg</td>
<td>1 hr</td>
<td>12 mg</td>
</tr>
<tr>
<td>Iontophoretic transdermal (TDS)</td>
<td>6.5 mg</td>
<td>2 hrs</td>
<td>13 mg</td>
</tr>
<tr>
<td><strong>Suma + Naproxen</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tabs 85mg +500mg</td>
<td>1 tab</td>
<td>2 hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Zolmitriptan</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tabs 2.5,5 mg</td>
<td>5 mg</td>
<td>2 hrs</td>
<td></td>
</tr>
<tr>
<td>ZMT 2.5,5 mg</td>
<td>5 mg</td>
<td>2 hrs</td>
<td></td>
</tr>
<tr>
<td>NS 5 mg</td>
<td>5 mg</td>
<td>2 hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Naratriptan</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tabs 1,2.5 mg</td>
<td>2.5 mg</td>
<td>4 hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Rizatriptan</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tabs 5,10 mg</td>
<td>10 mg</td>
<td>2 hrs</td>
<td>30 mg</td>
</tr>
<tr>
<td>MLT 5,10 mg</td>
<td>10 mg</td>
<td>2 hrs</td>
<td>30 mg</td>
</tr>
<tr>
<td><strong>Almotriptan</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tabs 6.25,12.5 mg</td>
<td>12.5 mg</td>
<td>2 hrs</td>
<td>25 mg</td>
</tr>
<tr>
<td><strong>Frovatriptan</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tab 2.5 mg</td>
<td>2.5 mg</td>
<td>2 hrs</td>
<td>7.5 mg</td>
</tr>
<tr>
<td><strong>Eletriptan</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20, 40 mg</td>
<td>40 mg</td>
<td>2 hrs</td>
<td>80 mg</td>
</tr>
</tbody>
</table>

Tip: In general, give the highest dose tablet available

Exception: If patient is on propranolol, use rizatriptan 5 mg not 10 mg
<table>
<thead>
<tr>
<th>TRIPTAN</th>
<th>Initial 2 hour relief</th>
<th>Sustained pain free</th>
<th>Consistency</th>
<th>Tolerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatriptan 50 mg</td>
<td>=</td>
<td>=</td>
<td>=/-</td>
<td>=</td>
</tr>
<tr>
<td>Sumatriptan 25 mg</td>
<td>-</td>
<td>=/-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Zolmitriptan 2.5 mg</td>
<td>=</td>
<td>=</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>Zolmitriptan 5 mg</td>
<td>=</td>
<td>=</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>Naratriptan 2.5 mg</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Rizatriptan 5 mg</td>
<td>=</td>
<td>=</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>Rizatriptan 10 mg</td>
<td>+</td>
<td>+</td>
<td>+(+)(+)</td>
<td>=</td>
</tr>
<tr>
<td>Eletriptan 20 mg</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>=</td>
</tr>
<tr>
<td>Eletriptan 40 mg</td>
<td>=/+</td>
<td>=/+</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>Eletriptan 80 mg</td>
<td>+(+)</td>
<td>+</td>
<td>=</td>
<td>-</td>
</tr>
<tr>
<td>Almotriptan 12.5 mg</td>
<td>=</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

- = no difference when compared with sumatriptan 100 mg
- + better when compared with sumatriptan 100 mg
- - inferior when compared with sumatriptan 100 mg
- No Triptan is more safe than another as far as cardiac or vascular risks

*Cephalalgia, 2002;22:633-658*
<table>
<thead>
<tr>
<th>Tier</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier 1G - Generic (preferred - lowest copay)</td>
<td>• Ergotamine/caffeine PO</td>
</tr>
<tr>
<td></td>
<td>• Isometheptene/Acetaminophen/Dichloralphenazone</td>
</tr>
<tr>
<td>Tier 1R - Generic, Restricted (preferred - lowest copay)</td>
<td>• Naratriptan PO</td>
</tr>
<tr>
<td></td>
<td>• Sumatriptan PO</td>
</tr>
<tr>
<td></td>
<td>• Rizatriptan PO (generic as of Jan 2013)</td>
</tr>
<tr>
<td>Tier 2 - Brand (generic not available)</td>
<td>• Ergotamine/caffeine PR</td>
</tr>
<tr>
<td>Tier 2R - Brand, Restricted</td>
<td>• Almotriptan PO</td>
</tr>
<tr>
<td></td>
<td>• Dihydroergotamine NS</td>
</tr>
<tr>
<td></td>
<td>• Eletriptan PO</td>
</tr>
<tr>
<td></td>
<td>• Ergotamine SL</td>
</tr>
<tr>
<td></td>
<td>• Sumatriptan NS</td>
</tr>
</tbody>
</table>
## Formulary at my institution

<table>
<thead>
<tr>
<th>Tier</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier 2R - Injection, Restricted</td>
<td>• Dihydroergotamine SC or IM (ampules and vials are generic)</td>
</tr>
<tr>
<td></td>
<td>• Sumatriptan SC</td>
</tr>
<tr>
<td>Tier 3R - Non-preferred or Lifestyle, Restricted</td>
<td>• Needle-free sumatriptan SC=Sumavel Dosepro</td>
</tr>
<tr>
<td></td>
<td>• Zolmitriptan NS</td>
</tr>
<tr>
<td>Tier 4R - Non-formulary, Restricted</td>
<td>• Frovatriptan PO</td>
</tr>
<tr>
<td></td>
<td>• Zolmitriptan PO (both tab and rapid dissolve)</td>
</tr>
<tr>
<td>Tier 5 - Excluded from the formulary, No Coverage</td>
<td>• Sumatriptan succinate/ naproxen sodium PO</td>
</tr>
</tbody>
</table>
## Dispensing limits at my institution

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dispensing limit</th>
<th>Can refill every</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatriptan, naratriptan, rizatriptan, eletriptan, almotriptan, zolmitriptan</td>
<td>54 tabs (all strengths)</td>
<td>100 days</td>
</tr>
<tr>
<td>DHE nasal spray</td>
<td>6 kits (48 vials)</td>
<td>100 days</td>
</tr>
<tr>
<td>DHE injection</td>
<td>20 vials</td>
<td>100 days</td>
</tr>
<tr>
<td>Sumatriptan SC</td>
<td>6 kits (12 vials)</td>
<td>100 days</td>
</tr>
<tr>
<td>Sumatriptan NS</td>
<td>36 sprays</td>
<td>100 days</td>
</tr>
<tr>
<td>Generic name</td>
<td>Trade name</td>
<td>Anticipated patent expiration</td>
</tr>
<tr>
<td>----------------</td>
<td>------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Zolmitriptan</td>
<td>Zomig</td>
<td>5/1/2013</td>
</tr>
<tr>
<td>Frovatriptan</td>
<td>Frova</td>
<td>12/2013 to 11/2015</td>
</tr>
<tr>
<td>Almotriptan</td>
<td>Axert</td>
<td>11/1/2015</td>
</tr>
<tr>
<td>Eletriptan</td>
<td>Relpax</td>
<td>12/1/2016</td>
</tr>
</tbody>
</table>

These dates are projections and could change with patent and legal challenges.

Zolmitriptan generic as of 5/2013, but has not moved up on my local formulary yet.
Tip

- Consider switching to nasal or injectable formulation after a patient has failed three oral triptans

Goadsby and Sprenger, Lancet Neurol, 2010
Contraindications to triptans

- Know or suspected ischemic heart disease
- Cerebrovascular disease
- Peripheral vascular disease
- Uncontrolled HTN
- Severe hepatic disease
- Use of ergot-alkaloid or other 5-HT$_1$ agonist (i.e. a different triptan) within preceding 24 hours
- Patients should avoid sumatriptan, rizatriptan, and zolmitriptan within 2 weeks of MAO inhibitor use (phenelzine)
- Hemiplegic or basilar-type migraine
- Typically avoid during pregnancy
Rational polytherapy

- Antiemetic (metoclopramide 10 mg) plus NSAID (Naproxen sodium 550 mg)
- NSAID plus triptan
- Antiemetic plus triptan
- Antiemetic plus NSAID plus triptan
What not to use (or use with caution)

■ Barbiturate containing compounds
  - Implicated in overuse headache (rebound) and as a risk factor for headache progression
  - Lack evidence base, associated with dependence, habituation, and sedation

Exceptions
  • Established, infrequent, non-escalating use
  • Better alternatives contraindicated
What not to use (or use with caution)

- Opioids
  - Implicated in overuse headache (rebound) and as a risk factor for headache progression
  - Associated with dependence, habituation, addiction, and sedation

Exceptions
- Established, infrequent, non-escalating use
- Better alternatives contraindicated
- Rescue when 1st-line treatment fails
Acute treatment plan

Initial Therapy

- First dose of triptan

If Fails

Back-up Therapy

- Repeat dose of triptan

If Fails

Rescue Therapy

- Trying to keep out of ED
- Prochlorperazine 25 mg or chlorpromazine 100 mg PR
- Indomethacin 50 mg PR
- Ketorolac 31.5 mg IN
- Ketorolac 30-60 mg IM
- Very rarely opioid

- If has early or severe nausea and vomiting, or if wakes up with migraine, or if severe migraine develops rapidly use non-oral meds (stratified care)

Whyte, Headache 2010; Turkewitz. Self-administration of parenteral ketorolac for head pain. Headache, 1992
General counseling

- Encourage patient to sleep, eat, and exercise regularly
- Limit caffeine to 2 normal sized beverages per day, or better yet avoid completely
- Avoid alcohol if it is a trigger
Address risk factors for progression from episodic to chronic migraine

<table>
<thead>
<tr>
<th>Not Modifiable by Health Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
</tr>
<tr>
<td>Low socioeconomic status</td>
</tr>
<tr>
<td>Head trauma</td>
</tr>
<tr>
<td>Genetic/epigenetic?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Modifiable by Health Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Medication overuse</td>
</tr>
<tr>
<td>Caffeine overuse</td>
</tr>
<tr>
<td>Stressful life events</td>
</tr>
<tr>
<td>Snoring</td>
</tr>
<tr>
<td>Depression</td>
</tr>
<tr>
<td>Allodynia</td>
</tr>
<tr>
<td>Anxiety</td>
</tr>
<tr>
<td>Attack frequency</td>
</tr>
</tbody>
</table>

Modifications Can Result in:

- Headache burden
- Migraine progression
- Rate of remission

Patient 2

- A 36-year-old female presents with worsening headache
- Her headaches started at age 26, initially occurred twice per month, associated with N/V/photophobia/phonophobia
- Headache frequency has gradually increased over the last year, associated with an increased use of Excedrin Migraine (acetaminophen, aspirin, caffeine)
- She has had a constant, background, holocephalic, non-throbbing headache associated with continuous photophobia for three months, rated 6/10

- Four times a week she has an exacerbation of this continuous headache, rated 9/10
- Exacerbations are holocephalic, throbbing, last 24 hours, and are associated with nausea, phonophobia, osmophobia, and increased photophobia
- Currently taking six Excedrin Migraine tablets per day
- No tobacco, alcohol, or caffeine
- Positive family history of migraine
- Exam normal
CHRONIC DAILY HEADACHE
Definition and Clinical Classification

Headache ≥ 15 days per month

Exclude secondary headache

Classify based on duration

Short Duration < 4 hours

Diagnose

Long Duration ≥ 4 hours
Chronic Daily Headache--Secondary Causes
Chronic Daily Headache
Secondary Causes
Chronic daily headache (≥15 d/M; ≥4 hours duration)

Migraine ≥ 8 days/month

Continuous unilateral pain with autonomic features

Clear onset as a daily syndrome

Pain and associated symptom profile

Primary CDH: Long Duration

Transformed or Chronic Migraine

Hemicrania Continua

New Daily Persistent Headache

Chronic Tension-Type Headache
2013 Criteria for CM

- Headache (TT and/or migraine) on $\geq 15$ days/month for $>3$ months
- Occurring in a patient who has had at least 5 attacks fulfilling migraine criteria
- On $\geq 8$ days/month for $>3$ months headache has fulfilled any of the following:
  - At least 2 of *unilateral, *pulsating, *moderate or severe, *worse with or avoids routine physical activity; AND at least 1 of *nausea and/or vomiting, *photophobia and phonophobia
  - Typical aura
  - Believed by the patient to be migraine at onset and relieved by a triptan or ergot
- Not better accounted for by another diagnosis
2013 Criteria for MOH

- Headache present on \( \geq 15 \text{ days/month} \) in a patient with a pre-existing headache disorder

- Regular overuse for \( >3 \text{ months} \) of one or more acute treatment drugs
  - Ergotamine, triptans, opioids, or combination analgesics \( \geq 10 \text{ days/M} \)
  - Simple analgesics on \( \geq 15 \text{ days/M} \)
  - Any combination of ergotamine, triptans, simple analgesics, NSAIDs and/or opioids on \( \geq 10 \text{ days/M} \) without overuse of any single drug or drug class alone

- No better diagnosis
Stating the obvious

- Chronic migraine and medication overuse frequently coexist
  - 45-80% of patients recruited into chronic migraine trials also meet criteria for MOH
- Difficult to make accurate dx of MOH at time of presentation
- Luckily, treatment approach is similar
New in 2013!

- Patients meeting criteria for chronic migraine and medication-overuse headache are given both diagnoses.
- After drug withdrawal, migraine will either revert to episodic subtype or remain chronic, and be re-diagnosed accordingly.

ICHD-3 beta, 2013
Treatment overview

- Provide patient education and address psychosocial issues
- Biobehavioral therapy (relaxation therapy, biofeedback)
- Withdraw overused acute medications
- +/- Initiate bridge therapy for withdrawal headache
- Initiate preventive medication
- Select acute therapy in the post-overuse setting; use ≤ 2 days per week
- Close f/u for 8-12 weeks
Nonpharmacological measures

- Eat, sleep, exercise in a regular pattern
- Limit caffeine
- Address comorbid depression and anxiety
- Training in relaxation techniques and biofeedback
- Educate that acute medication overuse may preclude the efficacy of preventives
  - Topiramate and onabotulinumtoxinA trials in chronic migraine cause some to this
- The headaches may get worse temporarily during withdrawal before subsequently improving
Fig 2.—Topiramate: impact of medication overuse on efficacy.

\[ ^a P < .02 \quad ^b P = .03 \] 

Diener, Cephalalgia, 2007; Aurora, Headache 2011;51(S2):93-100

Similar results found in PREEMPT trials of onabotulinumtoxinA: preventive was effective even if overusing acute headache medications

Silberstein et al. J Neurol Sci 2013;331:48-56
Behavioral and physical treatments

**Behavioral Treatments**
- Relaxation (Level A)
- Biofeedback (Level A)
- Cognitive Behavioral (Level A)
- Should be used

**Physical Treatments**
- Acupuncture (Level B)
- Cervical Manipulation (Level U)
- Mobilization (Level U)
- Probably not Effective
- Inadequate evidence

Updated American Academy of Neurology Guidelines; in progress
Outpatient withdrawal protocol A

■ Taper overused acute medication over 4 weeks
  – Make the goal one of two things:
    • Aim to quit the overused acute medicine completely at end of wean, and use another acute med ≤ 2 d/week, or
    • Get the overused acute med down to ≤ 2 d/week

■ Sometimes use long-acting NSAID daily as bridge therapy over that time period

■ In butalbital overuse, if there is a concern for withdrawal symptoms, provide tapering course of phenobarbital 30 mg BID for 2 weeks, followed by 15 mg BID for 2 weeks

■ In opioid overuse, if there is a concern for withdrawal symptoms, provide clonidine patch (0.1-0.2 mg/day/1 week) for 1-2 weeks

■ Start a preventive medication during the acute medication withdrawal

After Tepper, Continuum Headache, August 2012
Outpatient withdrawal protocol B

- I rarely use this approach
- This second outpatient approach is appropriate in the withdrawal of overused medications EXCEPT for barbiturates, opioids, or benzodiazepines
- Abrupt withdrawal of the overused medication
- Bridge therapy for 5-14 days (long-acting NSAID, prednisone, or SC dihydroergotamine)
- At the end of the bridge, provide migraine-specific treatment, limited to ≤ 2 d/week
- Start a preventive medication on day 1

After Tepper, Continuum Headache, August 2012
Inpatient withdrawal protocol

- **Abrupt withdrawal of the overused acute medication**
  - If abruptly withdrawing butalbital, start phenobarbital 30 mg BID for 2 weeks followed by 15 mg BID for 2 weeks
  - Opioids may need to be tapered rather than abruptly stopped if high doses are being overused
  - In opioid overuse, if there is a concern for withdrawal symptoms, provide clonidine patch (0.1-0.2 mg/day/1 week) for 1-2 weeks; alternatively clonidine can be given as needed for withdrawal symptoms (0.1-0.2 mg TID, titrated up or down based on symptoms)

- **IV bridge therapy** (dihydroergotamine plus metoclopramide or ondansetron or domperidone, prochlorperazine, valproate sodium, or methylprednisolone)

- **Start a preventive medication**

See Nagy et al Neurology 2011 for inpatient IV DHE protocol
Bridge therapies

- Naproxen
- Prednisone
- SC DHE
- IV DHE plus metoclopramide
- IV valproate sodium
- IV prochlorperazine
- IV methylprednisolone
Guidelines for initiating migraine preventive therapy

- > 3 headache days/M when acute treatment not reliably effective
- > 8 days/M even if acute medications effective
- Acute meds contraindicated, not tolerated, or ineffective
- Patient preference
- Uncommon migraine conditions (e.g., hemiplegic migraine)
Preventive therapy

- Goal is to decrease the headache frequency by **50%**
- Start low, go slow until therapeutic effects develop, side effects develop, or ceiling dose is reached
- Preventive should be continued for approx **2 months at target dose** or maximal tolerated dose before determining utility (some experts recommend a 6 month trial)
- If the first is not helpful, taper it and try another from a different class
- Monotherapy preferred, but sometimes necessary to combine preventives
- Reliable birth control
- If the preventive is effective, it can be **tapered after 6-12 months**
Malayan tapir; Tapirus indicus
Evidence-based episodic migraine prevention: Level A (established efficacy)

- Divalproex sodium
- Sodium valproate
- Topiramate
- Metoprolol
- Propranolol
- Timolol
- Petasites (butterbur)


I did not include preventives used to treat menstrually related migraine only
Evidence-based episodic migraine prevention: Level B (probably effective)

- Amitriptyline
- Venlafaxine
- Atenolol
- Nadolol
- Magnesium
- MIG-99 (feverfew)
- Riboflavin
- Histamine SC
- NSAIDs: fenoprofen, ibuprofen, ketoprofen, naproxen, naproxen sodium


I did not include preventives used to treat menstrually related migraine only
Evidence-based episodic migraine prevention: Level C (possibly effective)

- Lisinopril
- Candesartan
- Clonidine
- Guanfacine
- Carbamazepine
- Nebivolol
- Pindolol
- Cyproheptadine
- Co-Q10
- NSAIDs: flurbiprofen, mefenamic acid


I did not include preventives used to treat menstrually related migraine only
Evidence-based episodic migraine prevention: Level D (inadequate or conflicting data)

- Acetazolamide
- Acenocoumarol
- Coumadin
- Picotamide
- Fluvoxamine
- Fluoxetine
- Gabapentin
- Protriptyline
- Bisoprolol
- Nicardipine
- Nifedipine
- Nimodipine
- Verapamil
- Cyclandelate
- Omega-3
- NSAIDS: aspirin, indomethacin
- Hyperbaric oxygen


I did not include preventives used to treat menstrually related migraine only
2010 Migraine Prevention Recommendations from Canada

First-line agents
- Amitriptyline
- Propranolol
- Nadolol

Second-line agents
- Topiramate
- Gabapentin
- Venlafaxine
- Candesartan
- Lisinopril
- Magnesium
- Butterbur
- Coenzyme Q10
- Riboflavin

Third-line agents
- Flunarizine
- Pizotifen
- Divalproex sodium

### 2012 Migraine Prevention Recommendations from Canada

<table>
<thead>
<tr>
<th>Characteristic of the migraineur</th>
<th>Drug strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>First timer</td>
<td>Beta blocker, tricyclic</td>
</tr>
<tr>
<td>Side effect averse</td>
<td>Candesartan, Mg, riboflavin, butterbur, coenzyme Q10</td>
</tr>
<tr>
<td>Overweight</td>
<td>Topiramate</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>Beta blocker, candesartan, lisinopril</td>
</tr>
<tr>
<td>Depressed/anxious</td>
<td>Tricyclics, venlafaxine, dual therapy</td>
</tr>
</tbody>
</table>

*Canadian Journal of Neurological Sciences March 2012 supplement*
### Evidence base for preventive therapy in CHRONIC MIGRAINE

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Evidence class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>25-50 mg/day</td>
<td>II</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>20-40 mg/day</td>
<td>III</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>Mean dose 300 mg/day</td>
<td>III</td>
</tr>
<tr>
<td>Divalproex sodium, valproate sodium</td>
<td>500-2500 mg/day</td>
<td>II</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>2400 mg/day</td>
<td>II</td>
</tr>
<tr>
<td>Topiramate</td>
<td>100 mg/day</td>
<td>I</td>
</tr>
<tr>
<td>Tizanidine</td>
<td>Mean dose 18 mg/day</td>
<td>III</td>
</tr>
<tr>
<td>OnabotulinumtoxinA</td>
<td>155-195 U</td>
<td>I (combined results of PREEMPT 1 and 2 lead to FDA approval in 2010)</td>
</tr>
</tbody>
</table>
My typical regimens-ABCDE

- Nortriptyline or amitriptyline: Start 10 or 25 mg qhs, then increase by 10 or 25 mg q week until on 1mg/kg qhs
- Propranolol: Use extended-release formulation and start 80 mg qd, increase in one week to 160 mg per day, some patients need up to 320 mg per day
- Nadolol: Start 40 mg qd, increase by 40 mg q week up to target of 120 mg/day, some patients need up to 240 mg/day
- Atenolol: 25 mg qhs X one week, then increase by 25 mg q week until on 50 mg BID
- Verapamil: Use sustained-release formulation starting at 120 mg/ day (1/2 of a 240 mg scored SR tablet) and increase in two weeks to 240 mg per day
- Depakote: Use Depakote ER starting at 500 mg per day and increase in 1 week to 1000 mg per day
- Gabapentin: Start 300 mg qhs, increase by 300 mg q week until on 2400 mg per day (600/900/900)
- Topiramate: Start 25 mg qhs, increase by 25 mg q week until on 50 mg po BID (some need 100 mg po BID)
- Tizanidine: Start 2 mg qhs, increase by 2 mg q week as tolerated up to 8 mg TID (most patients only tolerate 2 mg TID)
- Candesartan 16 mg per day
- Lisinopril 10 mg per day for 1 week, then 20 mg per day
For chronic migraine, every 3 months
- I almost always do 2 cycles
- **150** Units total: 50 U anterior mm plus both temporalis; 25 U in SC total; 25 U in each trapezius; 25 U in occipitalis total
- Small number get neck pain post

After Garza, Cephalalgia 2010:30:500-503.
Doc, I don’t want to be:

**Overweight**
- Weight loss
  - Topiramate
  - Zonisamide
  - Naturals
  - ACE/ARB
  - Protriptyline
  - Metoprolol
  - Timolol
  - Propranolol
  - Nortriptyline
  - Venlafaxine
  - Amitriptyline
  - Divalproex sodium
  - Fluoxetine

**Sedated**
- (Onabotulinum toxin)
- Natural
- Vitamin B2
- Magnesium
- ACE/ARB
- Verapamil
- Beta Blockers
- Protriptyline
- Venlafaxine
- Valproate
- Topiramate
- Nortriptyline
- Gabapentin
- Amitriptyline

**Poor**
- Magnesium
- Amitriptyline
- Propranolol
- Butterbur
- B2
- Lisinopril
- Valproic acid

Courtesy of Dr. William Young
Scheduled opioid therapy

- One prospective study reported the outcome in 70 pts who remained on scheduled opioid therapy for at least 3 years.
- 74% either failed to show significant improvement or were discontinued from the program for clinical reasons.

Saper Neurology 2004
Other interventions
### GON Block for Primary Headaches
Prolonged Effects from a Single Injection

<table>
<thead>
<tr>
<th>Headache Disorder</th>
<th>Partial Response</th>
<th>Complete Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine</td>
<td>17</td>
<td>9</td>
</tr>
<tr>
<td>(54)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cluster</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>(19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NDPH</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>(10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemicrania Continua</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>(7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>(11)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean duration of complete response 20 days
Mean duration partial response 45 days
Mean latency to response: 2 days

---

Complete response: pain-free
Partial response: >30% decrease in severity or frequency

Afridi et al. Pain 2006;122;126-129
3/11/14: FDA allows marketing
Increased risk of ischemic stroke in MA (RR 2)

RR with OC 7, RR with smoking 9 in migraine of any type
- Some of this data collected when higher dose estrogen used

RR in MA currently using OC and smoking 10

Stroke can have significant morbidity/mortality

Discuss what WHO and ACOG recommend

Need an effective form of birth control when on a migraine preventive

I now recommend stopping estrogen-containing OC
- Change to progestin-only OC (or progestin implant, IUD, or injection), copper IUD, barrier method, or other

# U.S. Selected Practice Recommendations for Contraceptive Use, CDC, 2013

<table>
<thead>
<tr>
<th>Sub-condition</th>
<th>Combined pill, patch, ring</th>
<th>Progestin-only pill</th>
<th>Progestin Injection</th>
<th>Progestin Implant</th>
<th>Progestin IUD</th>
<th>Copper IUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine with aura, any age</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

1 = no restriction  
2 = advantages generally outweigh risks  
3 = risks usually outweigh advantages  
4 = unacceptable health risk

I = initiation of contraceptive method  
C = continuation of contraceptive method  
The issue of continuation is clinically relevant whenever a woman develops the condition while she is using the method

AHS Choosing Wisely 2013

- Don’t prescribe opioid or butalbital-containing medications as first-line treatment for recurrent headache disorders
- Don’t recommend prolonged or frequent use of over-the-counter pain medications for headache
- Don’t recommend surgical deactivation of migraine trigger points outside of a clinical trial

Loder et al Headache 2013
Outline

- Migraine
- Tension-type headache
- Cluster headache
Patient 3

- 58 year-old female with 15 years of headache
- 5 days per week, each headache lasts several hours
- Bifrontal and bitemporal ache, no throbbing, usually 4/10, does not interfere with daily activities
- No N/V, photo-, phono- or osmophobia
- No aura, does not wake her from sleep
- Worse when stressed
- No FH headache
- Exam normal
Chronic tension-type headache

A. Headache occurring on ≥15 d/mo on average for >3 mo (≥180 d/y), fulfilling criteria B-D
B. Lasting hours to days, or unremitting
C. ≥2 of the following 4 characteristics:
   1. bilateral location
   2. pressing/tightening (non-pulsating) quality
   3. mild or moderate intensity
   4. not aggravated by routine physical activity
D. Both of the following:
   1. not >1 of photophobia, phonophobia, mild nausea
   2. neither moderate or severe nausea nor vomiting
E. Not better accounted for by another ICHD-3 diagnosis
## Recommended acute treatment for tension-type headache

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Level of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen</td>
<td>200-800 mg</td>
<td>A</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>25 mg</td>
<td>A</td>
</tr>
<tr>
<td>Aspirin</td>
<td>500-1000 mg</td>
<td>A</td>
</tr>
<tr>
<td>Naproxen</td>
<td>375-550 mg</td>
<td>A</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>12.5-100 mg</td>
<td>A</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>1000 mg</td>
<td>A</td>
</tr>
<tr>
<td>Caffeine comb.</td>
<td>65-200 mg</td>
<td>B</td>
</tr>
</tbody>
</table>

Bendtsen et al, EFNS guideline, European Journal of Neurology, 2010
# Recommended preventive treatment TTH

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose</th>
<th>Level of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug of first choice</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>30-75 mg</td>
<td>A</td>
</tr>
<tr>
<td><strong>Drugs of 2(^{nd}) choice</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>30 mg</td>
<td>B</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>150 mg</td>
<td>B</td>
</tr>
<tr>
<td><strong>Drugs of 3(^{rd}) choice</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clomipramine</td>
<td>75-150 mg</td>
<td>B</td>
</tr>
<tr>
<td>Maprotiline</td>
<td>75 mg</td>
<td>B</td>
</tr>
</tbody>
</table>

Bendtsen et al, EFNS guideline, European Journal of Neurology, 2010
# Non-drug treatment of TTH

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Level of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psycho-behavioral treatments</td>
<td></td>
</tr>
<tr>
<td>EMG biofeedback</td>
<td>A</td>
</tr>
<tr>
<td>Cognitive-behavioral therapy</td>
<td>C</td>
</tr>
<tr>
<td>Relaxation training</td>
<td>C</td>
</tr>
<tr>
<td>Physical therapy</td>
<td>C</td>
</tr>
<tr>
<td>Acupuncture</td>
<td>C</td>
</tr>
</tbody>
</table>

Bendtsen et al, EFNS guideline, European Journal of Neurology, 2010
Outline

■ Migraine
■ Tension-type headache
■ Cluster headache
A 46-year-old lion-tamer has a ten year history of headaches occurring in bouts

Bouts often occur in the fall, last about 2 months

During the two-month-long bout, he will have 1-2 headaches in a 24-hour period, each lasting 1 hour

Almost always wakes up at 2 am with one of his headaches

Strictly right-sided, around eye

Throbbing pain, 10/10

Associated with ipsilateral tearing, conjunctival injection, ptosis, and rhinorrhea

No N/V

Very restless during headache attack--paces floor

Acetaminophen no help

Triggered by alcohol in 30 minutes, so avoids this during bout

Usually has four beers per day, does smoke 1 ppd

No FH of headache

Exam normal
Cluster Headache International Headache Society 2013 Diagnostic Criteria

- At least 5 attacks of severe or very severe unilateral orbital, supraorbital, and/or temporal pain lasting 15-180 min untreated
- Frequency between 1 qod and 8/day for > half of the time when the disorder is active
- Either or both of the following:
  - Associated with ≥1 of:
    - ipsi conjunctival injection and/or lacrimation
    - ipsi nasal congestion and/or rhinorrhea
    - ipsi eyelid edema
    - ipsi forehead and facial sweating
    - Ipsi forehead and facial flushing
    - ipsi sensation of fullness in the ear
    - ipsi miosis and/or ptosis
  - Sense of restlessness or agitation
- Not attributed to another disorder
Cluster Headache

■ Episodic cluster headache
  A. Attacks fulfilling criteria for Cluster headache and occurring in bouts (cluster periods)
  B. ≥2 cluster periods lasting 7 d to 1 y (when untreated) and separated by pain-free remission periods of ≥1 mo

■ Chronic cluster headache
  A. Attacks fulfilling criteria for Cluster headache and criterion B below
  B. Occurring without a remission period, or with remissions lasting <1 mo, for ≥1 y
### EFNS cluster headache guidelines

#### Acute:
- 100% oxygen, 15 l/min (A)
- Sumatriptan 6 mg s.c. (A)
- Sumatriptan 20 mg nasal (A)
- Zolmitriptan 5 mg nasal (A/B)
- Zolmitriptan 10 mg nasal (A/B)
- Zolmitriptan 10 mg oral (B)
- Zolmitriptan 5 mg oral (B)
- Lidocaine intranasal (B)
- Octreotide (B)

#### Preventive:
- Verapamil (A)
- Steroids (A)
- Lithium carbonate (B)
- Methysergide (B)
- Topiramate (B)
- Ergotamine tartrate (B)
- Valproic acid (C)
- Melatonin (C)
- Baclofen (C)

A denotes effective, B denotes probably effective, C denotes possibly effective

May, EJN, 2006
Acute treatment of cluster headache

- Oxygen 7-15L/min for 15-20 min via non-rebreathing face mask (give them prescription and send them to oxygen supply store, not pharmacy)
- Sumatriptan 6 mg SC, limit 2 inj/24 hours (can also use 4 mg SC, then limit is 3 inj/24 hours*)
  - Give them enough
- Sumatriptan 20 mg IN (only if attacks last at least 45 min)--used much less than SC because doesn’t work as well
- Zomig 5 mg IN

- DHE 1 mg SC or IV
- Lidocaine 4-6% nasal drops, 2 drops in each nostril
  - patient has to lie down after dosing for 2-5 minutes, with head extended out of bed, bent downwards 30-45 degrees and rotated 20-30 degrees towards side of headache
  - rarely adequate on own as acute therapy, and difficult for cluster headache sufferers to tolerate as they are restless

*Generic 4 mg suma injections on back order as of 2/14/14

Halker, Vargas, and Dodick, Sem Neurol, 2010
Transitional Prevention of Cluster Headache

- Prednisone 60 mg qd X 3 days, then decrease by 10 mg q 3 days until off
  - typically used once starting maintenance prevention as maintenance prevention takes a while to work
  - usually limited to 3 courses per year
- GON blockade
  - I typically use 1 injection, ipsilateral to pain
  - Can repeat every 3 months in CCH (Lambru et al Eur J Neurol 2014;21:338-343)

- *Ergotamine 1 mg po TID or 2 mg supp qd X 1-3 weeks
  - avoid triptan use acutely
- *DHE 0.5-1 mg SC or IM q 8-12 hours for 1-3 weeks or *repetitive IV DHE X 3 days
  - avoid triptan use acutely
- *Naratriptan 2.5 mg BID X 7 days or *eletriptan 40 mg BID X 6 days or *frovatriptan 2.5 mg qd X 7-20 days
  - avoid other triptan or ergot

*placebo-controlled evidence lacking
Maintenance Prevention of Cluster Headache

- Short duration bouts may not require this
- Effective dose continued for typical duration of bout plus 2 weeks pain-free, then slow taper
- Baseline ECG, then verapamil 80 mg TID, increase by 80 mg q 2 weeks with ECG before each dose increase looking for PR-interval prolongation, initial target 480 mg/day but some need up to 960 mg/day
  - Routine 6-month ECGs after dose is established
- Lithium 300 mg TID, check trough level in approximately 1-2 weeks, trying to achieve a level of 0.7 to 1.0, may need to increase to 300/300/450 or 450/300/450
- *Topiramate 25 mg qhs, increase by 25 mg every 3-4 days up to max of 200 mg po BID
- Melatonin 10 mg qhs

*placebo-controlled evidence lacking

Goadsby. TACs. Continuum 2012.
Goals/Objectives

At the end of this talk you should be able to:

- Explain the pathophysiology of common headache types
- Develop exam skills relevant to the evaluation of patients with headache
- Describe the basic approach to the management of common headache types
CCQ: Treatment of the Pregnant Migraineur

- Relaxation techniques and biofeedback, regular meals and sleep
- Acute:
  - For headache:
    - Acetaminophen, +/- codeine†
    - Codeine†
    - Ibuprofen, naproxen (use in 2nd trimester only)*
    - Hydrocodone, other narcotics†
  - For nausea:
    - Metoclopramide
    - Chlorpromazine
    - Prochlorperazine
    - Promethazine
    - Ondansetron**
- For severe acute attacks:
  - Hydration
  - Mag sulfate 1 gram IV***
  - Metoclopramide 10 mg IV#
  - Prochlorperazine 10 mg IV
  - IV narcotics† can supplement
- For prolonged attacks:
  - Corticosteroids**
  - Sumatriptan does not appear to increase risk of birth defects, but I still avoid
- Preventive:
  - I hardly ever use
  - Propranolol when benefits outweigh risks
  - Mag citrate 400-600 qd****

† 2011 case-control study found association between early pregnancy opioid tx and certain birth defects; Broussard AJOG 2011

# CHS acute migraine treatment during pregnancy strategy

<table>
<thead>
<tr>
<th>Phenotype/strategy</th>
<th>Medication options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine during pregnancy strategy</td>
<td>Avoid medication where possible 1. acetaminophen ± metoclopramide 2. acetaminophen with codeine ± metoclopramide 3. ibuprofen (avoid 1st trimester and at /after 32nd week gestation) ± metoclopramide 4. sumatriptan (if benefits outweigh risks – limited data but relatively safe) ± metoclopramide</td>
</tr>
</tbody>
</table>

Worthington et al. Can J Neurol Sci 2013
CHS migraine prevention during pregnancy

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<tr>
<td>Migraine prevention during pregnancy</td>
<td>• Drug avoidance if possible</td>
</tr>
<tr>
<td></td>
<td>• When necessary, magnesium, propranolol, metoprolol, amitriptyline and (nortriptyline) are</td>
</tr>
<tr>
<td></td>
<td>considered relatively safe options</td>
</tr>
</tbody>
</table>

Pringsheim et al Can J Neurol Sci 2012
CCQ: Treatment of the lactating migraineur

**Acute:**
- Acetaminophen
- Moderate caffeine
- Ibuprofen, naproxen
- AAP considers sumatriptan compatible with breastfeeding
  - Can try to take med just after breast-feeding or pump/discard following a dose
- InfantRisk Center at Texas Tech states eletriptan is safer than suma as less detected in milk*
- Magnesium sulfate
- Opioids (other than codeine)

Loder, Sem Neurology, 2007; AAP Committee on Drugs, Pediatrics, 2001; *Lucas, Curr Pain Headache Rep, 2009
## CHS acute migraine treatment during lactation strategy

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| Migraine during lactation strategy | Avoid medication where possible  
1. acetaminophen ± metoclopramide  
2. ibuprofen ± metoclopramide  
3. sumatriptan ± metoclopramide  
4. morphine (exceptional circumstances only - avoid high doses, maternal sedation, avoid when infant is premature, and use caution if infant under 1 month of age) |

Worthington et al. Can J Neurol Sci 2013
CCQ: Treatment of the lactating migraineur

- Preventive:
  - I nearly always recommend waiting until done breastfeeding
  - Propranolol, verapamil felt by AAP to be usually compatible with breast feeding
  - Canadians recommend magnesium and beta blockers, or amitriptyline/ nortriptyline if that doesn’t work*

*Pringsheim et al Can J Neurol Sci 2012
CCQ: Preventive treatment of frequent, prolonged, or prominent aura

- Verapamil
- Aspirin 81 mg (experience in polycythemia vera; picotamide has been studied open label)
- Magnesium oxide 400 mg BID (Personal communication, Rozen)
- Divalproex sodium
- Gabapentin
- Acetazolamide (500-1000 mg total)
- Lamotrigine (50 to 300 mg total; mean 150 mg/d)
- Memantine