Taking the Headache Out of Migraine Diagnosis & Management
Session 8: Taking the Headache Out of Migraine Diagnosis and Management

Learning Objectives

- Describe how to use standardized tools to guide you through the appropriate diagnosis and treatment of migraine.
- Describe a stratified care approach to management of migraine in order to tailor therapy to the patient.

Faculty

Frederick R. Taylor, MD, FAHS
Adjunct Associate Professor of Neurology
University of Minnesota School of Medicine
Minneapolis, Minnesota

Dr Frederick R. Taylor is an adjunct associate professor of neurology at the University of Minnesota Medical School. He is a board-certified headache specialist/neurologist and directs the Integrated Headache Clinic and Research Center at Park Nicollet Health Services in Minneapolis. He attended the University of New Mexico School of Medicine and received his MD in 1977. He then completed residencies and fellowship at the University of Wisconsin–Madison.

Dr Taylor is assistant editor of the headache subsection of the Cochrane Library of Pain, Palliative and Supportive Care systematic reviews; associate editor and abstracts and citations co-editor of Headache: The Journal of Head and Face Pain; a contributing editor to Headache Currents; and migraine subsection editor of Current Pain and Headache Reports. He serves on the governing board of the Migraine International Primary Care Advisors and previously served on the board of the American Council for Headache Education.

Dr Taylor is an active member and fellow of the American Headache Society, a member of the International Headache Society, and treasurer of the National Board for Certification in Headache Management. Extensively published in headache, he lectures worldwide, with a special interest in the role of patient as self-care healer.

Susan Hutchinson, MD
Associate Clinical Professor
Department of Family Medicine
University of California Medical Center
Irvine, California

Dr Susan Hutchinson received her bachelor’s degree in chemistry magna cum laude from Miami University of Ohio in Oxford, Ohio. She graduated from the Medical College of Ohio in Toledo, and completed her internship and residency in the Department of Family Medicine at the University of California, Irvine, Medical Center, where she is currently an associate clinical professor. Dr Hutchinson is board-certified in family practice, with a subspecialty in headache. She is also director and founder of the Orange County Migraine and Headache Center, also in Irvine.

Dr Hutchinson concentrates on the management of migraine and mood disorders, with a special interest in the relationship of both conditions to hormones. A national speaker on migraine and depression, in February 2003, she was awarded the National Headache Foundation Lectureship Award in recognition of her contribution to headache education. She was designated a Physician of Excellence by the Orange County Medical Association in January 2007. In recent years, Dr Hutchinson has co-authored numerous journal articles and book chapters on the subject of migraine.

Faculty Financial Disclosure Statements

The presenting faculty report the following:

- Dr Taylor serves as a speaker for and an advisor to Merck & Co., Inc.
- Dr Hutchinson serves as a speaker for Forest Laboratories, Inc.; Merck & Co., Inc.; and Ortho-McNeil Pharmaceuticals, Inc.; and as a speaker for and an advisor to Endo Pharmaceuticals, Inc., and GlaxoSmithKline.

Education Partner Financial Disclosure Statement

The content collaborators at MedicoAlliance, LLC, have nothing to disclose.
**Drug List**

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**Suggested Reading List**


Taking the Headache Out of Migraine Diagnosis and Management

Frederick R. Taylor, MD, FAHS
Adjunct Associate Professor of Neurology
University of Minnesota School of Medicine
Minneapolis, MN

Video Case Study: Part 1

Case Study Review: Part 1

- 28-year-old female, law school student
- Complains of bilateral, moderate in severity, headaches (HAs) with occasional nausea and mild photosensitivity but not phonophobia
- Over-the-counter (OTC) analgesics give her partial relief
- HAs occur several times/month and started when she began law school 1 year ago

Audience Response Question #1

Are these headaches?
1. Tension
2. Migraine
3. Mixed
4. Not enough information to diagnose

Migraine Overview

- Pathophysiology
  - Update
- Diagnosis
  - International Classification of Headache Disorders II
  - Pattern recognition
  - Brief screeners: ID migraine
  - Brief screeners: nausea
- Sinister headache
  - When to work up for secondary causes
- SNOOP
  - A mnemonic for secondary workup

Treatment Overview

- Acute treatment
  - How to get to the right treatment first time
  - The triptans
- Preventive treatment
  - When to add daily pharmacologic treatment
  - US Headache Consortium Guidelines and update
Pathophysiology of Migraine

3 Steps

1. Central generator: cortex or brainstem
2. Peripheral pain mechanisms in the meninges: inflammation and vasodilation
3. Central processing and sensitization

Migraine Neuroanatomy

Pathophysiology of Migraine

Central Generator
- Cortex?
- Brainstem?

Meningeal Events
- Inflammation
- Vasodilation
- Peripheral sensitization

Brainstem Events
- Pain signal to central nervous system (CNS)
  - Central sensitization
  - Allodynia

Activated neurons and glia release CGRP and substance P

Leads to:
- Vasodilation
- Mast cell degranulation
- Inflammation

Pathophysiology of Migraine

Approaches to Diagnosis

- International Headache Society (IHS), International Classification of Headache Disorders II (ICHD-II), 2004
- Pattern recognition
- Brief screeners

Abbreviations: CGRP, calcitonin gene-related peptide; 5-HT, 5-hydroxytryptamine (serotonin).
International Classification of Headache Disorders (ICHD-II/ IHS) Criteria for Migraine Without Aura

Migraine is episodic headache, ≥ 5 episodes, lasting 4-72 hrs

With any 2 of:
• unilateral
• throbbing
• worsened by movement
• moderate or severe

With any 1 of:
• nausea or vomiting
• photophobia and phonophobia

No secondary cause

\[2 + 1 = \text{Migraine}\]


International Classification of Headache Disorders (ICHD-II/ IHS) Criteria for Tension-Type Headache

ETTH is episodic headache, ≥ 10 episodes, 30 min-7 days long

With any 2 of:
• not unilateral (bilateral)
• not throbbing
• not worse with movement
• not severe (mild to moderate)

With both of:
• no nausea or vomiting
• Either photosensitivity or phonophobia, or neither (but not both)

\[-2 + (-1) = \text{Episodic tension-type headache}\]

Abbreviation: ETTH, episodic tension-type headache.


IHS (ICHD-II/IHS) Criteria for Migraine/Tension-Type Headache (TTH)

1.1 Migraine Without Aura (vs episodic TTH)

- At least 5 (10) attacks with
- At least 2 of the following 4:
  • unilateral (bilateral)
  • pulsating (not pulsating)
  • moderate to severe intensity, inhibits or prohibits activities (mod to moderate)
  • physical activity aggravates (does not aggravate)
- At least 1 of the following:
  • nausea and/or vomiting (no nausea or vomiting)
  • photophobia and phonophobia (either or neither, but not both)
- No evidence on history or exam of disease that might cause headache

1.6 Probable Migraine (Migrainous)

- Missing one of the above criteria


ID Migraine™ Validated Screener

During the last 3 months, did you have the following with your headaches?

1. You felt nauseated or sick to your stomach?
   Yes ___ No ___

2. Light bothered you (a lot more than when you don’t have headaches)?
   Yes ___ No ___

3. Your headaches limited your ability to work, study, or do what you needed to do?
   Yes ___ No ___

2/3 for migraine:

Sensitivity: 0.81
Specificity: 0.75


Sensitivity
Specificity

Nausea

Headache Clinic
Community-Based
Neurology Clinic
College Student

Overall sensitivity: 81%
Overall specificity: 83%

Global Prevalence of Episodic Headache Presenting to PCP Based Upon Expert Panel Diary Review

- 94% migraine/probable migraine
- Tension (N=11) 18%
- Probable Migraine (N=67) 3%
- Unclassifiable (N=11) 3%
- Migraine (N=288) 76%

N=377 patients who returned diaries

Abbreviation: M, migraine.


Migraine Prevalence

3 Population-Based Studies

- 1989
- 1999
- 2007


Algorithm for Headache Diagnoses

- Detailed history and examination
- Headache alarms (red flags) present
  - Yes: Exclude secondary headache using appropriate tests, if necessary
  - No: Consider primary headache
- Are there atypical features?
  - Yes: Reconsider secondary headache
  - No: Diagnose the primary headache disorder

Atypical features: consider referral


Worrisome Headache Red Flags

“SNOOP”

- Systemic symptoms (fever, weight loss) or
- Secondary risk factors: underlying disease (HIV, systemic cancer)
- Neurologic symptoms or abnormal signs (confusion, impaired alertness or consciousness)
- Onset: sudden, abrupt or split-second (first, worst)
- Older: new onset and progressive headache, especially in older age >50 (giant cell arteritis)
- Pattern change: first headache or different, change from
- Previous headache history: attack frequency, severity or clinical features

Clinical Pearl

When in doubt, investigate the atypical!

Treatment of Migraine

- Acute
- Preventive
- Medication-overuse headache (MOH)
Strategies for Outpatient Acute Migraine Treatment

- All migraine patients need acute treatment provided
- Selection of medication is based on disability
  - Standard of care for acute therapy: sustained pain-free response, reducing disability, optimally restoring function with minimal adverse events and cost
- Outcome of acute treatment also can be monitored by Migraine Assessment of Current Therapy (Migraine-ACT)

How to Get the Right Acute Treatment the First Time

- Assess disability, impact, or time loss

Video Case Study: Part 2

Case Study Review: Part 2

- Emily, now in her 3rd year at law school, states her headaches can become worse if she does not take her OTC analgesic soon enough into the HA
- Activity worsens her HA, and as a result, she misses running at least once/week
- She also is absent from school a few times/month; other times, she attends class with a HA but finds they greatly interfere with her ability to focus and concentrate on her studies
- Her Migraine Disability Assessment Scale (MIDAS) score is 22, indicating severe disability

Audience Response Question #2

The best treatment option for this patient would be?
1. A prescription-strength nonsteroidal anti-inflammatory drug (NSAID), such as naproxen 500 mg
2. Isometheptene/dichloralphenazone/acetaminophen combination
3. Butalbital-containing product
4. A triptan

MIDAS: Migraine Disability Assessment Scale*

1. On how many days in the last 3 months did you miss work or school because of your headache? 10 Days
2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headache? (Do not include days you counted in question 1 where you missed work or school) 10 Days
3. On how many days in the last 3 months did you not do household work because of your headache? 10 Days
4. How many days in the last 3 months was your productivity in household work reduced by half or more because of your headache? (Do not include days you counted in question 1 where you did not do household work) 10 Days
5. On how many days in the last 3 months did you miss family, social, or leisure activities because of your headaches? 10 Days

Add up the number of days from questions 1-6 (figure A and B). If the total is above 6, prevention and acute treatments need to be optimized Total 40 Days

1. On how many days in the last 3 months did you have a headache? (If a headache lasted more than 1 day, count each day) 10 Days
2. On a scale of 0-10, on average, how painful were these headaches? (Where 0=no pain at all and 10=pain as bad as it can be) 8

*Use in waiting room when possible

**MIDAS: Migraine Disability Assessment Scale**

- **MIDAS Grade I**  
  Little to no disability  
  Score 0-5
- **MIDAS Grade II**  
  Mild disability  
  Score 6-10
- **MIDAS Grade III**  
  Moderate disability  
  Score 11-20
- **MIDAS Grade IV**  
  Severe disability  
  Score 21+

Useful on initial screening and follow-up visits to assess level of function and determine if change in medication needed.

**Disabilities in Strategies of Care (DISC) Study**

- Compared 3 strategies of migraine management over 6 attacks
- Stratification based on disability (stratified care)
  - MIDAS Grade II: aspirin (ASA) + metoclopramide
  - MIDAS Grade III, IV: triptan (zolmitriptan)
- Step care within attacks
  - ASA + metoclopramide → Assess response at 2 hours
  - Rescue with triptan prn
- Step care across attacks
  - ASA + metoclopramide
  - Assess response after 3 attacks
  - Escalate treatment to triptan if ASA + metoclopramide fails 2/3 or 3/3

**Benefit of Stratified Care Over Step Care**

**Short Cuts to Optimal Acute Treatment of Migraine**

- Most patients in offices complaining of episodic headache have disabling migraine
- Therefore, in the absence of vascular contraindications, most patients complaining of episodic migraine in the office merit a triptan first line
- Since most attacks of migraine begin at mild and progress to disabling, in migraine attacks occurring <10 days/month, use of triptans early in the attack, <60 minutes into the attack, when pain is mild, is most likely to result in a sustained pain-free response (one and done)
- A Migraine-ACT score of ≤ 2 suggests a need to switch acute medications

**Success Outcome**

Migraine-ACT

**Impact**

Are you able to function normally within 2 hours?

**Global Assessment of Relief**

Does the HA pain disappear within 2 hours?

**Consistency of Response**

Does your migraine medication work consistently in the majority of your attacks?

**Emotional Response**

Are you comfortable enough with your medication to be able to plan your daily activities?
# Treatment

Susan Hutchinson, MD  
Associate Clinical Professor  
Department of Family Medicine  
UC-Irvine Medical Center

## Triptan Groups

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Fast onset, high potency</th>
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<tbody>
<tr>
<td>Sumatriptan</td>
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<tr>
<td>Sumatriptan/naproxen</td>
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<td>Zolmitriptan</td>
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<td>Rizatriptan</td>
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<td>Almotriptan</td>
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<td>Eletriptan</td>
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<table>
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<th>Group 2</th>
<th>Slower onset, lower potency</th>
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<tr>
<td>Naratriptan</td>
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<tr>
<td>Frovatriptan</td>
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## Formulations and Doses of Triptans

### Group 1  
Fast onset, high potency

<table>
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<tr>
<th>Formulation</th>
<th>Dose</th>
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<tr>
<td>Nasal 10, 20 mg</td>
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</tbody>
</table>

- **Sumatriptan**
- **Sumatriptan/naproxen**
- **Zolmitriptan**
- **Rizatriptan**
- **Almotriptan**
- **Eletriptan**

### Group 2  
Slower onset, lower potency

<table>
<thead>
<tr>
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<th>Dose</th>
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<tr>
<td>OD 2.5, 5 mg</td>
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<tr>
<td>Nasal 5 mg</td>
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</table>

- **Naratriptan**
- **Frovatriptan**

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## Selecting the Triptan

**The 3 F's**

- **Fast vs slow**
- **Formulation**
- **Formulary**

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## On the Horizon...

- **CGRP-receptor antagonist**
- **Dihydroergotamine (DHE) inhaler**
- **AMPA/kainate glutamate–receptor antagonist**
- **Gap junction inhibitor**
- **5-HT1F agonist**
- **Inducible nitric oxide synthase inhibitor**
- **Carbon dioxide inhaler**

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## New Triptan-NSAID Combination

- **Sumatriptan 85 mg with naproxen sodium 500 mg**
- **FDA approved April 2008**

**Rationale**

- Targets multiple pathways involved in migraine pathogenesis

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**Abbreviations:**  5-HT, 5-hydroxytryptamine (serotonin); AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; CGRP, calcitonin gene-related peptide.
Selecting the Right Acute Treatment Avoids Chronic Daily Headache (CDH)

- Most CDH evolves from episodic migraine
- Thus, most CDH is transformed migraine (transformed from episodic migraine to daily HA)
- Goal of treatment: sustained pain free, one and done
- The use of suboptimally effective treatment leads to relief but not pain free, recurrence of the same HA, repeat doses, and then overuse
- Most CDH seen in the office is associated with acute medication overuse for episodic migraine (≥10-15 days of use/month)

When to Start Daily Preventive Medication

Video Case Study: Part 3

Emily now works at a prestigious law firm
She experiences HAs 2-3 times/week, which interfere with her work, personal, and social life; this causes her to worry and lose sleep frequently
Emily is frustrated and plans to see her PCP but has missed several follow-up appointments
She recently missed an important client meeting due to a severe HA; the firm is concerned her HAs will impede her ability to successfully carry her full case load

Case Study Review: Part 3

For her headaches, she starts with an OTC combination product (acetaminophen/caffeine/aspirin) and waits to see how the HA evolves before taking her triptan
Emily takes the OTC product at least 2-3 times/week and the "rescuing" triptan at least 2 times/week
She often runs out of her #9 allotted triptan tablets/month

Audience Response Question #3

The best treatment option at this time would be?
1. Increase her quantity of triptans/month from #9 to #18
2. Prescribe an NSAID, such as naproxen 500 mg, and instruct her to take this for her milder HAs and "save" the triptan for the more severe HAs
3. Offer her a daily preventive medication
4. Quit her job!
When to Consider Daily Prevention

- Migraine that significantly interferes with the patient’s daily routine despite acute treatment
- Failure of, contraindication to, or troublesome side effects from acute medications
- Special circumstances:
  - Hemiplegic migraine
  - Attacks with a risk of permanent neurological injury


When to Start Daily Preventive Medication

The Frequency Strategy

- Clinic-based study on the development of CDH over 1 year
  - 0-5 vs 6-9 days/month, Odds Ratio (OR) 6.2 for developing over 1 year
  - 0-5 vs 10-14 days/month, OR 20.1 for CDH


Disability/Frequency Issues

- The US Headache Consortium suggests daily prevention with:
  - Migraine that significantly interferes with the patient’s daily routine despite acute treatment
  - ≥ 2 long, significantly disabling attacks/month
  - Infrequent attacks but producing profound disability
  - Failure of, contraindication to, or troublesome side effects from acute medications

- The American Migraine Prevalence and Prevention study (AMPP):
  - As disability increases, headache frequency at which you might intervene with daily prophylaxis decreases

American Migraine Prevalence and Prevention Study (AMPP) 2007

- AMPP expert consensus
  1. Prevention should be offered:
     - ≥ 5 HA days/month
     - ≥ 4 HA days with at least some impairment
     - ≥ 3 HA days with severe impairment or requiring bed rest
  2. Prevention should be considered:
     - 4-5 migraine days/month with normal functioning
     - 3 migraine days with some impairment
     - 2 migraine days with severe impairment
  3. Prevention not indicated:
     - <4 migraine days/month and no impairment
     - No more than 1 migraine day/month regardless of impairment


Goals of Preventive Treatment

- Decrease attack frequency (by 50%), intensity, and duration
- Improve responsiveness to acute medication
- Improve function and decrease disability
- Intervene to prevent rebound

Preventive Therapies for Migraine
US Headache Consortium Guidelines for Migraine Prophylaxis

Group 1
Medium to high efficacy, good strength of evidence, mild to moderate side effects.

- Amitriptyline (10-150 mg/day)
- Divalproex sodium (125-200 mg/day)
- Timolol (10-30 mg/day)
- Propranolol (20-160 mg/day)
- Topiramate (50-150 mg/day)

Group 2
Lower efficacy, limited strength of evidence, mild to moderate side effects.

- Aspirin (325 mg/day)
- Atenolol (25-100 mg/day)
- Fenoprofen (600 mg three times/day [tid])
- Flurbiprofen (1,000 mg two times/day [bid]-tid)
- Fluoxetine (10-80 mg/day)
- Gabapentin (300-2,400 mg/day)
- Ketoprofen (75 mg tid)
- Metoprolol (50-200 mg/day)
- Naproxen (200-550 mg bid)
- Nimodipine (30 mg tid)
- Verapamil (120-480 mg/day)
- Botulinum toxin type A (25-100 units/3 months)

Group 3
No scientific evidence of efficacy, but clinically efficacious based on consensus of experience.

- Low to moderate adverse events
- Frequent or severe adverse events (or safety concerns);
- Complex management issues

Group 4
Medium to high efficacy, good strength of evidence, but side effect concerns

Group 5
Evidence indicating no efficacy over placebo

- Acebutolol
- Pindolol
- Carbamazepine
- Nicardipine
- Nifedipine
- Indomethacin
- Cyproheptadine
- Antidepressants, such as nortriptyline, paroxetine, venlafaxine, doxepin, sertraline, and phenelzine
- Methysergide (discontinued)

Findings of US Headache Consortium

The following are all somewhat effective in preventing migraine compared with controls:

- Relaxation training
- Thermal biofeedback combined with relaxation training
- Electromyography biofeedback
- Cognitive-behavioral therapy

Hormonal Approach to Prevent Menstrual Migraine

- Continuous contraception (skip placebo)
- Estradiol patch 0.1 mg perimenstrually to prevent the drop in estradiol
- Transdermal estradiol patches < 0.1 mg not effective at preventing menstrual migraine compared with placebo

Randomized Controlled Trials (RCTs) for Prevention Update

- Topiramate, 100 mg, since guidelines, FDA approved (Group 1)
- Venlafaxine, 150 mg (Group 2)
- Lisinopril, 20 mg, 1 RCT since guidelines (Group 2)
- Candesartan, 16 mg, 1 RCT since guidelines (Group 2)
- Butterbur (petasites hybridus), 100-150 mg/d (Group 2)
- Coenzyme Q10, 1 RCT, 300 mg/d (Group 2)

Choose Preventive Medication Based on Pharmacologic Opportunity

- Go for a 2-Fer!
  - Hypertension
    - Beta-blocker, calcium channel blocker, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker
  - Anxiety
    - Beta-blocker
  - Depression and sleep disturbance
    - Tricyclic antidepressant (TCA)
  - Pain disorder
    - Gabapentin
  - Obesity
    - Topiramate

Principles for Preventive Treatment

- Start low and increase dose slowly
  - Use long-acting formulation if compliance an issue
- Adequate trial (2-3 months) at appropriate dosage
- Maximize treatment of comorbidity and avoid interfering and contraindicated medications
- Evaluate therapy
  - Use headache calendar (diary)
  - Attempt to taper and discontinue treatment when headaches well controlled
Avoid Medications That Worsen Comorbid Illnesses

- Depression or asthma
  - Beta-blockers
- Obesity
  - TCAs, divalproex

Patient Weekly Diary

<table>
<thead>
<tr>
<th>Day</th>
<th>Sunday</th>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
<th>Thursday</th>
<th>Friday</th>
<th>Saturday</th>
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<tbody>
<tr>
<td>Date</td>
<td>Prodrome</td>
<td>Aura</td>
<td>Time of pain onset</td>
<td>Severity of pain</td>
<td>Treatment 1 (dose)</td>
<td>Symptoms (nausea, throbbing, disability)</td>
<td>Treatment 2 (dose)</td>
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Prevention

What Goes Wrong

- Wrong drug
- Excessive initial dose
- Inadequate final dose
- Duration of treatment too short
- Combination treatment required
- Non compliance
- The presence of rebound/CDH/MOH nullifies effectiveness of preventive medication
- Expectations unrealistic
- Failure to provide acute medications (triptans) for breakthroughs

Conclusions

- Migraine is common
  - 12% of the general population and 94% of patients complaining of episodic headache in the PCP office
- Secondary headache is less common
  - SNOOP
- All migraine patients need to be provided acute treatment
- Selection of medication is based on disability
- Outcome can also be monitored by Migraine-ACT

Emily Returns

Emily returns 6 weeks after starting daily preventive therapy
- Review of her headache diary shows 1-2 headaches/week
- Many of her headaches are mild and do not require triptan therapy
- She is trying to practice good health habits, is running routinely again, and has not had to miss work for the past 4 weeks!