Myths of Migraine:
What is it? Who gets it? What can you do about it?

Robert E. Shapiro, MD, PhD
Robert Shapiro, M.D., Ph.D., is a professor of neurology and director of the Headache Clinic at the University of Vermont. Dr. Shapiro earned his medical degree from Columbia University, and a Ph.D. in anatomy from the University of Pennsylvania. Prior to joining UVM/Fletcher Allen in 1997, he served a residency in neurology and then held positions as an instructor and assistant professor of neurology at The Johns Hopkins University School of Medicine. Active in several professional organizations, Dr. Shapiro is a founding president of Alliance for Headache Disorders Advocacy.
Dr. Shapiro is also the organizer of ‘Headache on the Hill,’ an annual event designed to reach legislators to increase awareness of the crucial need for additional funding for research into migraine and other headache disorders. The recipient of several awards for scholarship, Dr. Shapiro has been actively involved in research activities throughout his career. His current research is focused on clinical trials to examine the effectiveness of medications for migraine.
Myth #1

Migraine is just a bad headache.
Migraine is **NOT** Headache

- Migraine is a chronic episodic state of the brain.
- Headache is a symptom of the migraine state.

- **migraine symptom patterns**
  - idiosyncratic
  - stereotypic
  - evolving

- **migraine susceptibility**
  - heritable
  - chronobiologic
  - stimulus-bound
Migraine Attacks: Clinical Features

Prodrome phase: ~ one third of patients, ~ hours to days
moodiness, fatigue, GI, muscle stiffness, fluid retention, yawning, cravings

Aura phase: (~ 20 % of patients): < 60 min
symptoms: visual, paresthesias, cognitive, behavioral, perceptual
sensory > motor, positive > negative, dynamic > static

Headache phase: ~4 hours to 3 days
pain: hemi-cranial, throbbing, moderate to severe
sensitivities: light, sound, odor, touch (alldynia), movement (vertigo)
autonomic: nausea (~90%), vomiting, gastric atony, sinus congestion

Recovery phase:
moodiness, fatigue, GI, muscle stiffness, diuresis
**Migraine Aura**

**Aura Features**
- **sensory** > **motor**
- **positive** > **negative**
- **dynamic** > **static**

**Aura Variants**
- acephalgic
- hemiplegic
- retinal
- ophthalmoplegic
- abdominal
- basilar
- paroxysmal vertigo
- “Alice in Wonderland”

Speirings, *Management of Migraine* 7-19
Phases of a Migraine Attack

Adapted from Cady RK. *Clin Cornerstone*;1:21-32. (1999)
Migraine without aura

A. At least 5 attacks fulfilling criteria B-D
B. Headache attacks lasting 4-72 h (untreated or unsuccessfully treated)
C. Headache has ≥2 of the following characteristics:
   1. unilateral location
   2. pulsating quality
   3. moderate or severe pain intensity
   4. aggravation by or causing avoidance of routine physical activity (e.g., walking, climbing stairs)
D. During headache ≥1 of the following:
   1. nausea and/or vomiting
   2. photophobia and phonophobia
E. Not attributed to another disorder
Tension-Type Headache: “The Un-migraine.”

Misleading terms: “tension”, “psychogenic”, “muscle contraction”

**timing:** episodic :~30min to 4 hours

chronic : up to 7 days

**pain:** location: bilateral / “band-like”

quality: pressing / tightening, non-throbbing

intensity: mild to moderate

**other symptoms:**

nausea / vomiting – absent, but anorexia may be present

sensitivity to light and sound – generally absent, but one or the other may be present

aggravation by physical activity - absent

tender scalp muscles - variably present
Migraine / Tension-type Spectrum

Silberstein, Phys Assist 67-81 (9/1991)
Frequency of Tension-Type Headache


Migraineurs

Non-migraineurs
Chronic Migraine

• Headache at least 15 days per month
• Migraine or probable migraine attacks at least 8 days per month
• Lasting at least 3 months
• No evidence of other cause of headache such as overuse of painkillers
Migraine is Underdiagnosed

- 94% of patients presenting to a PCP with recurrent headache meet diagnostic criteria for migraine or probable migraine.
- Nearly 90% of “sinus headache” patients meet diagnostic criteria for migraine or probable migraine.
- Nearly 90% of “tension/stress” headache patients meet IHS criteria for migraine or probable migraine.
Misperceptions of Headache Diagnosis in Primary Care

Primary Care Diagnoses

"Expert Panel" Diary Review Diagnoses

Tepper et al. Headache 2004;44:856
Migraine –

what does it look like?
You can’t diagnosis migraine by looking at someone’s face.

Wong-Baker FACES Pain Rating Scale

- 0: No Hurt
- 1: Hurts Little Bit
- 2: Hurts Little More
- 3: Hurts Even More
- 4: Hurts Whole Lot
- 5: Hurts Worst
Myth #2

Everyone gets headaches sometimes.

Migraine is due to a character flaw. It only affects a few people who can’t cope with a little pain.
“For, in the migrainous, there is often a curious impulsion to do what they know is ‘the wrong thing’ in the practical conduct of their lives: as if it were their fate, or as if they wished it to be their fate. They then derive some measure of satisfaction from a demonstration of how well they behave under adverse circumstances, hampered as they are by their own ill-health and the bludgeonings of fate. They know subconsciously that, in spite of their own ability, they have failed, in perhaps quite ordinary circumstances, and they are almost to the end, reluctant to acknowledge where and how they have been wrong and have created for themselves the difficulties from which they escape by means of the brain-storms that afford them their excuse. It is, in fact, the consciousness of their own errors in the management of their lives (though unadmitted frankly, even to themselves) that prevents them facing any given situation boldly and that impels them to go on suffering and struggling in ‘rage and humiliation’.”
Headache Disorders are the Most Prevalent Neurological Disorders

This year…

- Half of Americans will experience headache
- 4% of Americans will have headache 15 or more days per month

Lifetime prevalence…

- 30% of Americans will have episodic migraine
- 43% of American women will have episodic migraine
- 18% of American men will have episodic migraine

Stewart et al. Cephalalgia 2008; 28:1170
US One Year Prevalence of Migraine

- 19.5% - any type of migraine (60.2M people)
  - 3.9% - any migraine with aura (12M people)
- 13% - Episodic migraine (40M people)
- 2% - Chronic migraine (6.2M people)
- 4.5% - Probable migraine (14M people)
- 25% of American families have a member with episodic migraine
- 35% of Iraq war veterans will experience migraine
- 60% of Iraq war veterans with mild TBI will experience migraine
Episodic Migraine is More Prevalent than Asthma & Diabetes Combined

Disease Prevalence in the US Population

- Rheumatoid arthritis: 1%
- Asthma: 5%
- Diabetes: 6%
- Osteoarthritis: 7%
- Migraine: 13%

Data from the Centers for Disease Control and Prevention, US Census Bureau, and the Arthritis Foundation, 2002.
So what causes migraine?
Migraine Susceptibility

- Probably anyone could have a migraine attack if the conditions were just right. Maybe it’s not a disease.

- People who have recurrent disabling attacks have some enhanced genetic susceptibility.

- 50% of the likelihood of developing recurrent migraine is genetic, the rest is environmental.
  - Usually, the small contributions of many genes are involved. These genes are hard to find.
  - Rarely, migraine susceptibility can be linked to a single genetic change. These genes are a bit easier to find.
Migraine with Aura *Plus*
Familial Advanced Sleep Phase Syndrome

A single change in a gene called *casein kinase 1 delta*

“Cortical Spreading Depression”

http://hartp.neurology.ucla.edu/CLINICALRESEARCH.html
Migraine and Gender


Fox and Davis, Headache 38: 436 (1998)

1966 Attacks in 1208 Women
Migraine occurs more often...

on awakening

3582 Attacks in 1698 Patients


don weekends

during winter
Migraine & Behavioral Disorders

One year prevalence
Rates per 100 subjects

Major Depression
- With migraine: 14.7
- Without migraine: 7.3

Mania / Hypomania
- With migraine: 8.8
- Without migraine: 3.3

Generalized Anxiety
- With migraine: 9.8
- Without migraine: 2

Social Phobia
- With migraine: 6.6
- Without migraine: 2

Merikangas, et al. Arch Gen Psych 1990; 47:849
Chemical Triggers for Migraine

There is little direct proof of chemical triggers for migraine...

...but patients often report sensitivities

- estrogens - OCPs, HRTs
- caffeine
- chocolate
- tobacco smoke - nicotine, carbon monoxide?
- odors: perfumes, diesel, etc.
- MSG - beware “natural” products
- processed, pickled or fermented foods or meats - nitrates, nitrites?
- some dairy products - aged cheeses, yogurt, sour cream (tyramines?)
- nuts
- alcohols (e.g. red wines) / Balsamic vinegar
- some fruits & vegetables - citrus, avocados, bananas, raisins, plums, beans, onions
- aspartame
What is the “burden” of migraine?
Individual Burden of Migraine

Lipton RB, et al. *Headache* 2001;41:638-45

- Missed Family/Social Leisure Activity: 59%
- Reduced by ≥50%
- Unable to Do Chores/Household Work: 76%
- Reduced by ≥50%
- Household Work Productivity: 67%
- Reduced by ≥50%
- Work/School Productivity: 51%
- Reduced by ≥50%
Societal Burden of Migraine and Headache Disorders

Total Annual US Costs = $31B / yr
- greater than the economic costs of epilepsy, asthma, and ovarian cancer combined

Direct Costs = $11B
- Presenteeism ($16.4B)
- Absenteeism ($3.6B)

Indirect Costs = $20B
- 9% of all health-related lost US labor

NIH annually reports its expenditures for 229 disease and diagnostic categories.
Impact of NIH Funding: Migraine vs. Epilepsy

Migraine is 7 times more prevalent
Migraine results in >3 times more DALYs
Epilepsy causes <2.8 times more deaths.

NIH also reports 9 new compounds in clinical trials for epilepsy

- Chronic paroxysmal disorders
- Pathophysiologies in common
- Preventative drugs in common
- Often occur in the same people

New Molecular Entities Approved by the FDA since 1992 by Indication

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NIH also reports 9 new compounds in clinical trials for epilepsy

Greater NIH funding correlated with a wave of “innovative” new epilepsy drugs

Shapiro, Headache 47:993 (2008)
The North Korea of Diseases

Migraine

Epilepsy
Bipartisan Joint Congressional Letter to NIH Director Francis Collins

April 20, 2010

The Honorable Francis S. Collins
Director
National Institutes of Health
Building 1
One Center Drive
Bethesda, Maryland 20892-1875

Dear Director Collins:

During the last two Small Grants (R01) from the National Institute of Neurological Disorders and Stroke (NINDS), we found that headache disorders in a few mechanisms with the disease’s prevalence. While we are encouraged that the workshop is being held in May to develop a plan for the study and research on headache disorders, we remain concerned that NIH is not fulfilling adequate resources in this field.

Headache disorders are the most prevalent of all neurological disorders. This year, 36 million adults will experience a migraine and 12 million will suffer from chronic daily headaches. Collectively, headache disorders will cost the United States economy more than $51 billion annually, including 30 percent of all lost productivity. Despite this tremendous burden, migraine research receives the lowest amount of public funding compared to other brain disorders relative to its societal impact.

Increased research in this area could bring transformative changes in headache conditions and lead to better treatment of the daily, contributing to the quality of life for those struggling with these conditions.

The report recently issued by Congress on the appropriateness of research funds in this area states that the National Institutes of Health (NIH) should be allocated more funding for research on headache disorders. We request that as a result of the planned research, NIH provide Congress with updated projections for developing a long-term strategic approach to develop new headache research and treatment for these disorders. We believe that the NIH should provide peer review by headache scientists of submitted research grant applications.

We hope NIH will make additional efforts to solicit studies on headache disorders and we encourage you to consider additional steps to incentivize research and study in this area. The NIH has the opportunity to lead the way in making headache research a priority and we hope the workshop in May produces a proactive plan to achieve that goal.

Sincerely,

The Honorable Franeker S. Collins
April 20, 2010

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We request... a long-term strategy including a proposal to increase scientific participation in headache research, a strategy for the creation and funding of academic headache centers, a plan to encourage and fund new investigators with career training and transition awards, and a plan to provide peer review by headache scientists of submitted headache research grant applications.”
How can migraine be treated?
Migraine Rewards
Boring Predictable Lifestyles

regulate schedules:
- stable sleep hours (avoid oversleeping)
- stable meal times (avoid hunger)
- integrate exercise

reduce exposures:
- hormonal fluctuations (estrogen / progesterone)
- stress (e.g. biofeedback and relaxation training)
- changing weather
- glaring sunlight
- noise
- chemical triggers
- head trauma
- painkillers and caffeine
Medications for the Acute Treatment of Migraine Attacks

- **NSAIDs or aspirin** (e.g. diclofenac, ibuprofen, naproxen sodium, indomethacin, cox-2 inhibitors, etc.)

- **Dopamine antagonists** (e.g. metoclopramide, prochlorperazine, chlorpromazine)

- **5-HT\textsubscript{1} agonists** (specific: triptans / non-specific: ergotamines – DHE nasal spray)

- **Caffeine combinations** (e.g. APAP/ASA/caffeine, APAP/butalbital/caffeine, etc.)

- **Opioid “rescue medications”** (e.g. butorphanol)

FDA approved migraine therapies
Medications for Prevention of Migraine

First line agents

♦ β blockers (propranolol *, nadolol, atenolol)
♦ Tricyclics (amitriptyline ¶, nortriptyline, doxepin)
♦ Anticonvulsants (divalproex sodium *, topiramate *)
♦ Botox * for chronic migraine

Other “off-label” agents

♦ methysergide *, timolol *, riboflavin, magnesium, lithium, estradiol, gabapentin, nardil, SSRIs, lisinopril, cox-2’s, co-Q10, memantine, flunarizine, amlodipine, verapamil, feverfew, butterbur, candesartan, pizotifen, metoprolol, protriptyline, cyproheptadine, tizanidine etc.

* FDA-approved for migraine prophylaxis
Myth #3
Got migraine?
Just take some more painkillers.
The Limits of Acute Migraine Therapy:
Treat early in the attack, but don’t treat too often.

Substances which can acutely relieve migraine … may provoke migraine upon their withdrawal.

Frequent exposure to such substances over sufficient duration may transform episodic migraine to chronic daily headache in susceptible individuals – “Rebound”
Which substances are implicated in rebound?

- Caffeine often involved (coffee, Excedrin, Fioricet, Mt Dew, etc.)
- Probably ANY acute medication for migraine… and others too: opioids, barbiturates, ergots, triptans, NSAIDs, etc.

What is “frequent exposure”?

- More than ~ 8 days / month; more than 5 days / month for opioids…
- Dosage per day seems to be less significant

What is “sufficient duration” of exposure?

- Very gradual development:
  Analgesics ~ 4.9 yrs; ergots ~ 2.7 yrs; triptans ~ 1.7 yrs

Evolution of Medication Overuse Headache

Tablets / day of caffeine-containing analgesics over 10 years

“Take one of these every four hours. If pain persists, see another doctor.”
Medication Overuse Headache ("Rebound") is Common

- ~4% of adults have chronic daily headache (CDH)
  - ≥ 15 days with headache per month
  - ≥ 4 hours per day with headache

- Almost 20,000 adult Vermonters have CHD

- Almost 6,000 adult Vermonters have MOH

The Migraine Threshold

- Lifestyle Changes
- Preventive Medications
- Behavioral Therapy

- Genetic Factors
- Biorhythms

- Head Trauma
- Overuse of Acute Medications
- Estrogens

Migraine in Women, A. MacGregor, Martin Dunitz, 1999