
KNOW
HEADACHE
& MIGRAINE
PAIN

Migraine Module Development Committee

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Learning objectives

After completing this module, participants will be able to:

- Understand the pathophysiology of migraine
- Discuss the prevalence of migraine
- Recognize the signs and symptoms of migraine
- Assess the impact of migraine on patients' quality of life and ability to work
- Apply diagnostic criteria at the appropriate time
- Understand the goals of managing migraine
- Understand the impact of migraine and comorbidities
- Select appropriate pharmacological and non-pharmacological strategies for the management of migraine

Headache Classification

- 1988: International Headache Society (IHS)
- 2003: International Classification of Headache Disorders-II (ICHD-II)
- **2013: ICHD-III-beta: Headache Classification Committee of the IHS: The International Classification of Headache Disorders, 3rd edition (beta version)**

Access the current IHS classification:

ICHD-3, International Classification of Headache Disorders – 3rd Edition, Beta

Learners should consult both the *classification* and the *accompanying notes* for full information

ICHD-3, International Classification of Headache Disorders (3rd Edition, Beta Version)

Part One: The Primary Headaches
1. Migraine
2. Tension-type headache
3. Trigeminal autonomic cephalalgias
4. Other primary headache disorders
Part Two: The Secondary Headaches
5. Headache attributed to trauma or injury to the head and/or neck
6. Headache attributed to cranial or cervical vascular disorder
7. Headache attributed to non-vascular intracranial disorder
8. Headache attributed to a substance or its withdrawal
9. Headache attributed to infection
10. Headache attributed to disorder of homeostasis
11. Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cervical structure
12. Headache attributed to psychiatric disorder
Part Three: Painful Cranial Neuropathies, Other Facial Pains and Other Headaches
13. Painful cranial neuropathies and other facial pains
14. Other headache disorders

ICHD = International Classification of Headache Disorders

Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia*. 2013;33(9):629-808.

Headache Disorders

- Among the most common disorders of the nervous system
- Associated with
  - Personal burden of pain
    - Negative impact of pain
    - Reduced quality of life
    - Disability
  - Societal burden of pain
    - Direct costs
    - Indirect costs
- A minority of people with headache disorders are appropriately diagnosed

Headache has been underestimated, under-recognized, and under-treated throughout the world

WHO 2012. Headache disorders. Available at: http://www.who.int/mediacentre/factsheets/fs277/en/. Accessed March 31, 2015.

What Is Migraine?

- Central nervous system disorder
- Common clinical syndrome
- Characterized by recurrent episodic attacks of headache with pulsating quality and moderate to severe intensity, *which serve* ***no protective purpose***
- Migraine can be accompanied by the following symptoms
  - Aura
  - Nausea / Vomiting
  - Sensitivity to light (photophobia)
  - Sensitivity to sound (phonophobia)
  - Sensitivity to head movement
- Vulnerability to migraine is inherited in many people

Lance JW, Goadsby PJ. Mechanism and Management of Headache. London, England: Butterworth-Heinemann; 1998; Silberstein SD, Lipton RB, Goadsby PJ. Headache in Clinical Practice. 2nd ed. London, England: Martin Dunitz; 2002; Olesen J, Tfelt-Hansen P, Welch KMA. The Headaches. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2000.

Classification of Migraine

Migraine without aura
- Recurrent attacks
- Attacks and associated migraine symptoms last 4-72 hours

Migraine with aura (migraine with typical aura, migraine with brainstem aura, hemiplegic migraine, retinal migraine)
- Visual and/or sensory and/or speech/language symptoms and/or motor weakness
- Gradual development of aura
  - At least one symptom spreads gradually over ≥5 minutes
  - Symptoms last ≥5 and ≤60 minutes
- Can be positive or negative symptoms or a mixture
- Complete reversibility

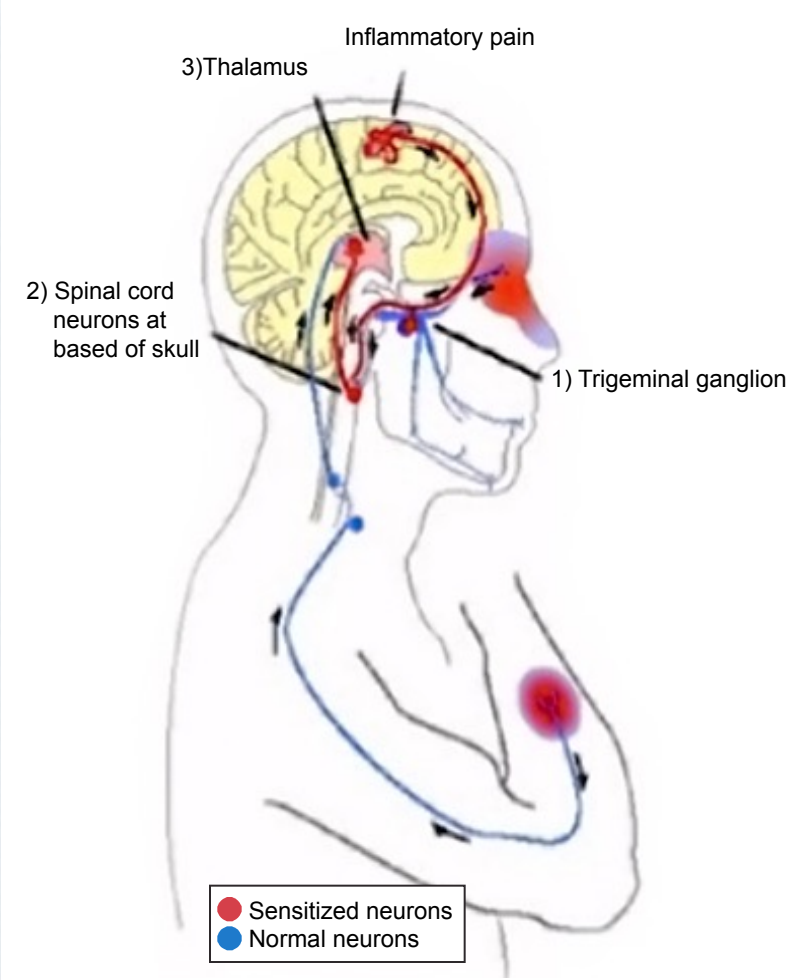
Chronic Migraine
- In a patient with previous episodic migraine
- Headache on ≥15 days/month for >3 months
- Headache has features of migraine on ≥8 days/month

Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia*. 2013;33(9):629-808.

WHAT ARE THE MOST COMMON TYPES OF HEADACHES YOU SEE IN YOUR PRACTICE?

Pathophysiology of Migraine

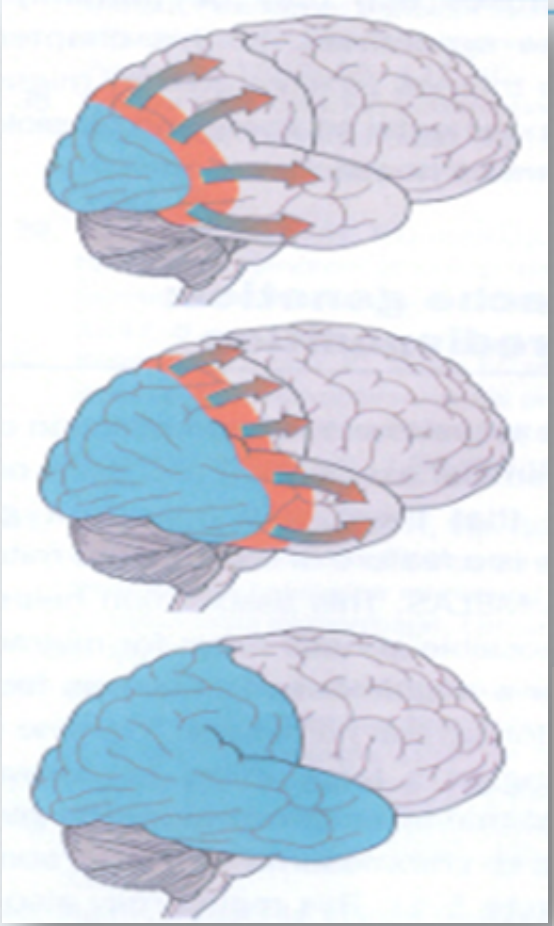
Central Sensitization/Allodynia in Migraine



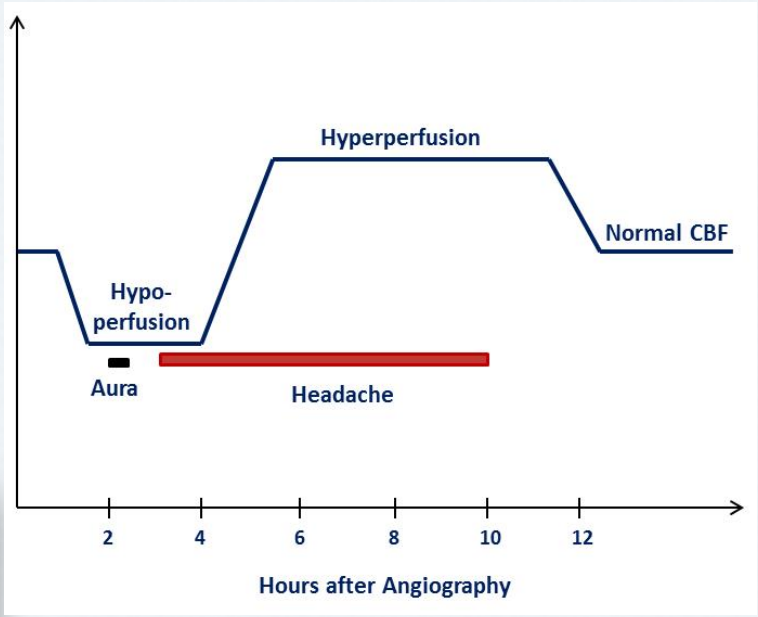
- Sensory sensitivity is increased during a migraine attack
- Symptoms are regulated by **central** or **peripheral** mechanisms
  - Peripheral sensitization leads to throbbing and exacerbation of pain with movement
  - Central sensitization leads to cutaneous allodynia

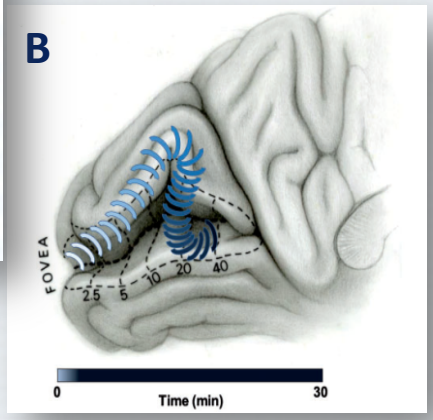
American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

Migraine Aura



Relative timing of cerebral blood flow (CBF), aura, and headache*





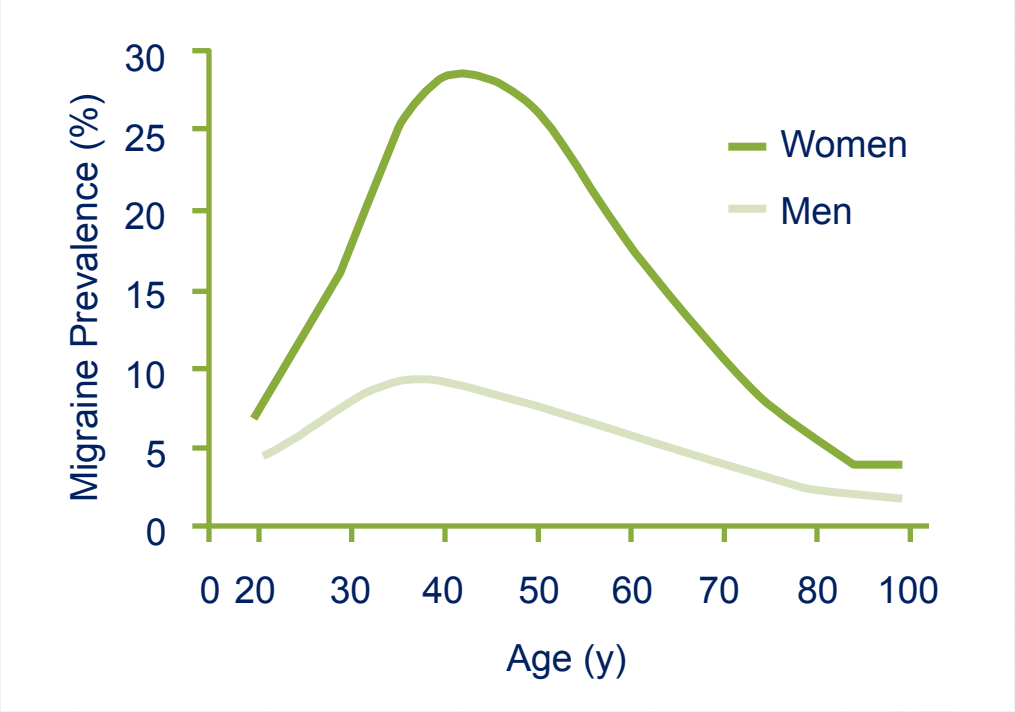
CBF = cerebral blood flow

*Original study disproving the vascular hypothesis of migraine
Olesen J *et al. Ann Neurol.* 1990;28(6):791-8.

Prevalence of Migraine

Prevalence of Migraine

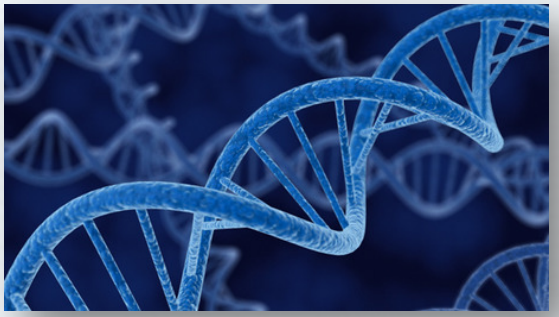
- Prevalence of migraine in the general population is 10 to 12%
  - Prevalence of chronic migraine is 2 to 4%



*Symptomatic at least once within the last year

1. WHO 2012. Headache disorders. Available at: http://www.who.int/mediacentre/factsheets/fs277/en/. Accessed 20 May, 2015; 2. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. *Headache.* 2001;41:646-57.

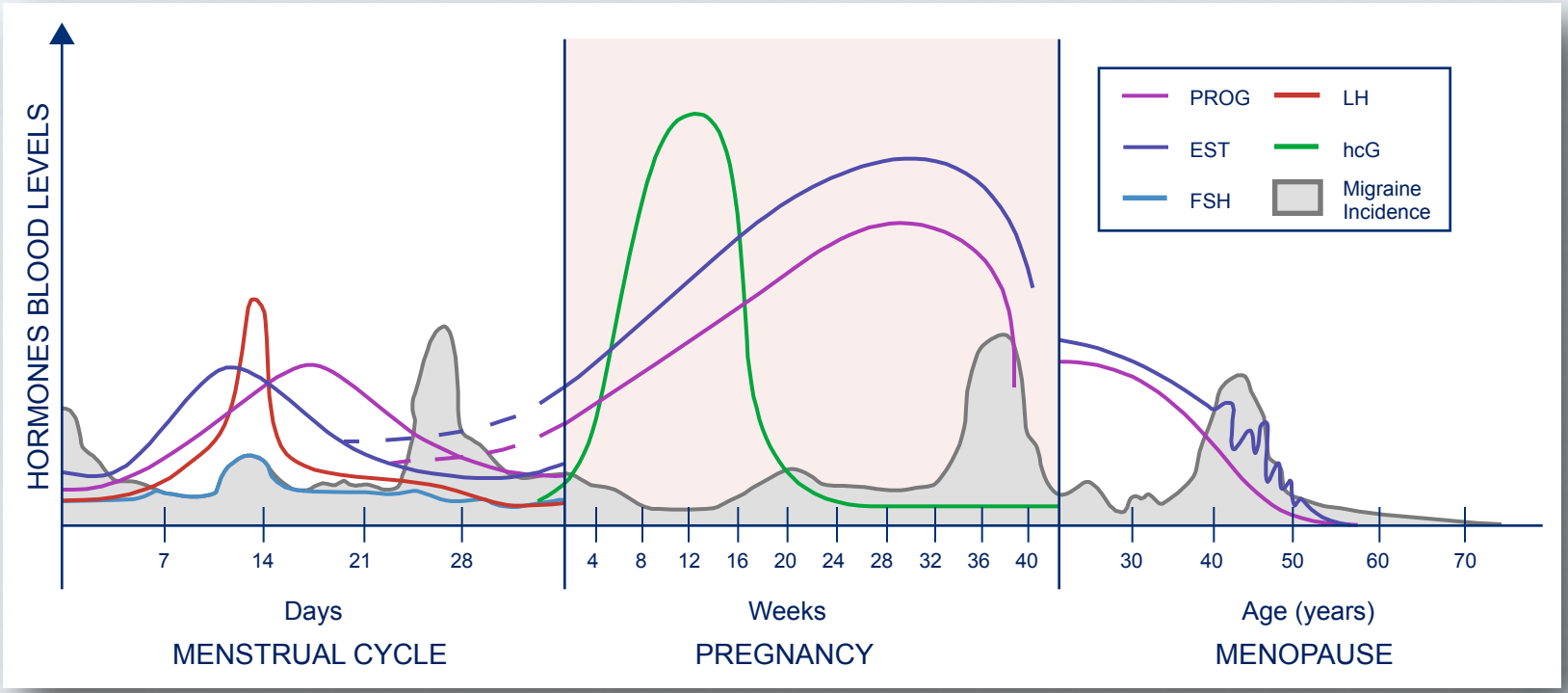
Heritability of Migraine: When Patients Ask "Why Me?"



- Studies have identified 13 migraine-associated variants pointing at genes that cluster in pathways for glutamatergic neurotransmission, synaptic function, pain sensing, metalloproteinases, and vasculature
- Individual pathogenic contribution of each gene variant is difficult to assess
  - Small effect sizes and complex interactions
- Six genes with large effect sizes identified in patients with rare monogenic migraine syndromes in which hemiplagic migraine and non-hemiplagic migraine with or without aura are part of a larger clinical spectrum
- Transgenic mouse models with human monogenic-migraine-syndrome gene mutations showed migraine-like features and increased susceptibility to cortical spreading depression

Ferrari MD *et al. Lancet Neurol.* 2015;14:65-80.

Hormonal Changes and Incidence of Migraine without Aura in Women



Sacco S *et al*. *J Headache Pain*. 2012;13:177-89.

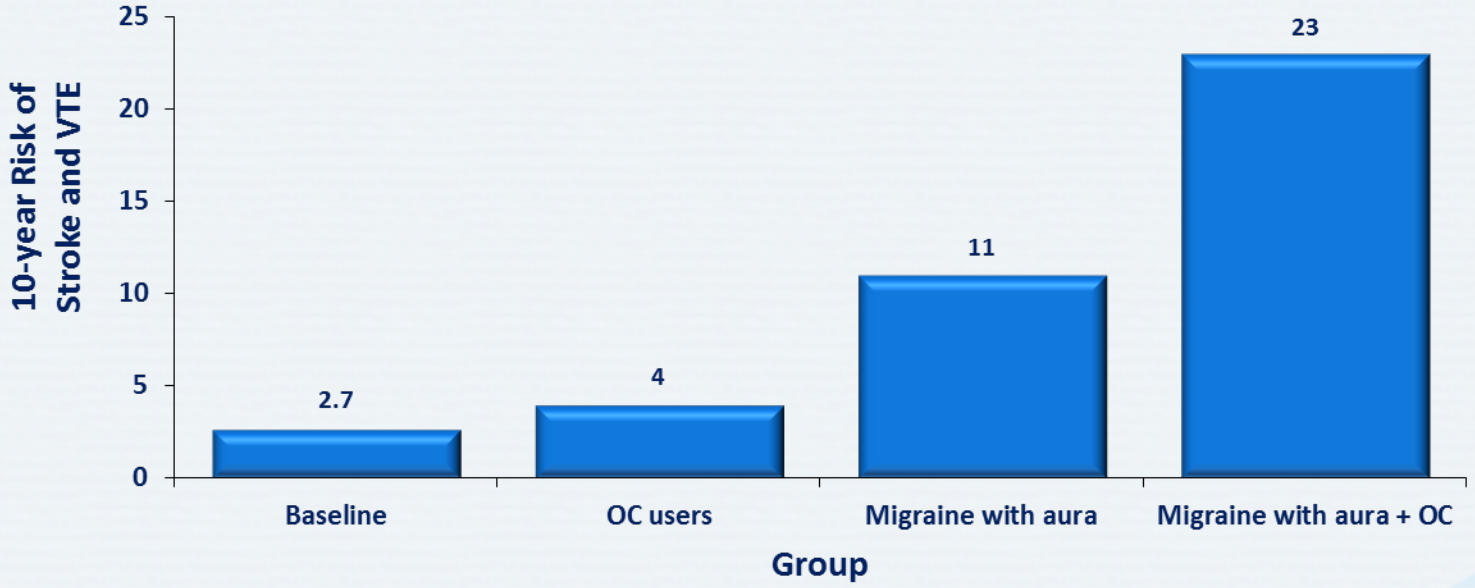
Pregnancy and Migraines

- Most female migraineurs (up to 80%) note remarkable and increasing improvement of their attacks during pregnancy
  - Fewer attacks
  - Improvement more likely in women with menstrual migraine
- If migraine does not improve by end of first trimester, it will likely continue throughout pregnancy
- In some women, migraine worsens during pregnancy
  - Involves women with migraine with aura
- Some women develop de novo migraine during pregnancy
  - Mostly migraine with aura
- Migraine attacks return after delivery in nearly all women

Sacco S *et al*. *J Headache Pain*. 2012;13: 177-89; MacGregor A. *Progress Neurol Psychiatry*. 2009;13:21-24.

Migraine and Oral Contraceptives

- Must consider the risk of stroke and venous thromboembolism in migraine
  - Combination oral contraceptives (OCs) increase risk
- Risk is similar in women with migraine without and women without migraine



- WHO recommends women with migraine with aura avoid combination OCs

WHO = World Health Organization

Hutchinson S. Use of oral contraceptives in women with migraine. Available at: http://www.americanheadachesociety.org/assets/1/7/Susan_Hutchinson_-_Use_of_Oral_Contraceptives_in_Women_with_Migraine.pdf. Accessed March 31, 2015.

Signs and Symptoms of Migraine

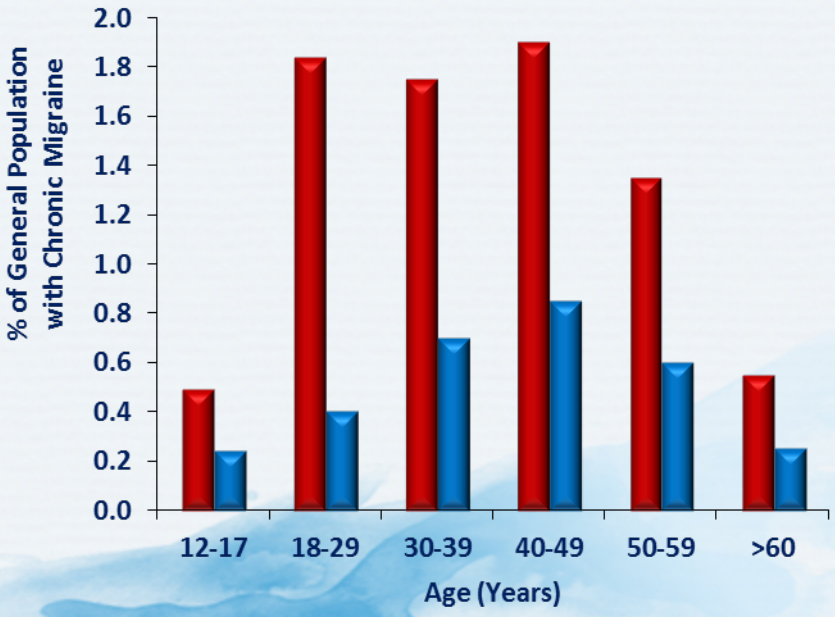
Core Symptoms of Migraine

- Duration: 4 to 72 hours if untreated/unsuccessfully treated
  - Duration of 2 to 72 hours in patients <18 years of age
- Pain:
  - Throbbing or pulsatile headache
  - Moderate to severe; intensifies with movement/physical activity
  - Unilateral pain in 60%, bilateral in 40%
  - Pain can be felt anywhere around the head or neck, and location does not make the diagnosis
  - Pain be rapid onset or more indolent
- Nausea (80%) and vomiting (50%)
  - Can have anorexia, food intolerance, light-headedness, frank nausea or dislike of light and noise during the premonitory phase and during the attack itself

Tepper SJ, Tepper DE. Diagnosis of Migraine and Tension-type Headache. In: Tepper SJ, Tepper DE, eds. The Cleveland Clinic Manual of Headache Therapy. 2nd Edition. NY: Springer, 2014; Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia*. 2013;33(9):629-808.

Chronic Migraine (CM)

- Typically develops after a slow increase in headache frequency over years to months ("migraine transformation")
  - 2-4% of people with episodic migraine transform to CM yearly
- Population studies indicate a prevalence of 1.4% to 2.2%
- ≥50% of patients with CM have medication overuse headache
- Patients with CM often revert to episodic migraine with treatment



Schwedt TJ. *BMJ.* 2014;348:g1416; Bigal ME *et al*. *Headache.* 2008;48:1157-68; Lipton RB *et al*. *Neurology.* 2015;84:688-95.

Factors Associated with Transformation and Reversion of Chronic Migraine (CM)

Transformation to CM	Reversion of CM
• High baseline headache frequency • Overuse of migraine acute drugs • Ineffective acute migraine treatment • Nausea • Obesity • Snoring • Sleep disorders • Excessive caffeine intake • Psychiatric disease • Major life changes • Head or neck injury • Cutaneous allodynia • Female gender • Comorbid pain disorders • Lower socioeconomic status	• Adherence to migraine prophylactic drugs • Lower baseline headache frequency • Absence of cutaneous allodynia • Physical exercise • Withdrawal of overused migraine abortive drugs

Schwedt TJ. *BMJ.* 2014;348:g1416; Lipton RB *et al*. *Neurology*. 2015;84:688-95; Reed ML *et al*. *Headache*. 2015;55:76-87.

Medication Overuse Headache (MOH)

- Headache occurring on >15 days/month
- Develops as a consequence of regular overuse of acute or symptomatic headache medication (on ≥10 or ≥15 days per month, depending on the medication) for >3 months
- Usually, but not invariably, resolves after the overuse is stopped
- Around 50% of patients with chronic migraine revert to an episodic migraine subtype after drug withdrawal

Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia*. 2013;33(9):629-808.

Subtypes of Medication-overuse Headache (MOH)

- Intake on ≥10 days/month on a regular basis for >3 months:

  - Ergotamine-overuse headache
  - Triptan-overuse headache
  - Opioid-overuse headache
  - Combination analgesic-overuse headache

Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia*. 2013;33(9):629-808.

Typical Features of Migraine Aura

- May precede or accompany headache phase or may occur in isolation
- Usually develops over 5 minutes and lasts <1 hour
- Typical aura is most commonly visual, but can be sensory or speech/ language, or a combination
- Visual symptoms can be positive or negative
- Most common positive visual phenomenon is the scintillating scotoma, an arc or band of absent vision with a shimmering or glittering zigzag border

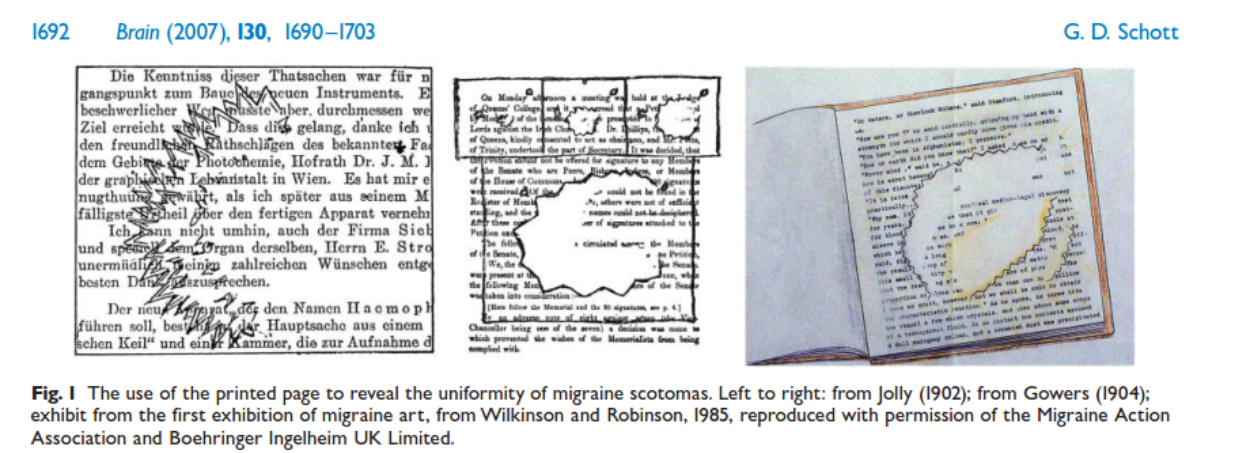
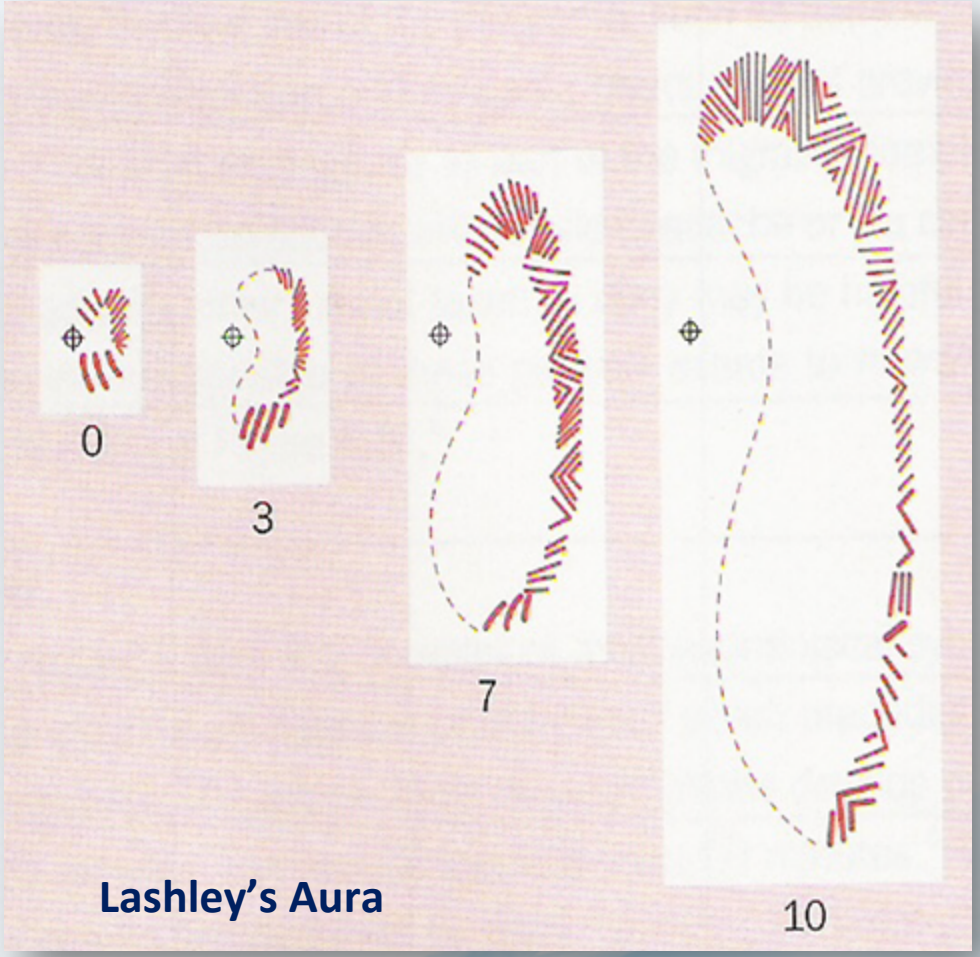


Fig. 1 The use of the printed page to reveal the uniformity of migraine scotomas. Left to right: from Jolly (1902); from Gowers (1904); exhibit from the first exhibition of migraine art, from Wilkinson and Robinson, 1985, reproduced with permission of the Migraine Action Association and Boehringer Ingelheim UK Limited.

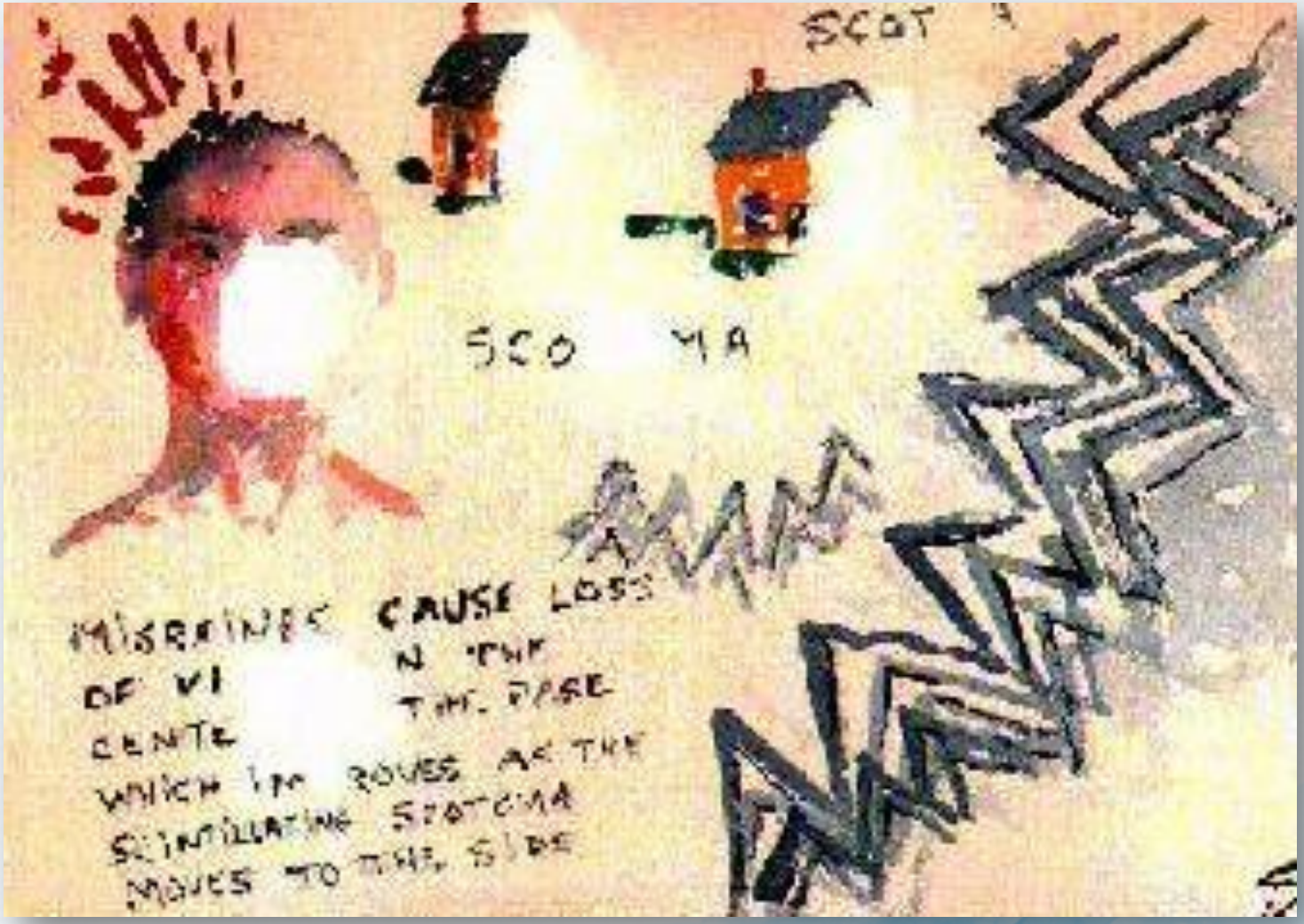
Chawla J. 2014. Available at http://emedicine.medscape.com/article/1142556-overview. Accessed 05 January 2014.

Migraine Visual Aura

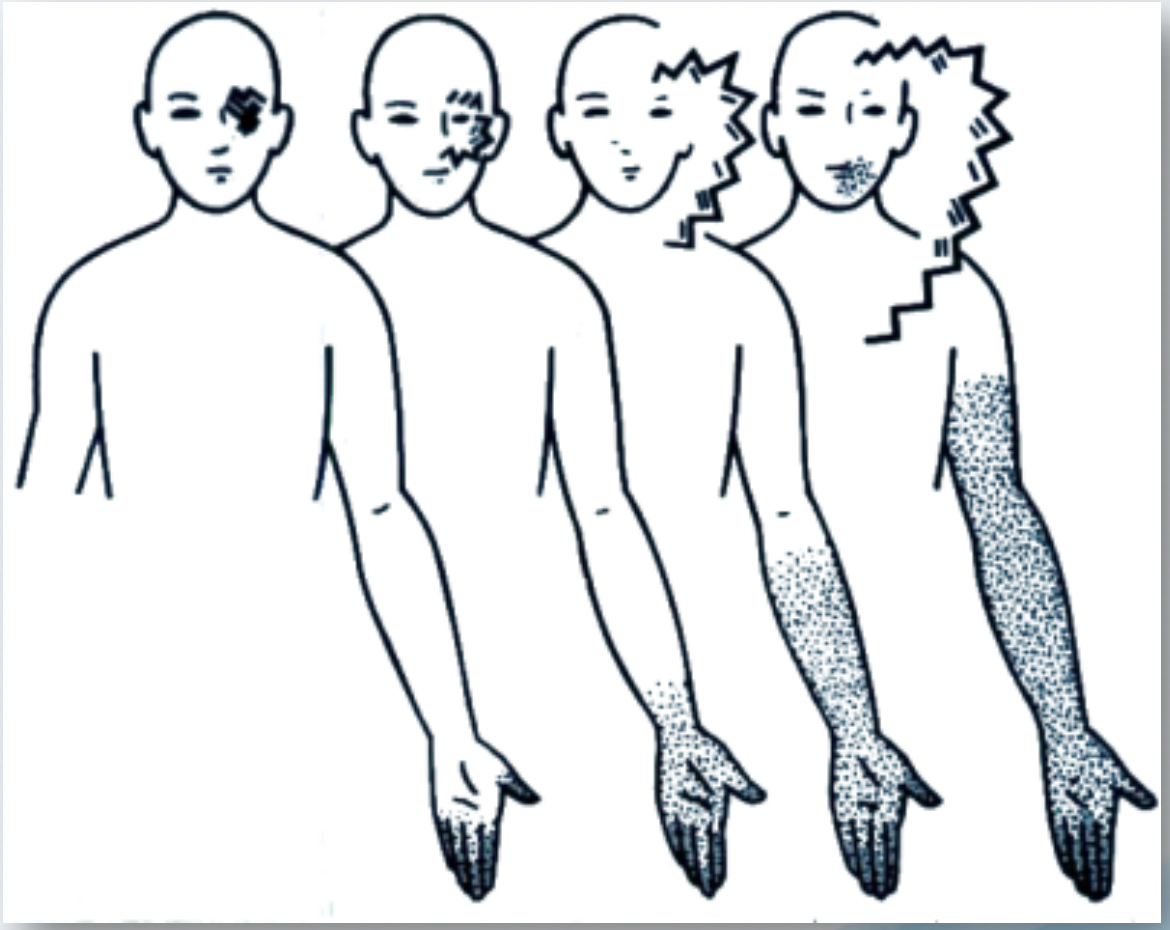


Lashley's Aura

Migraine Aura



Somatosensory Symptoms in Migraine (Paresthesia-hypoesthesia)



Podoll K. 2005. Somatosensory symptoms. Available at: http://www.migraine-aura.com/content/e27891/e27265/e26585/e26970/index_en.html. Accessed 20 May, 2015.

Assessment and Diagnosis of Migraine

Discussion Question

HOW DO YOU ASSESS MIGRAINE IN YOUR PRACTICE?

Importance of Diagnosing Migraine

- **Improved** quality of life
- **Reduced**
  - Disability
  - Patient dependence on opioids
  - Overuse of analgesic medications or opioids
  - Risk of complications or medication overuse headaches
  - Chance of progressing to chronic daily headache (CDH)

Consequences of non-diagnosis include disabling illness, reduced quality of life, and loss of opportunities for early intervention

American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

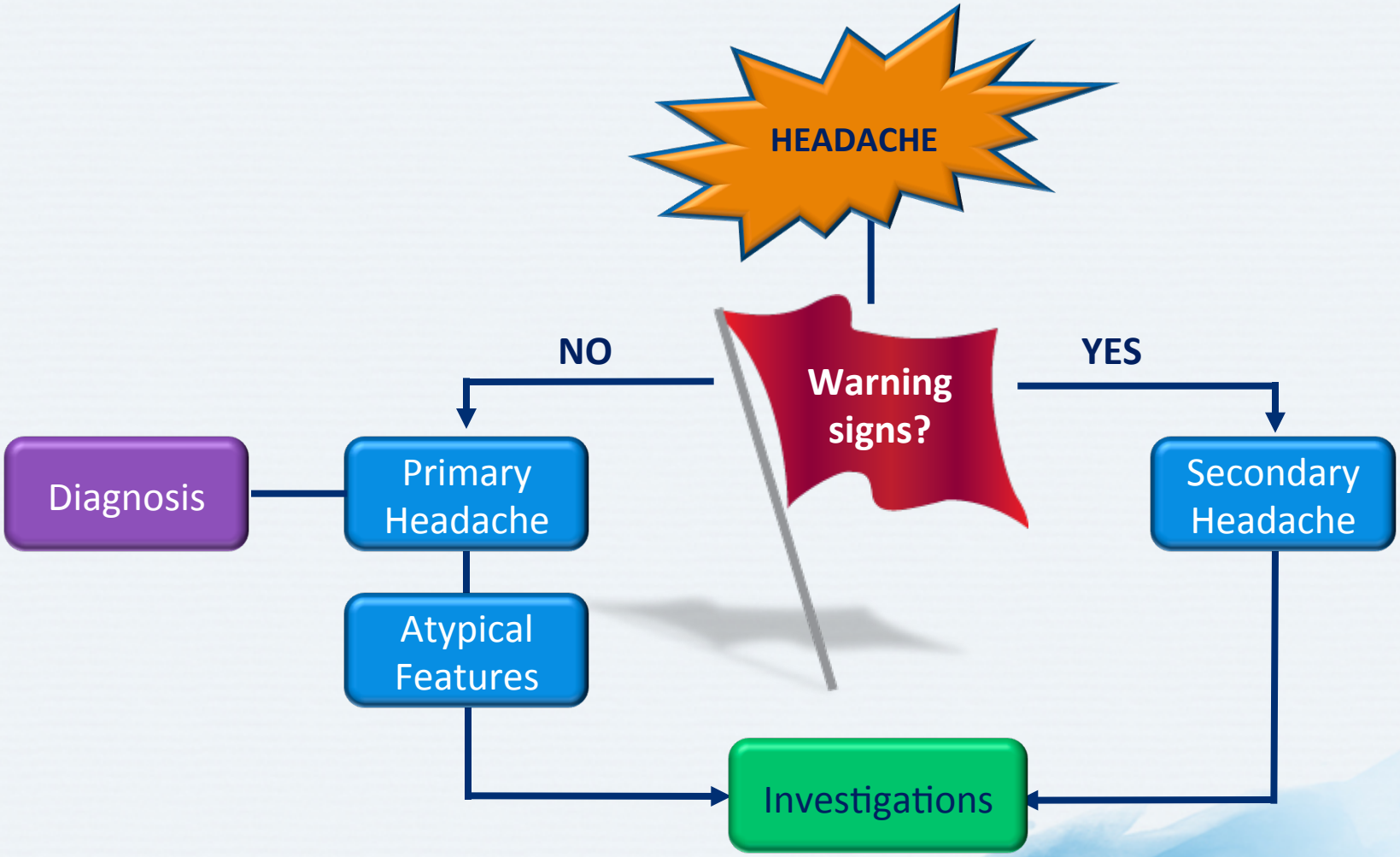
Headache and Patient History: Key Questions to Ask Patients

- **Onset**: Abrupt? Gradual?
- **Frequency/duration:**
  - How many times per week/month/year?
  - Approximate duration (two hours, 12 hours, two days etc.)
- **Location***: Uni- or bilateral? Frontal, temporal or fronto-temporo-occipital ?
- **Severity of pain:** Worst-ever headache? Mild, moderate, severe?
- **Characteristics and other accompanying symptoms**
- **Medication use:** Direct relationship with a certain medication?
- **Family history of migraine?**
- **What makes the headache better or worse?**
- **Any recent change in headache pattern?**
- **Degree of disability?**
- **Comorbid conditions?**

*If episodic headache

American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December,

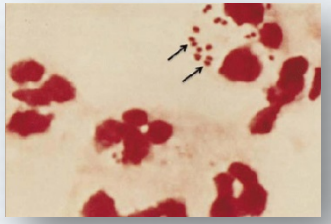
Diagnostic Evaluation for Migraine



American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

Red Flags in Headache Diagnosis

Red Flag	Differential Diagnosis
Headache with systemic illness (fever, stiff neck, rash)	• **Meningitis** • Encephalitis • Lyme disease • Systemic infection • Collagen vascular disease
Red Flag	**Differential Diagnosis**
New onset headache in a patient with HIV or cancer	• **Meningitis** • Brain abscess • Metastasis
Red Flag	**Differential Diagnosis**
Presence of neurological deficits, **papilledema** or change in cognition	• Mass lesion • Stroke • Intracranial hypertension

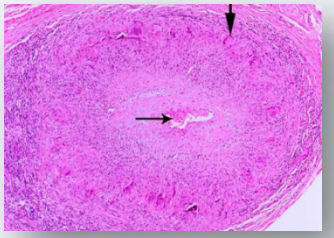


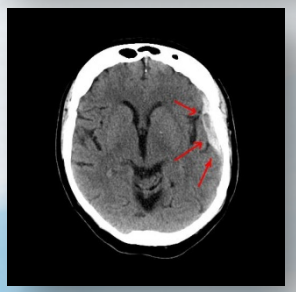
Images represent conditions in boldface

American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

Red Flags in Headache Diagnosis

Red Flag	Differential Diagnosis
Sudden onset headache	• **Subarachnoid hemorrhage** • Reversible cerebral vasoconstriction syndrome • Cervical artery dissection • Cerebral venous thrombosis • Pituitary apoplexy • Bleed into a mass or arteriovenous malformation • Mass lesion
Red Flag	**Differential Diagnosis**
Headache begins in patient >50 years of age	• **Giant cell arteritis (temporal arteritis)** • Mass lesion
Red Flag	**Differential Diagnosis**
Accelerating pattern of headaches	• Mass lesion • **Subdural hematoma** • Medication overuse





Images represent conditions in boldface

American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

ICHD-3 Diagnostic Criteria for Migraine without Aura

A. At least five attacks fulfilling criteria B to D

B. Headache attacks lasting 4 to 72 hours (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*

D. During headache ≥1 of the following

1. Nausea and/or vomiting
2. Photophobia and phonophobia

3. Not better accounted for by another ICHD-3 diagnosis

Link to ICHD-3 Diagnosis of Migraine without Aura

*For example, walking or climbing stairs

ICHD = International Classification of Headache Disorders

Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia*. 2013;33(9):629-808.

ICHD-3 Diagnostic Criteria for 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:
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 to 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

Link to ICHD-3 Diagnosis of Migraine with Aura

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ICHD-3 Diagnostic Criteria for Chronic Migraine

A. Headache (tension-type-like and/or migraine-like) on ≥15 days/month for >3 months and fulfilling criteria B and C

B. Occurring in a patient who has had ≥5 attacks fulfilling criteria B to D for *Migraine with aura* and/or criteria B and C for *Migraine with aura*

C. On ≥8 days/month for >3 months, fulfilling any of the following:

1. Criteria C and D for *Migraine without aura*
2. Criteria B and C for *Migraine with aura*
3. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative

D. Not better accounted for by another ICHD-3 diagnosis

Link to ICHD-3 Diagnosis of Chronic Migraine

ICHD = International Classification of Headache Disorders

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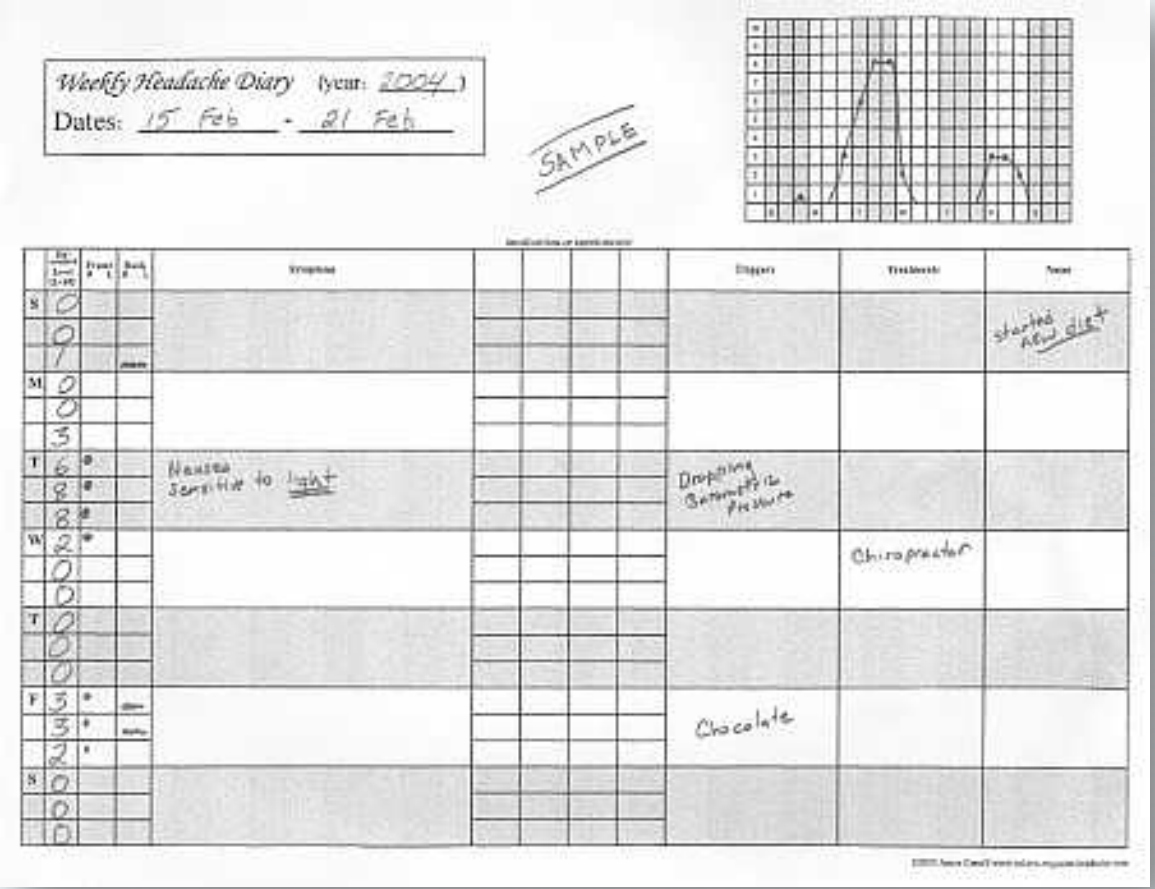
Tools for Migraine Evaluation, Treatment, and Imaging

Headache Diary



Patients should record:

- Date, time of onset and end
- Preceding symptoms
- Intensity on scale
- Suspected triggers
- ANY medication taken, including over-the-counter medication – note dosage taken, how many pills the patient took that day
- Relief (complete/partial/none)
- Relationship to menstrual cycle

American Headache Society, 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf; National Institute for Health and Care Excellence . Diagnosis and management of headache in young people and adults. CG150. London: NICE; 2012. Available at: https://www.nice.org.uk/guidance/cg150/resources/guidance-headaches-pdf. Accessed 20 May, 2015.

Brief Screeners for Migraine, Migraine Impact, and Response to Treatment

	Test	Comments
Screening and Diagnosis	ID Chronic Migraine[1]	• 12-items; identifies patients with chronic migraine • Can be used by patients or physicians
	ID-Migraine[2]	• 3-item tool • Simple and reliable; use in primary care
Assess Migraine Impact	MIDAS (Migraine Disability Assessment)[3]	• 5-item tool to score number of days of significant reduction in activity due to migraine in past 3 months
	Headache Impact Test™-6 (HIT-6)[4]	• Covers 6 categories • Useful in clinical practice and research
Assess Response to Therapy	Migraine Therapy Assessment Questionnaire (MTOQ®)[5]	• 5-item questionnaire suitable for use by GPs • Identifies suboptimal migraine treatment
	Migraine-ACT (Assessment of Current Therapy)[6,7]	• 4-item questionnaire • Identifies patients whose acute therapy should change

1. Lipton RB *et al*. *Neurology*. 2003;61:375-82; 2. Maizels M, Burchette R. *Headache.* 2003;43(5):441-50; 3. Stewart WF *et al. Neurology.* 2001;56(6 Suppl 1):S20-8; 4. Kosinski M *et al. Qual Life Res.* 2003;12(8):963-74; 5. Lipton RB *et al. Cephalalgia*. 2009;29(7):751-9; 6. Dowson AJ *et al. Curr Med Res Opin*. 2004;20(7):1125-35; 7. Kilminster SG *et al. Headache.* 2006;46(4):553-62.

Imaging for Migraine

American Academy of Neurology

- Consider only in patients with migraine with atypical headache patterns or neurologic signs

U.S. Headache Consortium

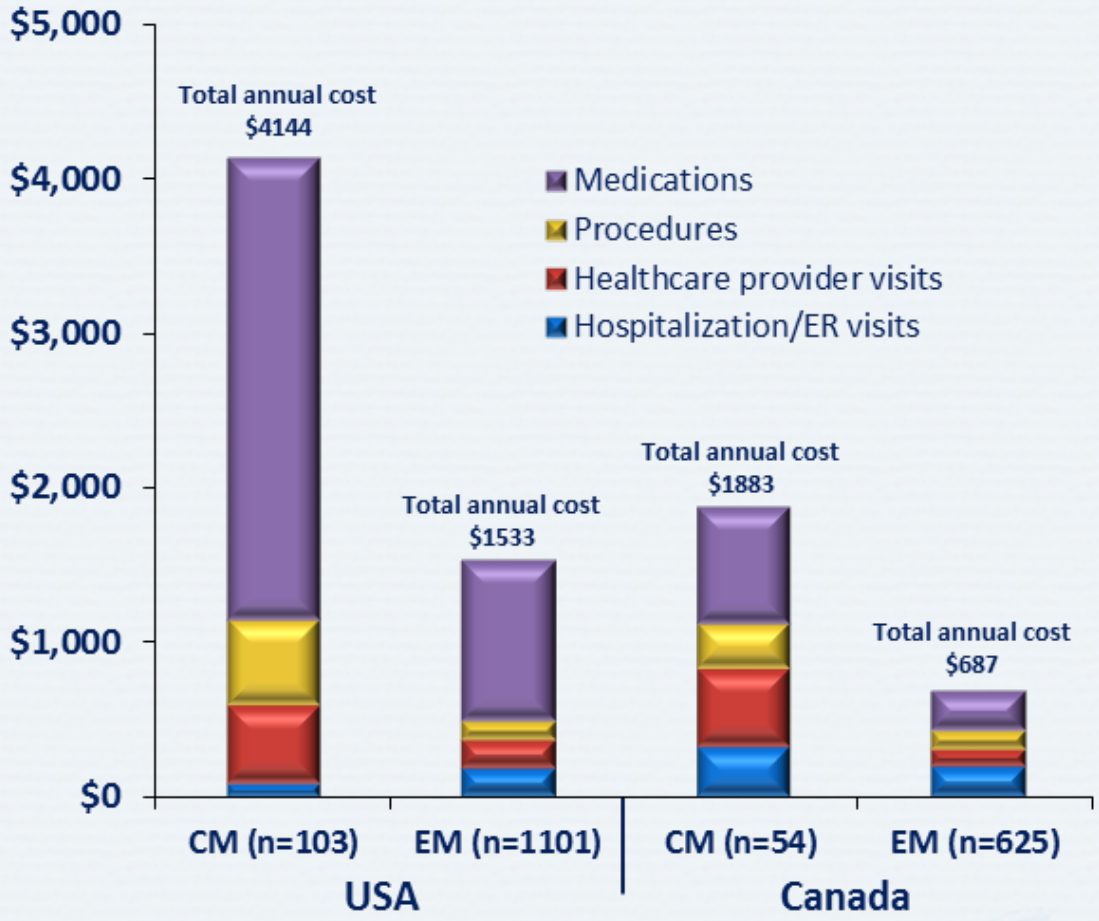
- Consider in patients with non-acute headache and unexplained findings on neurologic exam
- No usually warranted in patients with a normal neurologic exam
  - Lower threshold may apply if headache has atypical features or does not meet strict definition of migraine

- **Do not image patients with stable headaches that meet migraine criteria**
- **If MRI is available, do not perform CT, except in emergency settings**

Aukerman G *et al. Am Fam Physician.* 2002;66(11):2123-30; Loder E *et al. Headache.* 2013;53(10):1651-9.

Patient Burden of Migraine

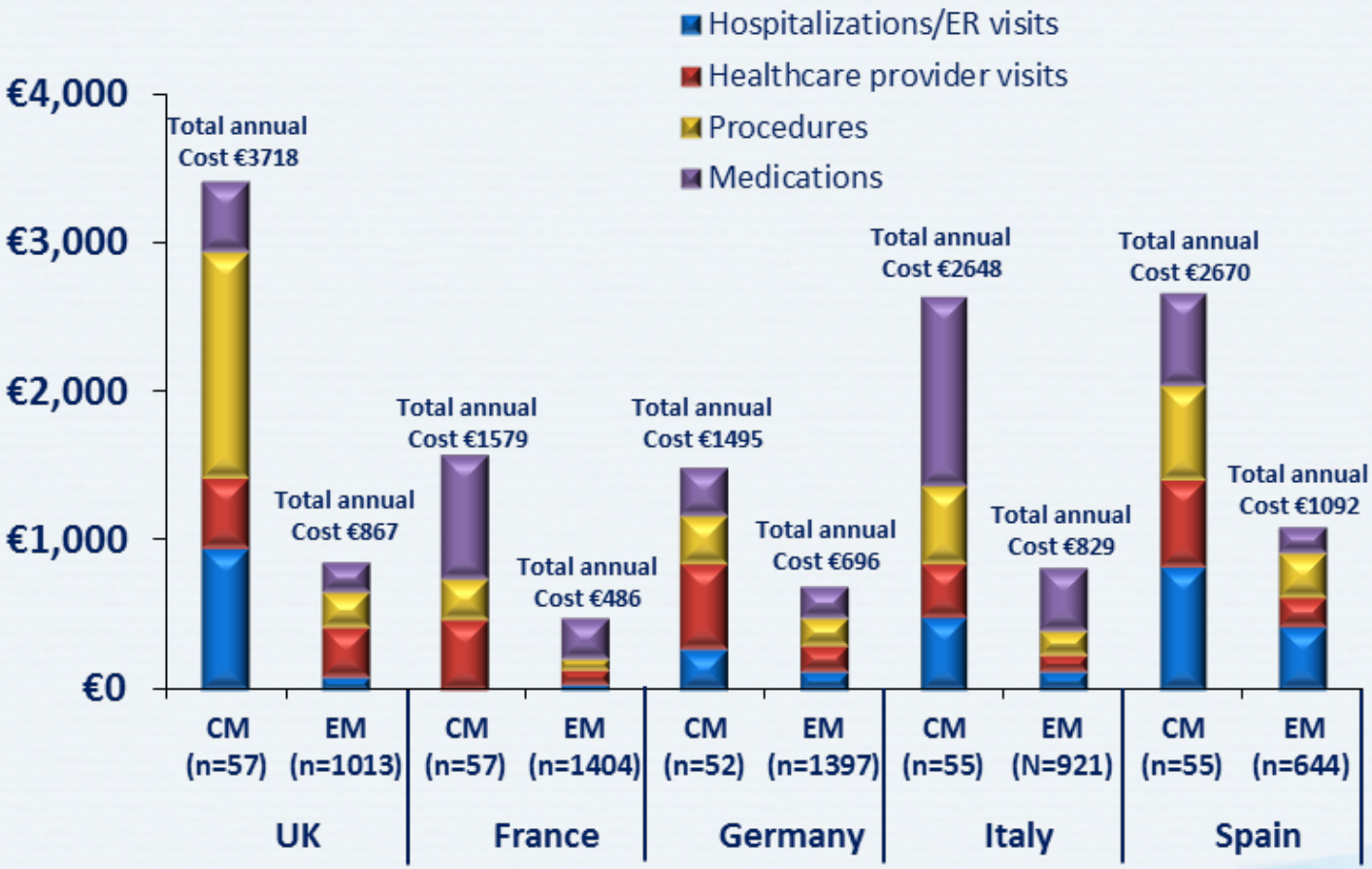
Economic Impact of Migraine – North America



*Migraine subject with a medical follow-up
CM = chronic migraine; EM = episodic migraine

1. WHO 2012. Headache disorders. Available at: http://www.who.int/mediacentre/factsheets/fs277/en/. Accessed December 1, 2014; 2. Harwood RH *et al. Bull World Health Organ*. 2004; 82(4): 251-8; 3. Steiner TJ *et al*. *J Headache Pain.* 2013;14(1):1; 4. Stokes M *et al. Headache*. 2011;51(7):1058-77; 5. Bloudek LM *et al. J Headache Pain.* 2012;13(5):361-78.

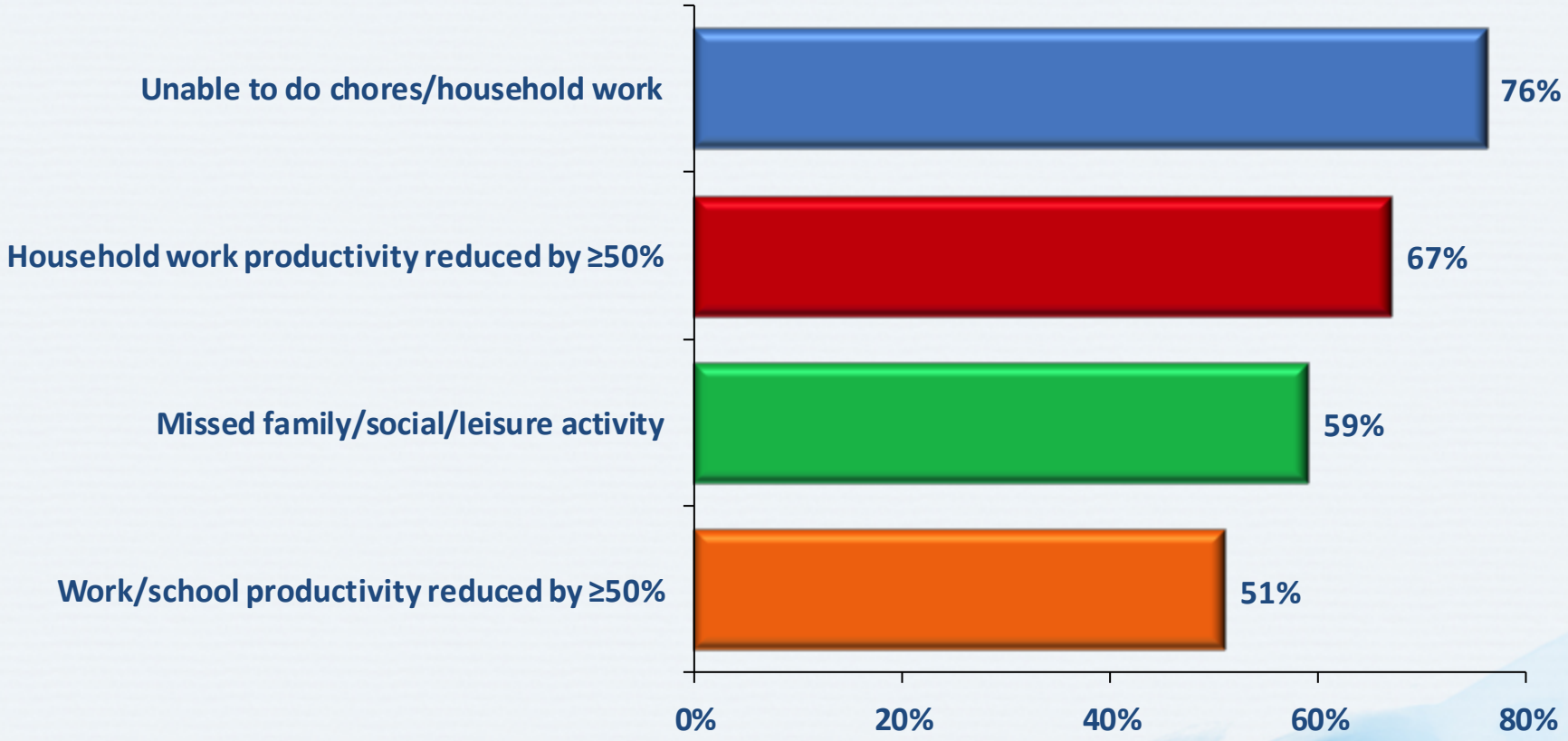
Economic Impact of Migraine - Europe



*Migraine subject with a medical follow-up
CM = chronic migraine; EM = episodic migraine

1. WHO 2012. Headache disorders. Available at: http://www.who.int/mediacentre/factsheets/fs277/en/. Accessed December 1, 2014; 2. Harwood RH *et al. Bull World Health Organ*. 2004; 82(4): 251-8; 3. Steiner TJ *et al. J Headache Pain.* 2013;14(1):1; 4. Stokes M *et al. Headache*. 2011;51(7):1058-77; 5. Bloudek LM *et al. J Headache Pain.* 2012;13(5):361-78.

Impact of Migraine on Patient's Daily Lives



Lipton RB *et al. Headache*. 2001;41(7):646-57.

Comorbidities of Migraine

- Strong association with[1]
  - Anxiety
  - Depression
  - Sleep disorders
  - Chronic pain disorders (fibromyalgia, chronic low back pain, irritable bowel syndrome)
  - Epilepsy
  - Vertigo

- Migraine with aura, but not migraine without aura, is a risk factor for ischemic stroke and silent brain lesions on MRI[2]
  - Particularly in women with frequent attacks

- Anxiety in childhood[3]
- History of abuse in childhood[4,5]
- History of motion sickness in childhood[6,7]

} Associated with headache development in adulthood

1. IASP Fact Sheet – Epidemiology of Headache 2012; Goodwin RD *et al. Am J Public Health*. 2003;93:1065-7; 2. Antonaci F *et al. J Headache Pain*. 2011;12:115-25; 3. Braccili T *et al. Eur Rev Med Pharmacol Sci.* 1999;3:37-9; 4. Tietjen GE *et al. Headache.* 2010;50:20-31; 5. Tietjen GE *et al. Headache.* 2010;50:32-41; 6. Cuomo-Granston A, Drummond PD. *Prog Neurobiol.* 2010;91:300-12; 7. Jan MM. *J Paediatr Child Health*. 1998;34:483-4.

Management of Migraine

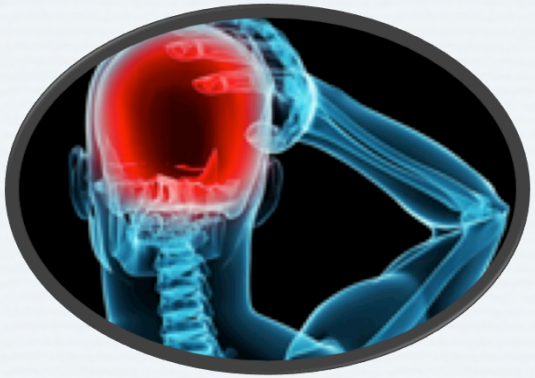
Discussion Question

HOW DO YOU TREAT MIGRAINE?

Management of Migraine

Pre-emptive Strategies
Used when a known headache trigger exists

Acute Strategies
To interrupt attacks



Preventative Strategies
To prevent attack recurrence

Fumal A, Schoenen J. *Neuropsychiatr Dis Treat.* 2008;4(6):1043-57; American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

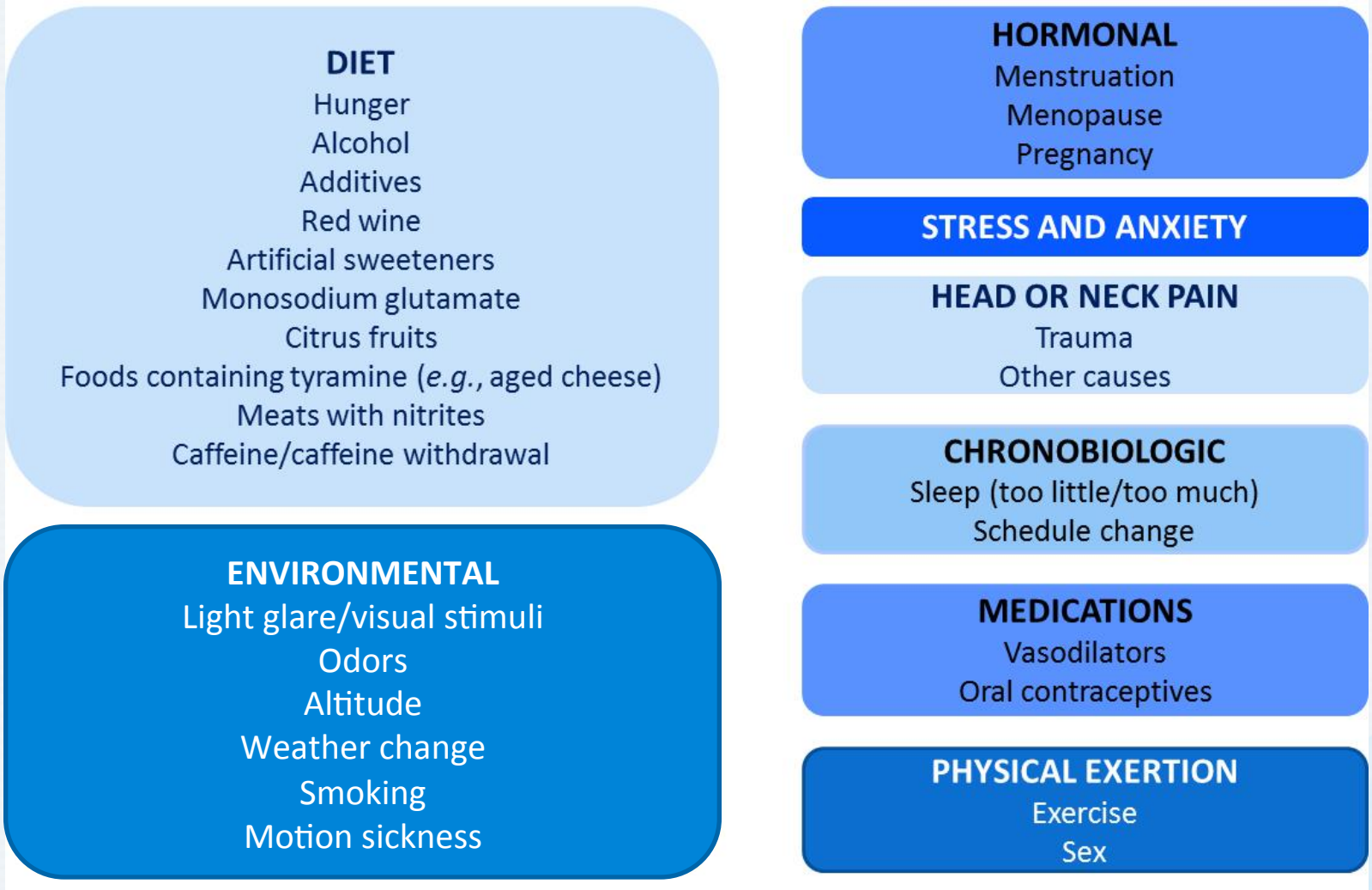
Evaluating Migraine Triggers

- Triggers should not be confused with cause of headache
- Not all triggers act equally to provoke headache
- Multiple triggers or combinations of triggers may be needed to provoke headache
- Types of triggers
  - Menstruation
  - Stress
  - Environmental
  - Hormonal
  - Dietary (*e.g.*, caffeine, fasting/skipping meals, alcohol)
  - Behavioral (sleep)

Patients should be advised to avoid known triggers if possible and should be counselled on lifestyle and stress management

American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

Commonly Reported Migraine Triggers



American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014; Chawla J. 2014. Available at http://emedicine.medscape.com/article/1142556-overview. Accessed 05 January 2014.

Goals of Acute Treatment for Migraine

- Treat attacks quickly and consistently and avoid recurrence
- Restore patient function in personal, social, and work domains
- Minimize the use of backup and rescue medications
- Eliminate or minimize adverse events
- Optimize self-care and reduce the need for resource use
- Provide cost-effective care

American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

What Is Successful Treatment of a Migraine Attack?

2 hour pain-free response and sustained pain-free response (*i.e.*, freedom from pain with no recurrence or use of rescue or study medication 2-24 hours post-dose)

Yes	No	Item
☐	☐	**Most times, I get relief from my migraine symptoms within 2 afters after I take my migraine medicine.**
☐	☐	Most times, I can get back to what I was doing within 2 hours after I take my migraine medication.
☐	☐	Most months, I get 3 or more migraines.
☐	☐	I take daily medicine to reduce how often I get migraines.
☐	☐	I know what may bring on my migraines.
☐	☐	Most times, I try *not* to use my migraine medicines right away.
☐	☐	In the past month, I missed some school, work, or other activity because of a migraine.
☐	☐	In the past 6 months, I had to go to an emergency or urgent care centre for a migraine.
☐	☐	I am satisfied with my migraine treatment.

Migraine Therapy Assessment Questionnaire (MTAQ®)

Silberstein SD *et al. Curr Med Res Opin.* 2013;29(7):861-7; Chatterton ML *et al. Headache.* 2002;42(10):1006-15.

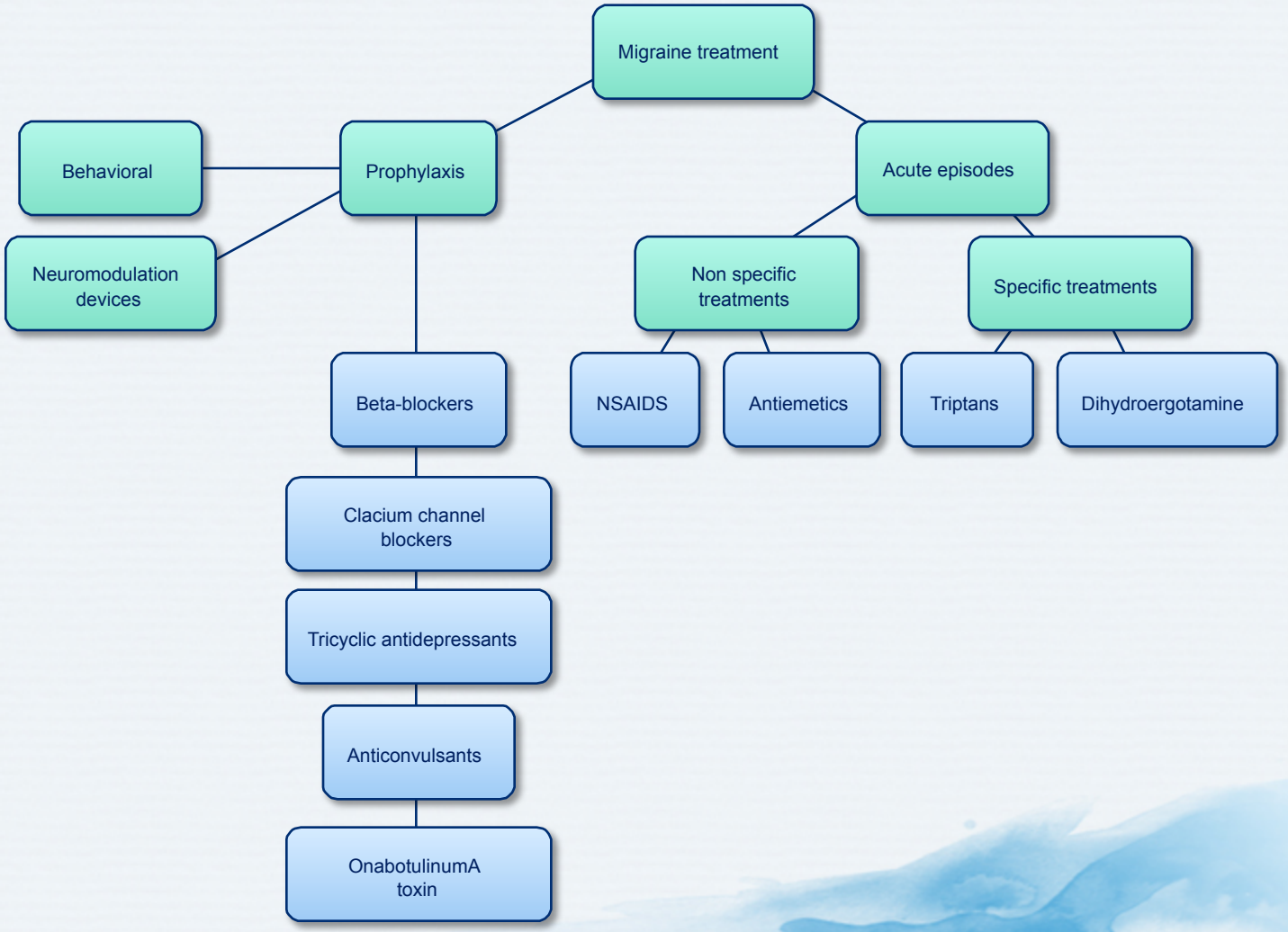
U.S. Headache Consortium – Goals for Migraine Treatment

Goals of Long-term Migraine Treatment
• Reduce migraine frequency and severity • Reduce disability • Improve quality of life • Prevent headache • Avoid escalation of medication overuse • Educate and enable patients to manage their disease

Goals for Successful Treatment of Acute Migraine Attacks
• Treat attacks rapidly and consistently without recurrence • Restore patient's ability to function • Minimize use of back-up/rescue medications • Optimize self-care for overall management • Be cost-effective in overall management • Cause minimal or no adverse effects

Matchar DB *et al.* Available at: http://tools.aan.com/professionals/practice/pdfs/gl0087.pdf. Accessed 27 November, 2014.

Overview of Migraine Treatment



Non-pharmacological Management of Migraine

Procedural

Behavioral

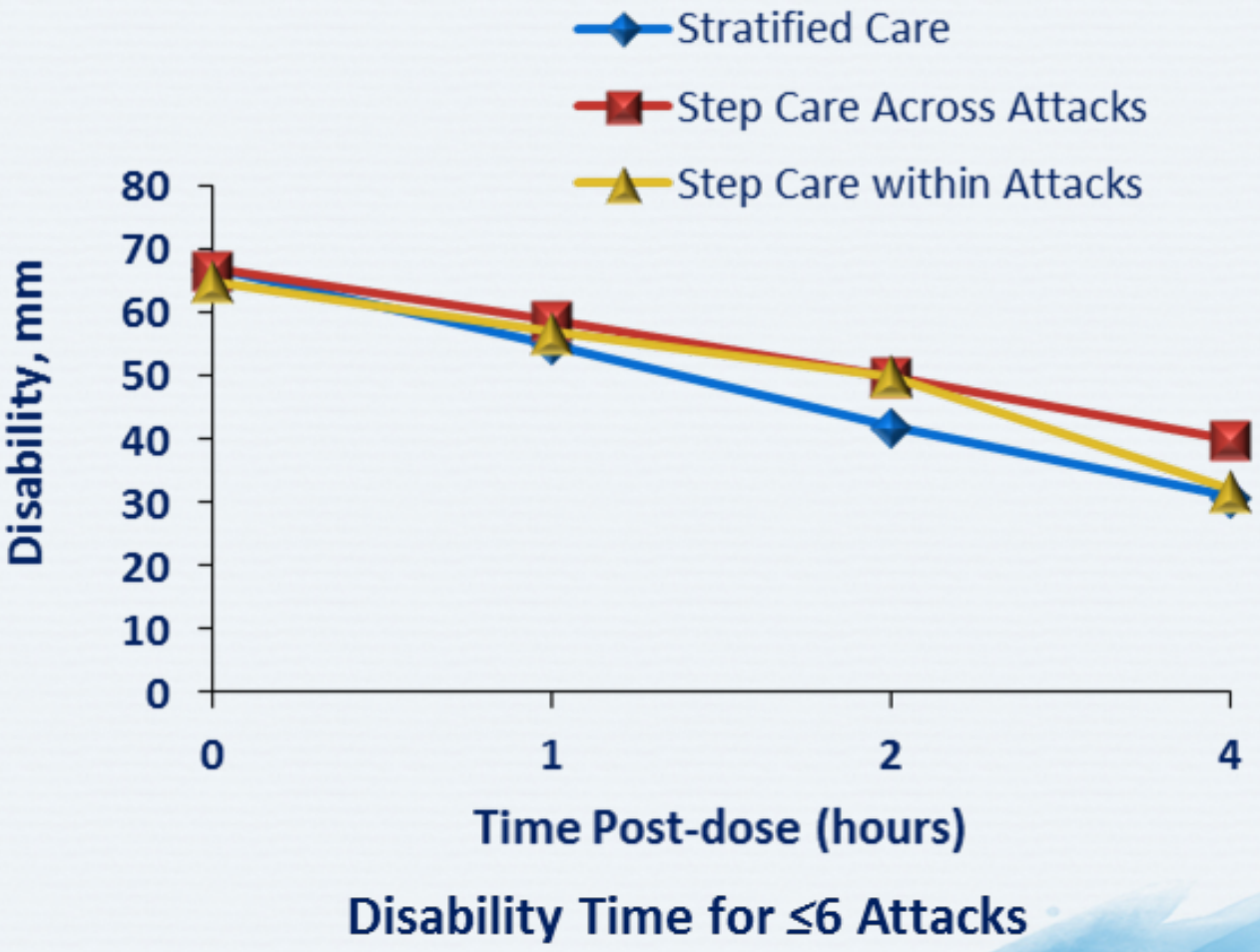
Non-pharmacologic Therapy for Migraine

Therapy	Comments
Massage	• Varying degrees of efficacy
Yoga	• Reduces migraine frequency and associated clinical features
Relaxation, biofeedback, and behavioral therapy	• Reduce migraine frequency and severity • Reduce the risk of episodic into chronic migraine • transformation,
Acupuncture/ Procedural	• Conflicting data • One study showed acupuncture was more effective than topiramate in chronic migraine prophylaxis

Holland S *et al. Neurology.* 2012;78(17):1346-53; Lester M. 2012. Available at: http://nccam.nih.gov/sites/nccam.nih.gov/files/D462.pdf. Accessed 14 December, 2014; John PJ *et al. Headache.* 2007;47(5):654-61; Mauskop A. *Continuum (Minneap Minn).* 2012;18(4):796-806; Linde K *et al. JAMA.* 2005;293(17):2118-25; Yang CP *et al. Cephalalgia.* 2011;31(15):1510-21; Guyuron B*et al. Plast Reconstr Surg.* 2009;124(2):461-8; Guyuron B *et al. Plast Reconstr Surg.* 2011;127(2):603-8; Mullally WJ *et al. Pain Physician.* 2009;12:1005-11; Pistoia F *et al. Curr Pain Headache Rep.* 2013;17:304.

Pharmacologic Management of Migraine Attack

Stratified Care for Migraine



Lipton RB *et al. JAMA*. 2000;284(20):2599-605.

Considerations when Selecting a Medication for Acute Treatment of Migraine

- Frequency of headaches
- Severity of headaches
- How quickly the headache builds
- Duration of the headache
- Tendency for headache recurrences
- Disability caused by headaches
- Associated symptoms (*e.g.*, nausea)
- Previous response to therapy
- Adverse events associated with medications
- Patient preference

- **Patients should be offered an appropriate backup medication if their initial acute medication does not provide relief**
- **Patients should have a rescue medication for use at home in case of complete treatment failure**

American Headache Society. Brainstorm. 2004. Available at: http://www.americanheadachesociety.org/assets/1/7/Book_-_Brainstorm_Syllabus.pdf. Accessed 04 December, 2014.

Medications for the Acute Management of Migraine

Level A Evidence

Analgesic
Acetaminophen

Ergot
Dihydroergotamine (DHE)

NSAIDs
Acetylsalicylic acid (ASA)
Diclofenac
Ibuprofen
Naproxen

Opioids
Butorphanol (nasal)
- Strong recommendation to **avoid** the use of butorphanol

Triptans
Almotriptan
Eletriptan
Frovatriptan
Naratriptan
Rizatriptan
Sumatriptan
Zolmitriptan

Combinations
Acetaminophen/ASA/caffeine
Sumatriptan/naproxen

Level B Evidence

Antiemetics
Chlorpromazine
Droperidol
Metoclopramide
Prochlorperazine

Ergots
Dihydroergotamine (DHE)
Ergotamine/caffeine
- Ergotamine is **not** recommended for routine use

NSAIDs
Flurbiprofen
Ketoprofen
Ketorolac

Others
Magnesium sulphate ($MgSO_4$) IV
Isometheptene

Combinations
Codeine or tramadol + acetaminophen
Strong recommendation to avoid the use of butorphanol
- Codeine- and tramadol combinations are **not** recommended for routine use

Level C Evidence

Antiepileptic
Valproate IV

Ergot: Ergotamine
- **Not** recommended for routine use

NSAID: Phenazone

Opioids
Butorphanol IM
Codeine
Meperidine IM
Methadone IM
Tramadol IV
- Strong recommendations to **avoid** use of butorphanol and opioid medications

Steroid: Dexamethasone IV

Others
Lidocaine intranasal
Butalbital
- Strong recommendations to **avoid** use of butalbital-containing medications

Combinations
Butalbital/acetaminophen/caffeine/codeine
Butalbital/acetaminophen/caffeine
- Strong recommendations to **avoid** use of butorphanol and opioid medications

NSAID = non-steroidal anti-inflammatory drug; IM = intramuscular; IV = intravenous

Marmura MJ *et al. Headache*. 2015;55(1):3-20.; Worthington I *et al. Can J Neurol Sci.* 2013;40(5 Suppl 3):S1-S80.

Acute Management of Migraine during Pregnancy

- Non-pharmacological approaches (relaxation, biofeedback, physical therapy) are safe and may be effective
- Acetaminophen (paracetamol) is the drug of choice for mild to moderate pain throughout pregnancy
- Acetylsalicylic acid (Aspirin®) are safe in the first and second trimesters but should be avoided near term
- If no other treatment is effective, sumatriptan is the triptan of choice
- Antiemetics (domperidone, metoclopramide) can be used

Ergotamine and dihydroergotamine are contraindicated during pregnancy

MacGregor A. *Progress Neurol Psychiatry*. 2009;13:21-24.

Migraine Prophylaxis during Pregnancy

- Non-pharmacological approaches (relaxation, biofeedback, physical therapy) are safe and may be effective
- Use migraine prophylaxis when patients have ≥3 prolonged severe attacks a month that are incapacitating or unresponsive to symptomatic therapy or are likely to result in complications
- Lowest effective dose of propranolol (10-20 mg twice daily) is the drug of choice
  - If beta-blockers are used in the third trimester, treatment should be stopped two to three days before delivery
- Low-dose amitriptyline (10-25 mg daily) is an option

Sodium valproate, topiramate and methysergide are contraindicated during pregnancy

Cassina M *et al. Expert Opin Drug Saf.* 2010;9:937-48; MacGregor A. *Progress Neurol Psychiatry*. 2009;13:21-24.

Pediatric Migraine

- Migraines are common in children
- Increase in frequency with increasing age
- Approximately 6% of adolescents experience migraine
- Mean age at onset: girls = 10.9 years; boys = 7.2 years
- Diagnosis is challenging because symptoms can vary significantly throughout childhood
- Not all adolescents will experience headaches throughout their lives
  - Up to 70% will experience some continuation of persistent or episodic migraines

Lewis D *et al. Neurology*. 2004;63:2215-24; Winner P. Pediatric and Adolescent Migraine. Available at: http://www.americanheadachesociety.org/assets/1/7/Paul_Winner_-_pediatric_and_Adolescent_Migraine.pdf. Accessed March 31, 2015.

Key Features for Diagnosis of Pediatric Migraine

- Duration tends to be shorter than in adults
- May be as short as 1 hour but can last 72 hours
- Often bifrontal or bitemporal rather than unilateral pain
- Children often have difficulty describing throbbing pain or levels of severity
- Using a face or numerical pain scale can be helpful
- Children often have difficulty describing symptoms
  - Symptoms often have to be inferred from the child's behavior
- Consider associated symptoms (difficulty thinking, fatigue, lightheadedness)

Winner P. Pediatric and Adolescent Migraine. Available at: http://www.americanheadachesociety.org/assets/1/7/Paul_Winner_-_pediatric_and_Adolescent_Migraine.pdf. Accessed March 31, 2015.

Red Flags in the Diagnosis of Pediatric Migraine

- Increasing frequency and/or severity over several weeks (<4 months) in a child <12 years of age
  - Even more important in children <7 years of age
- A change of frequency and severity of headache pattern in young children
- Fever is not a component associated with migraine at any stage – especially in children
- Headaches accompanied by seizures
- Altered sensorium may occur in certain forms of migraine but it is not the norm
  - Needs attention to determine appropriate assessment and intervention

Winner P. Pediatric and Adolescent Migraine. Available at: http://www.americanheadachesociety.org/assets/1/7/Paul_Winner_-_pediatric_and_Adolescent_Migraine.pdf. Accessed March 31, 2015.

Pharmacotherapies for Pediatric and Adolescent Migraine

- Acute therapies should be used as soon as it is clear the headache is migraine
  - Ibuprofen and sumatriptan nasal spray are effective
  - Acetaminophen is probably effective
- Almotriptan is the only triptan currently approved by the FDA for treatment of migraine in patients ≥12 years of age
- Analgesics or acute medications should not be used >2 times per week unless patient is under medical supervision
- Supplementation with magnesium, riboflavin, and coenzyme Q10 may be helpful
- No medication currently approved by FDA for migraine prophylaxis in children
  - Some studies have shown topiramate to be effective

Lewis D *et al. Neurology*. 2004;63:2215-24; Winner P. Pediatric and Adolescent Migraine. Available at: http://www.americanheadachesociety.org/assets/1/7/Paul_Winner_-_pediatric_and_Adolescent_Migraine.pdf. Accessed March 31, 2015.

Pharmacological Preventative Treatment of Migraine

EFNS Guidelines for Initiating Prophylactic Therapy for Migraine

Consider and discuss prophylactic drug when:

- Quality of life, business duties, or school attendance are severely impaired
- Patient experiences ≥2 attacks per month
- Migraine attacks do not respond to acute drug treatment
- Frequent, very long, or uncomfortable auras occur

EFNS guidelines exclude the regular use (≥2 days/week) of medication, which is a frequent indication for prophylaxis, regardless of quality of life level

Migraine prophylaxis is regarded as successful if the frequency of migraine attacks per month is decreased by ≥50% within 3 months

EFNS = European Federation of Neurological Societies

Evers S *et al. Eur J Neurol.* 2009;16(9):968-81.

Prophylactic Therapies in Migraine

- Antiepileptics
- Antidepressants
- Antihypertensives
- Vitamins/minerals/herbs
- OnabotulinumtoxinA
- Triptans (only in menstrual migraine- limit to 3-4 days)
- Antihistamines
- NSAIDs (only in menstrual migraine- limit to 3-4 days)

NSAID = non-steroidal anti-inflammatory drug

Pringsheim T *et al. Can J Neurol Sci.* 2012;39(2 Suppl 2):S1-59; Silberstein SD *et al. Neurology.* 2012;78:1337-45; Holland S *et al. Neurology*. 2012;78:1346-53..

Prophylaxis Treatments for Migraine

Drug(s)	Comments
Beta-blockers	• Most widely used drugs for migraine prophylaxis • 60 to 80% effective in decreasing migraine frequency by >50% • Similar efficacy to topiramate • Good tolerability • Excellent choice for patients with hypertension, CAD
Antidepressants	• TCAs most studied • Amitriptyline decreases number and intensity of migraines by 50-70%
Topiramate	• Rapid onset of action (within first month) • Shown to decrease mean monthly migraine periods • Good tolerability in most patients
Valproate, divalproex	• First-line agents • Divalproex is FDA approved • Several delivery modes • IV formulation of divalproex permit rapid achievement of therapeutic levels
OnabotulinumtoxinA	• FDA approved therapy for migraine • Significantly reduces headache days/month vs. placebo • Few associated adverse events

CAD = coronary artery disease; IV = intravenous; TCA = tricyclic antidepressant

Demaagd G. *P T.* 2008;33(7):480-7; Arulmozhi DK *et al. Vascul Pharmacol.* 2005;43(3):176-87; Silberstein SD. *Adv Stud Med.* 2005;5(6E):S666-S675; Garza I, Swanson JW. *Neuropsychiatr Dis Treat.* 2006;2(3): 281-91; Demaagd G. *P T.* 2008;33(7):480-7; Dodick DW *et al. Headache*. 2010 Jun;50(6):921-36; Allergan. Allergan Inc., Markham ON. BOTOX® (onabotulinumtoxinA) for injection. Product monograph. Date of approval: July 7, 2014; Mathew NT *et al. Headache*. 2001 Feb;41(2):119-28; Gallagher RM *et al. J Am Osteopath Assoc.* 2002;102:92-4; Freitag FG. *Psychopharmacol Bull*. 2003;3(Suppl 2):98-115; Parsekyan D. *West J Med.* 2000;173:341-5.

Discussion Question

WHAT PHARMACOLOGICAL APPROACHES TO MANAGING MIGRAINE DO YOU INCORPORATE INTO YOUR PRACTICE?

Guidelines for the Pharmacological Management of Migraine

- AAN/AHS Guidelines
- CHS Guidelines for Acute Migraine Therapy
- CHS Guidelines – Prophylactic Drug Treatment Strategies
- CHS Guidelines – Migraine Prophylaxis
- Latin American Consensus Guidelines for Chronic Migraine
- EFNS Guideline on the Acute Treatment of Migraine
- EFNS Guideline on the Prophylactic Treatment of Migraine

Continue to Key Messages

AAN/AHS Guidelines for Episodic Migraine Prevention in Adults

Level A Medications
Antiepileptic drugs (divalproex sodium, sodium valproate, topiramate)
Beta-blockers (metoprolol, propranolol, timolol)
Triptans (Frovatriptan)
Level B Medications
Antidepressants (amitriptyline, venlafaxine)
Beta-blockers (atenolol, nadolol)
Triptans (naratriptan, zolmitriptan)
Third-line (Level C)
ACE inhibitors (lisinopril)
Angiotensin receptor blockers (candesartan)
Alpha agonists (clonidine, guanfacine)
Antiepileptic drugs (carbamazepine)
Beta-blockers (nebivolol, pindolol)
Antihistamines (cyproheptadine)

AAN = American Academy of Neurology; ACE = angiotensin-converting-enzyme; AHS = American Headache Society; MRM = menstrually-related migraine; SSNRI = selective serotonin-norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant

[a]Classification based on original guideline and new evidence not found for this report

[b]For short-term prophylaxis of menstrually-related migraine

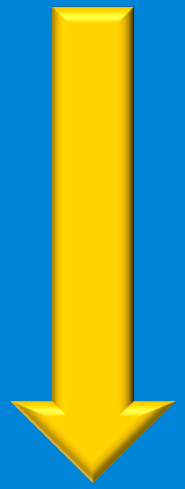
Silberstein SD *et al. Neurology.* 2012;78(17):1337-45.

Access full AAN/AHS guidelines

Return to guidelines list

CHS Guidelines for Acute Migraine Therapy

Acute Migraine Treatment Strategies and Medication Summary: General Strategies

Increasing migraine severity – Refractoriness to therapy 	Clinical Phenotype	Strategy
	Mild-moderate attack strategies	a. Acetaminophen b. NSAID
	Moderate-severe attack/ NSAID failure strategies	a. NSAID with triptan rescue b. Triptan
	Refractory migraine strategies	a. Triptan-NSAID combination b. Triptan-NSAID combination with rescue c. Dihydroergotamine

CHS = Canadian Headache Society; NSAID = non-steroidal anti-inflammatory drug

Worthington I *et al. Can J Neurol Sci.* 2013;40(5 Suppl 3):S33-S62.

Access full CHS guidelines

Return to guidelines list

CHS Guidelines for Migraine Prophylaxis

Clinical Setting	Strategy
First time strategy	a. Beta-blocker (propranolol, nadolol, metoprolol) b. Tricyclic antidepressant
Low side effects	a. Candesartan, lisinopril b. Herbal/vitamin/mineral (*e.g.*, butterbur, riboflavin, magnesium
Increased body mass	Topiramate
Hypertension	Propranolol, nadolol, metoprolol, candesartan, lisinopril
Depression/anxiety	Amitriptyline, venlafaxine
Additional monotherapy	Topiramate, divalproex, gabapentin, pizotifen, flunarizine, verapamil
Pregnancy	Drug avoidance if possible When necessary, magnesium, propranolol, metoprolol, amitriptyline
Lactation	Drug avoidance if possible When necessary, magnesium, propranolol, metoprolol, amitriptyline, valproate

Access full CHS guidelines

Return to guidelines list

CHS = Canadian Headache Society

Worthington I *et al. Can J Neurol Sci.* 2013;40(5 Suppl 3):S33-S62.

CHS Guidelines for Migraine Prophylaxis

Drug Class	Drugs
Antiepileptics	Divalproex sodium, valproic acid, sodium valproate, topiramate, gabapentin
Antidepressants	Amitriptyline, venlafaxine extended release
Beta-blockers	Propranolol, nadolol, metoprolol
Calcium channel blockers	Flunarizine, verapamil (not recommended for routine use)
ACEIs/ARBs	Candesartan, lisinopril
Serotonin agonists	Pizotifen
Vitamins/minerals/herbals	Riboflavin, coenzyme Q10, magnesium citrate, butterbur (petasites)

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; AV = atrioventricular; BID = twice daily; CHF = congestive heart failure; CHS = Canadian Headache Society; CNS = central nervous system; CV = cardiovascular; GI = gastrointestinal; LA = long acting; MI = myocardial infarction; SNRI = serotonin-norepinephrine reuptake inhibitor; SR = sustained release; TCA = tricyclic antidepressant; TID = three times daily

Worthington I *et al. Can J Neurol Sci.* 2013;40(5 Suppl 3):S33-S62.

Latin American Consensus on Guidelines for Chronic Migraine Treatment

Drug(s)	Comments
Topiramate	Use in prophylaxis is based on class I studies with level A evidence
Sodium valproate, divalproate	Recommended in prophylaxis of episodic migraine (class I studies with level A evidence)
Amitriptyline Pregabalin Gabapentin Tizanidine	Studied for chronic daily headache by revealing efficacy (evidence levels I to III); not specifically researched for migraine
Type A botulinum toxin	For prophylaxis of chronic migraine in patients aged 18 to 65 years
Non-pharmacologic measures/ complementary therapies	Use is limited due lack of studies. Exception = acupuncture (promising results)

Medicines already proven as preventive for episodic migraine can be used alone or in combination, even without any evidence of their efficacy for chronic migraine

Access full Latin American guidelines

Return to guidelines list

Giacomozzi AR *et al. Arq Neuropsiquiatr.* 2013;71(7):478-86.

EFNS Guideline on the Treatment of Migraine – Acute Therapies

Drug(s)	Comments
Analgesics	• Drugs of first choice for mild or moderate attacks • Restrict intake of simple analgesics to 15 days/month • Restrict intake of combined analgesics to 10 days/month
Antiemetics	• Recommended for nausea and potential vomiting • Assumed to improve resorption of analgesics
Ergot alkaloids	• Restrict to patients with very long migraine attacks or with regular occurrence • Limit use to 10 days/month
Triptans	• Efficacy proven in large placebo-controlled trials and meta-analyses • Use restricted to maximum 9 days/month by IHS criteria • Should not be taken during the aura
Opioids Tranquillizers	• Should not be used in the acute treatment of migraine

Access full EFNS guidelines

Return to guidelines list

EFNS = European Federation of Neurological Societies; IHS = International Headache Society

Evers S *et al. Eur J Neurol.* 2009;16(9):968-81.

EFNS Guideline on the Treatment of Migraine – Prophylactic Therapies

First-line (Level A)	
Beta-blockers (metoprolol, propranolol)	
Calcium channel blockers (flunarizine)	
Antiepileptic drugs (valproic acid, topiramate)	
Second-line (Level B)	
Amitriptyline Venlafaxine Naproxen	Butterbur (petasites) Bisoprolol
Third-line (Level C)	
Acetylsalicylic acid (ASA) Gabapentin Magnesium Tanacetum parthenium Riboflavin	Coenzyme Q10 Candesartan Lisinopril Methysergide

Access full EFNS guidelines

Return to guidelines list

EFNS = European Federation of Neurological Societies; IHS = International Headache Society

Evers S *et al. Eur J Neurol.* 2009;16(9):968-81.

Key Messages

- Headache is extremely common
  - Migraine and tension-type headache are the most common presentation in primary care
- Clinicians should maintain high degree of awareness for "red flags" indicating potential serious disorders
  - When possible, clinicians should treat the underlying cause of headache
- The mechanisms of pain in migraine include meningeal vasodilation, neurogenic inflammation, and peripheral and central neuronal sensitization and pain processing
  - These may be modified using migraine treatments
- Timely and appropriate treatment may help prevent episodic migraine from becoming chronic migraine and medication overuse headache

References

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