

Migraine

What to Keep in Mind

Cory Toth, BSc, MD, FRCPC; and Werner J. Becker, MD, FRCPC

As presented at the University of Calgary's
28th Annual Family Practice Review (November 2003)

In North America, 18% of women and 6% of men have at least one migraine attack each year.¹ Fortunately for migraineurs, advances in the understanding of pathophysiology of migraine, as well as new treatment options, have been developed over the past decade.

What are the components of migraine?

Migraine has four main phases (Figure 1):

Phase 1—*Premonitory*

This phase is a prodrome, characterized by changes in mood and behaviour. These changes include euphoria, irritability, drowsiness, poor concentration, food cravings, and changes in gastrointestinal function.

Phase 2—*Aura*

Aura may occur in as many as one-third of migraineurs. It usually develops over five to 20 minutes and lasts < 60 minutes (Table 1). Headache usually occurs within 60 minutes after the aura has ended, but may begin before resolution, or even before initiation of the aura.

Erin's case

Erin, 28, has had severe headaches for the past 16 years. Her headaches began around the time of menarche and now occur five to six times per month. Each episode lasts at least six hours. She misses at least one to two days of school or work per month due to her headaches. Prior to onset, she notes increased appetite and emotional lability.



Erin's headaches are severe, generalized, throbbing, and associated with nausea and vomiting. Often she must sleep in a dark, quiet room for her symptoms to improve. Ibuprofen, taken at the peak of headache, has been ineffective for her.

Her mother and grandmother had migraine, but her other medical history is negative and her neurologic exam is normal.

She is diagnosed with migraine without aura. Prophylactic therapy, in the form of amitriptyline, 25 mg, as needed, is initiated.

For a followup on Erin, go to page 78.

Phase 3—*Typical headache*

A migraine headache is unilateral, throbbing, at least moderate in severity, and worsened by physical activity; not all of these features are required for

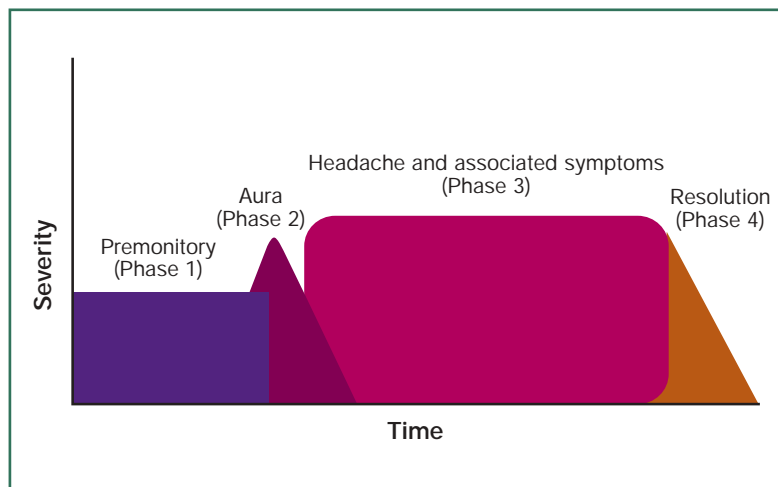


Figure 1. Four phases of a migraine attack.

a headache to be considered a migraine.

Headache pain onset is typically gradual, but may fluctuate over its course before peaking and subsiding. The typical duration of the headache phase is between four and 72 hours. Other typical associated features of Phase 3 include changes in appetite, nausea and vomiting, photophobia, phonophobia, and osmophobia. During this phase, patients often seek a dark and quiet room.

Phase 4—Resolution phase

During resolution, feelings of fatigue, irritability, poor concentration, mood changes, and malaise often develop, although some patients experience euphoria.

Dr. Toth is a clinical fellow/associate member, division of neurology, department of clinical neurosciences, University of Calgary, Calgary, Alberta.

Dr. Becker is a professor, department of clinical neurosciences, University of Calgary, and the director, division of neurology, Calgary Health Region, Calgary, Alberta.

How can migraine be diagnosed?

Clinical diagnosis of migraine is dependent on clinical criteria formulated by the International Headache Society (IHS) (Tables 2 and 3). These criteria have recently been revised and will soon be published.

The IHS criteria have understandable limitations, but nevertheless represent the gold standard for diagnosing migraine. In

In North America, 18% of women and 6% of men have at least 1 migraine attack each year.

most cases, further diagnostic testing is not required if the IHS criteria are met. In other cases, neuroimaging and referral to a neurologist or headache specialist may be necessary.

How can migraine be treated?

Migraine treatment can be divided into abortive and prophylactic therapy. In general, if the number of migraine attacks is greater than twice monthly and the patient has significant disability despite symptomatic therapy, prophylactic therapy should be attempted.

Migraine

Often, migraine therapy can be tailored to the individual. For example, a patient with migraine and essential tremor in the absence of asthma and diabetes, would best be treated with a beta blocker; a patient with migraine and epilepsy would best be treated with anticonvulsant therapy, *etc.*

Abortive therapy

Abortive therapy of migraine should be tailored to the individual patient. If over-the-counter (OTC) non-steroidal anti-inflammatory (NSAIDs) agents, such as acetylsalicylic acid (ASA), ibuprofen, or naproxen, are effective, this may be sufficient. In many cases, addition of metoclopramide is beneficial for nausea and headache.

When efficacy, side-effects, and cost are considered, a beta blocker or tricyclic antidepressant should be the prophylactic agent of choice.

If gastroparesis and vomiting are excessive, alternative routes of administration (nasal or parenteral) should be considered.

If these measures are sub-adequate, triptans are good abortive agents (Table 4). Some of these

Table 1

Characteristics of a migraine aura

<u>Visual</u>	<u>Sensory</u>	<u>Motor</u>	<u>Cognitive</u>
Fortification spectra	Paresthesias	Heaviness	Drowsiness
Object oscillation	Slowly spreading	Fatigue	Aphasia
Flickering lights	Numbness	Dysarthria	Apraxia
Multi-coloured	Hand and face		Delirium
Visual blurring			Dreaminess
Excessive brightness			
Marching spectra			
Visual hallucinations			
Visual scotoma			

A followup on Erin

Three months later, the frequency of Erin's headaches has fallen to two to three times per month, with decreased severity of headache intensity (except for headaches occurring around her menses). She is advised to take ibuprofen daily, starting three days before menses and ending four days after menses, in addition to increasing her amitriptyline dosage to 50 mg, as needed.

Three months later, her headache frequency is down to one per month without any disability. In this case, the non-steroidal anti-inflammatory drug acted as a prophylactic agent during the hormonal fluctuation associated with Erin's menstruation.

triptans have subcutaneous, intranasal, and oral wafer delivery formats to circumvent absorption difficulties.

Dihydroergotamine (DHE) is also used to treat severe migraine attacks and can be delivered intranasally. Although the triptans have been regarded as the best in migraine abortive therapy over recent years, the Acetaminophen, aspirin, and

Table 2

International Headache Society criteria for migraine with aura

1. At least 2 attacks meeting criteria 2 to 4
2. Aura consisting of at least one of the following, without true weakness:
 - a. Fully reversible visual symptoms including, scintillations and loss of vision
 - b. Fully reversible sensory symptoms, including pins and needles sensations, as well as numbness
 - c. Fully reversible language dysfunction (aphasia)
3. At least two of the following:
 - a. Homonomous visual symptoms and/or unilateral sensory symptoms
 - b. At least one aura symptom develops gradually over at least 5 minutes and/or different aura symptoms occur in succession over at least 5 minutes
 - c. Each symptom lasts between 5 to 60 minutes
4. Headache fulfilling criteria for migraine without aura beginning during the aura or follows aura within 60 minutes
5. Clinical syndrome cannot be attributed to another disorder; a normal neurologic exam is present and no evidence of organic disease that could lead to headaches is present

caffeine with Sumatriptan Succinate in the Early Treatment of migraine (ASSET) study demonstrated that, for some patients, a combination of ASA, acetaminophen, and caffeine may be more effective than oral sumatriptan in moderately severe migraine attacks.²

The patient who requires too many visits to find an effective therapy may become discouraged, spending many years using less effective OTC analgesics, with the potential for developing

Table 3

International Headache Society criteria for migraine without aura

1. At least 5 attacks meeting criteria 2 to 4
2. Untreated or unsuccessfully treated headache attacks lasting 4 to 72 hours.
3. Headache has at least two of the following characteristics:
 - a. Unilateral location
 - b. Pulsating quality
 - c. Moderate or severe intensity
 - d. Aggravation by or causing avoidance of routine physical activity (*i.e.*, climbing stairs)
4. At least one of the following during headache:
 - a. Nausea and/or vomiting
 - b. Photophobia and/or phonophobia
5. Clinical syndrome cannot be attributed to another disorder; a normal neurologic exam is present and no evidence of organic disease that could lead to headaches is present

rebound headache. In view of these considerations, a “stratified care approach” has been advocated.³ This approach allows the physician to make clinical determination of the patient’s treatment needs based on headache attack severity⁴ or overall headache-related disability.³

With the latter approach, patients with severe migraine attacks should receive triptan therapy or other migraine-specific medications at first; patients with moderately severe migraine attacks should initially receive NSAIDs and be upgraded to a triptan if the therapeutic response is sub-optimal. Another option for patients with moderate migraine attack severity is to start with an NSAID and use a triptan two hours later, if needed.

Some patients will not respond to triptans. In these cases, a satisfactory response may be

Table 4

Commonly used triptans in Canada

Triptan	Methods of delivery (mg/dose)
Sumatriptan	Injectable (6), nasal spray (20), oral (50, 100)
Naratriptan	Oral (2.5)
Zolmitriptan	Oral (2.5), oral wafer (2.5)
Rizatriptan	Oral (5, 10), oral wafer (5, 10)
Almotriptan	Oral (6.25, 12.5)

obtained with a triptan plus a NSAID, or even a triptan, NSAID, and metaclopramide combination.

Prophylactic treatment

A large number of drugs have now been shown to have significant efficacy as prophylactic agents. There are a wide variety of prophylactic therapeutic agents to treat migraine (Table 5).

Besides pharmacologic agents, behavioural interventions, such as biofeedback and relaxation techniques, can be useful adjuvant therapy.

Lastly, precipitants of headache, such as excessive caffeine, monosodium glutamate, tyramine-containing foods, and a number of medications, should be avoided. In particular, oral contraceptive pill (OCP) use needs to be reviewed; OCP use may be contraindicated in some female migraineurs who suffer migraine with aura.

Most often, when efficacy, side-effects, and cost are considered, a beta blocker or tricyclic antidepressant should be considered prophylactic agents of choice.

Frequently Asked Questions

- 1.** Can migraine be associated with stroke?
Yes, but rarely. If strokes do occur, they will occur during the aura. The infarct must be documented by neuroimaging, and other causes of cerebral infarction must be ruled out.
- 2.** Can prophylactic agents be combined?
Yes, if they are tolerated. (Example: Flunarizine and riboflavin may be used together in most patients.)
- 3.** Can migraineurs use prophylactic and abortive therapy?
Yes, if they are tolerated. (Example: Amitriptyline in combination with a triptan may be effective.)
- 4.** What is the best prophylactic/abortive agent for migraine?
The ideal agent is the one tailored to the individual patient. (Example: A patient with migraine and premenstrual symptoms may benefit most from a NSAID; one with migraine and hypertension may benefit most from a beta blocker or a calcium channel blocker.)
- 5.** Can prophylactic agents be used in patients with migraine and tension-type headaches?
Yes, certain prophylactic agents, such as tricyclic antidepressants, are beneficial in both syndromes.

Table 5

Commonly used prophylactic agents

Type	Examples
Beta blockers	Propranolol, nadolol, metoprolol, atenol
Tricyclic antidepressants	Amitriptyline, nortriptyline
Serotonin agonists	Pizotifen, methysergide
Calcium channel blockers	Flunarizine, verapamil
Anticonvulsants	Divalproex sodium, topiramate, gabapentin
ACE inhibitors & ARBs	Lisinopril, candesartan
Other	Riboflavin, magnesium, botulinum toxin

ACE: Angiotensin-converting enzyme
ARB: Angiotensin II receptor blocker

When should primary physicians refer?

In cases where headaches do not meet the outlined diagnostic criteria, and for patients without successful therapeutic intervention, referral to a headache specialist or neurologist can be beneficial.

In some situations, such as in a patient with migraine and chronic daily headache due to excessive analgesic use, intervention with a specialist (and sometimes admission to hospital) is required.

In those patients who do not respond to initial or standard abortive or prophylactic treatment, referral for further therapeutic options is often beneficial. **Dx**

Take-home message

- Migraine is a neurologic disorder of the brain due to an intrinsic abnormality within the brainstem.
- The IHS migraine diagnostic criteria represents the gold standard for diagnosis.
- Migraine therapy can be divided into abortive and prophylactic therapies; both consist of numerous options tailored to the individual patient.

References

1. Lipton RB, Stewart WF: Migraine in the United States: Epidemiology and healthcare utilization. *Neurology* 1993; 43(6 Suppl 3):S6-10.
2. Goldstein J, et al: A placebo-controlled comparison of the combination of Acetaminophen, Aspirin, and Caffeine with Sumatriptan Succinate in the Early Treatment of Migraine: Results from the Asset trial. AAN 2003 Meeting, Honolulu. Abstract S22.005.
3. Lipton RB, Stewart WF, Stone AM, et al: Disability in strategies of care study group. Stratified care vs step care strategies for migraine: The Disability in Strategies of Care (DISC) study: A randomized trial. *JAMA* 2000; 284(20):2599-2605.
4. Pryse-Phillips WE, Dodick DW, Edmeads JG, et al: Guidelines for the diagnosis and management of migraine in clinical practice. Canadian Headache Society. *CMAJ* 1997; 156(9):1273-87.

www.stcommunications.com



For an electronic version of this article, visit:
The Canadian Journal of Diagnosis online.