Migraine Headache

INTRODUCTION
Migraine is the leading reason patients with headache seek help from primary care providers, yet migraine may be both under diagnosed and under treated. Differentiating migraine from other headache types and determining the optimal acute or preventive therapy for this complex patient population is often challenging.

OBJECTIVES
This module will enable clinicians to:
• Accurately diagnose migraine, including migraine with aura.
• Identify comorbidities relevant to migraine and determine the impact of migraine on quality of life.
• Use evidence-based management for acute migraine treatment and prophylaxis.

Note: Please refer to the following modules for additional information on the management of headache:
• Headaches: Children and adolescents, November 2013
• Headache disorders: Approach to non-migraine types, August 2010

These modules are available through members online at https://members.fmpe.org/

CASES

Case 1: Dora, female, age 35

Dora is new to your practice. She had previously been receiving care from a walk-in clinic. Today, Dora presents to you concerned about her longstanding headaches, which have been occurring about five or six times a month. She takes medication for her headaches three to four times a month. Acetaminophen or ibuprofen provides some acute pain relief, but the headaches still last up to 12 hours. Dora takes no chronic medication and reports that she is otherwise healthy. She is married with two grown children and had a tubal ligation several years ago. Dora works shifts as a nurse.

What further information would be helpful for you?

Part Two

Dora tells you her headaches began about 20 years ago. At that time she had one or two headaches per month. Dora experiences severe unilateral pain in the right temporal-occipital region which radiates into the right eye. Her headaches are always severe, unilateral and pulsating. She has not noted any triggers, other than maybe changes in the weather. Dora is frequently nauseated with the headaches and has to lie down in a dark room. Dora takes 1000 mg of acetaminophen or 600 mg of ibuprofen when the headache “gets bad enough,” but she has not tried anything else. She smokes half a pack of cigarettes a day and drinks a few glasses of wine on the weekend.

Physical examination showed that she was well. Her vital signs included pulse of 82 BPM and blood pressure of 126/80 mmHg. A brief neurological exam was performed with no abnormal findings. There were no abnormalities on head and neck examination including range of motion or tenderness.

What would you do next?
Part Three

Dora opted for acute management with a triptan. Three months later, she returns to discuss her headaches. She is still having five or six headaches a month. Dora found the triptan effective but it made her very drowsy. Dora wants to talk about what other therapy she can try.

How would you manage Dora now?

Case 2: Michael, male, age 52

Michael is quite anxious when he presents to you. He complains of frequent trouble with his eyesight. This seems to occur following days when he participates in soccer games or practices. He further describes his visual difficulty as ‘zigzag lines’ across both visual fields. Occasional numbness and tingling in his right hand and fingers may accompany the visual disturbance. Each episode comes on over about 5 to 10 minutes and lasts approximately 30 to 45 minutes, but he doesn’t really keep track.

When asked about headaches, Michael does not specifically recall having any headaches but has experienced nausea, vomiting, and photophobia on many occasions when he has these visual disturbances. He is concerned that he is suffering from mini-strokes and wants to know if he should give up soccer.

What additional information would be helpful?

Part Two

Michael says these symptoms occur approximately twice a week and started about three months ago. Activity, bright light, and strong odours seem to aggravate his symptoms, which are often relieved by rest and sleep in a dark room. He is a non-smoker, and his weight is normal, as is his lipid profile. There is a family history of migraine but not of cardiovascular illness. A recent eye examination was normal.

His pulse is 66 BPM and his blood pressure is 110/68 mmHg. Michael is afebrile. His neurological exam, including fundoscopic and cranial nerve assessment, is benign and non-lateralizing. He has no weakness.

What investigations might you order?

Part Three

Michael had magnetic resonance imaging (MRI). There were no abnormal findings.

What would be your approach for Michael?

Case 3: Connie, female, age 32

Connie presents to you concerned about her migraine headaches. She has had them on and off since she was an adolescent, but in the last several years they have become much worse. Now her headaches occur several times a week, and they occur daily before her menstrual period. Although she does not get an aura, fatigue and neck stiffness seem to signal that a migraine is starting. Her migraines are also aggravated by stress and changes in barometric pressure, but she has not been able to identify any additional triggers. Connie becomes quite incapacitated by her migraines and has to lie down in a dark room.

For acute pain relief, Connie has tried reasonable doses of acetaminophen (Tylenol®) and ibuprofen as soon as she feels a headache starting, without much relief. She experienced chest pain when taking sumatriptan, although it did help her headaches. She has resorted to taking Tylenol–Codeine No. 3 about three times a week, but avoids taking it daily. Last year her migraine pattern changed and a CT scan was ordered. It was negative for intracranial pathology. Prophylactic therapy with propranolol did not help her. Amitriptyline reduced her headache frequency slightly, from four to two or three headaches weekly, but she could not tolerate more than 50 mg at bedtime, due to daytime somnolence. She remains on amitriptyline.

Connie’s past history includes irritable bowel syndrome, depression, nonalcoholic fatty liver disease, and obesity. She takes a proton pump inhibitor but no other chronic medications. Her mood has been worse lately due to her frustration with the impact of her headaches on her life. She is married, with two healthy children, and she has a supportive partner. Currently, they are using foam and condoms for contraception. Connie does not work outside the home. She does not smoke and her blood pressure is normal.

How would you manage Connie?
**If Connie asked about other options for contraception, what would be your approach?**

**If Connie had migraine with aura, how might your approach to contraception differ?**

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**INFORMATION SECTION**

**DIAGNOSIS**

1. Although migraine is a common type of headache with a current global prevalence greater than 10% among adults, fewer than half of patients with migraine may be diagnosed correctly. This under-diagnosis, which results in only one-third of migraine patients being treated appropriately, can lead to considerable disability and quality-of-life problems.

2. About 10% of people with migraine meet the diagnostic criteria for generalized anxiety disorder. A “bidirectional association between migraine and major depression, as well as panic disorder, has also been consistently confirmed.”

3. *ID-Migraine™* is a three-item, validated screening tool to identify the presence of disability, nausea, and photophobia. This test has a sensitivity of 0.82 and specificity of 0.75 for the diagnosis of migraine, if the patient responds positively to two or three of the following questions:
   - Has a headache limited your activities for a day or more in the last three months?
   - Are you nauseated or sick to your stomach when you have a headache?
   - Does light bother you when you have a headache?
   This is available at WebMD [http://www.webmd.com/migraines-headaches/news/20030818/3-question-test-identifies-migraine](http://www.webmd.com/migraines-headaches/news/20030818/3-question-test-identifies-migraine)

4. The mnemonic POUND is an evidence-based tool for migraine diagnosis, where POUND stands for the following:
   - Pulsatile quality of headache
   - One-day duration (4 to 72 hours)
   - Unilateral location
   - Nausea or vomiting
   - Disabling intensity
   In primary care, there is a 92% probability of migraine in patients with at least four of the POUND criteria. This decreases to 64% with three criteria.

5. Although the Migraine Disability Assessment Scale (MIDAS) assesses frequency of disability due to migraine and can be a good screening tool, the scale requires the patient to recall migraines that occurred over the previous three months. A score of at least 21 indicates severe disability due to headache. The five-question MIDAS scale can be found at [http://uhs.berkeley.edu/home/healthtopics/pdf/assessment.pdf](http://uhs.berkeley.edu/home/healthtopics/pdf/assessment.pdf).

6. A *headache diary* is a valuable tool that eliminates recall bias. A diary can identify headache frequency, severity, features, and triggers. It can also help tailor acute and prophylactic treatment, as medication use and responses are recorded. Various headache diaries are available online at:
   - Headache Network Canada: [http://headachenetwork.ca/](http://headachenetwork.ca/) and click the “publications” tab.
   - Institute of Health Economics: [http://www.ihe.ca/research/--the-alberta-ambassador-program/--headache-guideline/headache-guideline-1/clinical-resources/This Diary is available in both a long and short form and also as a smart phone app.](http://www.ihe.ca/research/--the-alberta-ambassador-program/--headache-guideline/headache-guideline-1/clinical-resources/)

7. The American Headache Society makes the following recommendations for investigation of migraine:
   - “Don’t perform neuroimaging studies in patients with stable headaches that meet criteria for migraine.” Migraine diagnosis is based on history and physical examination that documents the *absence of any neurologic findings*, such as papilledema.
   - “Don’t perform computed tomography (CT) imaging for headache when magnetic resonance imaging (MRI) is available, except in emergency settings.” CT is preferred when acute stroke or head trauma may be present. MRI is more sensitive for detecting various other lesions, such as neoplasms and vascular disease.

8. The diagnosis of migraine is based on the International Headache Society (IHS) criteria for migraine. There is also a revised International Classification of Headache Disorders, ICHD-3-beta edition. These criteria are presented combined in Appendix 1. A complete physical examination and history can assist in diagnosis, and rule out other potentially serious causes of the symptoms (see Appendix 2). For “red flag” headache features that demand investigation, consult the previous PBSG module, *Headache disorders: Approach to non-migraine types, August 2010, Appendix 2* (https://members.fmpe.org/).
9. Chronic migraine is defined as “the occurrence of headache on at least 15 days a month, with at least eight days a month on which headaches and associated symptoms meet diagnostic criteria for migraine.”
   • Episodic migraine may transform to chronic migraine. Risk factors for transformation include obesity, snoring, sleep disorders, psychiatric disease, frequent acute medication use, female sex, excessive caffeine intake, lower socioeconomic status, comorbid pain disorders, history of head or neck injury, and cutaneous allodynia.
   • Chronic migraine may also revert to episodic migraine. Factors associated with reversion include lower baseline frequency (15–19 vs. 25–31 headache days per month), absence of allodynia, prophylactic treatment adherence, withdrawal of overused acute medications, and physical exercise.11

10. Migraine aura, a transient neurologic phenomenon, usually involves visual symptoms and occurs before headache onset. The proportion of migraine patients who have aura varies from 10 to 46% with references from European populations citing about 33%.6,12 The Visual Aura Rating Scale (VARS) can help clinicians better recognize aura (see below).

11. Aura may also occur without headache. This situation is more common in older individuals with a history of migraine with aura, but it can occur at any age, and in people who have not experienced migraine headache. The prevalence of “migraine aura without headache” varies according to the study, from 1 to 2% of elderly individuals to 44% of patients with migraine with aura.
   • If a history of typical recurrent aura symptoms is present, with no neurologic deficits, workup is usually unnecessary.
   • On initial presentation, other possible causes, such as transient ischemic attack, retinal disease, partial seizures, polycythemia, thrombocytosis, and vasculitis should be excluded based on clinical assessment and/or investigations where appropriate.
   • Anticonvulsants and calcium antagonists, such as verapamil, may reduce severity and frequency of migraine aura without headache.13

12. A systematic review and meta-analysis found that a patient experiencing migraine with aura has twice the risk of ischemic stroke compared with the general population. This risk is substantially increased in smokers (relative risk [RR] 9.03, 95% confidence interval [CI] 4.22–19.34) and in women taking oral contraceptives (RR 7.02, 95% CI 1.51–32.68). The risk of ischemic stroke does not appear to be increased in patients experiencing migraine without aura. Analysis did not suggest an increased risk of death from cardiovascular disease.14

### ACUTE TREATMENT

13. Determining the optimal acute therapy for an individual patient can be challenging. Although medications from several different classes, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and triptans may be effective in the acute treatment of migraine, it is difficult to determine the preferred regimen as the classes have not generally been compared to each other. Complete pain relief is not always possible to achieve,8 and the individual response to specific acute therapy is difficult to predict.15

14. The following general principles apply in determining the appropriate acute therapy for an individual patient.
   • Several trials of acute medication may be necessary to determine the best option.
   • Different medications may be needed for attacks of varying severity.
   • Patients with severe migraines should have a rescue plan if their usual medication does not consistently provide relief.

### The Visual Aura Rating Scale (VARS)6

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<tr>
<th>Description</th>
<th>Duration</th>
<th>Scoring</th>
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<tr>
<td>Duration</td>
<td>5 to 60 minutes</td>
<td>3 points</td>
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<tr>
<td>Gradual development</td>
<td>≥ 5 minutes</td>
<td>2 points</td>
</tr>
<tr>
<td>Scotoma</td>
<td></td>
<td>2 points</td>
</tr>
<tr>
<td>Zigzag lines</td>
<td></td>
<td>2 points</td>
</tr>
<tr>
<td>Unilateral presentation</td>
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A VARS score ≥ 5 has a sensitivity of 91 to 96% and a specificity of 96 to 98% for migraine aura.
• Combinations of acute medications may be effective for some patients. (i.e., triptan plus NSAID)
• Medication is most effective if taken early in the attack. For instance, it is best to take triptans at headache (but not aura) onset.15

15. Two treatment approaches may be useful to manage acute headache.
• Stratified care: Medication choice is based on severity of attack, degree of disability, and previous response. This is likely the most effective approach.
• Step care across attacks: A medication is used for several attacks. If it is not effective enough, a different medication, such as a triptan, is then prescribed.15

16. Medications commonly used for acute treatment may result in medication overuse headache. Limiting their use can prevent this complication.
• Limit acetaminophen, acetylsalicylic acid (ASA), and NSAIDs to a maximum of 14 days per month.
• Limit triptans, ergotamine, opioids, and combination analgesics to a maximum of nine days a month.

17. The Canadian Headache Society guidelines for the use of acute migraine medications provide the evidence level and strength of recommendation for each medication. See Appendix 3 for a summary of these recommendations.15

18. Clinical trials evaluating the efficacy of triptans generally compare the medications to placebo, and not to each other. To estimate the relative potential benefits of triptans compared to each other, a network meta-analysis of 74 randomized controlled trials was undertaken. A network meta-analysis approach uses statistical methods to indirectly infer the relative benefits of the various triptans based on how they perform against placebo. The analysis looked at pain-free response at 2 and 24 hours and found that eletriptan, rizatriptan, zolmitriptan and sumatriptan statistically tended to provide better two-hour pain free responses than other triptans; there were no major clinically relevant differences in the efficacy of the medications at 24 hours. The study was funded by the makers of an eletriptan. The results of the analysis are summarized in Appendix 3.16

a) Triptans should not be used in patients with ischemic cardiac or cerebrovascular disease, hemiplegic migraine or in patients taking monoamine oxidase inhibitors.8

b) Although there is a risk of serotonin syndrome in patients taking selective serotonin reuptake inhibitors, they are not contraindicated and the reported absolute risk of serotonin syndrome is generally low (< 0.03%).17,18

c) Patients with a poor response or side effects with one triptan can benefit from a therapeutic trial of a different triptan.15

19. It has been reported that, within 48 hours following the initial acute treatment, migraine headaches recur in more than 50% of cases presenting to an emergency department. A meta-analysis of 905 patients in eight high-quality RCTs showed that steroids reduced the rate of recurrence of moderate-to-severe headache within 72 hours following acute migraine treatment (RR 0.71; 95% CI 0.59–0.86 for all headaches; NNT=10 and RR 0.68; 95% CI 0.55–0.84 for headaches that were moderate-to-severe at presentation).19
• Although intravenous doses of 15 mg or more of dexamethasone appeared to be the most effective, more research is needed on the optimal preventive dosage for emergency room treatment of migraine.

PROPHYLAXIS

20. Although the evidence related to migraine triggers is not robust, it is worthwhile to have patients examine potential triggers that may contribute to their headache frequency. The five most common triggers identified by migraine patients are stress, skipped meals, weather change, lack of sleep, and, in women, hormonal changes. Food triggers can be individual and are identified only by about one-third of migraine sufferers, but may involve additives, such as monosodium glutamate and aspartame, alcohol, and higher doses of caffeine (> 300 mg daily). Although not all triggers are avoidable, a headache diary (see Info point 6) may help to identify modifiable triggers.15

21. For patients who require prophylaxis of their migraine headache, choosing when to start and what to use is challenging for both patient and clinician, as all drugs have incomplete efficacy and most are associated with side effects. About 25% of all patients with migraine may benefit from prophylaxis. General principles of prophylaxis are the following:
• Clinical judgment determines when to initiate prophylaxis and which drug to try first.
• Prophylaxis does not replace lifestyle and migraine trigger management.
• As migraine is a chronic medical condition, effective management requires a patient and clinician partnership.
Patients starting prophylaxis should first be evaluated for medication overuse.\textsuperscript{20}

22. Prophylaxis is a reasonable option for the following patients:
   • **Patients who suffer significant disability despite appropriate acute therapy** – patients with more than three moderate or severe headache days a month when acute medications are not reliably effective.
   • **Patients with a high frequency of medication use (i.e., more than eight headaches a month)** – even though headaches may respond well to treatment; which patients may be at risk of medication overuse headache or significant systemic side effects.
   • **Patients with contraindications or intolerance to acute therapies.\textsuperscript{20}**

23. Migraine prophylaxis should be discontinued in the following situations:
   • **Int tolerable adverse effects** – Another prophylactic medication should be tried.
   • **Insufficient efficacy** – If no benefit after two months at target dose, it is appropriate to trial a second prophylactic medication.

24. Little evidence indicates the optimal duration of successful prophylaxis, which is defined as at least a 50% reduction in headache days. Generally, discontinuation may be considered after six to 12 months of successful prophylaxis. Most patients eventually relapse after discontinuation. Long-term prophylaxis may be appropriate for patients with very disabling migraine and for those with a long history of frequent migraine.\textsuperscript{20}

25. **Medication overuse headache** – Analgesics taken for painful conditions other than headache may also produce medication overuse headache. Medication overuse makes prophylaxis less effective. Evidence from two small, double-blind, randomized controlled trials (n=59 and 50 respectively), however, suggests prophylaxis using topiramate may be effective and well-tolerated in patients experiencing medication overuse, and may reduce acute medication use.\textsuperscript{20,22} A small open-label withdrawal study (n=56) found that initiation of prophylaxis prior to discontinuation of acute medication reduces total headache frequency better than abrupt withdrawal alone of acute medication.\textsuperscript{23}


27. The Canadian Headache Society guidelines for migraine prophylaxis also indicate the evidence level and strength of recommendation for each medication. See Appendix 4 for a detailed summary of these recommendations. The following medications are recommended for prophylaxis:

**Strong recommendation**\textsuperscript{20} (Applicable to most patients and benefits outweigh risks):
   • High-quality evidence for efficacy: Amitriptyline, metoprolol, propranolol, topiramate
   • Moderate-quality evidence for efficacy: Butterbur, candesartan, nadolol
   • Low-quality evidence for efficacy: Coenzyme Q10, magnesium citrate, riboflavin

**Weak recommendation**\textsuperscript{20} (Balance between risks and benefits closer or more uncertain and whether the intervention is suitable for an individual patient depends on clinical situation):
   • High-quality evidence for efficacy: Divalproex sodium, pizotifen
   • Low-quality evidence for efficacy: Lisinopril, venlafaxine, verapamil.

**Note:** A recent meta-analysis of five RCTs of gabapentin (900–3000 mg) showed no evidence of efficacy for migraine prophylaxis.\textsuperscript{24}

28. Consider the patient holistically when selecting initial prophylactic therapy. Amitriptyline or venlafaxine may be most useful if the patient has depression. Similarly, as topiramate is associated with weight loss, this agent may be preferred for patients with obesity. An antihypertensive may be useful for patients with hypertension.\textsuperscript{20}

29. Menstrual migraines can often be more frequent, severe, and more refractory to standard treatment than non-menstrual migraine. Prophylactic therapy is often the best approach. For patients with predictable cycles, short-term prophylaxis with a triptan can be considered, beginning two days before menstruation and lasting six days. A 2012 meta-analysis of six good quality RCTs suggests that frovatriptan and zolmitriptan are the preferred agents balancing side effects and efficacy.\textsuperscript{25}
   a) Estrogen withdrawal is the likely pathophysiology of menstrual migraine. Extended-use oral contraceptives may play a role in otherwise healthy women, particularly if reliable contraception is needed, there is no migraine with aura, and no other contraindications exist.
   b) Migraine without aura is not considered a contraindication to combined oral contraceptive use, and literature suggesting even a small increased risk of stroke in this situation is inconsistent (see info point 12).\textsuperscript{15,26}
30. Acupuncture for prophylaxis was reviewed in a Cochrane meta-analysis of 22 trials with 4419 participants. Compared with either usual care, (which generally involved treatment of acute attacks), or prophylactic drug therapy, overall headache frequency was slightly reduced at 3 to 4 months following treatment. (standard mean difference -0.43 (-0.60 to -0.27) and -0.26 (-0.41 to -0.11) respectively)

- Acupuncture had fewer adverse effects than drug therapy, when compared with sham acupuncture alone. Five higher quality studies showed no significant differences between the acupuncture and sham procedures for migraine prophylaxis. Sham procedures may have some therapeutic benefit themselves, which could account in part for this result. Clinicians may wish to consider acupuncture as a treatment option in patients interested in this therapy.27

31. OnabotulinumtoxinA has been compared to placebo and to amitriptyline in chronic migraine. Two large placebo-controlled trials included 1384 participants, two-thirds of whom met medication overuse criteria. A pooled analysis of the trials found onabotulinumtoxinA was significantly more effective than placebo in reducing the number of headache days.28 A randomized, but not blinded, trial compared onabotulinumtoxinA with amitriptyline in 72 patients and found similar benefits with both therapies. The number of days with pain was reduced by 50% in 72% for patients in the amitriptyline group and in 68% of the onabotulinumtoxinA group.29

PATIENT RESOURCES

32. Patient handouts on migraine, tension headache, medication overuse headache, and migraine prophylaxis are available at http://www.ihe.ca/research/the-alberta-ambassador-program/headache-guideline/headache-guideline-1/patient-resources-1/ (also see Patient Handout at the end of the module)

THE BOTTOM LINE

- Screen patients with headache for migraine.
- Suspect migraine in patients who appear to have recurring “sinus” headache.
- Develop a strategy to implement acute therapy for patients with migraine.
- Consider prophylaxis for patients with disabling headaches, those with insufficient relief from acute therapies and those with frequent use of acute therapies

CASE COMMENTARIES

Case 1: Dora, female, age 35

What further information would be helpful for you?

A more detailed history including headache characteristics and symptoms would be useful (Info points 4, 8; Appendix 1). Knowing what impairment was associated with the headaches would also help in determining treatment (Info point 3). Knowing how much medication she is taking and when during the headache she is taking it can confirm if these are being used in the most effective fashion (Appendix 3). It may also be useful to determine Dora’s risk factors and/or triggers for her headaches. Physical examination with a neurologic examination is appropriate.

Part Two

What would you do next?

Dora’s headaches meet the criteria for migraine headache (Appendix 1). It may be useful to have Dora keep a headache diary for a month (Info point 6). In terms of acute treatment of headache, Dora may be taking the medication too late to derive the maximum benefit from it (Info point 14). If she is willing to continue her current medication, she should take it as soon as the headache begins. Other options for acute management include the triptans (Info point 18; Appendix 3). At six headaches a month, it may be worthwhile to consider prophylactic therapy (Info points 21, 22; Appendix 4).

Part Three

How would you manage Dora now?

Dora may do better with another triptan with a different side effect profile (Info point 18). It is important to note that triptans may not be covered on provincial formularies. It is also appropriate to discuss prophylaxis with her (Info points 21, 22). Numerous medications have been found to be effective, including amitriptyline, propranolol, and topiramate, and several non-prescription options (Info point 27; Appendix 4). Side effect profile and cost are factors to consider when deciding on the most appropriate medication (Info point 28; Appendix 4).

Case 2: Michael, male, age 52

What additional information would be helpful?

It is important to determine his cardiovascular risk factors and any family history of migraine and cardiovascular disease. With respect to these episodes, it is important
to determine whether there is any motor weakness, how long they have been going on, how frequently they occur, and whether they are unilateral or bilateral (Info points 9, 11, 12). It would also be useful to perform a physical examination and a neurological examination to assess for any focal findings.

**Part Two**

**What investigations might you order?**

If Michael’s symptoms had started only a few weeks ago, a transient ischemic attack (TIA) would be a real concern (Info point 11). In that situation carotid Doppler would be useful to rule out carotid pathology, and an MRI (if available) or CT scan (Info point 7) would have been useful to rule out a vascular or space-occupying lesion. Consider an ESR or CRP to screen for arteritis. Depending on resources, a referral to a stroke clinic or neurologist would also have been appropriate. In this case, with positive visual symptoms (as opposed to loss of vision) that have been stable for three months, this diagnosis is unlikely (Info point 11). Although his presentation has many characteristics of a typical aura (based on the history provided, he would score 7 on the VARS scale) (Info point 10), there are some red flags: new onset of symptoms over 50 years of age and atypical neurological symptoms occurring without actual headache (Info point 8; Appendix 2).

**Part Three**

**What would be your approach for Michael?**

Michael appears to be having a migraine aura without headache. Based on a frequency of one or two episodes a week, it is appropriate to discuss prophylactic therapy with Michael. Calcium channel antagonists and anticonvulsants have been shown to be effective in this migraine variant (Info point 11).

**Case 3: Connie, female, age 32**

**How would you manage Connie?**

Connie appears to have chronic migraine (Info point 9). It is important to find out if all Connie’s headaches are the same (i.e., similar symptoms, intensity, and impact). She also has a high risk of medication overuse headaches as she has used codeine-containing medication for 12 days out of the month (Info point 16).

Several options are available for addressing Connie’s migraines. If triggers and the potential impact of lifestyle factors have not been explored, this should be discussed with Connie (Info point 21). In terms of acute medication, another triptan may not have the same side effects as sumatriptan (Info point 18; Appendix 3). It is also worth noting that the chest pain occurring with triptans is not associated with cardiac ischemia. Although frovatriptan and zolmitriptan may be better for migraines that occur in close temporal relation to menstrual periods (Info point 29), if she requires treatment of acute attacks at other times, eletriptan or rizatriptan may give her the best 24 hour pain free response (Appendix 3).

It is worth starting an additional prophylactic medication at the same time as an analgesic washout (Info point 25, 26). In terms of prophylactic therapy, taking the amitriptyline 12 hours before she is due to get up in the morning may help deal with the daytime somnolence. Nortriptyline may be better tolerated. Given her mood disorder, if a different prophylactic medication is tried, an antidepressant, such as venlafaxine (Effexor®) may be an effective alternative (Info point 28; Appendix 4). Also, as she has problems with menstrual migraine, hormone manipulation may prove beneficial (Info point 29). A referral to a migraine expert or a migraine clinic may be helpful depending on community resources.

**If Connie asked about other options for contraception, what would be your approach?**

As long as there are no other contraindications, a trial of a birth control pill (particularly sustained use) may be useful, as her migraines worsen before her period (Info point 29).

**If Connie had migraine with aura, how might your approach to contraception differ?**

Oral contraceptive pills substantially increase the risk of ischemic stroke in migraine with aura but not in migraine without aura. A progesterone-only contraceptive or intrauterine device would be a better choice (Info point 12).

**Real case scenario**

Neurology saw her in consultation and tried her on gabapentin (Neurontin®) and topiramate (Topamax®), neither of which she could tolerate. She underwent massage therapy and chiropractic manipulation, but ended up having Botox® injections which have reduced her headaches to once weekly.

We always welcome your input. If you would like to provide feedback on this module, the following link will take you to an electronic survey: https://adobeformscentral.com/?f=H8YNukiMNdzZgrdNlzXIJg
Disclosures of competing interests:

No competing interests were declared for Christine Thornton, William Davenport, Elizabeth Shaw, and Joanna Gorski.

Ted Findlay is a member of the Guideline Development Group, Alberta TOP Guideline for Primary Care Management of Headache in Adults.

Werner Becker is on the Medical Advisory boards for Allergan, Amgen, Tribute, St. Jude and ElectroCore. He has received speaker honoraria from Allergan, Tribute, and Serono. Dr. Becker has participated in industry sponsored multicentre clinical trials with Amgen and St. Jude.

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Web-based resources cited within the module were active as of October 2014.

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<th>LEVELS of EVIDENCE</th>
<th>Evidence Level</th>
<th>Type of Evidence Included</th>
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|                   | High             | • Systematic reviews/meta-analyses that include a wide range of well-designed studies (few limitations/risk of bias, directly applicable to target population); summary estimate has a narrow confidence interval.  
• Large, well designed RCTs.  
Study conclusions are unlikely to be strongly affected by information from future studies. |
|                   | Moderate         | • Systematic reviews/meta-analyses of studies with more limitations/risk of bias (less well designed RCTs, cohort, case control studies), or when the summary estimate has a wide confidence interval.  
• Single, moderate sized, well-designed RCTs.  
• Well-designed, consistent, controlled but not randomized trials.  
• Large cohort studies.  
Study conclusions could change with additional information from future studies. |
|                   | Low              | • Small RCTs with a high risk of bias.  
• Controlled or cohort studies with significant limitations/risk of bias or significant variation between study results.  
Evidence from well-designed studies in representative populations is lacking or insufficient. |
|                   | Very Low         | • Expert opinion  
• Individual case reports or series |


### APPENDIX 1. International Headache Society Criteria for Migraine

#### Migraine without aura

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<tbody>
<tr>
<td>A</td>
<td>At least 5 attacks fulfilling criteria B–D</td>
</tr>
<tr>
<td>B</td>
<td>Headache attacks lasting 4–72 hours (untreated or unsuccessfully treated)</td>
</tr>
</tbody>
</table>
| C | Headache has at least 2 of the following characteristics:  
  • Unilateral location  
  • Pulsating quality  
  • Moderate or severe pain intensity  
  • Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs) |
| D | During headache, at least one of the following is present  
  • Nausea and/or vomiting  
  • Photophobia and phonophobia |
| E | Not attributed to another disorder |

#### Migraine with aura

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least 2 attacks fulfilling criteria B–D</td>
</tr>
</tbody>
</table>
| B | Aura consisting of at least one of the following, but no motor weakness:  
  • Fully reversible visual symptoms including positive features (e.g., flickering lights, spots, or lines) and/or negative features (i.e., loss of vision)  
  • Fully reversible sensory symptoms including positive features (i.e., pins and needles) and/or negative features (i.e., numbness)  
  • Fully reversible dysphasic speech disturbance |
| C | At least two of the following:  
  • Homonymous visual symptoms and/or unilateral sensory symptoms  
  • At least one aura symptom develops gradually over \( \geq 5 \) minutes and/or different aura symptoms occur in succession over \( \geq 5 \) minutes  
  • Each symptom last \( \geq 5 \) minutes and \( \leq 60 \) minutes |
| D | Headache fulfilling criteria B – D for migraine without aura begins during the aura or follows aura within 60 minutes |
| E | Not attributed to another disorder |

### Sources (reproduced with permission):


## APPENDIX 2. Differential Diagnosis of Migraine Headache and Migraine Aura

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute glaucoma</td>
<td>Associated with blurred vision, nausea, vomiting and seeing halos around lights; ophthalmologic emergency</td>
</tr>
<tr>
<td>Acute or chronic subdural hematoma</td>
<td>Antecedent trauma, may have subacute onset, altered level of consciousness or neurologic deficit may be present</td>
</tr>
<tr>
<td>Acute severe hypertension</td>
<td>Marked blood pressure elevation (systolic &gt; 210 mm Hg or diastolic &gt; 120 mm Hg); may have confusion or irritability</td>
</tr>
<tr>
<td>Benign intracranial hypertension (pseudotumour cerebri)</td>
<td>Often abrupt onset, associated with nausea, vomiting, dizziness, blurred vision and papilledema, may have cranial nerve VI palsy; aggravated by coughing, straining, or changing position</td>
</tr>
<tr>
<td>Carbon monoxide poisoning</td>
<td>May be insidious or associated with dyspnea; occurs more commonly in colder months</td>
</tr>
<tr>
<td>Carotid dissection</td>
<td>Cause of stroke; can be spontaneous or follow minor trauma or sudden neck movement; unilateral headache or face pain; ipsilateral Horner syndrome</td>
</tr>
<tr>
<td>Cervical spondylosis</td>
<td>Worse with neck movement, posterior distribution; pain is neuralgic in character and sometimes referred to vertex or forehead; more common in older patients</td>
</tr>
<tr>
<td>Cluster headache</td>
<td>Uncommon; sudden onset; duration of minutes to generally &lt; 3 hours; repeats over a course of weeks, then may disappear for months or years; may occur at the exact same time of day or night (“alarm clock headaches”); unilateral lacrimation and nasal congestion; severe unilateral and periorbital pain; more common in men; patient is restless or agitated during episodes</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>Neurologic abnormalities, confusion, altered mental status or level of consciousness</td>
</tr>
<tr>
<td>Frontal sinusitis</td>
<td>Usually worse when lying down; nasal congestion; tenderness over affected sinus</td>
</tr>
<tr>
<td>Greater occipital neuralgia</td>
<td>Occipital location; tenderness at base of skull; pain is neuralgic in character and referred to vertex or forehead</td>
</tr>
<tr>
<td>Intracranial, cerebral neoplasm</td>
<td>Worse on awakening; generally progressive; aggravated by coughing, straining, or changing position; neurological exam often abnormal</td>
</tr>
<tr>
<td>Medication-induced/medication overuse headache</td>
<td>Chronic headache with features of both migraine and tension-type; tends to occur daily; hormone therapy or hormonal contraceptives are frequent culprits; analgesic rebound/medication overuse headache – requires analgesia a minimum of 2-3 days weekly; (&gt; 10 days/month)</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Fever; meningeal signs</td>
</tr>
<tr>
<td>Migraine aura</td>
<td>Differential includes: transient ischemic attack (TIA); seizure; syncope; vestibular disorders; determine nature of symptoms, progression, duration, and timing as well as symptoms occurring both before and after the events; accompanying focal or nonfocal symptoms</td>
</tr>
<tr>
<td>Postconcussion syndrome</td>
<td>Antecedent head trauma; vertigo, lightheadedness; poor concentration and memory; lack of energy; irritability and anxiety</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>Explosive onset of severe headache (thunderclap headache); 10%-50% may be preceded by lower-grade sentinel headaches</td>
</tr>
<tr>
<td>Temporal arteritis</td>
<td>Almost exclusively in patients older than 50 years; associated with tenderness of scalp or temporal artery and jaw claudication; visual changes</td>
</tr>
<tr>
<td>Temporomandibular joint dysfunction</td>
<td>Pain generally involves the temporomandibular joint and temporal areas; associated with symptoms when chewing</td>
</tr>
<tr>
<td>Tension-type headache</td>
<td>Common; often co-exists with migraine; greater than 90% of tension-type headaches diagnosed in primary care are actually migraines; duration 30 minutes to 7 hours; attacks generalized throughout head; typically bilateral; nonpulsating; mild-to-moderate intensity without limiting activity; no or mild nausea or vomiting (moderate or severe nausea or vomiting rules out TT headache)</td>
</tr>
<tr>
<td>Trigeminal neuralgia</td>
<td>Brief episodes of sharp, stabbing pain and trigeminal face distribution</td>
</tr>
</tbody>
</table>

**Sources:**

### APPENDIX 3. Acute Management of Migraine Headache

#### Strong recommendation for use (general applicability)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Evidence Level</th>
<th>Migraine Severity</th>
<th>Dose Range</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylsalicylic acid</td>
<td>High</td>
<td>All severities</td>
<td>975–1,000 mg</td>
<td>First line</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>High</td>
<td>All severities</td>
<td>400 mg</td>
<td>First line</td>
</tr>
<tr>
<td>Naproxen sodium</td>
<td>High</td>
<td>All severities</td>
<td>500–825 mg</td>
<td>First line</td>
</tr>
<tr>
<td>Diclofenac potassium</td>
<td>High</td>
<td>All severities</td>
<td>50 mg</td>
<td>First line</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>High</td>
<td>Mild-moderate</td>
<td>1,000 mg</td>
<td>First line</td>
</tr>
<tr>
<td>Triptan</td>
<td>High</td>
<td>Moderate-severe</td>
<td>Second-line; See below</td>
<td></td>
</tr>
<tr>
<td>Add naproxen sodium to sumatriptan</td>
<td>High</td>
<td>Moderate-severe</td>
<td>500 mg</td>
<td>Third line</td>
</tr>
<tr>
<td>Add NSAID to other triptan</td>
<td>Low</td>
<td>Moderate-severe</td>
<td>See individual dosing</td>
<td>Third line</td>
</tr>
</tbody>
</table>

#### Weak recommendation for use (may be used for some patients)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Evidence Level</th>
<th>Migraine Severity</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dihydroergotamine</td>
<td>Moderate</td>
<td>Moderate-severe</td>
<td>–Intranasal or subcutaneous</td>
</tr>
<tr>
<td>Ergotamine</td>
<td>Moderate</td>
<td>Moderate-severe</td>
<td>–When triptans are unavailable or ineffective –Not for routine use</td>
</tr>
<tr>
<td>Tramadol plus acetaminophen</td>
<td>Moderate</td>
<td>Moderate-severe</td>
<td>–When triptans and/or NSAIDs are ineffective or contraindicated –As rescue medication when regular acute therapy is ineffective –Frequency of use should be monitored with headache diary –Not for routine use</td>
</tr>
<tr>
<td>Codeine-containing combinations</td>
<td>Low</td>
<td>Moderate-severe</td>
<td>–When triptans and/or NSAIDs are ineffective or contraindicated –As rescue medication when regular acute therapy is ineffective –Not for routine use</td>
</tr>
</tbody>
</table>

#### The triptans

<table>
<thead>
<tr>
<th>Triptan</th>
<th>Oral Dose*</th>
<th>Maximum Daily Dose</th>
<th>Cost of 6 doses</th>
<th>2-hour Pain-free Response OR** (95% CI)</th>
<th>24-hour Sustained Pain-free Response OR** (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eletriptan (Relpax®)</td>
<td>20–40 mg</td>
<td>80 mg</td>
<td>$80</td>
<td>4.95 (3.75, 6.59)</td>
<td>3.66 (2.63, 5.15)</td>
</tr>
<tr>
<td>Rizatriptan (Maxalt®)</td>
<td>5–10 mg</td>
<td>30 mg</td>
<td>$42–107</td>
<td>4.44 (3.51, 5.69)</td>
<td>2.85 (2.00, 4.10)</td>
</tr>
<tr>
<td>Zolmitriptan (Zomig®)*</td>
<td>1.25–2.5 mg</td>
<td>10 mg</td>
<td>$38–98</td>
<td>3.40 (2.54, 4.53)</td>
<td>3.35 (2.28, 4.96)</td>
</tr>
<tr>
<td>Sumatriptan (Imitrex®)*</td>
<td>25–100 mg</td>
<td>200 mg</td>
<td>$54–105</td>
<td>3.24 (2.45, 3.97)</td>
<td>1.94 (1.43, 2.63)</td>
</tr>
<tr>
<td>Almotriptan (Axert®)</td>
<td>6.25–12.5 mg</td>
<td>25 mg</td>
<td>$75</td>
<td>2.45 (1.77, 3.39)</td>
<td>2.98 (1.97, 4.51)</td>
</tr>
<tr>
<td>Naratriptan (Amerge®)</td>
<td>1–2.5 mg</td>
<td>5 mg</td>
<td>$50–104</td>
<td>1.68 (1.04, 2.72)</td>
<td>1.37 (0.64, 2.83)</td>
</tr>
<tr>
<td>Frovatriptan (Frava®)</td>
<td>2.5 mg</td>
<td>7.5 mg</td>
<td>$99</td>
<td>No data</td>
<td>No data</td>
</tr>
</tbody>
</table>

*Dose can be repeated in 2 hours
** OR compared with placebo
†available as a nasal spray; useful if nausea present
CI: Confidence interval; NSAID: nonsteroidal anti-inflammatory drug; OR: Odds ratio

Sources:


November 2014
# APPENDIX 4. Prophylactic Management of Migraine Headache

## Strong recommendation for use

<table>
<thead>
<tr>
<th>Agent</th>
<th>Evidence Level</th>
<th>Impression of Efficacy*</th>
<th>Initial dose</th>
<th>Titration</th>
<th>Target dose</th>
<th>Side effects</th>
<th>Cost per month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline†</td>
<td>High</td>
<td>Very effective</td>
<td>10 mg hs</td>
<td>10 mg/week</td>
<td>10–100 mg hs</td>
<td>Occasional dry mouth, drowsiness</td>
<td>$11–30</td>
</tr>
<tr>
<td>Topiramate†</td>
<td>High</td>
<td>Very effective</td>
<td>25 mg/day</td>
<td>25 mg/week</td>
<td>50 mg bid</td>
<td>Frequent, especially at high doses: Paresthesias, weight loss, altered taste, anorexia, fatigue, memory impairment</td>
<td>$74–77</td>
</tr>
<tr>
<td>Propranolol</td>
<td>High</td>
<td>Effective</td>
<td>20 mg bid</td>
<td>40 mg/week</td>
<td>40–120 mg bid</td>
<td>Infrequent fatigue, frequent reduction of heart rate and blood pressure</td>
<td>$10–15</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>High</td>
<td>Effective</td>
<td>50 mg bid</td>
<td>50 mg/week</td>
<td>50–100 mg bid</td>
<td>Infrequent fatigue, frequent reduction of heart rate and blood pressure</td>
<td>$10–16</td>
</tr>
<tr>
<td>Nadolol</td>
<td>Moderate</td>
<td>Effective</td>
<td>40 mg/day</td>
<td>20 mg/week</td>
<td>80–160 mg/day</td>
<td>Infrequent drowsiness</td>
<td>$23</td>
</tr>
<tr>
<td>Candesartan</td>
<td>Moderate</td>
<td>Effective</td>
<td>8 mg/day</td>
<td>8 mg/week</td>
<td>16 mg/day</td>
<td>Infrequent dizziness and fatigue</td>
<td>$9</td>
</tr>
<tr>
<td>Butcherb</td>
<td>Moderate</td>
<td>Effective</td>
<td>75 mg bid</td>
<td>NA</td>
<td>75 mg bid</td>
<td>Infrequent dizziness and fatigue</td>
<td>$50-65$</td>
</tr>
<tr>
<td>Coenzyme Q10</td>
<td>Low</td>
<td>Effective</td>
<td>100 mg tid</td>
<td>NA</td>
<td>100 mg tid</td>
<td>Infrequent dizziness and fatigue</td>
<td>$23</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>Low</td>
<td>Somewhat effective</td>
<td>400 mg/day</td>
<td>NA</td>
<td>400 mg/day</td>
<td>Infrequent dizziness and fatigue</td>
<td>$10</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Low</td>
<td>Somewhat effective</td>
<td>300 mg bid</td>
<td>NA</td>
<td>300 mg bid</td>
<td>Occasional soft stools and diarrhea</td>
<td>$10</td>
</tr>
</tbody>
</table>

## Weak recommendation for use (balance between benefits and harms less certain)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Evidence Level</th>
<th>Impression of Efficacy*</th>
<th>Initial dose</th>
<th>Titration</th>
<th>Target dose</th>
<th>Side effects</th>
<th>Cost per month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divalproex†</td>
<td>Moderate/high</td>
<td>Effective</td>
<td>250 mg/day</td>
<td>250 mg/week</td>
<td>750–1,500 mg divided bid</td>
<td>Hair loss.; Nausea, somnolence, dizziness, low platelet count, tremor (dose-related) Serious: agranulocytosis, aplastic anemia</td>
<td>$26–52</td>
</tr>
<tr>
<td>Pizotifen</td>
<td>Moderate</td>
<td>Effective</td>
<td>0.5 mg/day</td>
<td>0.5 mg/week</td>
<td>1–2 mg bid</td>
<td>Occasional weight gain, sedation</td>
<td>$20–47</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Low</td>
<td>Effective</td>
<td>37.5 mg/day</td>
<td>37.5 mg/week</td>
<td>150 mg/day</td>
<td>Occasional nausea, vomiting, drowsiness</td>
<td>$12</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>Low</td>
<td>Effective</td>
<td>20 mg/day</td>
<td>NA</td>
<td>20 mg/day</td>
<td>Infrequent</td>
<td>$6</td>
</tr>
<tr>
<td>Verapamil</td>
<td>Low</td>
<td>Somewhat effective</td>
<td>40 mg tid</td>
<td>40 mg/week</td>
<td>240–480 mg</td>
<td>Infrequent mild constipation</td>
<td>$30</td>
</tr>
</tbody>
</table>

*Impression of efficacy: Very effective: Most people experience clinically significant improvement; Effective: Some people experience clinically significant improvement; Somewhat effective: Few people experience clinically significant improvement.
† Shown to be effective in chronic migraine

**Sources:**


November 2014
Migraine Headaches

How do I know if I have a migraine?
You probably have migraines if your headaches come with two or more of these symptoms: nausea, light sensitivity, and problems doing usual activities.

Will I need x-rays, an MRI/CT, or laboratory tests?
For most people x-rays, MRI/CT and laboratory tests are not needed to diagnose headaches. Your doctor will order these tests only if a less common specific cause for headache is suspected.

Are there different kinds of migraines?
Migraines often start with a warning sign called an aura, lasting 15 to 30 minutes. During an aura, you may see flashing lights and colours, or have other changes in your vision. Many migraines do not start with an aura. They may start more slowly than migraines with aura and last longer. With both types of migraine, the pain may be on one or both sides of your head.

How long do migraines usually last?
Migraines may last for only a few hours or up to three days. They may happen only once or twice a year, or as often as daily. Migraines are different for each person.

What things may “trigger” a migraine?
In some people, certain things can set off a migraine, such as changes in weather, stress, missing meals, lack of sleep, menstrual periods, the birth control pill, certain foods or alcohol. It is often useful to keep a diary of your headaches to help identify your triggers. In some people, some foods can also trigger migraines, such as aged, canned, cured or processed meats or foods, such as bologna, pepperoni, hot dogs, and aged cheese; alcoholic beverages, especially red wine; aspartame (some brand names: NutraSweet™ and Equal™); too much caffeine; meat tenderizer or monosodium glutamate (MSG); chocolate, cocoa, and carob; nuts and peanut butter.

How are migraines treated?
A few things might help you feel better: lying down in a dark, quiet room; putting a cold, damp cloth over your forehead; massaging your scalp using a lot of pressure or putting pressure on your temples.

There are two types of medicines for migraines: some to help get rid of the pain and others to prevent headaches from happening. To treat the pain of a migraine, you can try over-the-counter medicines like acetaminophen (Tylenol®) and ibuprofen or naproxen (Advil®, Motrin® or Aleve®). These medications should be used as soon as the aura occurs or the headache starts. If they are not helpful, your healthcare provider may prescribe medicines called triptans. If one triptan does not work very well for you, another may work better. Seven different triptans are available in Canada. Narcotics may occasionally be necessary but are best avoided.

If your headaches occur more than two or three times a month and interfere with your daily life, you may discuss medication to prevent migraines from occurring with your healthcare provider. Preventive medications need to be taken every day and include beta blockers, such as metoprolol and propranolol; antidepressant medications, such as amitriptyline; and anti-seizure medications, such as topiramate. Some herbal medications, such as butterbur; and supplements, such as riboflavin, coenzyme Q10, and magnesium have also been shown to be helpful in some people. You may need to try several to find the right one for you.