>Statement of Objectives

After reading this lesson you will be able to:

1. Discuss and recognize symptoms of migraine headache.
2. Assess the level of disability associated with an individual's migraine headache condition.
3. Recognize headache alarm symptoms that must be referred for immediate medical attention.
4. Discuss the pathophysiology and triggers of migraine headache.
5. Recommend individualized, appropriate nonpharmacologic and pharmacologic treatment and prevention for migraine headache management.

>Instructions

1. After carefully reading this lesson, study each question and select the one answer you believe to be correct. Circle the appropriate letter on the attached reply card.
2. Complete the card and mail, or fax to (416) 764-3937.
3. Your reply card will be marked and you will be advised of your results in a letter from Rogers Publishing.
4. To pass this lesson, a grade of 70% (14 out of 20) is required. If you pass, your CEU(s) will be recorded with the relevant provincial authority(ies).
(Note: some provinces require individual pharmacists to notify them.)

>Disclosure

The author, expert reviewers and Pharmacy Practice magazine have each declared that there is no real or perceived conflict of interest with the sponsor company.

1 CEU

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THE ROLE OF THE PHARMACIST IN IDENTIFICATION, REFERRAL AND MANAGEMENT OF MIGRAINE HEADACHE

by Tom Smiley, BScPhm, Pharm D

INTRODUCTION

Severe migraine headache rates are one of the most disabling of chronic disorders according to the World Health Organization. In fact, in the Global Burden of Disease Study published by WHO and other groups, severe migraine ranked in the highest disability class along with additional conditions such as quadriplegia. The 1998/1999 Statistics Canada National population Health Survey reported that 7.9% of Canadians over age 12 have been diagnosed with migraine headaches.[1] Three times as many women as men suffer from this disabling disorder.[1] Many lifestyle factors as well as medication overuse may contribute to increased risk for onset of migraine symptoms. Management of migraine therefore should include patient education about the control of acute migraine attacks and prevention. Management plans that include patient goals and routine evaluation should be the cornerstone of migraine management.[2] Pharmacists are in an ideal position to assist patients through appropriate referral to physician for diagnosis, and collaborate with patients and physicians towards effective management of migraine headaches through well-developed patient care plans.

DEFINING MIGRAINE HEADACHES

Patients may confuse severe headache pain with migraine attacks and vice versa. This can potentially lead to inappropriate management and delayed treatment. It is therefore important to understand the difference between migraine and other types of headaches so that appropriate referral and management takes place. However, migraine symptoms vary considerably between and among individuals and can be difficult to diagnose.[3] Any patient with chronic, recurrent headache-type pain that interferes with quality of life, or headaches that have become more frequent or progressive should be referred to a physician for assessment and diagnosis.

Migraine has been described as an "idiopathic, recurring headache disorder manifesting as attacks typically lasting 4 to 72 hours. Typical characteristics of migraine headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity, and association with nausea, photo- and phonophobia."[3]

Migraine headaches can occur with or without aura. Aura symptoms occur in about 30% of migraine sufferers and most often precede the headache pain by 10 to 60 minutes.[4] Visual disturbances such as scotomata (patient perceives a blind or dark spot in the visual field) or photopsia (uniform flashes of light) are the most common type of aura. Many additional visual experiences with aura have been reported.

Migraine headaches can be classified as mild, moderate and severe.[3]

- With mild attacks, patients can continue their usual activities with only minimal disruption.
- In moderate attacks, the patient is still able to function but has some impairment with usual activities.
- In severe attacks, the patient is unable to continue their normal activities and can function in any capacity only with severe discomfort and impaired efficiency.
- In ultra-severe cases, there is inability to function for more than 72 hours in any useful capacity.

Symptoms of Migraine Headache

Table 1 outlines criteria for diagnosing migraine with or without aura according to guidelines published by the Canadian Headache Society.[3]

The MIDAS (MIgraine Disability ASsessment Program) may be helpful in assessing the severity of migraine headaches (see Table 2). It is downloadable online (in 10 different language options) at www.midas-migraine.net/edu/question/default.asp.

An additional tool that can be used to measure impact of headache on ability to function is the Headache Impact Test or HIT-6 test. It consists of 6 questions that are scored, with total scores indicating level of ability to function on the job, at school, at home and in social situations. It can be downloaded online at www.headachetest.com/HIT6/PDFS/English.pdf. It is available in 25 different languages.

Headache Alarm Symptoms

It is very important that migraine headache not be mistaken for pain caused by more serious underlying causes. Alarms that should prompt immediate referral include:[3,5]

TABLE 1 **Criteria for diagnosing migraine condition[3]**

1. At least 5 attacks fulfilling criteria 2 to 4.
2. Each attack, untreated or unsuccessfully treated, lasts 2 to 72 hours.
3. The attack has at least 2 of the following characteristics.
   - Unilateral location: Migraines can be bilateral in 30 to 40% of cases, and sometimes pain begins on one side and later spreads to the other.
   - Pulsating quality: Over 50% of people report nonthrobbing pain during some attacks, and 30% of patients with tension-type headaches may report pulsating pain.
   - Moderate or severe intensity (inhibits or prohibits daily activity).
   - Pain is aggravated by walking up and down stairs, or by a similar, routine physical activity.
4. During an attack, at least one of the following symptoms should be present.
   - Nausea or vomiting: Nausea must be differentiated from anorexia (common with anxiety or tension-type headaches).
   - Photophobia (aversion to light), phonophobia (aversion to sounds or noise) and olfactophobia (aversion to odours).
5. There is no evidence from the patient's history that any other disease might be causing the headaches.

- The first or worst headache of the patient's life, especially if the onset of pain was rapid.
- A change in the frequency, severity or clinical features of the attack.
- New onset of headache in middle-age or later, or significant change in long-standing headache pattern.
- New or progressive headache that persists for days.
- Precipitation of head pain by coughing, sneezing or bending down.
- Presence of systemic symptoms such as myalgia, fever, malaise, weight loss, scalp tenderness or jaw claudication.
- Presence of focal neurological symptoms, or confusion, seizures or any impairment in the level of consciousness.
- Onset of headache during the night or on awakening in the morning (possibility of brain tumor). Because migraines may occur upon awakening, a referral to a physician is in order, without unduly alarming the patient.

PATHOPHYSIOLOGY OF MIGRAINE HEADACHES

THE EXACT CAUSE OF MIGRAINE HEADACHES IS unknown. There may be a heritable component. The vascular hypothesis promoted the theory that vasoconstriction and reduction in cerebral blood flow followed by compensatory vasodilatation and displacement of pain-sensitive intracranial structures was responsible for migraine headache.[4] However, recent research involving functional brain imaging suggests that symptoms are associated with episodic dysfunction of neural structures that control the cranial circulation.[4] The trigeminovascular system contains neurons that innervate the cerebral circulation. Potent vasodilator neuropeptides such as calcitonin gene-related peptide,

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ABOUT THE AUTHOR

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REVIEWERS

All lessons are reviewed by pharmacists for accuracy, currency and relevance to current pharmacy practice.

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TABLE 2 The MIDAS Questionnaire - Assessment of all headaches within the past 3 months

1. On how many days in the last 3 months did you miss work or school because of your headache?	_____ days
2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? (do not include days you counted in question 1 where you missed work or school)	_____ days
3. On how many days in the last 3 months did you not do household work because of your headaches?	_____ days
4. How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches? (Do not include days you counted in question 3 where you did not do household work)	_____ days
5. On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches?	_____ days
TOTAL	_____ **days**
A. On how many days in the last 3 months did you have a headache? (if a headache lasted more than 1 day, count each day)	_____ days
B. On a scale of 0 to 10, on average how painful were these headaches? (Where 0 = no pain at all, and 10 = pain as bad as it can be)	_____ days

Once questionnaire is complete, add up the total number of days from questions 1 to 5 (ignore A and B)

GRADE

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

* Questions A and B have been added to gain a basic understanding of the number of days that you are affected by a headache and how painful your headaches are.

TABLE 3 Factors that may precipitate migraine headache[4, 5,6]

- Stress
- Emotions
- Glare
- Hypoglycemia
- Altered sleep pattern
- Menses
- Exercise
- Weather changes
- Allergens
- Alcohol
- Carbon monoxide
- Excess caffeine use or withdrawal
- Foods containing MSG (e.g., Chinese food, canned soups, seasonings), tyramine, (e.g., red wine, ripened cheeses), nitrites (e.g., cured meat products), phenylethylamine (e.g., chocolate, cheese), aspartame (e.g., artificial sweeteners, diet sodas)
- Drugs
- Excess use or withdrawal (ergots, triptans, analgesics)
- Estrogens (e.g., oral contraceptives)
- Cocaine
- Nitroglycerin, antihypertensives (e.g., nifedipine, methyldopa, ACE Inhibitors, beta-blockers), selective serotonin reuptake inhibitors, danazol, indomethacin

substance P, and neurokinin A are released from these neurons and are likely involved in the etiology of migraine headache. Abnormalities in serotonin (5-hydroxytryptamine or 5-HT) are also likely involved in migraine pathophysiology. This theory is supported by the fact that 5-HT levels drop by nearly 50% during a migraine attack and that medications that stimulate 5-HT_1 receptors or increase 5-HT levels are therapeutic in the management of the condition.[4]

Migraine Triggers

Migraine headaches are often "triggered" by one or more factors. Although triggers of migraine headache have been identified, there is variance in the sensitivity of the brain to such triggers at any given time. Irregular activities, such as irregular sleep, exercise, and meals seem to be the trigger rather than the activity itself. The key message is to aim for regularity in habits rather than compiling a long list of foods and activities that are prohibited.

Foods containing neurotransmitter precursors, such as tyramine, tyrosine and phenylalanine are known to be triggers of migraines in many people.[6] Additional triggers can be found in Table 3.

NONPHARMACOLOGIC MANAGEMENT OF MIGRAINE

PATIENT EDUCATION IS A VERY IMPORTANT component of migraine management. Helping patients understand their diagnosis and understand realistic benefits and limitations of treatment options will help them feel in control of their condition. Encouraging patients to identify and avoid triggers and to be actively involved in their own management by tracking their own progress (e.g., with a symptom diary) may be especially beneficial.[7]

Headache diaries can help to identify triggers, evaluate the effectiveness of management strategies and track time between headaches. Patients can track their headaches online at www.myheadachediary.com. A downloadable print version of a headache diary can be found at www.fmpe.org/en/documents/handouts/handout_migraines.pdf.

During a migraine attack, the following suggestions may be helpful.[6]

- Application of cold or pressure to the head.
- Reduction of activity and of sensory input in a quiet or dark environment.
- Sleep may help alleviate the symptoms of a headache.

The following therapies are associated with varying levels of evidence in attempting to prevent or reduce the number of migraine attacks (as outlined in the Canadian "Guidelines for the nonpharmacologic management of migraine in clinical practice.")[6]

- **Biofeedback:** This management strategy utilizes monitoring instruments to detect, amplify and display internal physiologic processes on-line. One of the most successful techniques for migraine prophylaxis is thermal control, where the patient learns to elevate finger temperature during therapy sessions using a digital temperature-reading device. A meta-analysis of 25 controlled studies suggests that biofeedback is comparable in efficacy to prophylactic pharmacotherapy. It requires a substan-

TABLE 4 Summary of medications for treatment of acute migraine[3]

Medication	Dose	Risk Profile	Comments
Acetaminophen	650-1,300 mg q4h x 2 doses prn. Pediatric: 10-20 mg/kg/dose q4h x 2 doses prn	Potential for liver (and sometimes kidney) dysfunction with chronic use of high doses or with acute overdose. May increase INR with doses ≥2 g/day.[5]	Effective in childhood migraine. Considered less effective than NSAIDs and ASA for adults. May be used alone or in combination with caffeine/codeine. Drug of choice during pregnancy.
NSAIDs (most consistent evidence exists for ibuprofen, naproxen sodium).[7]	Ibuprofen: 400-800 mg q4h x 2 doses prn. Pediatric: 5-10 mg/kg/dose q6h x 2 doses prn	Potential for GI upset or peptic ulcer or bleeding. Increased bleeding risk with warfarin.	First-line treatment choice for all severities of migraine attacks. Avoid use in 3rd trimester of pregnancy (relatively safe in intermittent doses during 1st and 2nd trimesters).
ASA	Dose (adults): 650-1,300 mg q4h x 2 doses prn. Pediatric (≥12 years): 500-650 mg q4h x 2 doses prn	Not to be used in children <18 years in presence of viral illness or fever (Reye's syndrome risk). Potential for GI upset or peptic ulcer or bleeding. Increased bleeding risk with warfarin.	Avoid use of enteric-coated products as onset of action is delayed. May be used alone or in combination with caffeine/ codeine.
Serotonin 1B/1D Agonists (Triptans)	See Table 5.	Contraindicated in patients with risk for heart disease, basilar or hemiplegic migraine, cerebrovascular or peripheral vascular syndromes, or uncontrolled hypertension. Inhibitors of CYP3A4 reduce clearance of almotriptan, and particularly eletriptan. (Eletriptan should not be used within 72 hours of potent CYP3A4 inhibitors).	Good evidence for effectiveness of oral, subcutaneous and intranasal routes of delivery.
Ergotamines (Dihydroergotamine [DHE] nasal spray, DHE injection, ergotamine oral tablets	Intranasal dihydroergotamine (DHE). Prime sprayer. 1 spray into each nostril at first sign of headache. If not sufficiently improved after 15 minutes, use 1 more spray in each nostril. Max. 4 sprays/attack, 8 sprays/day.	Adverse effects include nausea, rhinitis (with nasal spray), taste disturbance, vomiting, diarrhea. Contraindicated with history, symptoms or signs of ischemic cardiac, cerebrovascular or peripheral vascular syndromes, valvular heart disease or cardiac arrhythmias. Contraindicated with potent CYP 3A4 inhibitors (e.g., HIV protease or reverse transcriptase inhibitors, macrolide antibiotics and azole antifungals). Contraindicated with 5-HT agonists.	Good evidence for efficacy and safety of intranasal DHE as monotherapy. Inconsistent evidence to support efficacy of oral ergotamine or ergotamine-caffeine. Less risk for nausea and vomiting compared with parenteral or oral form. Should not be used in pregnancy due to oxytocic properties. Contraindicated for nursing mothers.
Opioids (Good evidence available only for efficacy of butorphanol nasal spray in treatment of acute migraine)[7]	Prn only. Butorphanol nasal spray - 1 spray in one nostril. If adequate pain relief not achieved within 60-90 minutes, additional 1 mg dose may be used. May repeat sequence in 3-4 hours if needed. Total daily doses >16 mg not recommended.	Opioids (general) - Somnolence, dizziness, nausea, vomiting constipation, potential for abuse, respiratory depression. Butorphanol half-life prolonged in patients with impaired hepatic function. Use caution in this population. Increase interval of initial dosage to 6-12 hours until response characterized. Dosage adjustments may also be necessary in renal dysfunction.	Good analgesics but good evidence for efficacy of butorphanol nasal spray only. Others commonly used, but until further research available, may be better reserved for use when other medications cannot be used.[7] Opioids affect cognitive function with no evidence of advantage over more migraine-specific therapy.

tial time commitment on the part of the patient. The guidelines suggest that candidates for biofeedback therapy should be selected according to their perceived motivation and financial resources.

- **Cognitive-behavioural therapy (CBT):** This therapy is designed to relieve anxiety and distress that have been identified as aggravators of an evolving migraine headache. The guidelines recommend that individual, group and self-help methods be utilized to encourage more adaptive thinking.
- **Hypnosis:** The guidelines suggest a limited role for hypnosis in the management of migraine in a small subgroup of patients who are willing and suitable. It is thought to reduce distressing sensory input and may be more beneficial when combined with CBT.
- **Chiropractic, osteopathy and acupuncture** have been used in the management of migraine but lack valid scientific basis or adequate documentation of their effectiveness. Patients strongly motivated to seek these alternative therapies should be referred to their doctors with awareness of the uncertain benefits of the techniques.
- **Transcutaneous electrical stimulation and acupuncture** have been found in small studies to provide some relief from migraine, but more evidence is

TABLE 5 Comparison of currently available triptans (5-$HT_{1B/1D}$ receptor agonists)

Triptan (dosage form)	T-max (hr)	Half-life (hr)	Response rate at 2 hr	HA recurrence within 24-48 hr	Dose/attack (mg)	Max. dose in 24 hr (mg)
Sumatriptan PO	1.2-2.3	2	50-69	25-41	25-100	200
Sumatriptan IN	1-1.5	2	62-78	10-40	20-40	40
Sumatriptan SC	0.2	2	63-82	10-40	6-12	12
Zolmitriptan PO	1.5	2.5-3	62-67	22-37	2.5-10	10
Zolmitriptan IN	3	2.5-3	69	N/A	5-10	10
Naratriptan PO	3-5	6	43-49	17-28	5-10	10
Rizatriptan PO	1.3	1.8	60-77	35-47	5-20	30
Almotriptan PO	1-3	3-4	55-65	18-30	6.25-25	25
Eletriptan PO	2	4	47-65	6-34	20-40	40

*PO = per os IN = Intranasal SC = Subcutaneous

required before recommending such treatment. Patients highly motivated should be made aware of the paucity of evidence existing for this technique.

- **Occipital or supraorbital nerve blockade** with local anesthetics, sometimes augmented by steroids, has been reported in uncontrolled studies to be effective in relieving migraine (when the pain of migraine occurs in this area).

PHARMACOLOGICAL MANAGEMENT OF MIGRAINE

Goals of treatment of acute migraine attacks include:

- Treating attacks rapidly and consistently to avoid headache recurrence.
- Restoring the patient's ability to function.
- Minimizing the use of back-up and rescue medications.

Patients need to be warned that overuse of analgesics can lead to medication-induced (rebound) headache and then to chronic daily headache (see the section on medication-induced headaches).[3]

Acute Pharmacological Treatment of Migraines

There is a range of treatment choices for management of acute migraine. Different treatment guidelines promote varying strategies for recommendation of initial pharmacologic therapy for migraine sufferers. Here are 3 different acute treatment strategies.[8]

1. **Step-care across attacks:** Patients begin with a simple or combination analgesic. If treatment result is unsatisfactory, they contact their doctor for treatment escalation to be used when next headache occurs. The process is repeated until migraine headache treatment is satisfactory.
2. **Step-care within attacks:** Migraine attack is treated initially with a non-specific therapy. After initial treatment (usually 2 hours), if relief is not satisfactory, the patient takes a different medication, which is often more migraine specific (e.g., triptan).
3. **Stratified care:** The initial treatment is selected based on the patient's treatment needs. For example, the MIDAS grade may be used to assess severity of illness, and treated accordingly.

Recently, these 3 strategies for treatment of acute migraine were assessed in a clinical trial. Patients were randomized to each of the 3 methods.[8] The study concluded that stratified-care strategies (e.g., patients with MIDAS grade III or IV headaches treated with a triptan) provide significantly better clinical outcomes than step-care strategies, as measured by headache response and disability time.[8] This study included 835 adult patients, but treatment strategies were limited to ASA 800 to 1,000 mg plus metoclopramide 10 mg (for nausea and to enhance gastric motility), or zolmitriptan 2.5 mg, and therefore interpretation of results must be made cautiously. Despite the outcomes of this study, the clinical guidelines for the management of migraine published by the American College of Physicians-American Society of Internal Medicine, and the American Academy of Family Physicians state that the best approach to initial management of acute migraine "is still an open question."[7]

If gastric stasis occurs during attacks, prokinetic agents such as metoclopramide or domperidone may be used with oral analgesics to enhance gastric motility and drug absorption and to help control associated nausea and vomiting.[9]

Which triptan and in what dosage form?

The triptan class (sumatriptan, zolmitriptan, naratriptan, rizatriptan, almotriptan, eletriptan) is effective and well-tolerated relative to other agents used for acute treatment of migraine. In the stratified model of care they are appropriate initial therapy for patients with moderate to severe migraine headaches and no contraindications to use.

Table 5 compares the currently available triptans.

In addition to dosage forms listed in Table 5, rizatriptan and zolmitriptan are both available as rapidly dissolving oral wafers. This freeze-dried formulation rapidly disintegrates within seconds on the tongue and is swallowed with saliva.[9] Onset of action of triptans in this dosage form is slower compared to the oral tablets.[9] The wafer formulation was developed as an alternative for patients who have difficulty swallowing tablets or liquids or who experience nausea and vomiting with their attacks. In addition, these dosage forms are convenient when liquids aren't readily available. Gastric stasis often occurs during migraine attacks and therefore patients sometimes absorb oral medications slowly. Prokinetic agents such as domperidone and metocloprmide may be given with oral analgesics to enhance gastric motility and drug absorption and to help control nausea and vomiting associated with attacks.[9]

The oral route of administration is generally preferred by patients. Those who suffer with nausea and vomiting along with their headache need to use the intranasal, subcutaneous or wafer form of triptan medications. Based on pharmacokinetic data, the parenteral route may be

TABLE 6 Summary of medications for prevention of migraine

Medication	Dose	Risk Profile	Comments
Beta-blockers[7]	Most studied. Propranolol: 40-120 mg twice daily Metoprolol: 50-100 mg twice daily. Timolol: 20-30 mg daily	Potential for fatigue, bradycardia, depression, nausea, dizziness, insomnia. Contraindicated in bronchospasm, allergic rhinitis during pollen season, greater than first-degree block sinus bradycardia, cardiogenic shock, congestive heart failure unless secondary to tachyarrhythmia treated with drug.	Propranolol and timolol shown to be consistently effective in clinical trials.[7] Beta-blockers with intrinsic sympathomimetic activity (acebutolol, alprenolol, oxprenolol, pindolol) seem ineffective for prevention of migraine.
Antidepressants[10]	Amitriptyline (most studied): 30-150 mg daily	Caution due to anticholinergic symptoms (e.g., constipation, urinary retention, narrow-angle glaucoma, dry mouth), drowsiness, weight gain. Caution in cardiovascular disease.	No evidence for nortirptyline, protriptyline, doxepin, clomipramine or imipramine. Limited evidence for modest effect for fluoxetine at doses from 20 mg every other day to 40 mg per day. No evidence for other SSRIs or MAOIs.
Calcium channel blockers[3,7]	Flunarizine: 5-10 mg daily Verapamil: 240-320 mg daily	Potential for fatigue, weight gain, depression (flunarizine). Potential for bradycardia, hypotension, constipation (verapamil).	Flunarizine has proven efficacy. Evidence for verapamil is poor quality, suggesting only modest effect. No evidence for use of diltiazem.
Anticonvulsants[10,11]	Divalproex sodium: 500-1,500 mg daily in divided doses. Sodium valproate: 800-1,500 mg daily in divided doses. Topiramate 50 mg bid (approved indication February 2005).	Contraindicated in patients with hepatic disease or significant hepatic dysfunction. Divalproex sodium contraindicated in patients with known urea cycle disorders. Cognitive side effects. Temporary paresthesia in up to 47% of users (inform patients). Taste perversion.	Carbamazepine and vigabatrin have been shown ineffective. Increased risk for teratogenic effects, such as neural tube defects, especially during first trimester. Cognitive side effects with topiramate can be minimized with gradual increase in dosing starting with 25 mg daily and increasing by 25 mg weekly until 50 mg bid.
Methysergide[10]	Adults only: Start with 2 mg at night, increase gradually to 2 mg 3 times daily with meals. Three-week trial period should be allowed to determine efficacy. Max daily dose 12 mg. Medication-free interval of 3-4 weeks every 6 months.	Contraindicated in peripheral vascular disorders, progressive arteriosclerosis, inadequately controlled hypertension, coronary heart disease, valvular heart disease, phlebitis or cellulites of the lower limbs, history of drug-induced fibrotic disorders, pulmonary fibrosis, collagen disease, severely impaired liver or renal function, obstructive disease of urinary tract.	Contraindicated for use with macrolide antibiotics, HIV-protease or reverse transcriptase inhibitors, azole antifungals due to increased risk for ergotism. Contraindicated in pregnancy and while breastfeeding. Dose should be reduced gradually over 2-3 weeks before discontinuing due to risk of headache rebound.
Pizotifen[12]	Adults only (>12 yrs): Start with 0.5 mg at bedtime. Increase gradually to 0.5 mg 3 times daily. Dosage range is 1-6 mg/day. Four-week trial period to determine efficacy.	Contraindicated with MAO inhibitors, pyloroduodenal obstruction and stenosing pyloric ulcer. Caution in narrow-angle glaucoma, urinary retention.	Reassess necessity of continuing treatment periodically (after several months) with drug-free period. Reduce dose gradually for 2 weeks before discontinuing to avoid headache rebound.
Feverfew[5]	Adults: 1-2 tablets standardized feverfew dried leaf powder 125 mg/day containing at least 0.2% parthenolide. Pediatric: No data in children <2 years.	Potential for mouth ulceration, GI symptoms, contact dermatitis. Syndrome including headache, anxiety, insomnia, muscle and joint stiffness possible following abrupt discontinuation in long-term users. Should be avoided in pregnancy due to potential to stimulate uterine contractions increasing abortion risk.	Should avoid use if previous contact dermatitis has resulted from plants in the Asteraceae family (e.g., chamomile, ragweed, chrysanthemum, sunflower, tansy, yarrow). Has been found effective in majority of small trials, but consensus to date is that effectiveness in prevention of migraine has not been established beyond reasonable doubt.
Magnesium[5]	Adults: 600 mg daily of elemental magnesium. No recommendations for children.	Diarrhea, GI upset. No significant drug interactions.	Magnesium deficiency suspected to play role in up to 50% of patients. Citrate salt appears to be best absorbed of magnesium salts.
Riboflavin[5]	Adults: 400 mg/day. No recommendations for children.	Causes harmless yellow discolouration of urine. No significant drug interactions.	Small trial (55 patients) suggests effectiveness. More trials required.

the fastest acting of the available triptan choices (only sumatriptan is available in this dosage form), although clinical trials are required to verify this assertion. Adverse effects are more common with the subcutaneous route, however, and include sensations such as tingling, warmth, heaviness or pressure in chest, neck, throat, jaw and arms, as well as dizziness, flushing and discomfort at the injections site which is usually mild and temporary.[9]

Preventing Migraine Attacks

Preventive therapy for migraines may be considered if:[5]

- the patient is having 2 to 3 attacks per month or more, especially when relief obtained from acute therapies is suboptimal.
- the patient is having severe attacks that result in an inability to function normally.
- the patient is psychologically not able to cope with attacks.
- acute therapies have failed, are contraindicated or have produced serious side effects.

Commonly-used agents for prevention of migraine are overviewed in Table 6.

Medication-Induced Headaches

Any type of headache syndrome, including migraine, can be worsened by analgesic overuse.[4] Medication-induced headache (also known as medication overuse headache) is associated with an increase in the use of analgesics, development of tolerance to the pain-relieving effect of the drugs, and an increase in headache intensity and frequency.[4] Analgesic abuse may lead to chronic daily headache, and is a common cause of failure of usual treatment measures (e.g., the triptans, NSAIDs and acetaminophen products).

In people with a history of analgesic overuse, successful migraine treatment may require detoxification from the previously overused agents. This is difficult, as headaches often worsen during the withdrawal period and may take several weeks for headache characteristics to return to baseline. Withdrawal may include symptoms such as anxiety, tremors, insomnia or diarrhea. The rate of drug withdrawal should be slowed should these symptoms occur. A tricyclic antidepressant (e.g., amitriptyline) may be prescribed if appropriate during this time period for it's centrally acting pain-relieving properties and as preventative therapy for migraine.[4] Encouraging patients to restrict their use of analgesics to no more than twice per week minimizes the risk of this occurrence.

THE ROLE OF THE PHARMACIST IN MIGRAINE MANAGEMENT

When considering options for headache management patients often turn to their pharmacist first, or at the very least make the trip to the local pharmacy to purchase over-the-counter remedies. Pharmacy staff should be trained to refer patients seeking pain relief to the pharmacist for assessment. The pharmacist should engage the patient in a discussion that includes the patient's description of the headache history including pain type, location, intensity, quality, frequency and duration. If headache pain is characterized by any other than intermittent, tension-type headache, a referral to a physician for diagnosis is indicated.[5] A doctor referral is also indicated if pain is chronic or progressive, or there is a significant change in the headache pattern.[5]

If migraine headache is diagnosed, the pharmacist can collaborate in patient care in the following manner.

- Education on control of acute attacks and role of preventive therapy. Also explain the risk for medication-induced headache and prevention principles.
- Regular re-evaluation of therapies should be a standard of care. Follow-up with patients after medications are started to aid patient in assessment of therapy effectiveness. Help patients with understanding about the level of severity of their migraine attacks using tools such as the MIDAS questionnaire.
- Help patients start a diary to measure migraine attack frequency, severity and duration, as well as response to type of treatment and adverse effects of medication. This will help to guide future treatment recommendations in collaboration with the patient's physician.
- Ensure patients understand expected benefits of their medication and how long it may take to be at maximal effectiveness. Patients must also understand any predictable side effects and adverse effects to be on the watch for (as well as action to take should adverse effects be encountered).

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QUESTIONS

Case #1: *Mary, a 22-year-old university student is in the pharmacy looking for the ibuprofen pills. In speaking with Mary, she says that her headaches are usually worse around exam time, but they seem to be getting even more bothersome. Ibuprofen used to work, but now she finds that even her usual dose of one 400 mg tablet just "takes the edge off." Mary says that her pain throbs on the right side of her head.*

1. Which statement about migraine headaches is TRUE?

a) Migraines are diagnosed in about 2% of all Canadians over the age of 12.
b) About three times as many women as men are diagnosed with migraine headaches.
c) Confirmed diagnosis of migraine headache can be made by the pharmacist.
d) Migraine symptoms are generally consistent from one individual to another.

2. Which quality regarding Mary's headache pain would be least indicative of migraine headache symptoms?

a) Throbbing quality of pain
b) Pain on one side of the head
c) Pain lasting about 30 to 60 minutes without treatment
d) Pain that is accompanied by nausea and vomiting

3. If Mary is diagnosed with migraine headache, which factor is likely to have triggered her current headache?
a) Stress over her exams
b) A large order of take-out Chinese food the night before
c) A long run to try and relieve the stress of exams
d) Any of the above might have triggered her current headache

4. In what percentage of migraine sufferers do aura symptoms occur?
a) 10% c) 50%
b) 30% d) 70%

5. What does "scotomata" refer to?
a) Bright flashes of light within the visual field
b) Seeing many colours in the visual field
c) A perception of floating objects in the visual field
d) A perception of a blind or dark spot in the visual field.

6. If Mary scores 8 on the MIDAS questionnaire, at what level of disability is she as a result of her migraine attacks?
a) Little or no disability
b) Mild
c) Moderate
d) Severe

7. Which etiology is thought to be most likely associated with increased risk for migraine headaches?
a) Release of vasoactive neuropeptides
b) Increase in 5-hydroxytryptamine levels
c) Reduction in 5-hydroxytryptamine levels
d) a and c

8. If Mary is otherwise healthy, what single dose of ibuprofen would be the maximum recommended for treatment of acute migraine?
a) 400 mg c) 800 mg
b) 600 mg d) 1,000 mg

Case #2: *Carla is a 28-year-old who has a 6-month-old child at home. She has recently been diagnosed with migraine headache. She reports to you that she always used to self-medicate, but her migraines are now more frequent (about 3 times monthly) and she finds it difficult to function and take care of her child when she has a migraine headache. Her doctor has recommended a triptan for acute management.*

9. Which suggestion is LEAST likely to help Carla with the symptoms of an acute migraine headache?
a) Rest in a quiet, dark room
b) Sleep
c) Go for a brisk walk outside
d) Apply a cold cloth to the head

10. The strategy of treating migraine attacks with a particular therapy, waiting for a few months to assess efficacy and then changing therapy if required is known as:
a) Step-care across attacks
b) Step-care within attacks
c) Stratified care
d) a or c

11. If Carla decided to use ASA before trying a triptan medication, what dose would be most appropriate for treating an acute migraine attack?
a) 325 mg qid for 2 days
b) 1,300 mg q4h for 2 doses
c) 650 mg q4h for 2 days
d) ASA is not appropriate therapy for treatment of migraine

12. If Carla were taking ketoconazole, which triptan would be most likely to interact?
a) Eletriptan c) Sumatriptan
b) Zolmitriptan d) Rizatriptan

13. The doctor decides to recommend rizatriptan wafers for Carla. Which statement is FALSE?
a) Wafers are a desirable dosage form because they can be used when water is not readily available.
b) Wafers are a desirable dosage form because they can be taken by people who have trouble swallowing water or tablets.
c) Wafers are a desirable dosage form because they are absorbed more quickly than tablets.
d) Wafers are a desirable dosage form because they may be associated with less nausea and vomiting than tablets.

14. Which of the following dosage forms takes the least time for active drug to reach maximum concentration in the blood?
a) Eletriptan tablets
b) Zolmitriptan intranasal spray
c) Sumatriptan subcutaneous
d) Almotriptan tablets

15. Carla continues to have 2 to 3 severe migraine attacks per month and her doctor and she ask you about preventive therapy. Which statement is FALSE?
a) Carbamazepine would not be a good choice if Carla desires to get pregnant again.
b) Propranolol is one of the most studied preventive agents and has been deemed effective.
c) Diltiazem is an effective calcium channel blocker for prevention of migraine.
d) Methysergide would not be a good choice for Carla if she is taking a reverse transcriptase inhibitor.

16. Which antidepressant is associated with good evidence for prevention of migraines?
a) Paroxetine
b) Doxepin
c) Imipramine
d) None of the above have been studied extensively for the prevention of migraines.

17. If Carla wanted to try magnesium to prevent migraine headache, what dose would you recommend?
a) 300 mg daily c) 1,200 mg daily
b) 600 mg daily d) 1,800 mg daily

18. When used chronically, which medication does not have potential for medication-induced headache?
a) Acetaminophen
b) Triptans
c) NSAIDs
d) All of the above have potential to cause medication-induced headache.

19. Which dosage form of ergotamine is LEAST likely to cause nausea or vomiting?
a) Dihydroergotamine intranasal spray
b) Ergotamine oral tablet
c) Dihydroergotamine parenteral form
d) All are equally likely to cause nausea or vomiting.

20. Carla is now inquiring about feverfew. Which statement about feverfew is FALSE?
a) Carla should not use feverfew during pregnancy.
b) Feverfew should not be stopped abruptly.
c) If Carla has a ragweed allergy she should not use feverfew.
d) Clinical studies have verified conclusively that feverfew is effective in preventing migraine headache.

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1. a b c d	**6.** a b c d	**11.** a b c d	**16.** a b c d
2. a b c d	**7.** a b c d	**12.** a b c d	**17.** a b c d
3. a b c d	**8.** a b c d	**13.** a b c d	**18.** a b c d
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Feedback on this CE lesson

1. Do you now better understand how to care for patients with migraine headaches? ❑ Yes ❑ No
2. Was the information in this lesson relevant to your practice? ❑ Yes ❑ No
3. Will you be able to incorporate the information from this lesson into your practice? ❑ Yes ❑ No
4. Was the information in this lesson... ❑ Too basic ❑ Appropriate ❑ Too Difficult
5. Do you feel this lesson met its stated learning objectives? ❑ Yes ❑ No
6. What topic would you like to see covered in a future issue? _____

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