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**Learning Objectives**

After reading the two-part newsletter series for 2005, participants should be able to:

- Conduct adequate patient assessment and correctly diagnose migraine to initiate targeted therapy.
- Provide individualized care for migraine patients, especially women and other high-risk groups, that promotes patient satisfaction and compliance.
- Appropriately prescribe treatments based on safety and efficacy data and evidence.
- Recognize impact on the patient of early intervention for minimizing migraine disability and improving lifelong care.
- Utilize strategies to reduce or prevent recurrence.
- Proactively monitor patients for long-term treatment success.
- Dispel the misconceptions and myths surrounding migraine management.

RELEASE DATE: JUNE 2005

EXPIRATION DATE: MARCH 2006

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This is the **second issue of a two-issue CME newsletter series.**

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This activity is conducted as a part of the National Initiative on Pain Control® (NIPC®), sponsored by Thomson Professional Postgraduate Services®, Secaucus, NJ.

Supported by an unrestricted educational grant from Endo Pharmaceuticals Inc.

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## Women With Migraine: Health Issues You Can't Ignore

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Twenty-four million American women are affected by migraine often throughout their lifetimes and the majority of these women will seek care from their primary care physicians. It has been estimated that 70% of migraine sufferers are female. Of these female migraine sufferers, 60% to 70% report a menstrual relationship to their migraine attacks.<sup>1</sup> Estrogen plays a key role in causing migraine, with both the natural and artificial hormonal fluctuations having an impact. Genetic, cultural, and ethnic differences in migraine are other contributing factors, which are not easily delineated. For example, biological factors between men and women, such as hormonal variances or differ-

ences in gene expression, may explain the observance of lower pain thresholds and/or pain tolerance in women. Yet cultural differences between men and women may contribute to differences in expectations and thus account for perceived differences in gender perception of pain.<sup>2</sup>

Women, perhaps partly as a result of their help-seeking and symptom-reporting behavior, are more likely than men to receive a diagnosis of migraine (41% vs 29%, respectively) (Figure), but migraine is seriously underdiagnosed in both groups (59% and 71%, respectively).<sup>3</sup> However, with appropriate diagnosis and treatment, migraine can be well controlled throughout the hormonal and chronologic stages of women's lives, and their health can be significantly improved.

**Hormones and Migraine**

Without proper management, women become disabled by migraine, impacting both their own

CONTINUED ON PAGE 3

**CASE STUDY**

## Faces and Phases of Menstrually Related Migraine

**Anne H. Calhoun, MD**

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Mrs P is a 38-year-old accountant being seen by a new physician for men-  
strually related migraine (MRM) of many years' duration. She recalled onset of moderate headaches in the sixth grade and had become aware of a menstrual association by the time she started high school. Until her later 20s, her only significant headaches were with menses. Over the next decade, these headaches became progressively more severe, and she began experiencing them at other times of the month. These migraines were most often on the right but occasionally on the left and were most often retro-orbital or temporal in location. She often noticed associated neck tension, as well as nausea, photophobia, phonophobia, and osmophobia. She denied both aura and prodrome. After the birth of her second child when she was 32 years of age, Mrs P's headaches became more frequent and she suffered from neck tension almost daily.

When seen, Mrs P reported experiencing headache or neck discomfort on 20 of the preceding 28 days (10 severe, 6 moderate, and 4 mild). She was regularly missing 1 to 4 days of work per month with her cyclic headaches and avoided scheduling important meetings for the days of her menstrual cycle. Her headache history followed an increasing pattern of visits for emergency care for intractable migraine.

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## EDITORS' PERSPECTIVES

### An Ounce of Prevention: What Is It Worth?

The ideal goal for most migraineurs would be to prevent migraine from ever occurring. Although this goal is rarely realistic, it does underscore the value and importance of considering preventive strategies for migraine. The traditional method of preventing migraine is to take medication on a daily basis in the belief that when a person becomes at risk for developing a migraine, the medication is already there and can stop the migraine before it starts. Those with few attacks see daily preventive medications as unnecessary except for the few days they are at risk for migraine. This has led to a new preventive treatment paradigm called "short-term preventive therapy" or "mini-prophylaxis," used only at those times a person is at risk for developing a migraine. Obviously, the challenge is deciding the time when a person is at risk for migraine.

The most predictable migraine for many women is migraine associated with their menstrual cycle. Most women will have migraine at other times of the month but will experience more severe and refractory attacks 1 to 2 days before or during their menstrual period. Another time when women are more likely to have severe attacks is at the time of ovulation. Studies have shown that menstruation and ovulation-related headaches occur when changing estrogen levels in the blood and in the brain evolve during the menstrual cycle. These changes in blood levels of hormone, rather than the presence of estrogen, can make women more susceptible to experiencing several different types of pain, such as headache, dysmenorrhea, musculoskeletal and temporomandibular pain, or joint aches, just before or during menstruation.

Clinical studies have demonstrated that several of the medications used more traditionally as acute treatments can be initiated to prevent severe attacks of pain. As was mentioned in the article by Dr Christine Lay, Women With Migraine: Health Issues You Can't Ignore (page 1), these medications include nonsteroidal anti-inflammatory drugs and triptan medications. Double-blind placebo-controlled studies have been completed for both naratriptan\* 1 mg and frovatriptan\* 2.5 mg, and both demonstrated statistically significant efficacy for preventing menstrual migraine. Timing is crucial with mini-prophylaxis. Preemptive therapy is most effective when begun 24 to 48 hours before the expected attack.

Although further study of short-term preventive therapy is needed, it represents an exciting and potentially very useful treatment paradigm.

—Roger K. Cady, MD *Co-Editor*

### Therapeutic Opportunity: Women With Migraine

Migraine can't be "cured" in the traditional sense, but it is eminently treatable. Since the majority of women with migraine note a connection between their headaches and the menstrual cycle, it is important to explore the relationship between the two with an eye toward possible treatment implications. A carefully kept headache diary should reveal the timing of both menstruation and any headaches that occur in relation to it. In women with regular menstrual periods and headaches that occur in predictable relation to menstruation, it may be possible to anticipate and, in some cases, even preempt attacks.

Accurate understanding of the response of menstrual migraine to treatment is important to avoid the misconception that this form of migraine responds poorly to any form of treatment. Such negative beliefs may discourage women or their physicians from attempting treatment in the first place, or they may become self-fulfilling prophecies. Women who seek treatment for menstrual migraine in specialty headache clinics often have headaches that have proved difficult to manage. Migraineurs in general practice settings, however, often respond extremely well to treatment.

A number of potentially useful and effective treatment strategies can be considered when menstrual migraine fails to yield to standard abortive or preventive therapies. The case study on page 1, Phases and Faces of Menstrual Migraine, by Dr Anne Calhoun, makes that clear. These strategies include the short-term, preemptive use of nonsteroidal anti-inflammatory agents, triptans, or estrogen supplementation. The largest and most carefully done studies to date have examined the role of scheduled doses of triptans for this indication. These studies have focused on triptans with longer half-lives because the need for fewer daily doses simplifies the treatment regimen.

Therapeutic nihilism about migraine in general, or menstrual migraine attacks in particular, serves no one well. A more appropriate view is of migraine as a treatable, manageable chronic illness, which, in some cases, demands considerable ingenuity in treatment strategies. Because they are so often predictable, migraine attacks that occur in conjunction with the menstrual cycle should more properly be considered a therapeutic opportunity rather than an obstacle.

—Elizabeth W. Loder, MD *Co-Editor*

**\*Not FDA approved for this use.**

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All NIPC programs are developed and continuously evaluated by the NIPC Education Council, an expert, multidisciplinary team of specialists, researchers, and practicing physicians in pain management. The NIPC Faculty includes nationally respected experts in the pain management field. The Headache and Migraine activities are developed and reviewed by NIPC Migraine Steering Committee.

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## Women With Migraine

CONTINUED FROM PAGE 1

lives and society as well, often at a tremendous financial and personal cost. Compared with nonmenstrual migraine (NM), menstrual migraine (MM) is often more severe, more debilitating, of longer duration, and less responsive to both acute and prophylactic treatment.<sup>4,6</sup> The decrease in estrogen in the luteal phase is a key trigger in MM and may prime blood vessels to be more susceptible to other factors, such as the prostaglandins, which likely promote neurogenic inflammation and inhibit norepinephrine release. The slight drop in estrogen occurring at ovulation similarly may trigger a migraine attack.

### Migraine Management

Acute therapy for MM is similar to therapy for NM. All of the triptans have proven efficacy in migraine, and most patients will require and respond to these migraine-specific agents, possibly with the addition of anti-emetics and NSAIDs. Preventive therapy is indicated in women experiencing 3 to 4 debilitating headaches per month, or in those who are unresponsive to abortive medications. Both daily preventive and mini-prophylactic therapy methods are employed, the latter requiring the predictable timing of MM. In nonhormonal prophylaxis, standard migraine prophylactic agents and some abortive medications are used perimenstrually, including nonsteroidal anti-inflammatory drugs (NSAIDs)\* and the long-acting triptans (frovatriptan and naratriptan).\* Timing is critical and cycles should be regular to predict migraine onset.

Hormonal prophylaxis\* may be considered for refractory MM provided there are no contraindications to estrogen therapy, including a history of migraine with aura, blood-clotting disorders, and risk factors for

arterial disease such as diabetes, hypertension, and tobacco use. Any patient who develops an aura while on hormones or experiences a change from simple aura, should discontinue use. This strategy attempts to counteract or prevent the luteal-phase decrease in estrogen and percutaneous and transdermal methods are preferred over oral supplementation. In refractory cases, synthetic androgens or gonadotropin-releasing hormone analogs can be considered. However, these methods have not been subjected to clinical trials and are not universally recommended.

### Migraine and Maturing

When patients of childbearing age experience migraine, birth control methods should be discussed. Oral contraceptives (OC) have variable effects on migraine often leading to a worsening during the placebo week. The low-dose, monophasic pills are the best in migraineurs, rather than the mid- or high-dose biphasic or triphasic pills. With respect to stroke risk, OC use is considered safe in women with migraine without aura or migraine with simple aura and in those without vascular risk factors.<sup>7</sup> Recent studies have demonstrated an increased risk of stroke in migraineurs with aura, although the absolute risk remains low.<sup>8</sup> However, an OC should be discontinued if the aura changes or develops for the first time after initiating an OC. The patch or vaginal insert contraceptive may provide more steady state levels and be less likely to negatively affect migraine as compared with OCs.

**Pregnancy and the postpartum.** In retro- and prospective studies, 47% of pregnant migraineurs without aura experienced improved symptoms in their first trimester, 83% in the second trimester, and 87% in their third trimester.<sup>9</sup> Improvement during pregnancy is more likely in migraineurs

without aura and in those who previously experienced menstrually related migraine. Migraine experienced for the first time during pregnancy is more often migraine with aura. In addition to the hormonal changes of pregnancy, disrupted sleep, nausea, dehydration, and stress likely contribute to migraine. If nausea and/or vomiting become problematic, therapy is indicated.

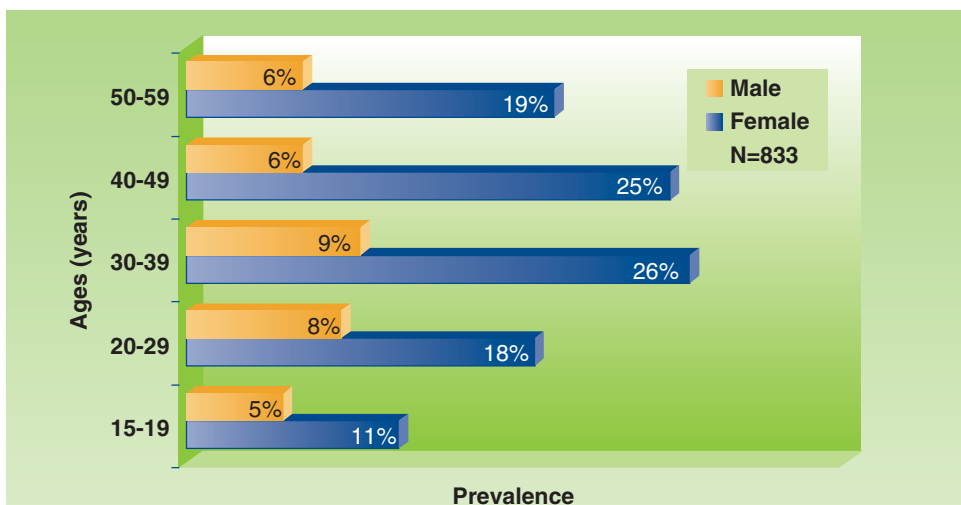
**“Without proper management, women become disabled by migraine.”**

Nonpharmacologic treatment measures as opposed to pharmacologic options should be emphasized because of the potential teratogenicity of drugs, especially during the first trimester. In the early stages of pregnancy, small doses of caffeine and acetaminophen are considered safe. During mid-pregnancy, several NSAIDs are listed as category B,<sup>†</sup> as are some narcotics and anti-emetics. Triptans, ergots, and aspirin should be avoided once pregnancy is established. Although pregnancy registries have been established for several of the triptans and no specific negative effects have been identified, proof of absence of risk is not absolute and as such triptans are not recommended without clear indication.<sup>10</sup>

Migraine often returns in the first 2 to 7 days postpartum, presumably related to the rapid fall in estrogen levels.<sup>9</sup> If headaches occur 3 to 4 times or more per week, prophylactic therapy may be indicated. Medication use in a migraineur who is nursing should be monitored and discussed with the pediatrician. Medications deemed safe in pregnancy are usually safe during nursing. A woman may pump and discard any breast milk for 4 to 6 hours following administration of sumatriptan for more severe migraine.

**Perimenopause and menopause.** Migraine tends to improve with age, especially during and after menopause. Worsening headaches often herald the onset of perimenopause and the chaotic hormonal fluctuations during perimenopause may contribute to the new onset or return of previously abated migraine. As irregular cycles set in, migraine treatment is more problematic. Blood hormone levels can be measured but the results are unlikely to significantly sway the diagnosis.

Hormone replacement therapy (HRT), often employed to manage the symptoms of perimenopause, has varying effects on migraines. For some women, HRT on a short-term basis to stabilize estrogen levels may be beneficial. For others, HRT may worsen migraine and strategies will need to be considered for these patients, including:



**Figure**

Female preponderance of migraine during reproductive years.<sup>17</sup>

CONTINUED ON PAGE 7

## CASE STUDY

### Faces and Phases of Menstrually Related Migraine

CONTINUED FROM PAGE 1

Her menses were regular: every 28 days, lasting 6 to 8 days with heavy bleeding for 2 days and severe cramps for 3 days. Her worst headache during the month is a predictable 4-day MRM that begins 1 to 2 days before the onset of bleeding. She also noticed a 1-day severe ovulatory migraine 2 weeks before MRM. The menstrual headaches frequently awaken her before dawn and are associated with vomiting. In addition, she has poor sleep habits and reports awakening “exhausted” every morning.

Last year, another physician had instituted migraine prevention with beta-blockers and amitriptyline. She discontinued amitriptyline due to weight gain. Beta-blockers were later discontinued due to lack of efficacy, and therapy with verapamil was started. Mrs P is now complaining of constipation with verapamil and is frustrated with the lack of improvement in her headaches.

Mrs P had previously tried traditional combination oral contraceptive (COC) regimens of estrogen and progestin (for treatment of co-occurring endometriosis) under guid-

ance from her gynecologist. She had discontinued each of them because of intensification of MRM. Three days before this visit, she began a 20- $\mu$ g esterified estrogens (EE) contraceptive patch.

Current medications include verapamil 240 mg/d, sumatriptan 50 mg/d (15/mon), butalbital compound (80–100/mon), caffeine/ASA/acetaminophen (22-25/mon), ibuprofen 800 mg (9/mon), acetaminophen (30–35/mon), and 20- $\mu$ g EE/150- $\mu$ g norelgestromin contraceptive patch.

### Discussion

For many women, menstruation is a predictable and potent trigger of migraine. Approximately 60% of female migraineurs report menstrual association of their headaches, making MRM a common disabling condition encountered in women. It strikes reproductive-aged women from puberty to perimenopause and exacts a high toll in clinical, social, and economic burden.<sup>1</sup> Before puberty, migraine is slightly more prevalent among boys; after puberty it is markedly more prevalent in women. That prevalence peaks at approximately 40 years of age and declines when hormone fluctuations stabilize after menopause.

MRM is not recognized as a formal headache diagnosis by the International Headache Society (IHS), although “candidate” criteria have been published by that organization to facilitate research. MRM is analogous to catamenial epilepsy, not a different *type* of epilepsy, but rather a seizure pattern that reflects changes in seizure thresholds that occur in conjunction with hormonal changes in the menstrual cycle.

Menstrual association of migraine is reported by a majority of childbearing-age women with migraine, but pure menstrual migraine—migraine that *exclusively* occurs with menses—is reported by only 14% of women with migraine.<sup>2</sup> This distinction between pure menstrual migraine and MRM may prove to be an artifact of disease progression. Many clinicians have noted histories similar to Mrs P’s: menstrual association with only one attack a month in the early years after onset and then development of a more frequent pattern of migraine over time. However, this conjecture remains to be proved.

Mrs P was quite certain that her own MRM was more disabling than her other attacks, although it has been debated whether this is true in larger populations. However, the work of MacGregor and Hackshaw has given strong credence to our patient’s observations. Diary data from 155 women attending a specialty headache clinic showed that—compared with all other times of the cycle—migraine was almost twice as likely to occur during the 2 days before or after menses. Furthermore,

migraines that occurred perimenstrually were 3 times more likely to be severe and 4 times more likely to be associated with nausea and vomiting.<sup>3</sup>

### Treatment

**Transformed or chronic migraine.** We should first approach Mrs P as a migraineur who has probable migraine without aura and probable medication overuse headache (MOH), using nonpharmacologic as well as pharmacologic strategies for her treatment. The IHS defines MOH as a chronic headache characterized by a patient’s overuse of analgesics, which improves after withdrawal from the overused agents, suggesting a causal relationship between medication overuse and chronicity. However, some patients develop chronicity without overusing medication,<sup>4</sup> suggesting that other factors may also be at work. When we examine chronic daily headache in its earliest presentation in children and adolescents, medication overuse is rarely seen.<sup>5</sup> However, sleep problems are common.<sup>6</sup>

In a 1996 survey of primary care physicians (PCPs) in the United States, MOH was reported to be the third most frequent form of headache observed in practice. Mrs P is a common example of a patient with a history of episodic migraine with or without aura, who complains of increased headache frequency that eventually transforms into a daily or near-daily headache lasting for prolonged periods. MOH must be treated with discontinuation of offending drugs, a transitional therapy, and preventive therapy to reduce the need to take analgesics frequently. Mrs P’s instructions were to discontinue all analgesics except ibuprofen 800 mg, which would remain limited to its current targeted pattern of use—as needed for severe dysmenorrhea once a month. The butalbital-containing medication was to be tapered and discontinued over 2 weeks while she also suspended sumatriptan. During these 2 weeks, “bridge therapy” was initiated with naratriptan (2.5 mg, dosed in a fixed schedule at 1 tablet bid for 2 days, then ½ tablet bid for 10 days). Naratriptan is one of two long half-life triptans, a category that also includes frovatriptan.

Strategies to revert patients out of chronic migraine (CM) emphasize not only discontinuing medication overuse, but also addressing nonpharmacologic issues, such as the frequently comorbid sleep issues. Mrs P was advised to set a regular sleep time that allows for 8 hours of nocturnal sleep, to discontinue her habit of watching television in bed, to move dinner to 4 hours before bedtime to reduce nocturia, and to discontinue her frequent naps.

**Acute therapy.** Most patients with menstrual migraine are treated with acute

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therapy to decrease the intensity and duration of individual attacks. Medications that have been proven effective or are commonly used for acute treatment include nonsteroidal anti-inflammatory drugs (NSAIDs), dihydroergotamine (DHE), triptans, and the combination of aspirin, acetaminophen, and caffeine.

After MOH therapy, Mrs P was to use a short-acting triptan (sumatriptan 100 mg) in the mild pain stage for migraine. All seven triptans have distinct pharmacologic, pharmacokinetic, and tolerability profiles (Table), and any triptan can be substituted for a previously unsuccessful trial. Onset of activity of fast-acting and long-acting triptans is in part a function of their half-life and delivery methods. When matching triptans to patients, clinicians must consider individual characteristics, preferences, efficacy of previous acute-care medications, and the specific features of the individual agents. If sumatriptan is not effective for Mrs P after three consistent headache episodes—or if she experiences side effects—another triptan may better target her individual needs.

**MRM.** Regarding her severe MRM, Mrs P was told that the new contraceptive patch would not be expected to make MRM worse (as the previous COCs had done), *but it was not likely to make it better either!* The 20- $\mu$ g EE dose in the patch produces a premenstrual decline in estrogen comparable with the decline in the native menstrual cycle; since she has MRM with her native cycle, she is likely to have MRM with these “lowest-dose” (20- $\mu$ g) pills or patches as well.<sup>7</sup>

However, COCs that produce greater declines in EE might be more likely to precipitate MRM, as with the three prior pills she had tried.<sup>8</sup> Two of the earlier oral contraceptives (OCs) contained 35- $\mu$ g EE and the third contained 30- $\mu$ g EE. Each might have been *predicted* to intensify MRM by virtue of the fact that they increased the magnitude of the premenstrual decline in estrogen concentration—to a greater extent than is seen with the native menstrual cycle. This likely explains why migraine was worse in the majority of women receiving a COC

dose of 50  $\mu$ g of ethinyl estrogen in a controlled study (although 50- $\mu$ g was termed “low dose” in the 1970s, it is the only remaining “high dose” COC today).<sup>9</sup>

The recapitulation of this initial step of treatment of MRM is simple. First, treat MRM in the same way as migraine occurring at any other time. At the same time, avoid concurrent treatments that would be expected to make migraine worse. In Mrs P’s case, this would include use of contraceptives that cause supraphysiologic declines in estrogen and analgesic overuse.

Mrs P was instructed to keep a 28-day menstrual migraine calendar and follow-up was scheduled immediately following her first menstrual week to assess whether specific prevention for MRM would be required.

### FOLLOW-UP

When Mrs P returned, she said that initially she was much improved, but the past week had been “awful.” Her calendar revealed that her headache frequency over the preceding 28 days had declined from 20 days to 11 days (4 rated as severe, 3 as moderate, and 4 as mild). Weighing heavy on her mind was the 4-day intractable MRM that preceded this office visit. It began 1 day before the onset of menstrual bleeding. As in previous months, she missed 2 days of work while home sick with migraine.

On a positive note, Mrs P’s calendar also revealed that she had registered 5 consecutive headache-free days while on the naratriptan taper. During this time she had successfully discontinued butalbital compounds and analgesics. In the week before the menstrual migraine, she had registered another 4-day headache-free stretch.

The first goal for Mrs P was to revert her to episodic migraine. One of the most important contributions the PCP can make in management of migraine is to prevent the evolution of episodic headaches into chronic or daily headaches. In this case, Mrs P was successful not only in discontinuing the overused medications, but also in achieving subjectively restorative sleep

by complying with recommended sleep habit modifications.

### Treatment at Follow-up

Since she was already achieving stretches of consecutive headache-free days during the nonmenstrual weeks, Mrs P was instructed to continue to treat each of her headaches early in the mild pain stage with a fast-acting triptan (ie, sumatriptan, zolmitriptan, almotriptan, rizatriptan, eletriptan).

Although her overall headache burden has improved substantially, Mrs P remains a candidate for migraine preventive therapy because of bouts of intractable, disabling MRM.

There are two traditional pharmacologic approaches to the treatment of menstrual migraine: acute (abortive) therapy and preventive (prophylactic) therapy. A third approach is pre-emptive treatment, sometimes referred to as short-term preventive therapy or “mini-prophylaxis.” In this strategy, treatment is started shortly before the anticipated menstrual headache and continued throughout the period of vulnerability. In most cases this is from 5 to 7 days during each month.

**Mini-prophylaxis.** Some women may require preventive treatment strategies that rely on perimenstrual targeted therapy (Figure). Agents that have been studied and appear effective for mini-prophylaxis include NSAIDs,\* triptans,\* methylergonovine,\* DHE,\* and magnesium\*; however, none are approved by the United States FDA for pre-emption of MRM. There are varying levels of evidence-based quality for the studies of these agents. In large and methodically rigorous clinical trials, frovatriptan\* and naratriptan\* have been shown to be effective in patients with MRM, reducing the headache frequency by as much as 50%.<sup>7</sup> Frovatriptan given prophylactically for 6 days, starting 2 days before anticipated attack, was effective in reducing the occurrence of MRM in more than half of patients (59%) vs 33% for placebo ( $P<.0001$ ). No MRM occurred

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**Table. Comparison of Triptans**

Name	Formulation	Usual Oral Dose (mg)	Most Common AEs	Serious Risks/Class
Almotriptan (Axert®)	Oral tablet	12.5	Nausea, dry mouth, paresthesia	Myocardial infarction, cerebro-vascular events, increased blood pressure
Eletriptan (Relpax®)	Oral tablet	40	Asthenia, nausea, dizziness, somnolence	
Frovatriptan (Frova®)	Oral tablet	2.5	Dizziness, fatigue, headache, paresthesia	
Naratriptan (Amerge®)	Oral tablet	2.5	Nausea, pain/pressure, paresthesia	
Rizatriptan (Maxalt®)	Oral tablet or MLT	10	Dizziness, somnolence, nausea, paresthesia	
Sumatriptan (Imitrex®)	Oral tablet, SQ, IN	50/100*	Paresthesia, pain/pressure	
Zolmitriptan (Zomig®)	Oral tablet, ZMT, IN	2.5	Dizziness, paresthesia, pain/pressure, somnolence	

\*While the PI states that the recommended dosage for this agent is 50 mg, common use is 100 mg.

Source: Package Inserts

## CASE STUDY

### Faces and Phases of Menstrually Related Migraine

CONTINUED FROM PAGE 5

in 23% of women treated with naratriptan compared with 8% in placebo-treated women ( $P < .05$ ). Targeted perimenstrual prophylaxis with frovatriptan\* (half-life of 26 hours) and naratriptan\* (half-life of 6 hours), has demonstrated positive prophylactic action in MRM in randomized controlled clinical trials.<sup>10,11</sup> How differences in pharmacologic profiles (long-acting vs short-acting) translate into clinical efficacy and tolerability for mini-prophylaxis of MRM is currently being studied.<sup>12</sup> Timing is crucial with mini-prophylaxis: pre-emptive therapy is most effective when begun 24 to 48 hours before the expected attack (see Figure).

Conventionally used agents include the NSAIDs, which interfere with prostaglandin formation, a possible factor in migraine. This class includes agents such as naproxen, ibuprofen, fluriprofen, and ketoprofen among others. When one NSAID is ineffective, another type of NSAID can be tried. Ergotamine agents, including DHE, methylergonovine maleate, and methysergide, may be used when the NSAIDs are ineffective.

**Preventive therapy.** Preventive therapy implies specific therapy taken daily to prevent the migraine occurrence. Mrs P had previously tried three migraine preventive therapies—amitriptyline,\* a beta-blocker, and verapamil\*—but did not notice any beneficial impact on MRM. Newer preventive strategies include neuronal stabilizers such as topiramate and divalproex, which are FDA approved for prevention of migraine. These agents

may diminish neuronal hyperexcitability and thus decrease migraine frequency.

There are many preventive therapies for migraine, but none specific to the menstrual setting or FDA approved for use in MRM. Hormonal therapies do target MRM specifically, but adequate controlled studies are lacking on which to base recommendations for treatment.

Estrogen administered via transdermal patches, applied to the skin immediately before menstruation, may be effective. There is little practical information in the literature regarding the specific precipitants of MRM. It is often reported to be triggered by “fluctuating hormone levels,” a statement that is nonspecific—not only regarding which hormones but also regarding the nature of the fluctuations. Examination of the literature gives better guidance: evidence is found only for the association of decreases in estrogen concentration with MRM. Consistent, stable estrogen concentrations—whether high, low, or physiologic—were associated with improvement in MRM.<sup>8</sup>

Mrs P had tried different COCs for treatment of her disabling endometriosis, but all were abandoned because they intensified MRM. Today there are 30 OCs available in the United States; all differ both pharmacologically and structurally. Even the lowest-dose COCs are unlikely to have beneficial impact on MRM. This is because the late luteal phase decline in estrogen in the native menstrual cycle is equivalent to the decline that accompanies the switch to placebo pills in the 20- $\mu$ g OCs. Menstrual migraineurs who want to use COCs may benefit from the addition of supplemental estrogen during the inactive pill week, thereby limiting the premenstrual decline in estrogen to the equivalent of 10- $\mu$ g EE. That

approach was examined in a small, open-label pilot study. All subjects responded with at least a 50% reduction in number of headache days per month; mean number of headache days per cycle declined from 7.6 to 1.6.<sup>13</sup>

Another treatment option is to use an extended-cycle COC regimen. A commercially available formulation provides 84 active contraceptive pills (30- $\mu$ g EE) followed by 7 inert pills. With successful prolonged suppression of ovulation, both menses and MRM can be postponed for months at a time. For specific prevention of her disabling MRM, Mrs P was prescribed a transdermal patch contraceptive that delivers 20  $\mu$ g of EE and 150  $\mu$ g of norelgestromin. She was instructed to apply the patch weekly for 3 weeks, followed by a transdermal patch containing 0.1 mg 17-beta estradiol during week 4 (the menstrual week). This limited the premenstrual decline in estrogen to the equivalent of only 10- $\mu$ g EE—half the decline experienced with the contraceptive patch alone or with the natural menstrual cycle.<sup>14</sup>

## Results

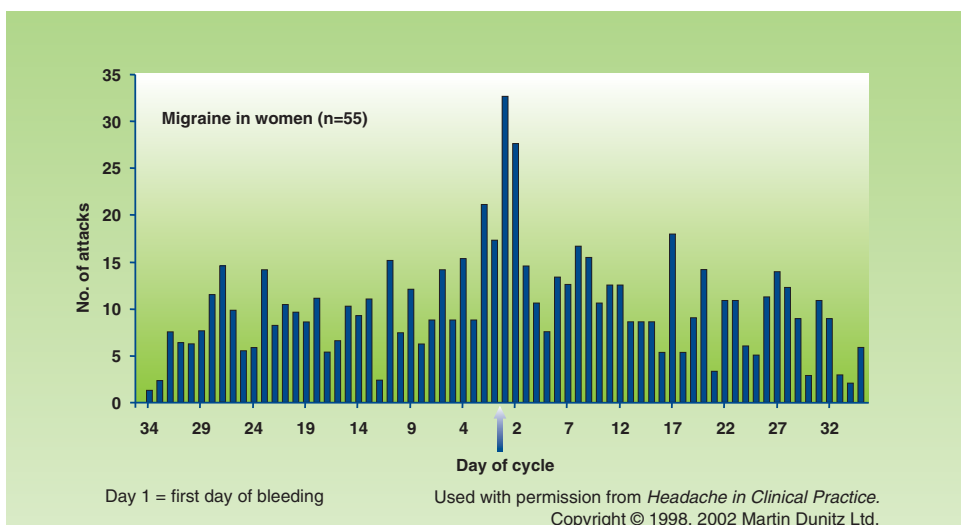
When seen in a follow-up visit 6 weeks later, Mrs P's calendar revealed that her headache frequency during the preceding 28-day cycle had declined to only 6 days: 2 rated as moderate and 4 rated as mild. Only 1 day of mild headache occurred during the menstrual week, and all headache attacks were reported to be quickly treated. Her endometriosis symptoms were significantly improved, with only 1 to 2 days of mild cramps, and she experienced no breakthrough bleeding. Three months later, she reported no lost workdays because of headache or dysmenorrhea.

In addition to their impact on migraine, potential side effects of OCs, such as breakthrough bleeding or breast discomfort, should be considered on an ongoing basis. Contraindications to the use of OCs include smoking (after 35 years of age), hypertension, diabetes with vascular disease, coronary disease, and “focal migraine with neurologic impairment,” which has been widely interpreted to mean migraine with aura.

## Discussion

Mrs P responded well both to initial attempts to achieve reversion to episodic migraine as well as to hormonal intervention for MRM. This approach was equally successful in treating her comorbid endometriosis; attempts at contraceptive therapy for endometriosis had been abandoned on three previous attempts because the products selected exacerbated MRM.

Migraine is one of the most important medical issues in women's health. It is



**Figure**

Menstrual migraine frequency and timing<sup>6</sup>

more common in women than in men, is influenced by hormonal levels that change throughout a women's menstrual cycle, and has great clinical, quality-of-life, and economic impact. PCPs have the unique opportunity to treat women throughout the chronologic and hormonal phases of their lives. Menstruation marks an impor-

**“Migraine is one of the most important issues in women’s health.”**

tant phase in a women's life that requires individualized pharmacologic and nonpharmacologic (including behavioral) treatment strategies for MRM.<sup>15</sup> Various challenges in treating MRM include the disability associated with MRM, frequently comorbid menstrual symptoms (eg, endometriosis), and issues related to pharmacologic management.

### References

- Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*. 2001;41:646-657.
- Edelson RN. Menstrual migraine and other hormonal aspects of migraine. *Headache*. 1985;25:376-379.
- MacGregor EA, Hackshaw A. Prevalence of migraine on each day of the natural menstrual cycle. *Neurology*. 2004;63:351-353.
- Bigal ME, Tepper SJ, Sheftell FD, Rapoport AM, Lipton RB. Chronic daily headache. *Headache*. 2004;44:684-681.
- Galli F, Patron L, Russo PM, Bruni O, Strambi LF, Guidetti V. Chronic daily headache in childhood and adolescence: clinical aspects and a 4-year follow-up. *Cephalalgia*. 2004;24:850-858.
- Smeyers P. Headaches in childhood: association with sleep disorders and psychological implications. *Rev Neurol*. 1999;28(suppl 2):S150-S155.
- Mannix LK, Calhoun AH. Menstrual migraine. *Curr Treat Options Neurol*. 2004;6:489-498.
- Calhoun A. Women's Issues in Headache. In: Loder E, ed. *Headache*. Philadelphia: American College of Physicians, 2004:157-177.
- Ryan RE. A controlled study of the effect of oral contraceptives on migraine. *Headache*. 1978;17:250-251.
- Newman L, Mannix LK, Landy S, et al. Naratriptan as short-term prophylaxis of menstrually associated migraine: a randomized, double-blind, placebo-controlled study. *Headache*. 2001;41:248-256.
- Silberstein SD, Elkind AH, Schreiber D, Keywood C. A randomized trial of frovatriptan for the intermittent prevention of menstrual migraine. *Neurology*. 2004;63:261-269.
- Allais G, Bussone G, De Lorenzo C, Mana O, Benedetto C. Advanced strategies of short-term prophylaxis in menstrual migraine: state of the art and prospects. *Neurol Sci*. 2005;26:S125-S129.
- Calhoun AH. A novel specific prophylaxis for menstrual-associated migraine. *South Med J*. 2004;97:819-822.
- Calhoun A. Menstrual and hormonally related migraine. UpToDate [Web site.] Available at: <http://www.uptodate.com>. Accessed August 22, 2005.
- Mannix LK, Diamond M, Loder E. Women and headache: a treatment approach based on life stages. *Cleve Clin J Med*. 2002;69:488-500.
- Silberstein SD, Lipton RB, Goadsby PJ. *Headache in Clinical Practice*. 2nd ed. London, England: Martin Dunitz Ltd; 2002.

\*Not FDA approved for this use.

## Women With Migraine

CONTINUED FROM PAGE 3

- dose reduction
- utilization of a noncycling method
- switching from conjugated estrogens to pure estradiol or from synthetic to bioidentical estrogen
- switching from oral to transdermal delivery.<sup>11</sup>

Women should be notified of the possibility that their migraine may worsen to ensure consent to treat. Because patients undergoing surgical menopause noted a worsening of their headaches and anecdotal reports of favorable effects are complicated by the post-operative use of daily estrogen replacement, there is no role in the management of MM for hysterectomy or oophorectomy.<sup>12</sup>

**“Treatment can be challenging and both pharmacologic and nonpharmacologic approaches are considered.”**

### Nonpharmacologic Treatment

Treatment of migraine in women can be challenging and both pharmacologic methods and nonpharmacologic approaches (ie, avoidance of known triggers, regular exercise, biofeedback, and acupuncture) are considered. Certain triggers may be critically important in avoidance of MM, yet be insufficient to trigger NM. A 3-month headache diary to record triggers and to ascertain the link between headaches and menses is helpful. In addition to hormonal factors, common migraine triggers for women include lifestyle factors—stress, skipped meals, lack of or excess sleep, post-stress letdown, foods and alcoholic beverages, perfume and smoke, as well as environmental factors such as weather changes and sunlight. Identification of triggers will help to ameliorate migraine or prepare for its possible onset. Behavioral treatments such as relaxation methods, biofeedback, acupuncture, and stress management can be effective in some patients who experience migraine and may complement treatment in patients with more severe or frequent migraine attacks.<sup>13</sup>

### Associated Comorbidities

Major depression and migraine are associated, and patients should be screened for depression since the lack of appropriate antidepressant treatment can hinder successful migraine management.<sup>14</sup> Similarly, anxiety disorders have been found to be comorbid with migraine.<sup>15</sup> In a recent study, migraine was found to be more common in women with endometriosis; however, the severity of endometriosis does not affect the migraine characteristics.<sup>16</sup> Irritable bowel syndrome (IBS) is often seen in migraineurs; however,

it is unclear whether the two conditions are comorbid or whether IBS symptoms are a presentation of migraine related to decreasing hormone levels or to other factors that vary with the menstrual cycle.

### Conclusions

Migraine is a common, progressive disease with significant potential for burden when not properly diagnosed or managed. While the effects of hormonal fluctuations can be unpredictable, a treatment approach based on life stages and perseverance by both physician and migraineur ultimately leads to effective control in the majority of female patients.

### References

- Allais G, Benedetto C. Update on menstrual migraine: from clinical aspects to therapeutic strategies. *Neurol Sci*. 2004;25(suppl 3):S229-S231.
- Robinson ME, Gagnon CM, Riley JL, Price DD. Altering gender role expectations: effects on pain tolerance, pain threshold, and pain ratings. *J Pain*. 2003;4:284-288.
- Lipton RB, Stewart WF, Celentano DD, Reed ML. Undiagnosed migraine headaches: a comparison of symptom-based and reported physician diagnosis. *Arch Intern Med*. 1992;152:1273-1278.
- MacGregor EA. Oestrogen and attacks of migraine with and without aura. *Lancet Neurol*. 2004;3:354-361.
- Couturier EG, Bomhof MA, Neven AK, van Duijn NP. Menstrual migraine in a representative Dutch population sample: prevalence, disability and treatment. *Cephalalgia*. 2003;23:302-308.
- Granella F, Sances G, Allais G, et al. Characteristics of menstrual and nonmenstrual attacks in women with menstrually related migraine referred to headache centers. *Cephalalgia*. 2004;24:707-716.
- Allais G, De Lorenzo C, Mana O, Benedetto C. Oral contraceptives in women with migraine: balancing risks and benefits. *Neurol Sci*. 2004;25(suppl 3):S211-S214.
- Kurth T, Slomke MA, Kase CS, et al. Migraine, headache, and the risk of stroke in women: a prospective study. *Neurology*. 2005;64:1020-1026.
- Sances G, Granella F, Nappi RE, et al. Course of migraine during pregnancy and postpartum: a prospective study. *Cephalalgia*. 2003;23:197-205.
- Fox AW, Chambers CD, Anderson PO, Diamond ML, Spierings EL. Evidence-based assessment of pregnancy outcome after sumatriptan exposure. *Headache*. 2002;42:8-15.
- Facchinetti F, Nappi RE, Tirelli A, Polatti F, Nappi G, Sances G. Hormone supplementation differently affects migraine in postmenopausal women. *Headache*. 2002;42:924-929.
- Martin V, Wernke S, Mandell K, et al. Medical oophorectomy with and without estrogen add-back therapy in the prevention of migraine headache. *Headache*. 2003;43:309-321.
- Holroyd KA, Penzien DB. Psychosocial interventions in the management of recurrent headache disorders. 1: Overview and effectiveness. *Behav Med*. 1994;20:53-63.
- Breslau N, Lipton RB, Stewart WF, Schultz LR, Welch KM. Comorbidity of migraine and depression: investigating potential etiology and prognosis. *Neurology*. 2003;60:1308-1312.
- Merikangas KR, Angst J, Isler H. Migraine and psychopathology: results of the Zurich cohort study of young adults. *Arch Gen Psychiatry*. 1990;47:849-853.
- Ferrero S, Pretta S, Bertoldi S, et al. Increased frequency of migraine among women with endometriosis. *Hum Reprod*. 2004;19:2927-2932.
- Henry P, Michel P, Brochet B, Dartigues JF, Tison S, Salamon R. A nationwide survey of migraine. GRIM. *Cephalalgia*. 1992;4:229-237.

\*Not FDA approved for this use.

<sup>†</sup>Pregnancy category B is the second-safest tier in the FDA 5-tier classification of fetal risk due to pharmaceuticals.

**WHAT'S HOT IN MIGRAINE****DAVID E. HARTREE, PhD**

Medical Writer,

Thomson Professional Postgraduate Services®

*No relevant financial relationships.***Increased Frequency of Migraine in Women With Endometriosis**

A recent study by investigators in Italy examined the relationship between endometriosis and headache. The study sample recruited women of reproductive age who were undergoing surgery for benign gynecological conditions. A diagnosis of endometriosis was made from histology and symptom intensity was determined from patient rating on a 10-point scale. A neurologist, unaware of subjects' endometriosis, interviewed

***“Diagnosis of chronic migraine can only be confirmed once medication overuse headache has been excluded.”***

those identified as suffering from headache. The study found that overall headache prevalence was significantly higher in women with endometriosis (63.9%) than in those without in the control group (36.1%) ( $P<.001$ ). There was no significant difference in mean age between the two groups. Migraine prevalence was 38.3% in women with endometriosis vs 15.1% in the control group ( $P<.001$ ). There was no increase in prevalence of other headache types. The presence of endometriosis did not have any effect on migraine attack frequency, migraine pain intensity, or menstrually associated migraine. Women with endometriosis, however, were more likely to miss workdays or experience reduced work effectiveness because of headache or dysmenorrhea. [Ferrero S, Pretta S, Petrerá P, et al. Higher frequency of migraine among women with endometriosis. Presented at American Academy of Neurology; April 13, 2005; Miami Beach, Fla. Abstract P04.050]

**Prevalence of Chronic Migraine and Medication Overuse as Defined by 2004 IHS Criteria**

Chronic migraine (CM) is a newly established headache type, defined as migraine headaches occurring 15 or more days per month for 3 or more consecutive months. A diagnosis of CM can only be confirmed once medication overuse headache has been excluded. The FRAMIG 3 population-based survey included 15,000 subjects from the French population. Subjects with CM were identified from questionnaire responses, and the diagnosis was subsequently confirmed by telephone interviews. Subjects were then classified as probable CM if they demonstrated medication overuse as defined by ICHD-II. There was a 1.7% prevalence of strict CM and a 0.8% prevalence of probable CM. The subjects with probable CM overused acetaminophen (41.9%) and fixed combinations containing opioids (33.7%). Overuse of NSAIDs and triptans occurred less frequently. Subjects with medication overuse showed greater impaired function and quality of life than those with CM with a trend toward greater psychiatric comorbidity. [Lantéri-Minet M, Chautard M-H, Lucas C. Chronic migraine and medication overuse: results of Framig 3, a French population-based survey carried out according to the 2004 IHS classification. Presented at American Academy of Neurology; April 12, 2005; Miami Beach, Fla. Abstract S09.004]

**Do Medications for Migraine Prevention Enhance the Effect of Triptans?**

Topiramate, in addition to its efficacy in migraine prevention, is commonly believed to enhance the responsiveness of individual migraine attacks to triptans. To study this effect, a post hoc analysis was made of the data from two 26-week clinical trials in which 445 patients took triptans and at least one post-baseline dose of topiramate. Pooled analysis showed that for individual triptan-treated migraine attacks, the use of topiramate 100 mg/d was associated with significant reductions vs placebo in migraine

severity ( $P=.007$ ) and nausea ( $P=.045$ ). In one trial there were statistically significant reductions in photophobia ( $P<.011$ ) and phonophobia ( $P<.018$ ). The findings of this exploratory analysis suggest that topiramate is effective in improving patient responsiveness to triptans and that future prospective studies are needed to investigate the hypothesis further. [Dodick DW, Hulihan J, Wu S-C. Do migraine preventive medications enhance the efficacy of triptans? Analyses from topiramate migraine trials. Presented at American Academy of Neurology; April 14, 2005; Miami Beach, Fla. Abstract S49.008]

**The Use of the Rudy Probability Model in Diagnosis of Menstrual Migraine**

The novel Rudy Probability Model has been devised to determine whether the timing of migraine attacks has any statistically significant connection to a woman's menstrual cycle. To test the usefulness of the model in diagnosis, women aged 18 to 45 years reporting significantly increased migraine with menses were recruited through study advertisements. For 3 continuous months, subjects recorded headache severity 4 times daily in diaries and made daily records of somatic and emotional complaints using the Calendar of Premenstrual Experiences (COPE). Sixty-two women completed the study. The Rudy model showed perfect diagnostic agreement with the International Headache Society (IHS) model for women with pure menstrual migraine and menstrually nonrelated migraine. In contrast, women identified as having menstrually related migraine using the Rudy model were more likely to show significant increases in headache and COPE scores during menstrual days than those identified using the IHS criteria. The results suggest that the Rudy criteria are more accurate than the new IHS criteria for identifying menstrual migraine. [Marcus DA, Bernstein C, Rudy TE. Prospective diagnosis of menstrual migraine: comparison of the IHS criteria and the Rudy probability model. Presented at Headache Update 2005; July 12-16, 2005; Lake Buena Vista, Fla. Abstract 305.]



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