



CASE VIGNETTE

“I feel so overwhelmed. How can I take care of my baby and deal with this pain?”

Jane, a 32-year-old white female, reports severe headaches worsening since the recent birth of her first child. She has no prior consultations for headache. Vital signs and physical exam are normal.

Jane, when did your headaches begin? Have there been any recent changes in the pattern of your headaches?

Her headaches started around age 13 or 14, and occurred about once or twice per month during her teenage years and 20s. Back then, she could generally manage them with over-the-counter analgesics and sleep. She had several bad headaches early in her pregnancy and then was headache free for about 6 months. But after the baby was born, her headaches came back with a vengeance.

That must be hard on you—how are you coping?

She feels terribly stressed, and she thinks maybe that makes the headaches worse. The baby seems to know it too, because he always seems to cry more when she has a headache. The child is still waking up two times per night, and she doesn't feel particularly supported by her husband, who has a demanding job as a physician.

Do you have one or more than one type of headache?

In addition to the severe headaches, she also experiences little “nagging” headaches maybe once or twice a week, but these don't really bother her.

Describe the more severe headaches. Where do you feel the pain and how severe is it? Do you have any other symptoms in addition to the head pain? Are there any warning signs that tell you a headache is coming on?

Her headaches are usually bilateral and frontal. The pain is throbbing and extremely severe—worse when she moves about. She has nausea as well as photophobia and phonophobia with the attack. She

has vomited with her headaches in the past, but typically only becomes nauseated with her headaches. She has no warning signs and when asked, specifically denies visual symptoms, one-sided weakness or numbness, and slurred speech. The mild headaches are experienced as a dull frontal ache, unaccompanied by nausea, photophobia or phonophobia.

How many days per month do you get your severe headaches? How long do the headache attacks last? How rapidly does the headache build to maximum intensity?

The severe headaches occur once or twice a month but last for 3 to 4 days and are quite debilitating. She is unable to perform her household duties and generally requires bed rest. The headaches build gradually in intensity over an hour or so.

How do you manage the severe headaches?

She has tried over-the-counter medications like Excedrin Migraine, which had been working in the past but now seems ineffective. She tries a double dose early in the attack, then gives up and goes to bed. She has never tried any preventive or abortive medications prescribed by a physician.

You mentioned you are under a lot of stress and you think this is making the headaches worse. Is there anything else that seems to be triggering your headaches? Is there any pattern in terms of day of the week or time of the month?

Aside from stress, red wine will trigger a headache, so she avoids it. She almost always gets a bad headache right before her period.

Do you have other premenstrual symptoms, any problems with mood, for example?

Jane says she is generally moody and irritable during the last 10 days of her menstrual cycle.

Has anybody in your family had similar headaches?

Her mother had severe headaches most of her adult life. When she went through menopause, her headaches got much better. Jane says she cannot wait that long for help.

Jane, there are a number of very effective headache medications available, and I feel confident we can find one that will work for you. I'm going to give you a prescription to try, and I'd like you to keep a headache calendar so you can keep track of possible triggers, including your monthly period, and also keep a record of how effective the medication is. If you bring that headache calendar with you on your next appointment, we'll have more information to help find the best possible therapy for your headaches.

PRETEST

1. What is the headache diagnosis?
2. What associated conditions or comorbidity may also be present?
3. Name two possible treatment strategies, with the rationales for your choices.
4. What would be important in the follow-up of this patient?

COMMENTARY

The patient's headaches are consistent with a diagnosis of migraine without aura. Her headaches can be further classified as menstrually related migraine, and on further investigation may prove to be true menstrual migraine. True menstrual migraine headaches are migraine headaches that occur exclusively between 2 days before to 3 days after the onset of menstruation. The headaches only occur around menstruation and not at other times of the month. This headache pattern accounts for approximately 5% to 10% of women with migraine.

Jane, when did your headaches begin? Have there been any recent changes in the pattern of your headaches?

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Her headaches are clearly linked to hormonal fluctuations—beginning around menarche, worsening in the first trimester of pregnancy when estrogen and progesterone levels are fluctuating, improving during the second and third trimesters when estrogen and progesterone levels are relatively high and stable, then resuming after childbirth with the return of the menstrual cycle. This is a common pattern for females with migraine and is not unique to menstrual migraine.

That must be hard on you—how are you coping?

Stress can have a major role in the provocation of migraine headache. Behavioral interventions such as relaxation training have proven efficacy in the management of migraine and should be considered if Jane reports continued stress and/or limited efficacy of medication. To the extent that her stress is a byproduct of the headaches, her mood and coping should improve with successful headache management. However, follow-up must include monitoring for possible coexisting depression. If comorbid depression is identified, then treatment with an antidepressant may be indicated. She is perceptive about her situation, but is not likely to volunteer information on her mood and family life unless specifically asked.

Do you have one or more than one type of headache?

More than one headache type often coexists in the same patient. Asking the more generic question “tell me about your headaches” will elicit a description of a combination of all headache types—usually migraine and tension-type headache. This will confuse the diagnosis.

Describe the more severe headaches. Where do you feel the pain and how severe is it? Do you have any other symptoms in addition to the head pain? Are there any warning signs that tell you a headache is coming on?

Bilateral head pain is less common than unilateral pain in migraine, but is not unusual or inconsistent with the diagnosis. The other features of her headaches and the associated symptoms are typical of migraine without aura. Her more frequent mild headaches do not have migrainous features and are likely tension-type headache.

How many days per month do you get your severe headaches? How long do the headache attacks last? How rapidly does the headache build to maximum intensity?

Here she provides useful information for selecting acute therapy. For her headaches, quick onset of action is less important than consistent response and low risk of headache recurrence. Once the severe

headaches are under control, it would be appropriate to ask again about the more frequent tension-type headaches and their management.

How do you manage the severe headaches?

Since the over-the-counter treatments are ineffective, she should be counseled not to use them. She should be given clear instructions on dosing and re-dosing of her prescription medication.

You mentioned you are under a lot of stress and you think this is making the headaches worse. Is there anything else that seems to be triggering your headaches? Is there any pattern in terms of day of the week or time of the month?

Red wine is a common dietary trigger. Some stress-prone patients will have a weekly pattern with a “let-down” headache striking on the weekends. The important information here is the apparent link to her menses, which needs to be confirmed by a 3-month headache calendar.

Do you have other premenstrual symptoms, any problems with mood, for example?

She likely suffers from premenstrual dysphoric disorder, which appears to be more prominent in patients with migraine headaches. This is probably secondary to the fact that the central nervous system of migraineurs seems to be hyperexcitable to a number of triggers, including hormones. If her premenstrual dysphoria is impacting her life, then treatment with an antidepressant may be indicated.

Has anybody in your family had similar headaches?

A positive family history is common in migraine, and here the mother would also appear to have had hormonally triggered headaches.

Jane, there are a number of very effective headache medications available, and I feel confident we can find one that will work for you....

Among the triptans, sumatriptan, rizatriptan and zolmitriptan have been shown to be effective as abortive therapy for menstrual migraine. The headache calendar is used to determine the relationship between her more severe headache and her menstrual period. If the calendar confirms a diagnosis of menstrual migraine, there are a number of strategies for prophylactic therapy, in which medication is started 2 days before the expected onset of headache and continued for at least 5 days, up to 7-10 days as needed for adequate prophylaxis.

—Case contributed by Vince Martin, MD, Division of General Internal Medicine, University of Cincinnati, Cincinnati OH

MANAGING MIGRAINE TRIGGERS

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Migraine headache syndrome is an inherited condition that predisposes to a “sensitive” or hyper-reactive CNS. Due to possible faulty modulation of nociceptive processing, minor alterations in the internal and external environment that may be well tolerated by others trigger headaches in a migraineur. Treat the headache with appropriate abortive and, if needed, prophylactic medications. Then address other factors that are likely to trigger an episodic migraine or transform episodic migraines into chronic daily headaches. (See tables 1 and 2 on page 4.)

The goal is to assure that the patient **RESUMES** a normal lifestyle:

Rule out and address coexisting disease: Always do an exam, paying particular attention to the eyes. Moderate to severe hypertension, usually >160/100, is a not uncommon headache trigger. Do routine blood tests, including thyroid function, to identify the most common disorders. If there is a family history of vascular disease or spontaneous abortions, particularly in women who are smokers and taking oral contraceptives, a workup for hypercoagulable disorders would be indicated. Mood disorders should be treated if present.

“Eat like a bird”: Fasting followed by a large meal is to be avoided. Eating low carbohydrate or small protein-rich meals every 4 – 5 hours helps maintain stable blood glucose levels.

Stress management: Stress is a given in our society. Daily, low-grade “hassles” are more likely to result in headaches than are major stressful events. Constant tension causes a miniature fight-or-flight response in the body: jaws clenched, shoulders hunched, neck turtled in, brow furrowed. Controlling these postural responses throughout the day is more effective than a 30-minute meditation every evening. Suggestions for patients:

- Take a brief break every 15 – 30 minutes and stretch the body and facial muscles.
- Upper body strengthening improves body posture and decreases the stress on the neck and shoulder muscles.
- Brief relaxation technique to keep tension at a minimum: pick a cue that occurs frequently in your particular environment (telephone ringing, a child calling “Mom”, typing the word ‘the’). With each cue occurrence take a deep breath, straighten your posture, and allow all your muscles to relax as you exhale.

- Control your time. Plan ahead and start early. Don’t expect to do more than is reasonable in a given time frame.
- Let go when you cannot control the situation. When caught in traffic there is nothing you can do to change the situation, so do relaxation techniques.

Unburden: Heavy bags, or coats with the pockets filled with heavy items, place a constant burden on the neck and shoulders, increasing nociceptive input into the upper cervical spinal nerve roots. This effects change in the trigeminal nucleus caudalis, an extension of the trigeminal nerve nucleus into the upper cervical spine, and can trigger headaches.

Modulate hormonal effects: Fluctuation in estrogen level is the major trigger factor for a woman with headaches. The most difficult times are at ovulation, perimenstrually, in the postpartum period, and in perimenopause. These fluctuations can be modified in a number of ways.

- By regulating the menstrual cycle, the newer oral contraceptives can modulate estrogen changes and may thus diminish the frequency or severity of migraine in some women. Be careful, however, as they can also exacerbate headaches, and there is no way of predicting which will occur. It takes several months to determine what effect an OC will have on headaches, so stopping or starting an OC for a month will not give you the answer. Many women are now controlling their menstrual cycle by using oral contraceptives for 3 consecutive months, ignoring the placebo week. Although it is not clear yet what long-term effects this practice may have, it is useful for women with severe, refractory menstrually related migraine.
- Mini-prophylaxis: for women with clear menstrually related migraines, daily NSAIDs, propranolol or verapamil for the 7 – 10 days around the onset of menses each month can be effective.
- In menopausal women, very low dose estradiol can be useful for low-grade daily headaches, and sometimes can improve the mood changes that accompany menopause. Some women benefit from low dose estradiol perimenstrually to modulate the rapid drop in estrogen, but often that simply delays the onset of the headache until the estrogen is stopped.

Exercise: Daily exercise relieves stress, a major trigger, and distracts from pain. Patients should be encouraged to develop a regular regimen, beginning with a minimum of 3 days/week, 20 minutes/day, but building to the equivalent of walking 12 miles/week (about 4 hours/week, based on a 20-minute mile).

Sleep: Alteration in sleep patterns is a more likely trigger than sleep deprivation. The three rules are:

get sufficient sleep at regular hours, avoid sleeping late on the weekends and avoid taking long naps. Jet lag is harder to control. The effect can be minimized by taking a *short* nap if needed and not over-sleeping the first night at one’s destination. Obstructive sleep apnea must be ruled out in patients who have cluster headaches or chronic morning headaches. Even if an individual does not have the expected characteristics of an apnea patient (obesity, hypertension, daytime sleepiness and snoring), ask about snoring, particularly if hypertension or nocturnal GERD is present.

Finally, as the presence and vigor of the response to headache triggers varies for each patient, and may not be consistent from week to week, patients should keep a simple headache diary. As we do not have the time to study an extensive list of headaches closely enough to identify patterns, rather than a journal, have the patient use a month-at-a-glance style of calendar to indicate headache days with a big X (severe) or a small x (mild), days of the menstrual period, and number of hours of sleep. Other items may be included, like medication usage, stressful days, vacations, and suspected triggers.

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CLINICAL PEARL: RELATIONSHIP OF QUESTION-ASKING TO COMPLIANCE

The fewer the questions the patient asks, the less the adherence to prescribed regimens!

Hall JA, Roter DL, Katz NR. Meta-analysis of correlates of provider behavior in medical encounters. *Medical Care* 1988;26:657-674.

Courtesy of Fred Sheftell, MD. New England Center for Headache. Stamford, CT

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TABLE 1. REPORTED PREVALENCE OF MIGRAINE TRIGGER FACTORS *

TRIGGER FACTOR	POPULATION-BASED STUDIES				SPECIALTY CLINIC-BASED STUDIES		
	Ulrich	Van den Bergh	Chabriat	Turner	Scharff	Robbins	Peatfield
Stress/poststress	36%	49%	42%	51%	72%	62%	—
Menstruation	—	8%	32%	54%	68%	50%	—
Changes in sleep	—	—	—	38%	52%	31%	—
Fasting	—	—	—	56%	45%	40%	—
Weather	—	7%	35%	52%	46%	43%	—
Food	—	44%	36%	22%	—	30%	—
Smoking	9%	4%	2%	—	—	26%	—
Chocolate	2%	23%	—	—	22%	—	19%
Alcohol	—	—	—	—	35%	—	29%
Caffeine	—	—	—	—	14%	—	—
Cheese	—	—	—	—	9%	—	18%
Monosodium glutamate	—	—	—	—	13%	—	—

*Adapted with permission from Martin VT. Toward a rational understanding of migraine trigger factors. *Med Clin North Am* 2001; 85: 911-41. Includes women and men as well as migraine with and without aura; represents the self-reported prevalence of migraine trigger factors.

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TABLE 2. STRENGTH OF EVIDENCE FOR MIGRAINE TRIGGER FACTORS*

TRIGGER FACTORS	STRENGTH OF EVIDENCE
Stress	Strong
Menstruation	Strong
Caffeine withdrawal	Strong
Visual stimuli	Strong
Weather changes (Chinook winds)	Strong
Nitrates	Moderate
Fasting	Moderate
Sleep disturbances	Moderate
Wine	Moderate
MSG	Moderate
Aspartame	Moderate
Smoking	Weak
Odor	Weak
Chocolate	Weak
Tyramine	Weak

*Adapted with permission from Martin VT. Toward a rational understanding of migraine trigger factors. *Med Clin North Am* 2001; 85: 911-41.

Strength of evidence was defined as: (1) strong—at least two prospective randomized, controlled or diary studies confirming an association with no dissenting studies; (2) moderate—at least one randomized, controlled trial or a prospective diary study confirming an association with no dissenting studies or two supporting studies with one dissenting study; (3) weak—two or more dissenting trials on a given trigger or no prospective trials at all.

HORMONAL INFLUENCES ON MIGRAINE IN WOMEN

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CLINICAL PRESENTATION OF MENSTRUAL MIGRAINE

In women, migraine attacks may occur mainly at the time of menses (*menstrually related migraine*) or exclusively with menses (*true menstrual migraine*) in some.¹ Menstrual migraine (MM) can be associated with other somatic complaints that arise before and often persist into menses, such as nausea, backache, breast tenderness, and cramps and, like these complaints, appears to be the result of falling sex hormone levels. When migraine occurs before menstruation (PMM), there may also be features of premenstrual syndrome (PMS).¹ Migraine that occurs during (rather than prior to) menstruation is usually not associated with PMS but is often associated with dysmenorrhea.² It is important to differentiate between the two conditions because medications that may be useful in treating MM may not help PMM.³

In general, migraine attacks occur more frequently with menstruation but are not longer in duration or clinically significantly more severe. In a population-based sample, 81 menstruating women with clinically diagnosed migraine were enrolled in a 98-day diary study and recorded the occurrence of menses, headache days, headache symptoms, and associated disability.⁴ Attacks of migraine without aura, but not migraine with aura, were significantly more likely to occur 2 days before the onset of menses (odds ratio 2.04) and on the first 2 days of menses (odds ratio 1.80). Migraine headache intensity was slightly greater during the first 2 days of menses. Otherwise, few significant differences were observed in headache severity, disability or symptoms by day of cycle.

PATHOGENESIS

MM begins at menarche in 33% of affected women.¹ Migraine may worsen during the first trimester of pregnancy and although many women become headache-free during the last two trimesters, 25% have no change in their migraine.⁵ MM typically improves with pregnancy, perhaps due to sustained high estrogen levels. Migraine prevalence decreases with advancing age but may either regress or worsen at the menopause. Both hormonal replacement with estrogens and oral contraceptives (OCs) can change its character and frequency. These phenomena indicate a relationship between migraine headaches and changes in sex hormone levels.

PREEMPTIVE TREATMENT OF MENSTRUAL MIGRAINE

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It is not surprising that Jane's headaches began at age 13. The incidence of migraine in girls peaks around the time of menarche, probably because of the provocative influence that cycling hormonal levels have on the headache-prone nervous system. About half of all women with migraine report that they are more likely to experience a headache attack around their period.¹ Research implicates falling estrogen levels as the most important trigger for these attacks.² Why this is an important trigger for some women with migraine but not others remains unclear, but the same variability is seen with other migraine triggers. Migraine occurring in association with menstruation is only slightly more severe than attacks that occur at other times of the month, so the popular belief that menstrual migraine is significantly more difficult to treat does not appear to be true for the majority of women with migraine.³ As with other forms of the disorder, though, some patients have particularly intractable headaches. Most women who have migraine attacks in association with menses also have attacks at other times of the month.

As a method of diagnosing menstrual migraine, patient recall is less reliable than diary information. In general, several months of headache and menstrual diary recordings are important to confirm a diagnosis of menstrual migraine. These diaries also show whether menstrual periods occur regularly and identify the timing of the menstrual attacks in relation to the period. In some cases, headache begins 1 or 2 days prior to the onset of the menstrual flow, although a large diary study showed that most begin during the first 2 days of bleeding. Most experts define a menstrual migraine attack as one that occurs during a window of 2 days before and up to 3 days after the first day of bleeding.⁴

Women with menstrual worsening of migraine rarely have hormonal abnormalities. Although many patients request them, "hormone tests" are invariably normal and unlikely to aid in diagnosis or treatment. What is abnormal in most of these patients is the way in which their headache-prone central nervous system responds to normal fluctuations in hormonal levels.

While the trigger in menstrual migraine attacks is hormonal, non-hormonal abortive and preventive treatments are effective in the disorder and recommended as initial treatment by most experts. The

SOME REGIMENS FOR PREEMPTIVE TREATMENT OF MENSTRUAL MIGRAINE*

DRUG	DOSAGE	COMMENTS
Naproxen sodium	550 mg po bid x 5 days	Other NSAIDs likely effective; dosing depends upon half-life
Estrogen patch	100 µg q 3 days x 5 days	There appears to be a dose threshold: 25 and 50 µg patches less effective. Other forms of estrogen supplementation (e.g., gel, oral) may also be helpful.
Naratriptan	1 mg po bid x 5 days	
Frovatriptan	2.5 mgs po bid x 5 days	
Ergotamine tartrate	1 mg po qd or bid x 5 days	

* Dosing generally begins 48 hours prior to expected onset of the headache.

exception to this is continuous use of oral contraceptives in those patients already using them for another medical reason, discussed in more detail later. Hormonal treatments can be attempted in those for whom first-line non-hormonal treatments are ineffective. Removal of the ovaries as a way of stopping hormonal cycling may actually provoke migraine rather than improve it and is thus not encouraged.⁵

Non-pharmacologic treatment strategies that are used for other forms of migraine are also helpful in menstrual migraine and should be encouraged or continued in most patients. Standard abortive treatment, such as the use of triptans at the onset of the headache, also works well for many women and may be all that is necessary for menstrual as well as non-menstrual attacks. There is little evidence that such treatment is less effective for menstrual attacks than for those occurring at other times of the month. Since Jane has never tried disease-specific medication such as the triptans for her severe headaches, this is where treatment for her should begin.

If Jane fails to respond to standard abortive therapy, preemptive treatment of the expected menstrual headache can be considered. Such treatment is practical only in women who have regular menstrual periods and whose headaches occur in predictable relation to the period, so Jane should be asked to keep a diary of her headaches and menstrual periods. Preemptive or "mini-prophylactic" treatment of menstrual migraine relies on starting a scheduled dose of a drug over a period of 4 or 5 days perimenstrually, with the goal of having a sufficient dose of medication on board before the headache starts in order to prevent or modify the expected attack. Some physicians may elect to extend mini-prophylaxis for up to 10 days, depending on the individual's time-frame of perimenstrual headache vulnerability and the regularity of her cycle.

Naproxen sodium 550 mg po bid given for 5 days has been well studied for menstrual attacks.⁶ This regimen is generally begun 1 or 2 days prior to the expected headache and continued for up to 5 days. Other NSAIDs are effective as well; the goal of treatment is to cover the window of susceptibility, so

dosing of the various drugs will depend upon the half-life. Ergotamine tartrate 1 mg at bedtime or twice a day for 5 days has also been studied in menstrual migraine and appears effective.⁷ Evidence from double-blind, placebo-controlled trials suggests that naratriptan 1 mg bid given perimenstrually is also beneficial.⁸ Preliminary double-blind, placebo-controlled trial results for a regimen using frovatriptan,⁹ also seem favorable. Only open-label evidence supports the use of sumatriptan 25 mg po tid.¹⁰ Mini-prophylaxis with both an NSAID and a triptan can be employed for women who fail to benefit from either regimen alone.

Continuous use of oral contraceptives in women who are already using them is another treatment option; such regimens eliminate the traditional pill-free or placebo pill week of each cycle for a period of up to 6 months, to minimize the number of times estrogen withdrawal occurs. Perimenstrual estrogen supplementation, started 48 hours before onset of menstruation and continued for a total of around 5 days, has also been studied and appears helpful for menstrual migraine. Such treatment maintains estradiol levels perimenstrually until endogenous levels rise naturally during the early part of the next menstrual cycle. Estradiol gel 1.5 mg qd and 100 µg estrogen patches appear to be most effective.¹¹

Other treatments for menstrual migraine, such as danazol, bromocriptine or tamoxifen, have only preliminary evidence for their usefulness. They are associated with many adverse effects, and their use should probably be limited to refractory patients in specialty care settings.

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DEFINITIONS¹

Migraine associated with menstruation is typically migraine without aura; women who have a history of migraine with and without aura often report that menstrual attacks are without aura.

Menstrual migraine: Migraine occurring exclusively on day 1 ± 2 of menstruation (i.e., days -2 to $+3$) in at least two out of three menstrual cycles. The first day of menstruation is day 1 and the preceding day is day -1 ; there is no day 0.

Menstrually related migraine: Migraine occurring on days 1 ± 2 of the menstrual cycle in at least two out of three menstrual cycles but with additional attacks of migraine at other times of the cycle.

POSTTEST—TRUE OR FALSE

1. Menstruation, stress, smoking and tyramine-containing foods are all common well-studied headache triggers.
2. Hormonal abnormalities are only rarely found in women with menstrual migraine.
3. A short perimenstrual course of NSAID therapy (e.g., naproxen) is often effective prophylaxis for menstrual migraine.
4. For women with severe refractory menstrual migraine, oophorectomy can be highly effective.
5. For women using oral contraceptives, continuous administration (eliminating the placebo week) can be effective in preventing menstrual migraine attacks.

The succession of shifting hormone levels in the menstrual cycle cause major changes in fluid balance, blood pressure, and uterine tone, and the transition between these states may not be smooth. The mean serum estradiol concentrations oscillate between 30 and 80 pg/ml during the first week of the menstrual cycle, between 80 and 300 during the second week, between 100 and 150 during the third week, and then drop to around 30 pg/ml again at the end of the fourth week of the cycle. Mean serum progesterone levels are below 1 ng/ml during the follicular phase, rapidly increasing after ovulation to around 20 ng/ml and dropping during the last few days of the cycle preceding menstruation.

Attempts to find differences in ovarian hormone levels in women with MM and controls have not yielded consistent results. Some authors have reported higher estrogen and progestin levels and others have not.¹ Most find that testosterone, FSH, and LH levels are similar to controls. Somerville⁶ reported that MM occurs during or after the simultaneous fall of estrogens and progesterone. Estrogens given premenstrually delay the onset of migraine but not menstruation.⁷ In contrast, progesterone administration delays menstruation but does not prevent migraine.⁸ Somerville concluded that estrogen withdrawal might trigger migraine attacks in susceptible women. Additional clinical observations support Somerville's conclusion. Women taking combined OCs often develop migraine headache during the steroid-free week, and postmenopausal women given Depo-Estradiol injections frequently develop estrogen-withdrawal migraine. The primary trigger of MM appears to be the withdrawal of estrogen rather than the maintenance of sustained high or low estrogen levels. However, changes in the sustained estrogen levels with pregnancy (increased) and menopause (decreased) also appear to affect headaches.

Estrogen and progesterone both modulate serotonin receptors (5-HT₁ and 5-HT₂).⁹ Prostaglandins, particularly PGE₂ and PGF₂, produced by the endometrium under the influence of estrogens and progesterone, intensify uterine contractions, which are responsible for much of the pain of dysmenorrhea. Prostaglandins have potent effects on nociception. Prostaglandin infusion produces menstrual symptoms, including dysmenorrhea and headache.¹⁰ Plasma PGF₂ levels, which are normal throughout the menstrual cycle, significantly increase during a migraine attack,¹⁰ which may explain the benefit frequently observed with NSAID mini-prophylaxis given for the days before and during menses.

Menstrual migraine is not psychological. Like menstruation, it is due to changes in sex hormone levels. Better treatments are now becoming available based on our new understanding of this condition.

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ANSWERS—PRETEST

1. Migraine without aura, further characterized as menstrually related migraine.
2. Premenstrual dysphoric disorder; possible depression.
3. Acute therapy with an oral triptan; if perimenstrual onset confirmed, short course prophylaxis with an NSAID, estradiol patch or other option.
4. Her depressive symptoms should be followed and treatment or referral considered as needed; her more frequent mild headaches should be monitored for increased frequency/severity or overuse of analgesics.

ANSWERS—POSTTEST

1. F 2. T 3. T 4. F 5. T