Headaches Through a Woman’s Life

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Importance: Headaches affect women across their life span, with menses, pregnancy, and menopause being times that pose unique challenges in diagnosis and treatment. The correct diagnosis and treatment of headache can prevent unnecessary interventions, the worsening of chronic headache disorders, and complications of secondary headaches.

Objective: The objective of this article is to educate women’s health care providers about the diagnosis, differential diagnosis, and treatment of headache during menses, pregnancy, the puerperium, and menopause to improve the quality of care for women with chronic and acute headache.

Evidence Acquisition: Current articles were reviewed addressing headache during menses, pregnancy, the postpartum period, and menopause. Articles with the highest level of evidence were compiled in this article to provide a summary of recommendations.

Results: Multiple diagnostic and therapeutic options for chronic and acute headache are available for women regardless of their stage in life or comorbidities.

Conclusions and Relevance: The effects of headaches span a woman’s life span, with puberty and menopause being times of increased frequency. Pregnancy is an at-risk time for women to develop secondary headache disorders. All women’s health care providers should know how to screen for, diagnose, and treat headache at all stages of a woman’s life. Effective treatment options are available for acute and chronic headache both during and outside pregnancy.

Target Audience: Obstetricians and gynecologists, family physicians.

Learning Objectives: After completing this activity, the learner should be better able to define the differences between primary and secondary headache disorders, interpret the differential diagnosis and treatment of menstrual-related migraines, analyze the diagnosis and treatment of headache in pregnancy, educate patients about secondary headaches in the postpartum period, discuss headache prevalence and treatment of headache during menopause, and propose treatment recommendations to women regardless of their comorbidities or stage in life.

Headaches affect women across their life span, with menses, pregnancy, and menopause being times of particular interest, in part because headaches are often more difficult to treat and diagnose during these epochs. To address these issues, it is important to establish a baseline understanding of primary and secondary headache in order to make a diagnosis.

The diagnosis of headache is divided into 2 general subgroups of primary and secondary headache. Primary headaches are often recurrent, with no underlying structural etiology. Secondary headaches are due to an underlying disease, such as infection, hypertensive disease, intracranial hypertension or hypotension, brain tumors, or a structural brain abnormality (or abnormalities).
Overall, 90% of headaches are primary in nature, with only 10% of headaches being attributed to secondary causes.

Primary headaches are divided into 3 subgroups, including migraine, tension, and cluster headache. The International Classification Headache Disorders, Third Edition, beta (ICHD-3 beta) has standardized all primary and secondary headache definitions to aid in diagnosis (Table 1). When approaching a patient with headache, it is important to keep all 3 subtypes of primary headache high on the differential but to likewise not miss any of the secondary forms.

**Primary Headache**

Tension headache is the most common type of primary headache. The ICHD-3 beta defines tension headache as lasting 30 minutes to 7 days. In addition, patients must meet 2 of the following 4 criteria: bilateral location (often described as a band around the head that spreads down the neck), nonpulsating pain quality (often described as tightening or pressure), pain intensity that is mild to moderate, and pain that is not aggravated by movement or changes in activity and with no associated nausea or emesis. Photophobia or phonophobia can be associated but not both.\(^1\) Tension headache has a female predominance, with 88% of all women meeting criteria for tension headache and 69% of men meeting criteria during their lifetime.\(^2\)

The ICHD-3 beta defines migraine headache as being recurrent, with patients having 5 or more distinct attacks in a lifetime. The duration of each episode must last between 4 and 72 hours. In addition, patients must meet at least 2 of the following 4 criteria: unilateral location (usually described as a band around the head that spreads down the neck), pulsating in quality, pain quality that is moderate to severe, and pain must be aggravated by, or cause avoidance of, routine physical activity (eg, walking or climbing stairs). In addition, patients must have nausea and/or emesis or photophobia and/or phonophobia at some time during the headache episode.\(^1\)

Although aura is not required for the diagnosis of migraine, it is important to address. Twenty percent of patients with migraine suffer from migraines with aura and/or a mixture of migraines with and without aura.\(^3\)

The classic migraine aura is a scotoma described as a perceptual disturbance of a strange light, which typically starts in a small portion of the visual field and then gradually enlarges or moves across the visual field. Auras may also involve other neurovascular symptoms such as vision loss, migratory weakness, paresthesias, or even speech impairment.

In 2007, Lipton et al\(^4\) published the results of a survey including 160,000 participants to assess migraine prevalence, disease burden, and need for preventive therapy. The results showed that migraine headache is more common in women, with increasing frequency at the time of menarche and decreasing intensity after menopause. Peak predominance occurs in the early 40s, with 17% of all women meeting the diagnosis of migraine headache.\(^4\)

As defined by the ICHD-3 beta, the diagnosis of cluster headache, the third and final primary headache disorder, is based on a history of at least 5 attacks meeting the following criteria: unilateral location (usually periorbital), associated with the sensation of severe agitation

**TABLE 1**

<table>
<thead>
<tr>
<th>Primary Headache Classification*</th>
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<tbody>
<tr>
<td><strong>Migraine headache</strong> Required criteria:</td>
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<tr>
<td><strong>Tension headache</strong> Required criteria:</td>
</tr>
<tr>
<td><strong>Cluster headache</strong> Required criteria:</td>
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*In all primary headache disorders, be sure to rule out any secondary cause.
and restlessness, and attack clustering (attacks occurring in multiple distinct episodes within a finite period of time). In addition, patients must have one of the following hallmark autonomic symptoms of conjunctival injection or lacrimation, nasal congestion or rhinorrhea, eyelid edema, forehead and/or facial sweating, sensation of ear fullness, or miosis/ptosis. Cluster headaches are more severe in nature and stand out because of their brief duration and unique autonomic involvement. Unlike tension and migraine headache, cluster headache is the only primary headache with a male predominance, being 4.3 to 6 times more common in men.  

Secondary Headache  
Secondary headaches are grouped into 6 general categories. These are medication overuse, pseudotumor
cerebri, cerebrovascular event, brain tumors, facial infections, and systemic conditions. All women's health care providers, including obstetrician-gynecologists, should be able to rule out secondary headaches by carefully reviewing the history and ensuring a normal neurological examination. When there are red flags or there is an abnormal neurological examination, patients should be referred to (or consultation should occur with) the appropriate provider for further evaluation of possible secondary causes of headache. The acronym SNOOPP, which stands for systemic symptoms, neurological symptoms, onset sudden, older age of onset, postural aggravation, precipitated by Valsalva, progressive, and pregnancy, can be used to remember these red flags. The only exception to referral to a specialist is the diagnosis and management of medication overuse headache.

Medication overuse headache is the result of long-term and often excessive use of acute rescue headache medications in individuals with a preexisting primary headache disorder. Medication overuse headache is often worse upon awakening and is the most common secondary headache, affecting 3% to 5% of the population. As with migraine and tension headache, medication overuse headaches are more common in women.

Although butalbital-containing medications are the most commonly overused headache medications in the United States, there are many other medications known to cause medication overuse headaches, including acetaminophen/aspirin/caffeine combination drugs, ibuprofen, opioids, and triptans. All of these medications can be used safely but should not be used more than 2 to 3 days a week in order to avoid overuse headache. If a patient is using any of the above medications for treatment of headache or chronic pain more than 2 to 3 days per week, they should first be encouraged to wean off their medication and to consider adding a preventive medication. If headaches do not improve, it is reasonable to change the management approach or pursue further workup.

### Premenarche Headaches

Headaches in the premenarche population are common, with 10% of children younger than 12 years experiencing headache. Because of the lack of controlled studies, the diagnostic criteria of tension, migraine, and cluster headache are the same as those used in the adult population, despite pediatric headaches typically being shorter in duration and more commonly associated with nausea and emesis. In addition, chronic headache characteristics vary with age and sex within the prepubertal population. Chronic daily headaches increase with age, with 4.5% of children aged 4 to 6 years meeting criteria and 27.4% of children aged 16 to 18 years meeting criteria. Chronic headaches are seen at the same frequency in males and females prior to the onset of puberty, with increased female predominance after puberty in the migraine and tension headache population.

As with headaches at any age, acute treatment in the premenarche population is imperative to avoid development of chronic daily headache syndromes. Acute abortive therapy is the same for the pediatric population as adults, with acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and triptans being the mainstay of therapy (Table 2). The role of prophylactic medications in the pediatric population is poorly understood. The CHAMP trial was done in an effort to compare amitriptyline, topiramate, and placebo but was discontinued for futility because neither of the 2 preventive medications was more effective than placebo in reducing headache days over a 24-week period. In addition, subjects who received amitriptyline or topiramate had higher rates of adverse events compared with those receiving placebo. As a result, the mainstay for treatment of headache in the pediatric population is focused on behavioral modifications, including expectation counseling, avoidance of headache triggers, daily exercise, cognitive behavioral therapy (CBT), and good sleep hygiene. Diagnosis of headache in the pediatric population should be approached in the same way as in the adult population. After evaluating the history for red flags suggesting a secondary headache type and ensuring that the neurological examination is normal, the provider should pursue a primary headache syndrome. Referral to neurology should be made if patients fail initial treatment, have refractory headache, or have atypical symptoms not commonly seen in migraine or tension headache.

### Menstrual Migraines

The diagnosis of menstrual migraine is divided into 2 subgroups: pure menstrual migraines (PMMs) and menstrual-related migraines (MRMs). More than 20% of women with migraine meet the diagnosis of menstrual migraine. Of these, approximately 15% meet the diagnosis of PPM, with the remaining having MRM. Clinically, both PMM and MRM are more severe, longer in duration, and more resistant to treatment than nonmenstrual migraines. Menstrual migraines of either type are rarely associated with aura. Pure menstrual migraines are rare. The ICHD-3 beta defines PMM as one meeting all of the following criteria: documented prospective evidence of migraine; 2 of 3 consecutive menstrual cycles being affected by...
migraine; migraine occurring only on days −2 through +3, with day 0 being the first day of the menstrual cycle; and migraine cannot be present at any other time of the month.1

The diagnosis of MRM, per the ICHD-3 beta, is almost identical to that of PMM requiring documented prospective evidence of migraine, 2 of 3 consecutive cycles being affected by migraine, and migraine occurring on days −2 through +3, with day 0 being the first day of the menstrual cycle, but headaches can also occur at other times during the month. As a result, the diagnosis of MMR is more common.1

Since the 1970s, it has been known that decreasing levels of estrogen in some women trigger migraine. In 1972, Somerville20 published a series of classic studies illustrating that administration of estradiol before menses delayed menstrual migraine attacks. This implied that menstrual migraine attacks might be due to an “estrogen withdrawal” effect.20 In 1975, Epstein et al21 further demonstrated that there are no significant differences in ovarian hormones between MRM patients and non-MRM patients at each stage of the menstrual cycle, confirming that MRM headaches were not primarily the result of abnormal hormone levels. In 1986, de Lignieres et al22 evaluated 18 women with PMM in a double-blind, placebo-controlled trial over the course of 3 months. They concluded that percutaneous estradiol has a preventive effect on PMM, further supporting the evidence that PMM is most likely triggered by estrogen withdrawal.22 Subsequent studies have confirmed the connection between estrogen withdrawal and migraine onset as the etiology of menstrual migraines.23–25

There are 4 approaches to the treatment of menstrual migraine: abortive treatment, mini prevention, daily prophylaxis, and menses suppression (Table 3). Although none of these approaches have US Food and Drug Administration (FDA)–specific approval for the treatment of menstrual migraine, many studies have demonstrated the effectiveness of acute abortive treatments and short-term prevention. Unfortunately, there are few head-to-head trials between medications and few meta-analyses, making direct comparisons limited.16

Because menstrual migraines are more severe and refractory to treatment, before choosing an acute abortive therapy it is important to consider efficacy of the treatment. In 2004, Granella et al26 published one of the few trials addressing acute therapy and showed that 7.7% of PMM patients received relief, 5.4% of MRM patients received relief, and 24.2% of patients with nonmenstrual migraine who experienced headache improved with acute treatment. Patients with MRM and PMM are less likely to experience improvement with acute abortive therapy compared with patients with nonmenstrual migraine, emphasizing the refractory nature of menstrual migraines.

Acute abortive treatment is used only at the onset of the headache. Rizatriptan and sumatriptan have shown the greatest efficacy for acute abortive therapy, but other triptans can be used. Injectable sumatriptan can also be helpful. Other acute treatment options, such as acetaminophen and ibuprofen, can be used, but because of the severe and refractory nature of menstrual migraine, treatment with triptans is a reasonable first-line therapy.27,28

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>Treatment of Menstrual Migraines</th>
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<tbody>
<tr>
<td><strong>Acute abortive treatment</strong></td>
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</tr>
<tr>
<td>Rizatriptan 10–30 mg every 2 h</td>
<td>(Max dose 30 mg/24 h)</td>
</tr>
<tr>
<td>Sumatriptan 50–200 mg every 2 h</td>
<td>(Max dose 200 mg/24 h)</td>
</tr>
<tr>
<td><strong>Mini prevention</strong></td>
<td></td>
</tr>
<tr>
<td>Frovatriptan 5 mg BID</td>
<td>Dosed day −2</td>
</tr>
<tr>
<td>Frovatriptan 2.5 mg BID</td>
<td>Dosed days −1 to +4</td>
</tr>
<tr>
<td>Naratriptan 2.5 mg BID</td>
<td>Dosed days −2 to +3</td>
</tr>
<tr>
<td>Zolmitriptan 2.5 mg TID</td>
<td>Dosed days −2 to +3</td>
</tr>
<tr>
<td>Naproxen 550 mg BID</td>
<td>Dosed days −7 to +6</td>
</tr>
<tr>
<td>Estradiol 1.5 mg every day</td>
<td>Dosed days −2 to +5</td>
</tr>
<tr>
<td><strong>Daily migraine prophylaxis</strong></td>
<td></td>
</tr>
<tr>
<td>Continuous OCPs</td>
<td>Daily OCP skipping placebo pills</td>
</tr>
<tr>
<td>OCP + estrogen supplementation:</td>
<td>Daily OCPs plus supplementation</td>
</tr>
<tr>
<td>10 μg ethinyl estradiol every day during placebo period</td>
<td>during placebo period</td>
</tr>
<tr>
<td>0.9 mg conjugated estrogen every day</td>
<td></td>
</tr>
<tr>
<td>100 μg estradiol patches every day</td>
<td></td>
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<tr>
<td>2 g estradiol every day</td>
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*Level A: high—several high-quality studies with consistent results; level B: moderate—1 high-quality study showing efficacy or several studies with some limitations showing efficacy; level C: low—1 study or more showing efficacy with severe limitation; level U: expert opinion—no direct research evidence.

BID indicates twice daily.
The use of mini prevention can be considered in women with regular menstrual cycles. Mini prevention is provided by using acute treatment agents beginning on day −2 through +2 of the menstrual cycle. Options include medications previously mentioned for acute abortive therapy: lower-dose rizatriptan, sumatriptan, and naproxen or ibuprofen. In studies, frovatriptan has been shown to have level A evidence, with naratriptan, zolmitriptan, naproxen, and estradiol also being shown to be efficacious as mini-preventive agents. Although recommended as mini treatment for menstrual migraine for several decades, estradiol has only FDA level C evidence for treatment of menstrual migraine.16 As a result, triptans and NSAIDs should be considered as first-line regimens.

Migraine prophylaxis is taken daily (Table 4) and is a good treatment option for patients with MRM plus high nonmenstrual migraine burden, patients with irregular menstrual cycles, or patients who have failed acute therapy. The adverse effects of daily prophylaxis vary widely based on which prophylactic agent was used, and adverse effects should be reviewed prior to prescribing. The β-blockers propranolol, metoprolol, and atenolol are commonly associated with fatigue, dizziness, bradycardia, and hypotension, whereas the antiepileptic agents valproate, topiramate, and gabapentin are commonly associated with sedation, depression, dizziness, word-finding difficulty, and weight changes. Propranolol, metoprolol, valproate, and topiramate all have FDA level A evidence for treatment of migraine. Although valproate and topiramate work well for migraine, they are not optimal for fertile women because both are known teratogens. Valproate during the first trimester has been reported to increase the risk of major malformations from 1.1% to 9.3%, with neural tube defects being the most commonly associated major malformation.29,30 Mothers exposed to topiramate during pregnancy have been reported to have an absolute risk of fetal oral clefts of 5 to 29 per 1000 births when compared with the unexposed population risk of 1 to 2 per 1000 births.30 Atenolol, amitriptyline, and venlafaxine are all FDA level B, cyproheptadine is level C, and verapamil and gabapentin are level U (no known benefit for migraine prophylaxis) medications.29 Verapamil is safe for use in pregnancy and is widely utilized for migraine prophylaxis, despite the absence of data confirming its efficacy.

The final menstrual migraine treatment option is menses suppression. This can be achieved with continuous oral contraceptive pills (OCPs) or with estrogen supplementation during the OCP placebo interval with either 10 μg ethinyl estradiol, 0.9 mg oral conjugated equine estrogens, 100 μg estradiol patches, or 2 g of estradiol.1 Menstrual suppression is not a first-line therapy, and a large majority of patients respond to other treatments. Many providers are hesitant to initiate OCP therapy in the setting of migraines with aura because of a reported increased risk of stroke based on data from the 1960s and 1970s at a time when OCPs contained much higher hormone concentrations. The stroke risk is not significantly increased with current OCP preparations, which include much lower hormone levels and should be considered a safe option for refractory headache even if aura is present.31 Much of the headache community does not encourage menses suppression unless the patient has failed abortive treatment, mini suppression, and daily prophylaxis or has another indication for menses suppression.32 However, the work of Calhoun33 has demonstrated that menses suppression is an effective treatment of MRM and PMM and should be readily used particularly if there is any other indication for menses suppression or if headaches are difficult to predict.

The importance of establishing an accurate diagnosis prior to initiation of menstrual migraine treatment is

<table>
<thead>
<tr>
<th>TABLE 4</th>
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<tr>
<td><strong>Migraine Daily Prophylaxis</strong></td>
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<tr>
<td><strong>Daily Dosing</strong></td>
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</tr>
<tr>
<td>Propranolol</td>
</tr>
<tr>
<td>Metoprolol</td>
</tr>
<tr>
<td>Valproate</td>
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<tr>
<td>Topiramate</td>
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<tr>
<td>Atenolol</td>
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<tr>
<td>Amitriptyline</td>
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<tr>
<td>Venlafaxine</td>
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<tr>
<td>Cyproheptadine</td>
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<tr>
<td>Verapamil</td>
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<tr>
<td>Gabapentin</td>
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</table>

*Refer to footnote to Table 2.

TID indicates thrice daily.
extremely important. Tepper\textsuperscript{34} published guidelines to help in the diagnosis for better direct treatment. Headache frequency should be assessed first. If headaches are infrequent (not associated with every menstrual period), acute abortive therapy is a reasonable first-line therapy, thus avoiding adverse effects of daily migraine prophylaxis. If headaches are frequent (associated with every menstrual period), then duration of headache should be considered next along with how responsive the headaches are to acute treatment. If headaches are highly responsive to acute treatment, abortive therapy is reasonable despite headache duration and frequency. If the headache is not responsive to acute treatment, then daily prevention or mini suppression should be considered even if headaches are infrequent or have a short duration. Headache predictability should be considered next. If headaches are highly predictable, acute abortive treatment or mini prevention can be beneficial. If headaches or menses are highly unpredictable, daily prophylaxis and ovulation suppression are preferable options.\textsuperscript{34}

In summary, menstrual migraines are difficult to treat and can severely affect the quality of a woman's life. Women's health care providers should be confident in using the ICHD-3 beta classification system to make the diagnosis of migraine, PMM, and MRM, so that timely treatment can be initiated.

**Pregnancy and Headache**

Pregnancy is a unique time in a woman's life, during which many changes in primary headache disorders can occur and pregnancy-specific secondary headache disorders can develop. Pregnancy is also a time when the diagnosis of headache can be made more difficult both because of concerns about some diagnostic options and because of confounding factors obscuring diagnosis. Treatment of headache in pregnancy can be difficult because of concerns of fetal and/or maternal risk associated with some treatments. Despite these limitations, accurate diagnoses of primary and secondary headache can be made in pregnancy and good treatment options exist.

Approximately 1 in 6 women of reproductive age will suffer from migraine.\textsuperscript{4} Of these, 92% of women will have their headaches resolved during pregnancy, most commonly after the first trimester, and 8% will have either no change or worsening of their headache.\textsuperscript{35} The remission of headache during pregnancy is thought to be due to increased and nonfluctuating estrogen levels. In 2011, Nappi et al\textsuperscript{36} published a study following estrogen levels during each trimester and resolution of headache. Fifty percent of women showed amelioration of headache during the first trimester, 83% in the second trimester, and 87% by the third trimester.

Migraine headache can initially present, or be initially diagnosed, during pregnancy. This almost always occurs in the first trimester. Because of this factor plus the common improvement in migraine during pregnancy, the new-onset migraine in the second and third trimester should always be considered a diagnosis of exclusion.

Diagnosis and treatment of acute headache in pregnancy are of great importance because they can dictate delivery and early interventions. Although primary headache is responsible for 90% of headaches outside pregnancy, only 65% of headaches during pregnancy are attributed to primary headache, whereas 35% are attributed to secondary headache.\textsuperscript{37} Headache from hypertensive disease of pregnancy is the most common type of secondary headache and is seen most frequently at advanced gestational age and in the setting of underlying asthma or a psychiatric disorder.\textsuperscript{37} Duration of headaches is also longer in the pregnant population.\textsuperscript{37} The observed increase in duration of headaches may be iatrogenic and due in part to the lack of knowledge and confidence many physicians have when treating headache in pregnancy.

**Diagnosis of Headache in Pregnancy**

The differential for headache in pregnancy expands with each progressive trimester (Table 5). In the first trimester, primary headache continues to be the most common etiology of headache, with secondary headache occurring roughly at the same frequency as it does in nonpregnant women. In the second trimester, although still rare, headache secondary to preeclampsia and venous sinus thrombosis increases in frequency. The third trimester is the time of greatest increased incidence of secondary headache. In addition to headache secondary to hypertensive disease of pregnancy, venous sinus thrombosis, cerebral vascular accident, posterior reversible encephalopathy syndrome (PRES), and reversible vasoconstriction syndrome need to be considered.

Although there is no evidence to suggest that pregnancy increases the incidence of brain tumors, they are more commonly diagnosed during pregnancy than during any other 9-month nonpregnant interval. This is thought to be due to decreased serum osmolality and increased extracellular fluid associated with pregnancy, causing tumors to become more symptomatic.\textsuperscript{38}

Obtaining a careful history is the key to a proper headache diagnosis, regardless of trimester. There are
6 key history points that can improve the accuracy of headache diagnosis during pregnancy.

First, obtain a family history. What is common in the family? Are genetic risk factors present that predispose this patient to experience headache? Second is life history. Is this her first headache, or does she suffer from a primary headache disorder and this is worsening of her chronic headaches? Third is attack history. Obtain details about the headache such as duration, location, intensity, and associated symptoms. Fourth is basic medical, surgical, and psychiatric history. As previously stated, asthma and the presence of underlying psychiatric disorder are risk factors for developing secondary headache during pregnancy. Fifth is medication history. Is she on medications that put her at risk of medication overuse headache or medications that have the common adverse effect of headache? And sixth is obstetrical history. Does she have a history of preeclampsia in prior pregnancy or other secondary headache disorders that pregnancy puts her at risk of recurrence?

Although nonultrasound imaging, specifically computed tomography but also to some degree magnetic resonance imaging scanning, is frequently avoided in pregnancy, there are situations in which it is important to consider in the workup of headache because it can expedite diagnosis and dictate treatment. Cranial imaging should always be obtained if there is an altered level of consciousness in the setting of headache. If any patient has recurrent seizure activity despite magnesium therapy in the setting of hypertensive disease of pregnancy, or if there is a prolonged alteration in consciousness following seizures, imaging should be obtained, first with CT (if bleeding is suspected) and more often with magnetic resonance imaging as needed. Imaging is also indicated in women who develop seizures more than 48 hours postpartum or if a patient has localizing neurological findings at any time during pregnancy or the puerperium. In addition, it is reasonable to obtain imaging if the constellation of signs and symptoms are atypical such as refractory headache or atypical headache. Many providers avoid imaging because of theoretical fetal risk or expense, but these are not reasons to delay diagnosis and potential treatment. In general, if nonultrasound cranial imaging would be indicated in a nonpregnant woman with similar signs and symptoms, it should at least be considered in a pregnant woman.

**Preeclampsia and Headache**

Differentiating primary headache disorders from preeclampsia-induced headache can be a particular challenge in pregnancy. Making this differentiation is of particular importance as headache is considered to be a “severe feature” in the diagnosis of preeclampsia with severe features and can be an indication for delivery because of risk of maternal neurological complications. Preeclampsia headaches are classically described as throbbing, persistent, frontal or occipital in location, associated with visual changes, and/or other systemic symptoms such as right upper quadrant pain and lower extremity swelling. Many of these symptoms are vague and are typical of both tension and migraine headache. Intravenous (IV) magnesium sulfate, administered as neuroprophylaxis either for maternal preeclampsia...
or for prevention of cerebral palsy in preterm labor, commonly causes headache and can further confound the diagnosis. There are some differences between primary headaches and preeclampsia-induced headaches that can be helpful in differentiating the 2 conditions. Preeclamptic headaches typically worsen with elevated blood pressure and improve with blood pressure control. As a result, if headaches seem to correlate with blood pressure changes, the diagnosis of preeclamptic headache becomes more likely. There are several long-acting antihypertensive medications typically used in pregnancy, and it is important to remember that nifedipine is frequently associated with a headache. The Amsler grid, a basic thin-lined, black-and-white grid with a black dot in the center, can be a useful tool in differentiating migraine from preeclamptic headache. Typically, patients with preeclampsia headache see large blotches on the grid, which patients with migraine without aura do not see. The presence of these blotches can raise the diagnosis of preeclampsia on the differential but again does not make a definitive diagnosis. Despite these considerations, it is frequently difficult to exclude the possibility of a preeclampsia-associated headache in the setting of elevated blood pressure.

A history of migraine is a reported risk factor for developing preeclampsia. Migraineurs are 4 times more likely to develop preeclampsia and experience preterm birth compared with patients without a history of migraine. This risk is further increased if patients do not experience amelioration of their migraines during pregnancy. The increased risk is thought to be due to a common endothelial dysfunction underlying both disease processes. It has also been shown that migraineurs are at slight increased risk of cerebrovascular events compared with the general population. Although lacking prospective confirmation, it has been suggested that low-dose aspirin might be a reasonable preventive therapy for patients who do not experience amelioration of headache in the first trimester, as it is known to decrease recurrent preeclampsia in patients with a prior history of preeclampsia.

Headache Treatment in Pregnancy

There are many good treatment options that can be utilized in the treatment of headache in pregnancy (Tables 2 and 4). For acute headache treatment in and outside pregnancy, there are 2 major treatment options, namely, triptans and nontriptans. There is FDA level A evidence for the use of acetaminophen, acetaminophen/aspirin/caffeine, and butorphanol for treatment of acute headache that are all safe for use during pregnancy. Ketorolac, naproxen, and ibuprofen are also FDA level A and can be safely used prior to 28 weeks for 48 to 72 hours. However, the potential risk of closure of the ductus arteriosus, platelet dysfunction, and/or fetal and maternal renal dysfunction limit usefulness of NSAIDs for treatment of headache in pregnancy, particularly in the third trimester. There is also concern for the use of regular-dose aspirin in the third trimester, which might discourage some providers from using the combination therapy of acetaminophen/aspirin/caffeine. An alternative is the use of acetaminophen 500 mg in combination with caffeine 130 mg every 6 to 8 hours. Headache improvement should still be anticipated without risks associated with full-dose aspirin administration.

Level B medications that can be used for the treatment of acute headache in pregnancy are the dopamine blockers: chlorpromazine, promethazine, metoclopramide, and prochlorperazine. The exact mechanism of dopamine blockade on headache is unknown but is felt to be safe in pregnancy and have the added benefit of treatment of nausea. There is also level B evidence for the use of codeine in combination with acetaminophen and tramadol in combination with acetaminophen, but these are used less commonly because of increasing awareness of the potential for maternal and fetal dependence.

There is no level A or B evidence for the use of butalbital-containing medications or hydrocodone/acetaminophen. Providers should be encouraged not to use butalbital-containing medications for treatment of headache inside or outside pregnancy because this barbiturate has a high addictive potential. When combination pills containing butalbital were first developed, migraine was thought to be a mental illness, and these medications were used in the treatment of mood changes. It has since been removed from the market in Europe, although it continues to be available and used in America.

Injection of local anesthesia into the greater or lesser occipital nerve, known as occipital nerve block (ONB), is an acute and prophylactic treatment of headache commonly used outside pregnancy. Occipital nerve block involves 5 to 10 mL of local anesthetic with or without steroids injected into the greater occipital nerve and/or lesser occipital nerve every 6 to 9 weeks. Although use of ONB has not been studied extensively in pregnancy, a case series has been published in 13 pregnant women who failed oral and IV treatment of migraine. Overall, 38% of these women suffered from chronic migraine, with 51% suffering from status migrainosus (migraine lasting >72 hours) at the time of injection. Of the 13 patients, 11 patients had acute pain relief and resolution, whereas 2 patients had no
pain relief and went on to be diagnosed with preeclamp-
sia.\textsuperscript{45} It is felt that ONB is safe in pregnancy. The
American Headache Society distributed a member sur-
vey in 2010 with 161 responses. More than one half of
members surveyed preformed ONB in pregnancy and
felt it was safe. The majority of practitioners waited un-
til the second trimester to give injections and used lido-
caine only, although there is no evidence that ONB in
the first trimester or use of other types of local anes-
thetic is unsafe.\textsuperscript{45} In general, patients with a history of
successful treatment of chronic headache with ONB or
refractory headache should be considered good can-
didates for ONB in pregnancy.\textsuperscript{46}

There are many options for treatment with triptans
during pregnancy. Triptan medications have been used
for more than 2 decades in pregnancy and have con-
sistently shown no increased rate of complications or
teratogenicity above the background population. In
2015, a large meta-analysis was published with 4200
infants born with triptan exposure and 1,466,994
without. When comparing these 2 groups, there was
no difference in major congenital malformations or
prematurity between the 2 groups. There was, however,
an apparent increase (odds ratio, 3.54; 95% confidence
interval, 2.24–5.59) in spontaneous abortion in the first
trimester about which patients should be counseled.\textsuperscript{47}
Triptans should be considered safe for use after the
first trimester and have fewer adverse effects than barbiturate-
or opioid-containing medications.\textsuperscript{43}

**Headache Prophylaxis in Pregnancy**

There are 3 major approaches to headache prophy-
laxis in pregnancy, including nonpharmaceutical treat-
ments, daily prophylaxis (Table 4), and injectable
medications. Nonpharmaceutical treatment should always
be tried first, both in and outside pregnancy. The 3
branches of nonpharmaceutical treatment include life-
style modification, CBT, and nerve stimulation.

Lifestyle modifications include dietary, sleep hy-
genie, exercise, weight control, and limiting caffeine in-
take. All of these areas should be addressed in all
patients with headache. There is no level A evidence
that dietary restrictions affect headache in positive or
negative ways. However, some patients do report con-
sistent onset of headache following ingestion of certain
foods such as red wine or chocolate. These patients
should be counseled to avoid these substances. Ade-
quate sleep or good sleep hygiene is an important com-
ponent of headache prevention. Patients should be
encouraged to have standardized sleep wake times with
7 to 9 hours of sleep nightly. Regular exercise and
weight control during pregnancy should be encouraged
and can improve chronic headaches. Moderate caffeine
intake (roughly 1 cup of coffee a day) is recommended
in all patients with chronic headache.

Patients with chronic headache who undergo CBT
have been shown to have a 35% to 55% improvement
in headache.\textsuperscript{48} Cognitive behavioral therapy is typically
used to treat depression and is a form of talk therapy
emphasizing the development of personal coping stra-
egies. It is unclear how CBT leads to headache im-
provement, but it should be suggested in patients who
have refractory headache, have a lack of pharmaceutical
options, or have concurrent depression.

A more novel treatment is nerve stimulation. Some of
the more common types of nerve stimulation include
supraorbital nerve stimulation, transcranial magnetic
stimulation, and vagus nerve stimulation. Although
poorly studied in pregnancy, there has been 1 report
of 3 women who received transcranial magnetic stimu-
lization during pregnancy, and all 3 women showed im-
provement.\textsuperscript{49} A neurologist should evaluate patients
prior to initiation of nerve stimulation to see if this form
of treatment would be a good therapeutic option.

Patients should be offered daily headache prophyl-
axis if they have 6 or more headache days a month,
more than 4 headache days with mild impairment, or
more than 3 headache days a month with severe impairment\textsuperscript{49} (Table 6). Ideally, headache prophylaxis should
be initiated prior to pregnancy, but if a patient has
worsening symptoms at any point in pregnancy, it is
reasonable to start preventive treatment during pregnancy.

Medications used for daily headache prophylaxis dur-
ing pregnancy are the same as those used outside preg-
nancy and have been previously discussed in Table 4.\textsuperscript{41}
The first-line headache prophylactic agents used during
pregnancy should be the β-blockers, followed by amitriptyl-
ine, venlafaxine, cyproheptadine, and verapamil.

As previously discussed, ONBs are considered both
and acute and prophylactic treatment of headache in
and outside pregnancy. Other types of nerve blocks that
can be considered are sphenopalatine injections and
trigger point injections. These injections use a similar
mixture of local anesthesia and steroid. Injectable
agents are good treatment options when given by a well-trained
provider and should be considered safe in pregnancy.

Botulinum toxin is another injectable prophylac-
tic treatment. Botulinum toxin A has a high molecular
weight and does not cross the placenta; there are no

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**TABLE 6**

Criteria for Daily Headache Prophylaxis

| >=6 Headache days per month |
| >=4 Headache days per month plus mild impairment in activities |
| >=3 Headache days/month plus severe impairment in activities |
known negative pregnancy outcomes. A postmarketing trial reported on 232 women who received injections 3 months prior to conception and through the first trimester. There was no increase in spontaneous abortion or birth defects with the treatment.52

**Postpartum Headache**

Headaches are more common in the postpartum period than during pregnancy. There is a return of primary headache disorders due to hormonal changes and poor sleep hygiene. These changes also place patients at risk of developing new primary headache disorders. There is evidence that breastfeeding can provide a lower recurrence of primary headache for up to 6 months postpartum. In breastfeeding mothers, the rate of recurrent migraine was reported to be 50% at 1 month and 71% at 6 months compared with bottle-feeding mothers, who have an 86% recurrence at 1 month at 95% recurrence at 6 months.53

The postpartum period is also a time at increased risk of secondary headaches (Table 5). As a result, all headaches that develop in the postpartum period should be taken seriously. The differential for secondary headache is broad, but symptoms are usually distinct with many red flags (Table 7). For example, orthostatic changes in headache often indicate a postepidural headache, usually a result of an inadvertent cerebrospinal fluid leak. The symptom of “thunder clap” headache, described as a severe, acute headache of sudden onset, is seen in reversible vasoconstriction syndrome, hemorrhagic stroke, venous sinus thrombosis, and carotid artery dissection. Hypertension associated with headache is seen in PRES, reversible vasoconstriction syndrome, preeclampsia, and hemorrhagic stroke. Vision loss can be seen in preeclampsia, PRES, and pituitary apoplexy. Focal neurological findings should prompt evaluation for cerebrovascular events, venous sinus thrombosis, PRES, and reversible vasoconstriction syndrome. Seizures associated with headache should suggest eclampsia if occurring within 24 to 48 hours of delivery. If further removed from the time of delivery, seizures are more likely a manifestation of venous sinus thrombosis, PRES, reversible vasoconstriction syndrome, and/or bacterial meningitis.

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**TABLE 7**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Differential Diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthostatic headache changes</td>
<td>Spinal or postpuncture headache</td>
</tr>
<tr>
<td>Relapsing thunderclap headache</td>
<td>Reversible vasoconstriction syndrome</td>
</tr>
<tr>
<td>Single thunderclap headache</td>
<td>Subarachnoid hemorrhage, reversible vasoconstriction syndrome, venous sinus thrombosis, carotid artery dissection, pituitary apoplexy</td>
</tr>
<tr>
<td>Hypertension with headache</td>
<td>Preeclampsia, eclampsia, PRES, reversible vasoconstriction syndrome, hemorrhagic stroke</td>
</tr>
<tr>
<td>Visual loss with headache</td>
<td>Preeclampsia, eclampsia, pituitary apoplexy</td>
</tr>
<tr>
<td>Seizure with headache</td>
<td>Eclampsia, venous sinus thrombosis, PRES, reversible vasoconstriction syndrome</td>
</tr>
<tr>
<td>Horner syndrome</td>
<td>Carotid artery dissection</td>
</tr>
<tr>
<td>Focal neurological findings with headache</td>
<td>Cerebrovascular event, PRES, reversible vasoconstriction syndrome, venous sinus thrombosis</td>
</tr>
<tr>
<td>Fever with headache</td>
<td>Bacterial meningitis</td>
</tr>
</tbody>
</table>

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**TABLE 8**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>650 mg PO every 4–6 h PRN</td>
<td>Max dose 4000 mg/24 h</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>800 mg PO every 8 h PRN</td>
<td>Max dose 3200 mg/24 h</td>
</tr>
<tr>
<td>Eletriptan</td>
<td>20–40 mg PO PRN</td>
<td>Max dose 80 mg/24 h</td>
</tr>
<tr>
<td>Caffeine</td>
<td>130 mg PO every 4–6 h PRN</td>
<td>Can lead to medication overuse headache</td>
</tr>
<tr>
<td>Dopamine antagonists: Chlorpromazine</td>
<td>25–50 mg IV/PO every 4–6 h PRN</td>
<td>Side effect of sedation</td>
</tr>
<tr>
<td>Promethazine</td>
<td>12.5–25 mg IV/IM/PO every 4–6 h PRN</td>
<td></td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>10 mg IM × 1 or 5–10 mg PO every 12 h PRN</td>
<td></td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>12.5–25 mg PO/IM/IV every 4–6 h PRN</td>
<td></td>
</tr>
</tbody>
</table>
The differential diagnosis for postpartum secondary headache is broad with the potential for severe morbidity if diagnosis is missed. As a result, if patients have concerning or atypical symptoms associated with postpartum headache, the threshold for central nervous system imaging and further evaluation should be thoughtful and expeditious.

There are many safe and effective treatments for acute headache in the puerperium (Table 8). Acetaminophen, ibuprofen, triptans, caffeine, steroids, and dopamine antagonists are all considered safe during breastfeeding and in the postpartum period, with low levels being found in breast milk. The only medications absolutely contraindicated in the postpartum period are dihydroergotamine and ergotamine. All preventive medications are felt to be safe in pregnancy, with the exception of zonisamide, atenolol, and tizanidine (Table 4).

**Menopause and Headache**

Headache, specifically migraine, is a common symptom during menopause. In 2007, a multinational study compared menopausal symptoms. In all locations, women reported headache as one of the most common symptoms of menopause. Despite the predominance of headaches during menopause, this is an underresearched area in the literature, and no significant longitudinal studies have been published.

Headache, and more specifically migraine, burden varies greatly during menopause. Sixty percent of women who go through surgical menopause report headache, 31% of women report headache late in menopause, 20% report headache early in menopause, and 13% of women report new onset of migraine during menopause. As with menstrual migraines, more women report migraine without aura than migraine with aura. The increased headache burden during menopause is thought to be secondary to estrogen changes, similar to that seen in menstrual migraine.

There are 4 treatment options for headache during menopause: acute abortive therapy, hormone replacement therapy (HRT), headache prophylaxis, and expectant management. If headaches are rare and not disabling, abortive therapy is always an option. The options for acute abortive therapy do not vary from those discussed for treatment of acute headache outside menopause (Table 2). Hormone replacement therapy, with a combination of estrogen and progesterone, will reduce headache burden during menopause, but with cessation of HRT, most patients will have recurrent headaches. Thus, HRT should be considered only a temporizing measure. It is important to stress that HRT is not contraindicated in women with aura, and if patients have severe headache that cannot be managed with acute treatment, HRT should be encouraged to improve their quality of life. Migraine prophylaxis is a good option for patients with frequent headaches or disabling headaches. Again, the options for headache prophylaxis do not differ from those discussed for women outside menopause (Table 4). Watchful waiting and reassurance should always be considered an option during menopause as only 5% of women suffer from migraine after the age of 60 years, showing that completion of menopause is a definitive treatment of migraine for many women.

**Postmenopausal Headache**

In the postmenopausal population older than 60 years, only 5% of women experience migraine. The literature addressing postmenopausal headache is scant and virtually nonexistent. As a result, it should be assumed that postmenopausal women should be treated using the same prophylactic agents and acute abortive agents that are used in the younger population. There is, however, more medical comorbidities that exist in this population, and a full review of each individual medical history and current medications should be done prior to initiation of treatment.

**SUMMARY**

The effects of headache span a woman's life, with puberty and menopause being times of increased frequency of migraine headache. Pregnancy is an at-risk time for women to develop primary and secondary headache disorders, with migraine being the most common primary headache disorder inside and outside pregnancy. All women's health care providers should know how to screen, diagnose, and treat headache at all stages of a woman's life. There are good treatment options for acute and chronic headache in and outside puberty, pregnancy, and menopause.

**REFERENCES**


