

## Headaches in Women

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Women have headaches more commonly than men. The prevalence of migraine is 18% of women and 6% of men. This gender ratio increases from menarche, peaks at 42 years of age, and then declines. For young women the incidence of migraine with aura peaks between the ages of 12 and 13 (14.1/1,000 person-years), and migraine without aura peaks between the ages of 14 and 17 (18.9/1,000 person-years) (1). Table 11-1 provides the lifetime prevalence of various headaches in women and men.

Estrogen levels are a key factor in the increased prevalence of migraine in women. Evidence includes the following: migraine prevalence increases at menarche; estrogen withdrawal during menstruation is a common migraine trigger; estrogen administration in oral contraceptives and hormone replacement therapy can trigger migraines; migraines typically decrease during the second and third trimesters of pregnancy, when estrogen levels are high; migraines are common immediately postpartum, with the precipitous drop in estrogen levels; and migraines generally improve with physiological menopause. Exactly how changes in estrogen levels influence migraine is not understood. Among numerous effects, fluctuations in estrogen levels can result in changes in prostaglandins and the uterus, prolactin release, opioid regulation, and melatonin secretion. These fluctuations can also cause changes in neurotransmitters, including the catecholamines, noradrenaline, serotonin, dopamine, and endorphins (2).

This chapter reviews some important headache issues for women, including menstrual migraine, menopause and migraine, oral contraceptive use in migraineurs, and headaches during pregnancy and postpartum.

### **MENSTRUAL MIGRAINE**

The reported prevalence of menstrual migraine varies from 4% to 73%, depending on the criteria used for the timing of the attack. According to the IHS 2nd edition appendix, pure menstrual migraine without aura are attacks that occur exclusively on day 1  $\pm$  day 2 of menstruation in at least two out of three menstrual cycles and at no other times of the cycle (3). Using this definition, about 7% (depending on the study) of female migraineurs have only menstrual migraine. Menstruation is a trigger for about 60% of migraineurs. Symptoms of the premenstrual syndrome, which occurs during the luteal phase, include depression, anxiety, crying spells, difficulty thinking, lethargy, backache, breast tenderness, swelling, and nausea. Both migraine and tension-type headaches can be associated.

### **Management**

The symptomatic treatment is the same as for other migraines and includes nonsteroidal antiinflammatory drugs (NSAIDs),

**Table 11-1. Lifetime prevalence of headaches in women and men**

| Type         | Women | Men |
|--------------|-------|-----|
| Any headache | 99%   | 93% |
| Migraine     | 25%   | 8%  |
| Tension      | 88%   | 69% |

Data from Rasmussen BK, Jensen R, Schroll M, et al. Epidemiology of headache in a general population—a prevalence study. *J Clin Epidemiol* 1991;44:1147–1157.

ergotamine, dihydroergotamine, and triptans (Chapter 2) (4,5). Triptans are just as effective for menstrual migraine. Women with frequent migraines, including menstrual migraine, may benefit from preventive treatment (Chapter 2). Increasing the dose perimenstrually can be helpful in some cases.

When menstrual migraine is the only migraine or the most severe and prolonged, a variety of short-term preventive treatments may be effective starting 2 to 3 days premenstrually and continuing during the menses for women with regular cycles (Table 11-2). NSAIDs can be especially helpful when migraine occurs with dysmenorrhea or menorrhagia (6). Some patients may respond to one class of NSAIDs and not another.

Hormonal treatments that may be effective include transdermal estradiol (Table 11-2), bromocriptine 2.5 mg three times a day (continuous treatment more effective than interval) (7), danazol 200 mg two or three times a day, and tamoxifen 5 to 15 mg daily for days 7 to 14 of the luteal cycle. (There are concerns about use because of an increased risk of uterine cancer [8].) Some women on estrogen-containing combination oral contraceptives may prevent their menstrual migraine from continuous use with breaks every few months or a brand with low-dose estrogen during the menstrual week and two inert pill days (e.g., Mircette). A short, tapering dose of corticosteroids or chlorpromazine 10 to 50 mg twice a day for 4 to 7 days may be effective. Oral magnesium (360 mg of magnesium pyrrolidone carboxylic acid) may also be effective (9). Hysterectomy is not recommended for the management of menstrual migraine.

## MENOPAUSE AND MIGRAINES

Two thirds of women with prior migraine improve with physiological menopause. By contrast, surgical menopause results in worsening of migraine in two thirds of cases.

### Estrogen Replacement Therapy

Hormone replacement therapy has a variable effect on migraine frequency: 45% improve, 46% worsen, and 9% are unchanged (10). Table 11-3 lists changes in hormone replacement therapy that may be helpful when migraines increase (11). The usual abortive and prophylactic migraine medications can also be used (Chapter 2).

**Table 11-2. Options for interval preventative treatment of menstrual migraine starting 2–3 days before and continuing during the menses**

| Medication                     | Dose  |
|--------------------------------|---|
| Amitriptyline or nortriptyline | 25 mg at bedtime (hs)                               |
| Propranolol long-acting        | 60–80 mg every day (qd)                             |
| Nadolol                        | 40 mg qd  |
| NSAIDs                         |   |
| Naproxen sodium                | 550 mg twice a day (bid)                            |
| Naproxen                       | 500 mg bid  |
| Ibuprofen                      | 400 mg three times a day (tid)                      |
| Mefenamic acid                 | 500 mg bid  |
| Ketoprofen                     | 75 mg tid   |
| Rofecoxib                      | 25 mg qd  |
| Ergotamine                     | 1 mg bid  |
| DHE                            | 1 mg SC or IM bid                                   |
| Sumatriptan                    | 50 mg qd  |
| Naratriptan                    | 1 mg bid  |
| Frovatriptan                   | 2.5 mg bid  |
| Transdermal estradiol          | 100 ( $\mu$ g on day –3 replaced on days –1 and +2) |

**Table 11-3. Treatment of estrogen replacement headache**

|   |
|---|
| Reduce estrogen dose  |
| Change estrogen type from conjugated estrogen (Premarin) to pure estradiol (Estrace) to synthetic estrogen (Estinyl) to pure estrone (Ogen) |
| Convert from interrupted to continuous dosing   |
| Convert from oral to parenteral dosing (Alora, Climara, Estraderm, or Vivelle-Dot)  |
| Add androgens   |

From Silberstein SD, Merriam G. Sex hormones and headache. *J Pain Symptom Manage* 1993;8:98–114, modified with permission.

## ORAL CONTRACEPTIVE USE AND MIGRAINE

### Influence on Onset and Frequency

Migraines may occur for the first time following oral contraceptive (OC) use. The effect of OC use is quite variable: migraines may increase, decrease, or stay the same. Much of the data on this topic is from older studies of the use of high-dose estrogen contraception, which often increased migraine frequency. Low-estrogen-dose OCs usually have no effect or may improve migraine. When new-onset migraine occurs or migraine frequency increases, 30% to 40% of this group may improve when OCs

are discontinued. However, improvement may not occur for up to 1 year.

### Risk of Stroke (12)

Since the 1970s, there has been concern that OCs taken by migraineurs may increase their risk of stroke. Review of the risk of stroke in young women, in female migraineurs, and in those using OCs helps clarify this issue.

#### *Stroke in Young Women*

The annual incidence of cerebral infarction in young women is low: about 4 in 100,000 for women aged 25 to 34 and 11 in 100,000 in women aged 35 to 44. For women who do not have migraine and do not take OCs, the annual incidence is perhaps 1.3 in 100,000 for women aged 25 to 34 and 3.6 in 100,000 for women aged 35 to 44.

Hypertension, diabetes, cigarette smoking, and cocaine use are significant risk factors.

#### *Stroke and Migraine*

There is an increased risk of stroke in women with migraine (13,14). Using a variety of assumptions, Becker has calculated the approximate risk of stroke in young women not on OC with and without migraine (Table 11-4) (12).

#### *Stroke and Use of Oral Contraceptives*

Stroke and the use of OCs is a controversial topic because studies of low-dose estrogens have yielded conflicting results (15). The risk of stroke associated with OCs may vary with the estrogen dose. Based on numerous studies, OCs with different estrogen doses have an increased risk of thromboembolic stroke (odds ratio) as follows: more than 50 mg, 8 to 10; 50 mg, 2 to 4; and 30 to 40 mg, 1.5 to 2.5. However, more recent studies have not shown an increased risk of stroke in women who use low-estrogen-dose OCs (16–19). OCs containing only progesterone do not increase the risk of stroke (20).

#### *Use of Oral Contraceptives in Migraineurs*

Some evidence suggests that OC use in migraineurs increases the risk of stroke. Tzourio et al. reported the odds ratio (increase of relative risk) of ischemic stroke in young women using low-estrogen-dose OCs as follows: without migraine, 3.5, and with

**Table 11-4. Approximate incidence of ischemic stroke (strokes per 100,000 women per year) in women with and without migraine who do not use oral contraceptives**

| Age   | Without migraine | Migraine     |           |
|-------|------------------|--------------|-----------|
|       |                  | Without aura | With aura |
| 25–34 | 1.3              | 4            | 8         |
| 35–44 | 3.6              | 11           | 22        |

Data from Becker WJ. Migraine and oral contraceptives. *Can J Neurol Sci* 1997;24:16–21.

migraine, 13.9 (13). The significance of this finding is uncertain in view of the more recent OC use and stroke studies showing no increased risk.

Most women with migraine without aura can safely take low-dose-estrogen OCs when there are no other contraindications to OC use. Similarly, those with migraine with auras such as visual symptoms lasting less than 1 hour can use OCs. Women with aura symptoms such as hemiparesis or dysphasia or prolonged focal neurological symptoms and signs lasting more than 1 hour might best avoid starting low-dose-estrogen OCs and stop the medication if they are already taking it. In addition, the physician should consider other factors in prescribing OCs, such as older age, cigarette smoking, and comorbidity such as diabetes, uncontrolled hypertension, and coronary artery disease. Progesterone-only OCs and the many other contraceptive options can be considered.

## HEADACHES DURING PREGNANCY AND POSTPARTUM

About 90% of headaches occurring during pregnancy and the postpartum period are benign. The frequency of tension-type headaches generally does not change. Migraine headaches usually occur less often. Management of frequent benign headaches can be challenging because of restrictions on medication use. Life-threatening causes of headache that can occur during this time include preeclampsia and eclampsia, subarachnoid hemorrhage, intracerebral hemorrhage, and cerebral venous thrombosis. There are numerous other secondary causes, including pseudotumor cerebri, brain tumors (including choriocarcinoma), and infections such as those arising from *Listeria*.

### Neuroimaging (21)

When there are appropriate indications (Chapter 1), neuroimaging should be performed during pregnancy. With the use of lead shielding, a standard computed tomography (CT) scan of the head exposes the uterus to less than 1 mrad. A radiation dose of equal to or more than 15 rad is necessary to result in deformities that might justify termination of the pregnancy. CT scan is the study of choice for the evaluation of head trauma or acute subarachnoid hemorrhage. Magnetic resonance imaging (MRI) is more sensitive for disorders that may occur during pregnancy, such as pituitary apoplexy, cerebral venous sinus thrombosis (with the addition of magnetic resonance venography), and metastatic choriocarcinoma. There is no known risk of MRI during pregnancy, but there is some controversy because the magnets induce an electric field and raise the core temperature slightly (less than 1°C). Although there is no known risk of intravenous (IV) contrast for CT scan or gadolinium for MRI, contrast should be avoided if possible. The radiation dose to the uterus for a typical cervical or intracranial arteriogram is less than 1 mrad.

## Migraine

### *Epidemiology*

The new onset of migraine has been variably reported as occurring in 1% and 10% of migraineurs during pregnancy, usually

during the first trimester. During pregnancy, preexisting migraine improves or disappears in about 60% or more, is unchanged in 20% or less, and grows more frequent in 20% or less (21). Improvement often occurs during the second or third trimester. In one study, menstrual migraine disappeared or improved in 85% and worsened in 7%, in contrast to nonmenstrual migraine, which disappeared or improved in 60% and worsened in 15% (22). When improvement occurs with the first pregnancy, improvement also occurs during subsequent pregnancies in about 50%, whereas an increased frequency occurs in the other 50% (23). Migraineurs do not have an increased risk of miscarriages, toxemia, congenital anomalies, or stillbirth.

One study reported that 38% of women had headaches during the first postpartum week, especially between days 3 and 6 (24). These headaches occurred more often in women with either a personal or family history of migraine. Many of the women described a mild to moderately severe bifrontal pain associated with photophobia and nausea. These headaches may be triggered by rapidly falling estrogen levels. In another study, 4.5% of women had the new onset of migraine during the postpartum period (25).

### *Management (26–30)*

Fortunately, migraines usually improve or disappear during pregnancy. Nonmedication approaches include avoidance of triggers, ice, sleep, and biofeedback.

Before prescribing medication, the patient should be advised of the potential risk during pregnancy. For many drugs there is insufficient knowledge about the risks of birth defects despite the fact that perhaps 67% of women take medications during pregnancy and 50% take them during the first trimester. The Food and Drug Administration (FDA) drug-risk ratings provide some guidance for medication during pregnancy. If nonobstetricians (such as neurologists or internists) are managing the migraines, they should confer with the obstetrician about medication use.

**SYMPTOMATIC MEDICATIONS.** Many migraineurs want to take medication during pregnancy, especially for moderate to severe migraines. Concerns include not only the potential of risk for the fetus, but also medication rebound headaches from overuse as well as habituation with the overuse of butalbital and narcotics.

Acetaminophen, which is an FDA Class B drug (no evidence of risk in humans, but there are no controlled human studies), is the medication of choice because there is no evidence of any teratogenic effect. Aspirin is rated Class C (risk to humans has not been ruled out) during the first and second trimesters and Class D (positive evidence of risk to humans from human or animal studies) during the third trimester. Although there is no definite evidence of teratogenicity, there are multiple possible adverse effects, including the following: inhibition of uterine contraction, longer gestation and labor, increased maternal and newborn bleeding, narrowing of the ductus arteriosus, and hyperbilirubinemia. Low-dose daily aspirin is generally safe when used to prevent preeclampsia or for the treatment of antiphospholipid antibody syndrome, although there may be an increased risk of abruptio placentae.

Caffeine in small doses of less than 300 mg a day is Class B and probably safe. Although butalbital is Class C, there has been no evidence of an association with malformations. However, prolonged overuse can result in fetal dependence and severe neonatal withdrawal. If acetaminophen alone is ineffective, some patients will benefit from the addition of butalbital (Phrenillin) or butalbital and caffeine (Fioricet), which can also be combined with codeine.

Codeine in reasonable amounts is probably safe. However, indiscriminate use of codeine (Class C) during the first and second trimesters has a potential for risk because defects such as cleft lip or palate and hip dislocation have been reported. Meperidine, methadone, and butorphanol (all Class C) are probably not teratogenic.

NSAIDs such as ibuprofen and naproxen are Class B during the first two trimesters but should be avoided during the third trimester because of the potential of inhibiting labor, prolonging the length of the pregnancy, and decreasing amniotic fluid volume. There is also concern about the possibility of causing pulmonary hypertension or premature closure of the ductus arteriosus.

Ergotamine and dihydroergotamine (both Class X, contraindicated in pregnancy) should not be used during pregnancy, although the actual risk is not clear. Triptans such as sumatriptan (Imitrex) are Class C. Although there is no evidence of a large increase in birth defects at this time, the use of triptans during pregnancy should be avoided because current information is not sufficient to exclude small increases in the risk of birth defects (31).

Antiemetics may be necessary if the headache is associated with prominent nausea or vomiting, and their use may prevent dehydration that can pose a risk to both the mother and fetus. Prochlorperazine, promethazine, and chlorpromazine (available orally, parenterally, and by suppository) are all Class C. Metoclopramide and ondansetron are Class B. These drugs are generally considered reasonably safe during pregnancy, especially with occasional use. No congenital malformations have been reported with the use of metoclopramide.

Prolonged migraine may be treated with 10 mg of prochlorperazine intravenously and IV fluids. The addition of parenteral narcotics may help some patients. Migraine status may respond to the administration of intravenous corticosteroids such as dexamethasone 4 mg IV.

**PREVENTIVE MEDICATIONS.** Frequent severe migraines associated with nausea and vomiting may justify the use of preventive medications.

Valproic acid, which is Class D (positive evidence of risk to humans from human or animal studies), should be avoided because of the 1% to 2% risk of neural tube defects when taken between day 17 and day 30 after fertilization. Topiramate, which is Class C, should only be used if the potential benefits outweigh the potential risks because there is inadequate information on the possibility of birth defects and its use (although there are reports on birth defects in animal studies).

Beta-blockers, routinely used during pregnancy for the treatment of hypertension, are the preventive of choice if medical contraindications are not present. Atenolol, nadolol, propranolol,

metoprolol, and timolol are all Class C. Although there is no evidence of teratogenicity, there may be an increased incidence of small-for-gestational-age infants. Propranolol may cause fetal and neonatal toxicity.

Antidepressants might be considered in some cases. The class rating of some tricyclic antidepressants are as follows: amitriptyline and nortriptyline, Class D; and doxepin and protriptyline, Class C. Tricyclics should be stopped at least 2 weeks before the due date. There are reports of infants with respiratory distress and feeding difficulties born to women who took tricyclics through delivery. Fluoxetine (Class C), a selective serotonin reuptake inhibitor (SSRI), is questionably effective for migraine prevention, but there is evidence of efficacy for chronic daily headache. Fluoxetine might be considered in a patient with frequent headaches and depression. None of the SSRIs or tricyclic antidepressants have been associated with an increased risk of congenital malformations, although information on long-term neurobehavioral effects remains limited (32).

Another option is the calcium channel blocker verapamil (Class C), which is probably safe during pregnancy. This drug is preferable to beta-blockers for prevention of migraine with prolonged aura. In addition, verapamil can also be considered in women with hypertension and frequent migraines who cannot take beta-blockers.

**BREASTFEEDING AND MIGRAINE MANAGEMENT.** The American Academy of Pediatrics Committee on Drugs has made recommendations based on their review of drug use during lactation (Table 11-5) (33). Ergotamine is contraindicated during breastfeeding. Drugs whose effect on nursing infants is unknown but may be of concern include such antidepressants as amitriptyline and fluoxetine. Their use is probably safe because there are no reported adverse effects.

Maternal medications usually compatible with breastfeeding include the following: acetaminophen; barbiturates (which may cause infant sedation); caffeine (which may cause irritability or

**Table 11-5. Drug therapy in lactating women: questions and options**

1. Is the drug therapy really necessary? Consultation between the pediatrician and the mother's physician can be most useful.
2. Use the safest drug—for example, acetaminophen rather than aspirin for analgesia.
3. If there is a possibility that a drug may prevent a risk to the infant, consideration should be given to measurement of blood concentrations in the nursing infant.
4. Drug exposure to the nursing infant may be minimized by having the mother take the medication just after she has breastfed the infant and/or just before the infant is due to have a lengthy sleep period.

From The American Academy of Pediatrics Committee on Drugs. The transfer of drugs and other chemicals into human milk. *Pediatrics* 1994;93:137–150.

poor sleeping pattern if the mother uses a lot of it); NSAIDs, such as ibuprofen and naproxen; beta-blockers, such as propranolol and nadolol; narcotics, including codeine, morphine, and butorphanol; valproic acid; and verapamil. Triptans (not listed in the report) should be used with caution.

### **Preeclampsia and Eclampsia (34)**

#### *Epidemiology*

Preeclampsia occurs in up to 7% of pregnancies, and eclampsia is found in up to 0.3%. The criteria for preeclampsia include the following: proteinuria of more than 300 mg/day or two spot urines with more than 1 g protein/liter collected more than 6 hours apart; edema; hypertension persistently greater than 140/90 or relative hypertension with a rise over a first-trimester baseline blood pressure of at least 30 mm Hg systolic or 15 mm Hg diastolic; and onset after the 20th week of gestation up until 48 hours postpartum. Eclampsia occurs with the additional complications of seizures or coma. As many as 45% of cases of eclampsia have an onset postpartum, with a mean of 6 days and up to 4 weeks.

Risk factors for preeclampsia in primigravida are prepregnancy hypertension, obesity, multiple abortions or miscarriages, and cigarette smoking. The incidence of pregnancy-induced hypertension is greater in first or multiple pregnancies and in younger and older women. Black women have twice the incidence of whites.

#### *Clinical Manifestations*

Nonneurological complications include the following: renal dysfunction with oliguria, casts, and elevated serum uric acid, urea, and creatinine; pulmonary edema; vomiting and epigastric pain; subcapsular hepatic hemorrhage; and hemolysis, elevated liver enzymes, and low platelets (HELLP syndrome), which can be further complicated by disseminated intravascular coagulation (DIC) in up to 40% of patients.

Neurological complications consist of the following: headaches that are typically bilateral; dizziness; tinnitus; altered consciousness or coma; seizures; and visual disturbances, including diplopia, scotomas, blurring, and blindness. Blindness, which can occur in up to 15% of eclamptics, may be due to retinal hemorrhages, edema, or detachment or occipital ischemia.

#### *Subarachnoid Hemorrhage*

Nontraumatic subarachnoid hemorrhage (SAH) during pregnancy has an incidence of about 20 per 100,000 deliveries. This is the third most common cause of nonobstetrical mortality, accounting for 5% to 10% of all maternal deaths. This risk is five times higher than that outside pregnancy. SAH is due to ruptured saccular aneurysms and arteriovenous malformations with equal frequency. Up to 20% of aneurysmal ruptures occur during pregnancy or in the early postpartum period. The risk of aneurysmal SAH is highest during the late third trimester, during delivery, and in the puerperium (35). The most common time for hemorrhage from an arteriovenous malformation (AVM) is

between 16 and 20 weeks' gestation or during parturition. About 25% of pregnant women who have already bled from an AVM will rebleed during the same pregnancy. Chapter 8 reviews the clinical manifestations of SAH.

Other causes of intracranial hemorrhage during pregnancy and the puerperium include eclampsia, cerebral venous thrombosis, choriocarcinoma, bacterial endocarditis, drug abuse, DIC, moyamoya disease, hematological disorders, tumor, ruptured spinal cord vascular malformations, and arterial hypertension.

### *Stroke and Cerebral Venous Thrombosis (36)*

The risk of ischemic stroke is 13 times higher during pregnancy and the puerperium than expected outside of pregnancy. Either ischemic or hemorrhagic stroke occurs in up to 19 in 100,000 deliveries. Arterial occlusions account for 60% to 80% of these strokes. The headaches associated with stroke are described in Chapter 13.

The numerous causes of arterial ischemic strokes include cardioembolic disorders (rheumatic heart disease, prosthetic heart valves, atrial fibrillation, bacterial and nonbacterial endocarditis, peripartum cardiomyopathy, mitral valve prolapse, and paradoxical embolus); cerebral angiopathies (atherosclerosis; arterial dissection; fibromuscular dysplasia; cerebral vasculitis, such as systemic lupus erythematosus, Takayasu's disease, periarteritis nodosa, and isolated angiitis of the brain; and postpartum cerebral angiopathy); hematological disorders (sickle-cell anemia; Sneddon's syndrome; antiphospholipid antibodies; thrombotic thrombocytopenic purpura; homocystinuria; deficiency of antithrombin II, protein C, and protein S; and DIC); and other causes (eclampsia, choriocarcinoma, amniotic fluid embolism, air embolism, fat embolism, drug abuse, and Sheehan's syndrome).

The only three pregnancy-specific disorders are eclampsia, choriocarcinoma, and amniotic fluid embolism. Postpartum cerebral angiopathy and peripartum cardiomyopathy have also been reported apart from pregnancy.

Pregnancy and the puerperium are associated with an increased risk of cerebral venous thrombosis (Chapter 13). Ninety percent of cases occur during the puerperium, most commonly in the second or third weeks postpartum.

Sheehan's syndrome is the spontaneous ischemic necrosis of the pituitary gland in the postpartum period, resulting in hypopituitarism. Most cases are due to hypotension and shock from acute blood loss, resulting in ischemia of a hypertrophied pituitary gland of pregnancy. About 1% to 2% of women who have a significant postpartum hemorrhage will have this syndrome. In contrast to pituitary apoplexy (Chapter 14), headaches and cranial nerve abnormalities are not usually associated.

### *Pseudotumor Cerebri*

Although pregnancy is not a risk factor, pseudotumor cerebri can develop or worsen during pregnancy. Visual outcome is the same for pregnant and nonpregnant patients (37). Subsequent pregnancy does not increase the risk of recurrent pseudotumor cerebri. This disorder is discussed further in Chapter 14.

### Brain Tumors

Pregnancy does not increase the risk of developing a primary brain tumor. Meningiomas may increase in size during pregnancy and then regress postpartum. Twenty-five percent of macroprolactinomas expand enough to cause problems during pregnancy.

Choriocarcinoma is due to malignant transformation of the trophoblast. Although choriocarcinomas usually follow a molar pregnancy, they can also follow term delivery, abortion, and ectopic pregnancy. Brain metastases occur in 20% of cases.

Trophoblasts can invade blood vessels and result in thrombosis and cerebral infarctions. Neoplastic aneurysms and cerebral hemorrhage can also occur.

### Infections

Pregnancy is a state of relative immunosuppression. Coccidiomycosis, tuberculosis, listeriosis, and malaria have an increased risk of spread to the central nervous system when acquired during pregnancy. Headache can certainly be a presenting or prominent symptom.

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## Author Queries

### Chapter 11

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