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*Neurologic emergencies of pregnancy range from life-threatening conditions such as eclamptic seizures (*see Hypertensive Disorders of Pregnancy, 2004;25:293-308*) to self-limiting disorders like meralgia paresthetica. This discussion will include those neurologic disorders directly resulting from pregnancy or the puerperium, those that are pre-existing conditions but now affect the pregnant patient or are affected by the gravid state of the patient, and those disorders that are not directly related to the pregnancy but may first become apparent during the gravid state. Most of the diseases presented are not a primary emergency department (ED) problem, but rather may intersect the ED due to time of day, day of week, or lack of other health care access. All disorders covered in this section occur in the non-pregnant patient as well, and therefore it is assumed that readers will consult a detailed text for specifics if they are unfamiliar with the disorder. Where appropriate, diagnostic pitfalls likely to present to the ED will be discussed.*

—The Editor

Neurologic Complications of Pregnancy

A Systematic Approach to Patient Evaluation and Management

Author: **Mary Hughes, DO**, **FACEP, FACOEP**, Professor, Emergency Medicine, Michigan State University College of Osteopathic Medicine (MSU-COM); Program Director, MSU-COM Emergency Medicine Residency, East Lansing, MI.

Peer Reviewers: **Charles Emerman, MD,** Chairman, Emergency Medicine, Case Western Reserve University, Cleveland, OH; and **Gary Hals, MD, PhD**, Department of Emergency Medicine, Palmetto Richland Hospital, Columbia, SC.

Epilepsy and the Pregnant Patient

Of all pre-existing neurological disorders in the pregnant patient, epilepsy is second only to migraines, affecting approximately 1:200 gravid patients, with a prevalence in the general population of 1%.[1-4] In the ideal situation, each female of childbearing age with epilepsy would be provided preconception vitamin and folic acid supplementation and counseling to decrease the risk of adverse events, including congenital anomalies, prior to becoming pregnant.[5] However, as greater than 50% of pregnancies are unplanned, pre-pregnancy counseling is lacking in many if not most epileptic females.[2,6] This partially is explained by the drug/drug interaction between the enzyme-inducing anti-epileptic drugs (barbiturates, phenytoin, carbamazepine, topiramate, and

tiagabine) and oral contraceptives (OC). They act by increasing the metabolism of the OC, making the OC less effective.[7]

Seizure control varies in pregnancy, with approximately one-third of patients having an increase in activity. Poor pre-pregnancy control predicts pregnancy control in many cases.[2] There are several reasons for this increased seizure frequency, including lack of compliance (often associated with withholding of medications by the mother to decrease the risk for congenital anomalies early in pregnancy), nausea and vomiting associated with pregnancy that limits intake and retention of medications, changes in intestinal absorption, increased clearance rates of anti-epileptic drugs, and changes in protein binding sites.[3] Because of changes in albumin and protein binding sites, the ideal way to monitor anti-epileptic drug therapy is to obtain a free blood level of the anti-epileptic drug pre-pregnancy, and then maintain this level during the pregnancy, assuming good seizure control pre-gestation.[3,5] The poorly controlled patient is the most likely patient to present to the ED, and measuring free drug concentrations in these patients may assist in the achievement of better control.[5,8]

Adverse Outcomes and Congenital Abnormalities in the Children of Women with Epilepsy

More than 90% of pregnant patients on anti-epileptic drugs will have a favorable fetal outcome,[8,9] but the incidence of congenital malformations in infants born to mothers on anti-epileptic drugs is 4-8%, which is 2-3 times the baseline rate.[2,4,10,11] The majority of malformations occur in the first trimester, often before the mother is even aware of her pregnant state.[12] Fetal anticonvulsant syndrome has been described with virtually all anti-epileptic drugs and is a term used to describe a constellation of major and minor anomalies that occur in infants born to mothers receiving anti-epileptic drugs.[13] The most common major fetal malformations due to anti-epileptic drugs include cleft lip/palate, congenital heart defects including Tetralogy of Fallot and atrial or ventricular septal defects, neural tube defects that often are open, and genitourinary defects.[7] Any patient newly diagnosed as pregnant in the ED who is noted to be on an anti-epileptic drug for any medical reason, including non-seizure related diagnoses, should be referred back to her treating physician for reevaluation and close monitoring to decrease the risk of these adverse events. Alteration of stable anti-seizure medication regimens by the ED physician is not indicated, but phone consultation with the prescribing physician to notify him or her of the pregnancy status of the patient and arrange for follow-up is. The lowest effective dose of the least number of medications while still maintaining adequate seizure control is the goal.

Although the newer anti-epileptic drugs, gabapentin (Neurontin), lamotrigine (Lamictal), and felbamate (Felbatol) have not been extensively studied, the five major anti-epileptic drugs, namely phenytoin (Dilantin), carbamezepine (Tegretol), phenobarbital (Luminal), primidone (Mysoline), valproic acid (Depakene, Depakote), have been. All have been associated with an increased risk of malformations, especially in patients on polytherapy with high anti-epileptic drug levels.[2,14] Ideally the patient should be placed on the least toxic monotherapy possible.[15] However, changing anti-epileptic drug therapy after 10 weeks gestation to alter side effect profiles will not change the final pregnancy outcome of birth defects, and therefore is not warranted. This is because all anti-epileptic drugs that cause fetal anomalies will do so during the organogenesis that occurs in the first 10 weeks, often well before the patient realizes she is pregnant.[16] Again,

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Editorial Group Head: Glen Harris
Specialty Editor: Shelly Morrow Mark
Marketing Manager: Nan Reeves
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90% of all patients on anti-epileptic medications will have a favorable fetal outcome,[9] and there is a 10-fold increase in maternal mortality in patients who suffer a seizure while pregnant.[17] The Gabapentin Pregnancy Registry has reported on 51 fetuses exposed to the drug during gestation for any reason, including epilepsy. To date, there is no increased risk above the general population in fetal malformations or maternal complications. Caution should be used, however, because the number of studied patients is small.[18] A history of maternal epilepsy without the concomitant use of anti-epileptic drugs is not associated with a greater frequency of congenital malformations.[14,19]

Patients who suffer a seizure during their pregnancy, regardless of the presence or absence of anti-epileptic drugs, may have an increased risk of congenital abnormalities or other pregnancy-related complications that may be the result of hypoxia, acidosis, or trauma during the seizure. A study conducted in Finland did not show an increase in fetal malformations in women who suffered a grand mal seizure during the first trimester.[20] However, a study in the United Kingdom of maternal mortality from 1985-1999, noted a 10-fold increase in mortality in women with epilepsy when compared to those without. Epilepsy was the third leading cause of maternal death, behind cardiac deaths and stroke. Most of these deaths were seizure related, and often in women who discovered they were pregnant, discontinued their anti-epileptic medication, and then suffered a seizure. Seizure medications should not be changed in the ED.[17]

Trauma during a seizure may cause abruptio placenta, premature rupture of membranes, premature delivery, or fetal demise.[21] These facts should be communicated to the female patient who is non-compliant secondary to worries about effects of anti-epileptic drugs on her fetus. For the pregnant patient prior to 20 weeks gestation, although the fetus is non-viable, the potential for these complications should be explicitly documented, and the mother should be instructed to contact her obstetrician should she experience a sudden leak of fluids, abdominal pain, vaginal bleeding, or a spontaneous abortion. If any of these occur and the mother in unable to contact her obstetrician, she should be instructed to return to the ED for re-evaluation. For any pregnant patient past 20 weeks gestation who suffers a seizure, these complications must be ruled out, which often necessitates the observation of the mother and fetus for several hours in an obstetrical observation ward or the ED if no such space is available. In addition, any seizure that occurs past 20 weeks gestation, even in a known epileptic patient, should prompt an evaluation for eclampsia. In all cases except maternal allergy, benzodiazepines are the drug of choice for acute control regardless of etiology.[3]

Nutritional Recommendations

Folic Acid. Folic acid is involved in the process of closure of the neural tube and development of red and white blood cells.[22] Supplementation in the periconceptual time period is recommended for the female of childbearing age, with higher doses recommended for those with a prior history of an infant with a neural tube defect.[7,22] Folates are cofactors in many biochemical reactions, including one-carbon metabolism. Barbiturates, carbamazepine, valproic acid, and phenytoin interfere with folic acid metabolism, and the enzyme inducing anti-epileptic drugs (barbiturates, phenytoin, carbamazepine, topiramate, and tiagabine) decreases absorption. Any of the anti-epileptic medications that induce the cytochrome p450 system can lower plasma folate levels as well.[17] The recommended dose for folic acid in patients receiving anti-epileptic drugs is 10 times the dose (4 mg daily) of that recommended to women not on anti-epileptic drugs (0.4 mg daily). This should be started at the time of the first diagnosis of pregnancy, even if that occurs in the ED, unless obstetrical consultation can be obtained within the following 24 hours.[3,5] Doses greater than 5 mg daily may impair seizure control and lower serum phenytoin levels.[23-25] Even with the larger doses given to women on anti-epileptic drugs, especially those taking valproic acid or carbamazepine, supplementation has had less than expected results in neural tube defect prevention, although all studies to date have been quite small.[7,22]

Vitamin K. All commonly used anti-epileptic drugs except valproic acid and clonazepam (Klonopin) can decrease the fetal vitamin K dependent clotting factors, leading to an increased risk of neonatal hemorrhage. It is recommended by the American Academy of Neurology[4] that oral vitamin K should be administered to the mother during the last month of gestation at a dose of 10 mg daily. If this has not been done and the patient presents for delivery, 10 mg of vitamin K may be given IV during delivery. The newborn also should receive 1 mg IM of vitamin K. Fresh frozen plasma may be necessary to manage hemorrhagic complications.[1-3,5,7,12,16] A more recent study questions the need for oral supplementation for the final month of pregnancy and did not note an increased risk of hemorrhagic events in newborns born to mothers not receiving supplemental vitamin K, but was underpowered to evaluate the true risk of hemorrhage in those infants born to mothers on anti-epileptic drugs.[26] It is a current recommendation by the American Academy of Pediatrics that all newborns receive 0.5-1.0 mg of vitamin K IM immediately after delivery.[16] This includes infants born to mothers on anti-epileptic medications.

Neonatal Exposure. Finally, the neonate exposed to phenobarbital or primidone (whose active metabolite is phenobarbital) may present approximately one week post-delivery with signs and symptoms of phenobarbital withdrawal, which may last for months.[12,27] Withdrawal symptoms include hyperexcitability, irritability, and regurgitation.[1] This should be one of the many items on the differential of the irritable newborn with a history of maternal gestational phenobarbital use, and following a complete work-up may be the diagnosis of exclusion.

ED Management of the Possibly Pregnant Seizing Patient

The management of the female patient presenting to the ED with a new-onset seizure should follow standard therapy and is beyond the scope of this article. Oxygen and benzodiazepines should be used for immediate control. The seizure evaluation, including a pregnancy test, serum chemistries, urine drug screen and dip for protein, head computed tomography (CT) scan, and

possibly magnetic resonance imaging (MRI) or lumbar puncture should be completed if indicated, regardless of the results of the pregnancy test. If the patient is found to be gravid, an ultrasound should follow a quantitative HCG level to determine the fetal age and viability. If the fetus is determined to be greater than 20 weeks or the patient is within two weeks post-partum, then eclampsia must be included in the differential, and magnesium sulfate started to prevent further seizures. In addition, fetal and maternal monitoring should be conducted following the seizure, preferably in an obstetrical observation unit equipped to handle an imminent delivery if necessary.

Summary

The ED physician who is presented with a pregnant or newly delivered patient suffering from a seizure, in addition to managing airway, breathing, and circulation (ABCs), should:

• Assess the mother for eclampsia if past 20 weeks gestation or within two weeks postpartum. (*See Hypertensive Disorders of Pregnancy, 2004;25:293-308.*)

• Provide oxygen therapy and place the patient in the left lateral position if pregnant and past 20 weeks.

• Treat the initial seizure, regardless of etiology, with benzodiazepines.

• Place the eclamptic patient on magnesium sulfate to prevent further seizures.

• If past 20 weeks gestation, monitor the mother and fetus for placental abruption, premature rupture of membranes, premature delivery, or fetal demise—this may require an observation period in the obstetrical unit depending on institutional protocols.

• If fewer than 20 weeks gestation, explain that the fetus is not viable outside the uterus, but that there are potential complications of the seizure that may occur, including: premature membrane rupture causing fluid leak; placental abruption, which may cause abdominal or pelvic pain or vaginal bleeding; spontaneous abortion; or stillbirth.

• Evaluate the new-onset seizure patient with the same diagnostic modalities that one would use if the patient were not pregnant, including CT of the head, drug screen, and possible MRI or lumbar puncture, depending on the scenario.

• Be aware that protein binding changes during pregnancy and free anti-epileptic drug levels are more accurate.

• Arrange follow-up with the physician managing the patient's seizures or other medical conditions being treated with anti-epileptic drugs to occur within the following few days, if the patient is found to be pregnant in the ED.

• Write a prescription for folic acid 4 mg daily until the patient can be seen by the neurologist and/or obstetrician in follow-up.

• Arrange obstetrical follow-up for the newly diagnosed patient on an urgent basis.

• If a pregnant patient on anti-epileptic drugs presents to the ED for delivery and cannot be taken to the labor and delivery floor, give vitamin K 10 mg IV to the mother and 1 mg IM to the infant at the time of birth, unless the mother has received vitamin K orally for the preceding month. In this case, give the infant the AAP recommended dose of vitamin K 1 mg IM.

Table 1. Patient Education for Women on Antiepileptic Drugs for Any Reason[28]

• You have been diagnosed with pregnancy, and are noted to be on one of several anti-epileptic drugs.
• If these medications are being taken for the management of epilepsy you should consult the health care provider managing your seizures.
• If these medications are being taken for migraine prophylaxis or as a mood stabilizer, consult the health care provider managing these conditions.
• Anti-epileptic drugs have been associated with an increased risk of birth defects in infants born to mothers who take them. These abnormalities occur during the first 10 weeks of your pregnancy.
• This risk is 2-3 times that of the population not taking these medications. However, more than 90% of pregnancies that occur while the mother is taking one of these medications produce healthy newborns.
• DO NOT stop taking these medications without consulting your physician, particularly if you are using them for seizure control. A seizure is also harmful to you and your baby. It may cause chemical imbalances in the blood, and trauma-related injuries to you or the baby may be fatal to one or both of you.
• If you are not already doing so, DO begin taking folic acid. A prescription for 4 mg/day is being provided until you can visit the obstetrician.
• DO arrange obstetrical follow up and follow their recommendations regarding the use of medications.
• DO adjust your lifestyle to avoid known triggers for your seizures. This includes getting enough rest; avoiding illicit drugs, alcohol, cigarettes, and prolonged exposure to flashing lights from any source (i.e., video games, computer

• Document in the chart patient education regarding seizure disorders and pregnancy, and the use of anti-epileptic drugs during pregnancy. (*See Table 1.*)

• In addition, the ED physician, when presented with an irritable newborn, should explore the medication list of the mother and include in the lengthy differential of this disorder possible withdrawal from maternal phenobarbital or mysoline.

• Although the pregnant patient in status is rare, she should be treated in the same fashion as the non-pregnant status patient.

Stroke and Cerebral Venous Thrombosis

Introduction. As if pregnancy weren't fraught with enough potential disasters, the pregnant patient also is at increased risk for a cerebrovascular accident (CVA). Cerebrovascular disease in

pregnancy accounts for more than 12% of maternal deaths.[29] Two recent large studies have placed the incidence of stroke (non-hemorrhagic and hemorrhagic combined) at 8.9-26/100,000 deliveries, approximately twice the incidence for females of the same age who weren't pregnant.[30-32] In these studies, which controlled for the "referral center factor" if necessary, the greatest risk was in the first few weeks postpartum, with less of a risk during the pregnancy itself.[30] In his population-based study in the Washington, D.C. area, Kittner noted a 0.7 relative risk of ischemic stroke during pregnancy, which rose to an 8.7 relative risk postpartum. Likewise, the relative risk of intracerebral hemorrhage from any cause was 2.5 during pregnancy, and 28.3 in the postpartum period.[30] One study revealed a nearly equal incidence of hemorrhagic and non-hemorrhagic strokes,[32] whereas others demonstrate a preponderance of ischemic (arterial and venous) events.[30,31]

A greater percentage of ischemic cerebral infarctions in this patient population are arterial rather than venous, but combined account for up to 69% of CVAs in pregnancy.[29] Etiologies range from cardiac emboli and arterial dissections to coagulopathies. Peripartum cardiomyopathy, hypertension, diabetes, underlying cardiac disease, smoking, and thrombophilic conditions increase the risk for ischemic stroke. In addition, pregnancy itself induces a relative hypercoagulable state, increasing the patient's risk for a cerebral event.[29,33]

The most common etiologies of hemorrhagic strokes include ruptured aneurysms, followed by arteriovenous malformation (AVM) and disseminated intravascular coagulopathy. Preeclampsia-eclampsia is an important cause of cerebral hemorrhage but not infarction.[33,34] Overall, patients with hemorrhagic strokes have a higher mortality rate when compared to ischemic events in these more recent studies.[31,32] A prior history of stroke does not preclude a subsequent pregnancy, and patients with a prior history of non-pregnancy related stroke have a 0-1% risk of a subsequent stroke during pregnancy. For patients with a thrombophilia, the recurrence rate is as high as 20%.[33,35]

Diagnostic Evaluation for Suspected Strokes in the Pregnant Patient

The diagnostic workup for the pregnant patient with a suspected stroke should be the same as for the non-pregnant one. Initially, a thorough history and physical exam with attention to the blood pressure, the neurological examination including funduscopic, the cardiovascular exam for rate and rhythm disturbances as well as murmurs, and the urine for drug screen as well as proteinuria should be conducted. The examination of the skin may reveal evidence of emboli or markers of connective tissue diseases.

A CT scan with abdominal shielding has minimal fetal exposure (2mRad).[36] Cerebral angiography with shielding is similar in skilled hands. Iodinated contrast may be given with good IV hydration, but poses a risk for fetal hypothyroidism if given after 6 months gestation. This easily is diagnosed and treated at birth if the initial benefit of the test in the mother outweighs the fetal risk.[36]

MRI appears to be safe but has not been studied extensively, and gadolinium is an unknown risk, which should be avoided if possible.[37-39] The latest American College of Obstetrics and Gynecology recommendations published in 1995 advise against an MRI in the first trimester, but other more recent studies have not shown deleterious fetal effects.[40] In 2002, the American College of Radiology published a white paper on the safety of MRI. Their position is that any pregnant woman may undergo MRI regardless of pregnancy stage, providing a Level Two MR Personnel-designated attending radiologist believes the benefits outweigh the risks and no other non-ionizing means can be utilized to gain the information. In addition, the information gained must be needed to affect care of the mother and/or fetus during the pregnancy, and the referring physician does not feel that it is prudent to wait until the patient is post-partum. MR contrast agents should *not* be given routinely, and on a case-by-case basis the MR attending radiologist must feel the benefits outweigh the risk. The mother should sign an informed consent form.[41] Therefore, it is recommended that the emergency physician discuss the benefits and risks of the study with the radiologist, patient's obstetrician, and the patient before ordering an MRI, especially if it is in the first trimester. Contrast should be avoided.[42] It should be noted that several studies have been conducted on the evaluation of the fetus for defects utilizing MRI, but they generally are in the third trimester.[43-45] Fortunately, the majority of the CVAs occur in the post-partum period, and thus carry no risk to the fetus from the MRI.

Determining the exact etiology of an ischemic event is paramount to providing the correct treatment, and this may necessitate studies outside the CNS, including electrocardiography and transesophageal echocardiography. Coagulation studies and a search for the common thrombophilias are indicated.[33]

Cerebral Venous or Sinus Thrombosis

Cerebral venous thrombosis (CVT) is another vascular event that is more common in the pregnant than non-pregnant patient, with 80% of cases occurring in the second and third postpartum weeks.[37] However, the diagnosis often is difficult to make and generally requires an MRI or, occasionally, a cerebral angiogram to reach a definitive answer. The initial presentation is one of a headache and variable neurological findings depending on the venous system or sinus thrombosed, and often is accompanied by an elevated intracranial pressure and normal cerebrospinal fluid (CSF) studies. The absolute mortality is unknown, but is somewhat greater than 5% in developed countries, and reported as high as 30%.[33,46] There appears to be a high prevalence of thrombophilia (up to 20% Factor V Leiden) in patients with CVT.[33]

Current treatment of CVT includes heparin initially with anticoagulation continued for 2-3 months, anticonvulsants for patients who suffer seizures, and intracranial pressure lowering medications or procedures for those in which it is indicated.[46] In addition, dehydration should be avoided.[33] If the diagnosis of CVT is made in the ED, therapy should be instituted in the ED.

Treatment of Stroke

Admission is required for all pregnant patients diagnosed with a suspected CVA from any cause. Management begins with stabilization of the maternal vital signs, including blood pressure

control. The underlying cause must be determined to provide appropriate therapy. For the treatment of hemorrhagic strokes, all management, including surgical procedures, should proceed as if the patient were not pregnant.[37,47]

In ischemic strokes, the etiology should be determined and appropriate treatment instituted based on the final cause. Anticoagulation with unfractionated heparin or low molecular weight heparin is reasonably safe in pregnancy, as neither molecule crosses the placenta. Anticoagulation should be based on the etiology of the stroke and should commence in the ED in consult with obstetrics and neurology.[29] Thrombolytic therapy may be indicated for a pregnant patient who presents within three hours of symptoms and is diagnosed with an ischemic stroke, but all studies evaluating thrombolytics for CVA excluded the pregnant patient, so very little data is available. Pregnancy is not an absolute contraindication to the use of t-PA, which is a Category C drug, meaning that the benefit of its use should outweigh the risks to the fetus.[29,33,40,48] Newer, mechanical clot disruption devices or snares may be a more attractive option in the pregnant patient, but still are considered investigational procedures and are not readily available.[29,33] From the ED perspective, making the diagnosis of a CVA should prompt the physician to consult the patient's obstetrician, neurology, and/or neurosurgery, depending on the etiology if the patient still is pregnant. As most CVAs occur in the first few postpartum weeks, the risk is only to the mother, and therefore proceeding with t-PA is based solely on maternal indications without worry about the fetus. The patient and/or her family should be informed of the potential risks and benefits and be included in the decision-making process.

Summary

• Any pregnant or newly delivered patient presenting with a headache or focal neurological deficits should undergo a thorough neurologic exam and be evaluated for hypertension and proteinuria.

• The risk of stroke is greatest in the puerperium.

• Rapid evaluation in patients suspected of having a stroke, including a head CT scan with abdominal shielding if pregnant, should be conducted.

• Pregnant patients who present with symptoms of stroke or cerebral venous thrombosis should be treated as those who aren't pregnant, including the use of t-PA if the patient presents within the three-hour window and the benefits to the mother outweigh the risk to the fetus.

• Lumbar puncture should be conducted if indicated.

• MRI should be obtained regardless of the pregnancy status of the patient, provided there is no alternative non-ionizing study to obtain the information, and the results will have an impact during the pregnancy and it would be deleterious to wait until the patient is postpartum.

• IV iodinated contrast for CT scan may be used, but may cause fetal hypothyroidism if used in the third trimester.

• MRI contrast should be given only if absolutely essential, as it does cross the placenta and is renally excreted by the fetus, although no studies have demonstrated adverse effects.

• If eclampsia is the final diagnosis, magnesium sulfate should be used to prevent further seizures.

• Anticoagulation with heparin or low molecular weight heparin should be used where indicated.

• Neurosurgical procedures should be conducted if indicated.

• The patient and her family should be kept apprised of the benefits and risks of all procedures, and it is recommended that informed consent be obtained before obtaining an MRI in the first trimester.

Headache

Initial Evaluation. The ED physician's role is to evaluate the patient for a life-threatening condition when a patient with a severe headache presents to the ED. A pregnant patient who presents with a chief complaint of headache should undergo a thorough history and physical exam with attention to prior history of headache, similarities between the current headache and previous headaches, results of any prior workup, and a physical exam with special attention to the blood pressure and neurologic exam. New headaches, changes in the character of the headache, neurologic findings, proteinuria, or other constitutional findings warrant further workup. Of particular concern, preeclampsia, eclampsia, and cerebral venous thrombosis all may present with headache as an initial symptom. A CT scan or MRI is necessary if headache character has changed or neurologic abnormalities are noted. A headache history suspicious for subarachnoid hemorrhage also should prompt a workup, including a CT with or without lumbar puncture (LP), depending on the CT results.[49] See discussion on stroke regarding the use of MRI in the pregnant patient. The contrast media used has been shown to cause adverse effects on animal fetuses at doses 2.5-7.5 times the human dose, but there are no human studies of safety of MRI contrast in pregnant females. It is recommended to defer contrast agents in pregnant patients unless the benefit is greater than the risk.[38,39]

Usual Course of Migraines. Migraines affect 15-17% of the female population and often are linked to the sex hormones.[50,51] In pregnant patients with migraines, there is a 60-70% improvement in the frequency of attacks, especially in the second and third trimesters, independent of migraine type,[51] which often worsen again after delivery.[49] In one prospective study, 18% of patients presenting to a university based obstetrics and gynecology clinic in their first trimester suffered from migraines, with 83% having migraines without aura. Migraines improved substantially throughout the pregnancy (47% in the first trimester, 83% in the second, and 87% in the third), recurring in the first postpartum week in 34% and within the first month in 55%.[52]

Management of Headaches in the ED. Once the ED physician has conducted an appropriate workup to discern the etiology of the headache, and comes to the conclusion that it is not life-threatening or related to a complication of pregnancy that might require additional treatment, such as preeclampsia or eclampsia, he or she should provide the least toxic acute therapy to control the symptoms. Attempts to avoid all triggers should be encouraged. In addition, preventive medications such as valproic acid should be avoided.[49] If the physician discovers that the patient is

pregnant in the ED and notes the use of valproic acid as a migraine prevention medication, the ED physician should notify the prescribing physician. If the patient is less than one trimester in gestation, she should be encouraged to discontinue the valproate if the sole use is for migraine prevention. As migraines generally improve greatly during pregnancy, this medication is likely unnecessary, and is known to cause serious fetal anomalies. In addition, a prescription should be written for folic acid 4 mg daily. If the patient is past the tenth week of gestation, the patient should be referred to obstetrics for a detailed evaluation of the fetus for birth defects. (*See previous discussion under seizures.*)

Acute measures for headache management may be as simple as a quiet environment and an ice pack. Non-pharmacological measures such as biofeedback and relaxation techniques may be effective, although not readily available in the ED.[53,54] Acutely, acetaminophen with codeine (Tylenol #3), prochlorperazine (Compazine), metoclopramide (Reglan) , trimethobenzamide (Tigan), or promethazine (Phenergan) are thought to be safe and effective. Parenteral narcotics such as morphine or meperidine (Demerol) may be necessary on rare occasions.[49,51,55] Aspirin and non-steroidals may be used, but should be avoided in the third trimester because their use has been associated with preeclampsia, prolonged labor, persistent pulmonary hypertension in the neonate, premature narrowing of the ductus arteriosus, and an increased fetal and maternal risk of hemorrhage.[51]

Pseudotumor Cerebri

Although not the most accurate term to describe this condition, pseudotumor cerebri (PC) has been defined and studied since the late 1800s.[56] It is a condition of elevated intracranial pressure in the absence of intracranial space occupying lesions, abnormal ventricles, infections, or other CSF abnormalities. PC most often is associated with papilledema and headache, but lacks focal neurological deficits.[57] Another common but more recent term is idiopathic intracranial hypertension (IIH).[58] This disorder must be differentiated from CVT, which often presents similarly to IIH.[46] Pregnancy is a predisposing factor for both, and MRI or cerebral angiography should be performed to rule out CVT before assigning the diagnosis of IIH.[59,60] Most patients with CVT present with an abrupt headache, which is considered severe and often is associated with papilledema, visual field and/or acuity loss, and diplopia.[61] The patient with PC generally will have a more gradual onset of cephalgia, with concomitant papilledema, normal CSF studies with the exception of the opening pressure, and without focal neurologic deficits.[57] A small series of patients studied revealed that the pregnant patient with pseudotumor has an elevated cardiac output when compared to a non-affected pregnant patient.[57]

The ED physician's role is to evaluate the patient for a life-threatening condition when a patient with a severe headache presents to the ED. If PC is the final diagnosis, consultation with neurology and obstetrics will determine the best course of action for the individual patient. Treatment for PC often is undertaken using acetazolamide (Diamox) to decrease the intracranial pressure. This poses some risk to the fetus, as diuretics have been shown to decrease amniotic fluid levels. Response to acetazolamide with or without a beta-blocker was not shown to decrease the cardiac output below the mean expected.[57]

Peripheral Neuropathies

Carpal Tunnel Syndrome (CTS). CTS, characterized by paresthesias in the median nerve distribution, is more common in females and may be hereditary. It is postulated that the reason for the nocturnal increase in symptoms is a result of blood volume redistribution from the legs while in the recumbent position. This is exacerbated by the pregnant state, especially the third trimester when blood volume is greatest. Symptoms often resolve after childbirth. When patients present to the ED with CTS, reassurance and the use of wrist splints may help alleviate the symptoms. Analgesics may be necessary initially, and their use should be based on the current age of the fetus. Occasionally surgery is necessary.[62]

Meralgia Paresthetica. This mononeuropathy involving the lateral femoral cutaneous nerve (LFCN) results in paresthesias and dysesthesias in the anterior lateral middle third of the thigh. Occasionally symptoms may extend into the lateral calf. The LFCN is primarily a sensory nerve with variable nerve root origins in the upper lumbar spine. It most often passes medial and inferior to the anterior superior iliac spine and as such is exposed to compressive forces as the gravid uterus enlarges.[63,64] This mononeuropathy occurs more frequently in those who suffer from CTS.[65] In pregnancy, conservative therapy often is all that is necessary because resolution after delivery is the norm. The diagnosis can be confirmed by injecting local anesthesia at the site where the nerve exits the pelvis, and occasionally surgical decompression or resection of the nerve is necessary in patients whose symptoms do not resolve within a few weeks postpartum.[63,64] Presented with this patient in the ED, the physician can often make the diagnosis, provide reassurance and analgesia, and refer the patient to her obstetrician for further treatment.

Bell's Palsy. A peripheral 7th nerve disorder of uncertain etiology, the majority of cases that occur in pregnancy do so in the third trimester.[66,67] Pregnant women are three times more likely than their non-pregnant cohort to develop Bell's palsy.[68] Of interest, gestational hypertension or preeclampsia was present or developed in 22.2% of cases of Bell's palsy, which is 3-5 times the rate for pregnancy in general.[66,67] If complete facial paralysis is present, the prognosis for total recovery is significantly less in the pregnant patient than in the general population.[69] Neuroimaging is not necessary.[66] The Cochrane Database recently reviewed (May 2004) the use of acyclovir (Zovirax) or valacyclovir (Valtrex) for Bell's palsy and concluded that, although probably safe in pregnancy, more data are needed from large randomized studies to show definite benefit.[70] The practice parameter published in 2001 by the American Academy of Neurology regarding Bell's palsy gives acyclovir a safe but possibly effective recommendation for the general population. Regarding steroids, the rating was safe and probably effective, again for the general population. Because of the lack of randomized clinical trials, the natural course of the disease to improve to complete recovery in approximately 80% of those afflicted (albeit some-

what less in the pregnant patient) no recommendations are made by these two review bodies regarding steroids, acyclovir, or the combination of the two.[71]

In a Japanese study published in 2003, a retrospective comparison of prednisolone (Delta-Cortef) (1 mg/kg/day for 4 days then decreased over the following two weeks) with or without acyclovir (2000 mg/day for 7 days) concluded that the overall rate of improvement in patients treated with acyclovir and prednisolone was significantly better than those treated with just prednisolone, and complete recovery was 100% in the population that received therapy within 3 days of symptom onset. Therapy begun 4 days or later in the course of the disease showed no benefit to adding acyclovir to the prednisolone. No placebo was used for comparison. However, because this study was conducted on the general population with Bell's palsy, not the pregnant population, no recommendations can be made regarding this subset of patients with Bell's palsy.[72]

The pregnant patient with Bell's palsy should receive artificial tears eye drops for daytime use and artificial tears ointment with patching for nighttime use. Serious consideration should be given to the use of prednisone and acyclovir, especially in the patient with complete facial hemiparalysis who presents within 3 days of symptom onset, in consultation with the patient's obstetrician. Acyclovir is pregnancy category B, meaning it is presumed safe based on animal studies, while prednisone is pregnancy category C, meaning there are no human studies, and animal studies reveal an adverse profile.[48]

Movement Disorders

Restless Legs Syndrome (RLS). RLS is a disorder with an uncertain pathogenesis that is characterized by deep paresthesias and dysesthesias, primarily in the calves. The sensations are worse at rest and resolve with movement, often causing a marked disturbance of sleep. Conditions other than pregnancy associated with this disorder include iron, folic acid, or B-12 deficiency; uremia; diabetes mellitus; rheumatoid arthritis; and a multitude of other conditions. Twenty-five to 50% of patients have idiopathic disease. Diagnosis usually is made by conducting a thorough history, and treatment often revolves around correcting the underlying cause. Up to 19% of pregnancies are affected by RLS.[73-77]

If the patient has no obvious vitamin deficiency, then treatment may include levodopa (Dopar, Larodopa), bromocriptine mesylate (Parlodel), narcotic analgesics, benzodiazepines, carbamazepine, or clonidine (Catapres).[73,74] Phone consultation with the patient's obstetrician prior to prescription of any of these medications is in order, as the disorder usually subsides within a few weeks postpartum.[75-78] Carbamazepine has been associated with congenital anomalies and should not be used in the first trimester.[2,14]

Chorea Gravidarum. Chorea gravidarum has been described since the mid 1600s[79] and is a rare choreiform movement disorder that occurs in pregnancy. The estimated incidence is 1:139,000 pregnancies.[80] Now that cardiac evaluation is more sophisticated in the evaluation of patients with rheumatic fever, it is believed that most cases of what was thought to be chorea gravidarum actually are associated with a prior history of rheumatic fever, and may be as a result of hormonal effects on an already damaged basal ganglia. Occasional cases have been associated with lupus, antiphospholipid antibodies, syphilis and encephalitis.[81] Dopamine receptor blockers may be used to control the symptoms when severe, again in consultation with the patient's obstetrician.[82]

Multiple Sclerosis (MS)

MS is an autoimmune disease thought to be mediated by T-lymphocytes, with an as yet undefined pathogenesis. Numerous studies have been conducted on the effect of pregnancy on MS and relapses, with variable results. Compared to the pre-pregnancy year, MS patients have fewer relapses while pregnant, but experience an increased rate within the first three post-partum months.[83-86] Despite an increased risk for the three months post-partum, 72% of women with MS did not experience a relapse during this time frame.[84] Other than an increased risk of maternal anemia, MS has no untoward effects on the pregnancy itself.[86] Women with MS are twice as likely to be re-hospitalized in the first three post-partum months when compared to their non-MS counterparts.[86]

Infants born to women with MS were significantly more likely to experience meconium aspiration, but this did not correlate to prolonged complications. They are not more likely to have malformations.[86] Female, but not male, offspring have a 50-fold increase of developing MS when compared to the general population. This correlates to a 5% risk of developing the disease.[83]

Treatment is based on symptoms and ED management should proceed similar to the non-pregnant patient. The effects of treatment modalities including interferon injections and high dose steroids for MS relapses have not been studied in infants exposed in-utero, and therefore no recommendations can be provided regarding these therapies.[86]

Myasthenia Gravis

Myasthenia gravis (MG) is an autoimmune disorder in which 85% of patients have antibodies to the acetylcholine receptors, causing disordered neuromuscular transmission and weakness of various muscle groups.[87] A 2:1 female to male ratio is noted, and it often affects women during their reproductive years.[88] Pregnancy has a variable effect on the course of this disease, even varying from pregnancy to pregnancy in the same patient. Fifty-nine percent of patients in one study had no change in their disease, while in 19% the disease worsened, and in 22% the disease improved.[89] Another reports a more even distribution of one-third each for improved, worsened, and no change. Postpartum exacerbations often are sudden and severe, resulting in maternal death. Maternal mortality has been reported at 40/1,000 live births.[88] In a 33-year retrospective study utilizing the Medical Birth Registry of Norway, Hoff et al reports on 127 births to mothers with MG. Women with MG have a higher rate of delivery complications, especially preterm membrane rupture, and a cesarean section rate twice that of the general pregnant population, with the majority being elective.[90]

The mainstay of therapy is anticholinesterase medications, with pyridostigmine (Mestinon, Regonal) being the most common. Of importance, an overdose of these medications can cause an

increase in the weakness the patient experiences, along with respiratory failure requiring intubation, and occasionally results in death. Changes in intestinal absorption and renal excretion during pregnancy may alter blood levels and therefore therapeutic effects. Often high dose corticosteroids are used in the initial management of the patient, and antimetabolites such as azathioprine, gamma globulins, plasmapheresis, and thymectomy may be necessary.[88]

Various studies report a 4-20% incidence of symptomatic neonatal myasthenia gravis (NMG) in infants born to mothers with MG.[89-91] This is due to the transfer of maternal antibodies to the acetylcholine receptor to the fetus. Symptoms may range from transient hypotonia, weak suckling, or a feeble cry to respiratory failure, and usually begin within hours of delivery and last for 2-3 weeks or more.[88,92] Although many newborns test positive for the antibody to the acetylcholine receptor, the occurrence of NMG and maternal disease severity do not correlate.[89] It has been shown that mothers who transmit NMG to their infants have a higher ratio of antibody to fetal vs. adult acetylcholine receptors throughout their pregnancy, and this may have predictive value in determining which infants will develop the transient disease in the newborn period.[93] If these infants present to the ED due to failure to eat, apnea, or hypotonia, they should be treated with standard anticholinesterase medications.

MG is known for its multitude of drug/disease interactions. Amide anesthetics are safer than ester anesthetics due to metabolism of the latter by plasma cholinesterase.[88] Of note, magnesium sulfate is contraindicated in this patient population. Other medications that have been shown to be problematic include narcotics, tranquilizers, barbiturates, lithium, certain antibiotics, beta-blockers, and some inhalation anesthetics.[88,94] These agents have been reported specifically, but caution should be used with any member of the same drug class, and before prescribing medication for the patient with MG, the ED physician should consult a reference. An extensive list of drugs that should be used with caution in the patient with MG is listed on page 1425 of the sixth edition of the *Emergency Medicine Comprehensive Study Guide* by Tintinalli et al.[95]

Brain Tumors

Although not specifically a disease of pregnancy, tumors involving the nervous system may first become apparent during the pregnancy period. The incidence is the same as for the non-pregnant patient, with the exception of metastatic choriocarcinomas, melanoma, and breast carcinoma, which have an increased rate of occurrence. The incidence of choriocarcinoma is 1:50,000 after full-term pregnancy, but 1:30 following a molar pregnancy. Meningiomas and pituitary adenomas have increased growth during the pregnant period due to hormonal effects.[96,97] Patients presenting to the ED with headache or what they assume to be protracted nausea and vomiting due to morning sickness should undergo a thorough neurologic exam to rule out focal neurologic deficits that may indicate a space occupying lesion. If there is any suspicion that a more serious condition exists, the ED physician should complete a further diagnostic evaluation, including a CT scan if indicated.

Summary

In summary, neurologic complications of pregnancy may range from life-threatening to merely a nuisance to be endured by the gravid patient. Bearing in mind that there are two patients when dealing with the myriad of neurologic disorders possible, and keeping rare but important items in the differential when evaluating the pregnant patient with such common complaints as headache when they present to the ED, is essential to thorough EM care. A thorough neurological examination should be included in the evaluation of every pregnant patient that presents with a complaint of headache or nausea and vomiting. Early consultation with the patient's obstetrician is often necessary for definitive care, and in addition, the ED physician should not hesitate to consult neurology early to assist in the management of these neurologic disorders.

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Physician CME Questions

21. The usual course of migraine headaches in pregnancy is:
    A. most patients have a decrease in frequency during pregnancy, returning to baseline in the first few weeks postpartum.
    B. decreased frequency in first trimester, return to baseline during third trimester.
    C. increased frequency during first trimester, decreasing for remainder of pregnancy.
    D. no change in frequency.
    E. no trends have been noted.

22. Regarding strokes in pregnancy, which of the following is the period of greatest risk?
    A. First trimester
    B. Second trimester
    C. Third trimester
    D. Puerperium
    E. The risk is similar throughout pregnancy.

23. Intracranial hypertension:
    A. always is associated with high blood pressure.
    B. often presents with a headache and photophobia.
    C. is defined as elevated intracranial pressure without focal neurologic deficits, often with papilledema.
    D. most commonly causes seizures as an initial presentation.

24. Which of the following statements is true of Bell's palsy?
    A. It occurs at a rate less than that of the general population during pregnancy, but fewer patients affected undergo complete resolution of the facial palsy.
    B. All patients should be prescribed steroids and acyclovir.
    C. It is an eighth nerve palsy, afflicting hearing and balance.
    D. Although 80% of the general population with Bell's palsy experience complete recovery, the prognosis is worse for pregnant patients with the condition.

25. Which drug routinely used to treat the eclamptic patient suffering from a seizure is absolutely contraindicated in the patient with myasthenia gravis?
    A. Phenobarbital

B. Phenytoin
C. Magnesium sulfate
D. Diazepam
E. Midazolam

26. Anti-epileptic drugs such as valproic acid, phenytoin, carbamezepine:
    A. cause a 10-fold increase in congenital anomolies in fetuses exposed during the first 10 weeks of gestation.
    B. should be discontinued if pregnancy in the first trimester is diagnosed in the ED
    C. rarely interfere with the metabolism of birth control pills.
    D. should be monitored using free drug levels.
    E. often cause anencephaly.

27. Regarding diagnostic testing for suspected neurologic disorders (CT, MRI, lumbar puncture), which of the following is true?
    A. Tests should be delayed until the post-partum period in most cases.
    B. Tests should proceed as if the patient were not pregnant, providing the conditions being evaluated will result in therapeutic changes for the mother during the pregnancy.
    C. Tests should never utilize iodinated contrast agents due to fetal hypothyroidism that may occur with their administration in the third trimester.
    D. MRI, in particular, is contraindicated during the third trimester.

28. Regarding seizures in pregnancy, which of the following is true?
    A. There is a 10-fold increase in maternal mortality in patients who suffer a seizure while pregnant.
    B. Seizures often result from maternal non-compliance with medications.
    C. Seizures may cause abruption of the placenta, premature rupture of membranes, and fetal demise.
    D. Initial management includes benzodiazepines.
    E. All of the above

29. Neonatal withdrawal symptoms due to maternal use of phenobarbital never is observed beyond one week after birth.
    A. True
    B. False

30. Both multiple sclerosis and migraine headaches experience a rate increase postpartum compared with during pregnancy.
    A. True
    B. False

In Future Issues:

Common Dermatology Presentations

Emergency Medicine Reports CME Objectives

To help physicians:

- quickly recognize or increase index of suspicion for specific conditions;
- understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- apply state-of-the-art diagnostic and therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;
- understand the differential diagnosis of the entity discussed;
- understand both likely and rare complications that may occur.

CME Answer Key

21. A	26. D
22. D	27. B
23. C	28. E
24. D	29. B
25. C	30. A

CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to evaluate their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. *After completing this activity, you must complete the evaluation form that will be provided at the end of the semester and return it in the reply envelope provided to receive a certificate of completion.* When your evaluation is received, a certificate will be mailed to you.

Emergency Medicine Reports®
The Practical Journal for Emergency Physicians

Neurologic Complications of Pregnancy

Patient Education for Women on Antiepileptic Drugs for Any Reason

- You have been diagnosed with pregnancy, and are noted to be on one of several anti-epileptic drugs.
- If these medications are being taken for the management of epilepsy you should consult the health care provider managing your seizures.
- If these medications are being taken for migraine prophylaxis or as a mood stabilizer, consult the health care provider managing these conditions.
- Anti-epileptic drugs have been associated with an increased risk of birth defects in infants born to mothers who take them. These abnormalities occur during the first 10 weeks of your pregnancy.
- This risk is 2-3 times that of the population not taking these medications. However, more than 90% of pregnancies that occur while the mother is taking one of these medications produce healthy newborns.
- DO NOT stop taking these medications without consulting your physician, particularly if you are using them for seizure control. A seizure is also harmful to you and your baby. It may cause chemical imbalances in the blood, and trauma-related injuries to you or the baby may be fatal to one or both of you.
- If you are not already doing so, DO begin taking folic acid. A prescription for 4 mg/day is being provided until you can visit the obstetrician.
- DO arrange obstetrical follow up and follow their recommendations regarding the use of medications.
- DO adjust your lifestyle to avoid known triggers for your seizures. This includes getting enough rest; avoiding illicit drugs, alcohol, cigarettes, and prolonged exposure to flashing lights from any source (i.e., video games, computer screens, strobe lights).

Supplement to *Emergency Medicine Reports*, January 24, 2005: Neurologic Complications of Pregnancy. A Systematic Approach to Evaluation and Management." *Author:* **Mary Hughes, DO, FACEP, FACOEP**, Professor, Emergency Medicine, Michigan State University College of Osteopathic Medicine (MSU-COM); Program Director, MSU-COM Emergency Medicine Residency, East Lansing, MI.
 Editor-in-Chief: Gideon Bosker, MD. **Vice President and Group Publisher:** Brenda Mooney. **Editorial Group Head:** Glen Harris. **Specialty Editor:** Shelly Morrow Mark. For customer service, call: **1-800-688-2421.**

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Volume 25 SUPPLEMENT

For a complete title index, please see page 20.

2004 Subject Index: Volume 25, Numbers 1-26

Entries are organized alphabetically by subject matter and key words, with entries followed by the issue number and page number (e.g., issue number 2, page 20 would be listed as 2:20). Tables are indicated by a lowercase t, figures by a lowercase f. Supplements are indicated by an uppercase S or their report number. Trauma Reports *is indicated by Trauma and then the issue number and page number.*

B

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Z

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