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Acute Complications of Preeclampsia

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Preeclampsia is an idiopathic multisystem disorder specific to human pregnancy and the puerperium.[1] More precisely, it is a disease of the placenta, because it has also been described in pregnancies where there is trophoblast but no fetal tissue (complete molar pregnancies). Although the pathophysiology of preeclampsia is poorly understood, it is clear that the blueprint for its development is laid down early in pregnancy. It has been suggested that the pathologic hallmark is a complete or partial failure of the second wave of trophoblast invasion from 16 to 20 weeks' gestation, which is responsible in normal pregnancies for destruction of the muscularis layer of the spiral arterioles.[2] As pregnancy progresses, the metabolic demands of the fetoplacental unit increase. However, because of the abnormally shallow invasion of the placenta, the spiral arterioles are unable to dilate to accommodate the required increase in blood flow, resulting in "placental dysfunction" that manifests clinically as preeclampsia. Although attractive, this hypothesis remains to be validated.

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Preeclampsia is a clinical diagnosis. The classic definition of preeclampsia encompasses three elements: new-onset hypertension (defined as a sustained sitting blood pressure ≥140/90 mm Hg in a previously normotensive woman); new-onset proteinuria (defined as >300 mg/24 hours or ≥2+ on a clean-catch urinalysis in the absence of urinary tract infection); and new-onset significant nondependent edema.[1] However, more recent consensus reports have suggested eliminating edema as a criterion for the diagnosis.[3]

A more extensive synopsis of preeclampsia is beyond the scope of this discussion. This monograph serves to review in detail the diagnosis and management of several acute maternal complications of preeclampsia: eclampsia, HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome, liver rupture, pulmonary edema, renal failure, disseminated intravascular coagulopathy (DIC), hypertensive emergency, and hypertensive encephalopathy and cortical blindness.

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Eclampsia

Eclampsia refers to the occurrence of one or more generalized convulsions and/or coma in the setting of preeclampsia and in the absence of other neurologic conditions.[1] In the past, eclampsia was thought to be the end result of preeclampsia, hence the nomenclature. However, it is now clear that seizures are only one of several clinical manifestation of "severe" preeclampsia. The precise cause of seizures in women with eclampsia is not known. Proposed etiologies include cerebral vasospasm with local ischemia, hypertensive encephalopathy with hyperperfusion, vasogenic edema, and endothelial damage.[4] Despite recent advances in detection and management, preeclampsia/eclampsia remains the second most common cause of maternal death in the United States (after thromboembolic disease), accounting for 15% of all maternal deaths.[5] It is estimated that eclampsia accounts for 50,000 maternal deaths per year worldwide.[6]

EPIDEMIOLOGY AND INCIDENCE

Eclampsia is most common in nonwhite, nulliparous women from lower socioeconomic backgrounds. Peak incidence is in the teenage years and early 20s, but there is also an increased prevalence in women older than 35. Eclampsia before 20 weeks' gestation is rare; this should raise the possibility of an underlying molar pregnancy or antiphospholipid antibody syndrome.

The overall incidence of eclampsia is relatively stable, at 4 to 5 cases per 10,000 live births in developed countries.[7] In developing countries, however, the incidence varies widely from 6 to 100 per 10,000 live births.[8]

CLINICAL MANIFESTATIONS AND DIAGNOSIS

Eclampsia is a clinical diagnosis based on evidence of one or more generalized convulsions and/or coma in a preeclamptic woman and in the absence of other neurologic conditions. Eclamptic seizures are almost always self-limiting and seldom last longer than 3 to 4 minutes. Eclamptic seizures are clinically and electroencephalographically indistinguishable from other generalized tonic-clonic seizures. In general, women with typical eclamptic seizures who do not have focal neurologic deficits or prolonged coma do not require either electroencephalographic or cerebral imaging studies.[9] Clinical conditions other than eclampsia that should be considered when evaluating a pregnant woman who has had a seizure are listed in Table 1.

Approximately half of all cases of eclampsia occur before term, with more than 20% occurring before 31 weeks' gestation.[7] Three quarters of the remaining cases occur at term, developing intrapartum or within 48 hours of delivery. Seizures due to eclampsia always resolve postpartum, often within a few hours to days. Diuresis (>4 L/day) is believed to be the most accurate clinical indicator of resolution of preeclampsia/eclampsia, but it is not a guarantee against the development of seizures.[10] Indeed, late postpartum eclampsia (eclamptic seizures developing >48 hours postpartum but <4 weeks postpar-

TABLE 1. Differential Diagnosis of Eclampsia

Cerebrovascular accident
Intracerebral hemorrhage
Cerebral arterial or venous thrombosis
Hypertensive diseases
Hypertensive encephalopathy
Pheochromocytoma
Space-occupying lesions of the central nervous system
Brain tumor
Abscess
Metabolic disorders
Hypoglycemia
Uremia
Inappropriate antidiuretic hormone secretion resulting in water intoxication
Infectious etiology
Meningitis
Encephalitis
Thrombotic thrombocytopenic purpura
Idiopathic epilepsy

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tum) accounts for 25% of postpartum cases and up to 16% of all cases of eclampsia.[10,11]

MANAGEMENT

A number of management strategies have been developed to prevent maternal and fetal complications resulting from eclampsia during the peripartum period. The immediate issues in caring for an eclamptic woman include maintenance of maternal vital functions, control of convulsions and blood pressure, prevention of recurrent seizures, and evaluation for delivery. If the seizure is witnessed, maintenance of airway patency and prevention of aspiration should be the first responsibilities of management. The parturient should be rolled onto her left side and a padded tongue blade placed in her mouth, if possible.

Control of Convulsions

Although eclamptic seizures usually resolve without treatment within 3 to 4 minutes, an anticonvulsant can be administered to achieve resolution of an ongoing convulsion. The treatment of choice is magnesium sulfate. In women already receiving magnesium seizure prophylaxis, a serum magnesium level should be obtained immediately and a rapid intravenous infusion of 1 to 2 g administered while awaiting the results. In women not receiving seizure prophylaxis, magnesium should be given as a rapid intravenous infusion of 2 g repeated every 15 minutes to a maximum of 6 g. This loading dose may be given safely even in the presence of renal insufficiency. Exactly how magnesium acts as an anticonvulsant in eclampsia is not known. Several mechanisms have been proposed, including selective vasodilatation of the cerebral vasculature, protection of endothelial cells from damage by free radicals, prevention of calcium ion entry into ischemic cells, and/or as a competitive antagonist to the glutamate N-methyl-D-aspartate receptor (which is epileptogenic).[12] Benzodiazepines have been used in the past for eclamptic seizures. Diazepam rapidly enters the central nervous system, where it achieves anticonvulsant levels within 1 minute, and it will control seizures in greater than 80% of patients within 5 minutes.[13] However, most investigators recommend avoiding benzodiazepines because of the potentially profound depressant effects on the fetus. This effect becomes clinically significant when the total maternal dose of diazepam exceeds 30 mg.

Treatment of Hypertension

Cerebrovascular accident accounts for 15–20% of deaths from eclampsia. The risk of hemorrhagic stroke correlates directly with the degree of elevation in systolic blood pressure and is less related to, but not independent of, the diastolic pressure.[14] It is not clear whether there is a threshold pressure above which emergent therapy should be instituted.[14] Most investigators recommend aggressive antihypertensive therapy for sustained diastolic pressures of more than 105 to 110 mm Hg and systolic blood pressures of 160 mmHg or greater,[3] although these thresholds have not been tested prospectively. The cerebral vasculature of women with underlying chronic hypertension can probably tolerate higher systolic pressures without injury, whereas adolescents with normally low blood pressures may benefit from starting treatment at lower levels. Persistent, severe elevation in blood pressure ($\geq$160/110 mm Hg) should be treated to prevent cerebrovascular accident. Initial treatment options include hydralazine (5 mg intravenous push followed by 5- to 10-mg boluses as needed q 20 minutes) or labetalol (10–20 mg intravenous push, repeat q 10–20 minutes with doubling doses not to exceed 80 mg in any single dose, for a maximum total cumulative dose of 300 mg). Women who do not improve rapidly after control of seizures and hypertension or those who develop localizing neurologic signs should be evaluated further.

Prevention of Subsequent Seizures

Approximately 10% of eclamptic women will have repeated seizures if managed ex-

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pectantly.[15] There is universal agreement that women with eclampsia require anticonvulsant therapy to prevent further seizures and the possible complications of repeated seizure activity: neuronal death, rhabdomyolysis, metabolic acidosis, aspiration pneumonitis, neurogenic pulmonary edema, and respiratory failure. However, the choice of agent is controversial. Obstetricians have long favored magnesium sulfate as the drug of choice for prevention of recurrent eclamptic seizures, whereas neurologists favor anticonvulsants traditionally used in nonpregnant individuals, such as phenytoin or diazepam. This dispute appears to have been resolved by a number of recent clinical studies:

- The Eclampsia Trial Collaborative Group conducted a prospective trial in which 905 eclamptic women were randomly assigned to receive either magnesium or diazepam and 775 eclamptic women were randomly assigned to receive either magnesium or phenytoin.[16] Primary measures of outcome were recurrence of seizures and maternal death. Women allocated to magnesium therapy had half the rate of recurrent convulsions compared with those allocated to diazepam (13% and 28%, respectively). There were no significant differences in maternal or perinatal death or complication rates between the two groups. Similarly, women administered magnesium had one-third the rate of recurrent seizures of those taking phenytoin (6% vs. 17%). In this arm of the study, women who received magnesium were 8% less likely to be admitted to an intensive care facility, 8% less likely to require ventilatory support, and 5% less likely to develop pneumonia compared with women given phenytoin. There were no significant differences in the maternal death rate or perinatal outcome.
- A Cochrane review[17] reported that magnesium sulfate was safer and better than "lytic cocktail" (containing promethazine hydrochloride, chlorpromazine, and meperidine hydrochloride) for the prevention of repeat seizures in eclamptic women.

Additional advantages of magnesium sulfate therapy include lower cost, ease of administration (cardiac monitoring is not required), and less sedation than diazepam and phenytoin. Magnesium also appears to selectively increase cerebral blood flow and oxygen consumption in women with preeclampsia[18]; this is not true for phenytoin.[19]

The maintenance dose of magnesium sulfate is 2 to 3 g/h administered as a continuous intravenous infusion. The maintenance phase is given only if a patellar reflex is present (loss of deep tendon reflexes is the first manifestation of symptomatic hypermagnesemia), respirations are greater than 12 per minute, and urine output is greater than 100 mL in 4 hours. Following serum magnesium levels is not required if the woman's clinical status is closely monitored for evidence of potential magnesium toxicity. There also does not appear to be a clear threshold concentration for ensuring the prevention of convulsions, although a range of 4.8 to 8.4 mg/dL has been recommended.[20] The dose should be adjusted according to the clinical response of the patient (Table 2).

Evaluation for Delivery

The definitive treatment of eclampsia is prompt delivery, irrespective of gestational age, to prevent potential maternal and fetal complications. However, this does not necessarily preclude induction of labor.[21] After maternal stabilization, several factors should be considered before determining the most appropriate route of delivery. These include gestational age, Bishop score, and fetal condition and position. In general, less than one third of women with severe preeclampsia/eclampsia remote from term (<32 weeks' gestation) with an unfavorable cervix will have a successful vaginal delivery.[22–24] Cervical ripening agents can be used to improve the Bishop score; however, long inductions should be avoided.

Fetal bradycardia lasting at least 3 to 5 minutes is a common finding during and immediately after an eclamptic seizure and does not necessitate emergent cesarean delivery. Maneuvers to stabilize the mother may help the fetus recover in utero from the

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TABLE 2. Prevention of Recurrent Seizures in Patients With Eclampsia

Drug	Loading Dose	Maintenance Dose	Therapeutic Level
Recommended first-line therapy			
Magnesium sulfate	4–6 g IV over 10–20 min 10 g IM (5 g into each buttock)	2–3 g/h IV infusion 5 g IM every 4 h	4–8 mEq/L* As above
Recommended therapy in women refractory to magnesium sulfate			
Phenytoin	1–1.5 g IV over 1 h (depending on body weight)	250–500 mg q 10–12 h orally or IV	10–20 μg/mL
Diazepam	–	10 mg/h IV infusion	–
Chlormethiazole†	40–100 mL of 0.8% over 20 min	60 mL/h IV infusion	–

* Not tested prospectively

† Not available in the United States

effects of maternal hypoxia, hypercarbia, and uterine hyperstimulation. Resolution of maternal seizure activity is often associated with compensatory fetal tachycardia and even with transient fetal heart rate decelerations, which typically resolve within 20 to 30 minutes.[25]

PROGNOSIS

Maternal complications occur in up to 70% of women with eclampsia and include DIC, acute renal failure, hepatocellular injury, liver rupture, intracerebral hemorrhage, cardiorespiratory arrest, aspiration pneumonitis, acute pulmonary edema, and postpartum hemorrhage.[26,27] Hepatocellular damage, renal dysfunction, coagulopathy, hypertension, and neurologic abnormalities typically resolve after delivery. However, cerebrovascular damage from hemorrhage or ischemia may result in permanent neurologic sequelae.[28]

Maternal death rates of 0–13.9% have been reported.[7,26,28] One retrospective analysis of 990 cases of eclampsia found an overall maternal death rate of 13.9% (138/990). The highest risk (12/54 [22%]) was observed in a subgroup of women with eclampsia previous to 28 weeks' gestation. Maternal death and severe complication rates are lowest among women receiving regular prenatal care who are managed by experienced physicians in tertiary centers.[29,30] An autopsy study performed shortly after death in eclamptic women found that the brains of more than 50% of the women who died within 2 days of seizures displayed cerebral hemorrhages and softening.[31] Petechial cortical hemorrhages were most common, especially involving the occipital lobe. Diffuse cerebral edema and gross hemorrhage were noted less frequently. Cerebral venous thrombosis was common in woman with postpartum eclampsia.

The perinatal death rate in eclamptic pregnancies is 9–23%[7,26] and is closely related to gestational age. For example, the perinatal death rate in one series of 54 parturients with eclampsia before 28 weeks' gestation was 93%[26]; this rate was only 9% in another study in which the mean gestational age at birth was 32 weeks.[32] Perinatal deaths are primarily the result of premature delivery, abruptio placentae, and intrauterine asphyxia.

FUTURE PREGNANCIES

Eclampsia can recur in a subsequent pregnancy.[33,34] The risk appears to be reduced by close maternal monitoring and timely intervention if preeclampsia develops.[35] However, there is as yet no effective way to prevent preeclampsia.[36] The rate of recurrent eclampsia is estimated to be around 2%.[37]

Subsequent pregnancies in women with a history of severe preeclampsia/eclampsia are also at increased risk of other obstetric complications compared with women with no such history, including placental abrup-

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tion (2.5–6.5% vs. 0.8%), preterm delivery (15–21% vs. 7–8%), intrauterine growth restriction (12–23% vs. 10%), and an increased perinatal death rate (4.6–16.5% vs. 1–3%).[32,33,38,39] Women with a history of preeclampsia/eclampsia remote from term (<28 weeks' gestation) are at highest risk for developing these complications.[38,39] This risk appears to be the same whether they had severe preeclampsia or eclampsia.

CAN ECLAMPSIA BE PREDICTED?

The relationship between hypertension, signs and symptoms of cortical irritability (headache, visual aberrations, nausea, vomiting, fever, hyperreflexia), and seizures remains unclear. A retrospective analysis of 383 cases of eclampsia in the United Kingdom found that only 59% of eclamptic women experienced one or more prodromal symptoms—headache, visual disturbance (scotomata, amaurosis, blurred vision, diplopia, homonymous hemianopsia), or epigastric pain—before their eclamptic seizure.[7] Moreover, the magnitude of blood pressure elevation does not appear to be predictive of eclampsia, although it does correlate well with the incidence of cerebrovascular accident. Retrospective analysis shows that eclampsia was the first manifestation of pregnancy-related hypertensive disease in 20–38% of cases.[7,28] Similar findings were reported in studies from Sweden, Scotland, and the United States.[40–42] In one of the latter reviews, the factors found to be at least partially responsible for failure to prevent eclampsia (179 consecutive cases) were physician error (36%), magnesium failure (13%), late postpartum onset (12%), early onset before 21 weeks (3%), abrupt onset (18%), and lack of prenatal care (19%).[41] Therefore, many cases of eclampsia appear not to be preventable, even among women receiving regular prenatal care.

PREVENTION OF FIRST ECLAMPTIC SEIZURE

Although not all cases of eclampsia can be predicted, anticonvulsant therapy administered to parturients at high risk can prevent a first seizure in women with severe preeclampsia. Two large studies have demonstrated the superiority of magnesium sulfate over phenytoin for the prevention of eclampsia.[43,44] The Parkland Hospital group, for example, randomly assigned 2,138 preeclamptic women to receive either magnesium or phenytoin.[43] Eclamptic seizures developed in 10 of 1,089 women assigned to phenytoin compared with none of 1,049 women assigned to magnesium (P = 0.004). Maternal and neonatal outcomes were similar in both groups. These data are supported by a recent study performed in South Africa in which 685 women with severe preeclampsia were randomly assigned to seizure prophylaxis with magnesium sulfate therapy or placebo.[45] Progression to eclampsia was lower in the magnesium group (0.3% vs. 3.2% [P = 0.003]).

Anticonvulsant therapy is generally initiated during labor or while administering antenatal corticosteroid therapy or cervical ripening agents previous to planned delivery in women with severe preeclampsia. Treatment should be continued until 24 to 48 hours postpartum, when the risk of seizures is low. The most common magnesium sulfate regimen is a loading dose of 4 to 6 g given intravenously over 20 minutes, followed by 2 to 3 g/h as a continuous infusion. It is unclear whether all women with preeclampsia require prophylaxis to prevent seizures in a small number of patients (0.6–3.2%[46]). Moreover in women with nonproteinuric hypertension, the incidence of seizures is so low (<0.1%[45]) that it may be safe to withhold seizure prophylaxis in such women.

HELLP Syndrome

HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) is a serious complication of preeclampsia that was first described by Pritchard et al in 1954,[47] although the term HELLP syndrome was coined by Weinstein in 1982.[48] Among women with severe preeclampsia, 6% will

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manifest with one abnormality suggestive of HELLP syndrome (usually elevated liver enzymes or low platelets), 12% will develop two abnormalities, and about 10% will manifest with all three abnormalities.[49] HELLP syndrome can manifest at any time during pregnancy and the puerperium but (like preeclampsia) is rare before 20 weeks' gestation. One third of all cases of HELLP syndrome occur postpartum, and only 80% of such patients were diagnosed with preeclampsia before delivery.

CLINICAL MANIFESTATIONS AND DIAGNOSIS

Although parturients with HELLP syndrome may be asymptomatic, 80% report right upper quadrant pain and 50–60% present with excessive weight gain and worsening edema. Not all women with HELLP syndrome have hypertension or proteinuria. Indeed, 20% of patients with HELLP syndrome have a maximum blood pressure less than 140/90 mm Hg, and 6% do not have significant proteinuria at the time of diagnosis.[49] Other clinical conditions that should be considered in women with features suggestive of HELLP syndrome include hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, and acute fatty liver.

The definitive laboratory criteria for the diagnosis of HELLP syndrome remain to be validated prospectively. However, the laboratory criteria most commonly used are those defined by Sibai in 1990.[49] In this review, Sibai defined hemolysis as the presence of an abnormal peripheral smear with schistocytes, serum lactate dehydrogenase (LDH) more than 600 U/L, and total bilirubin more than 1.2 mg/dL; elevated liver enzymes as serum aspartate aminotransferase more than 70 U/L (>3 standard deviations above norm) and LDH more than 600 U/L; and low platelet count as less than 100,000/mm^3. Based on the severity of the thrombocytopenia, Martin et al[50] further categorized HELLP syndrome into three classes. Class 1 is defined as a platelet count less than 50,000/mm^3, class 2 as a platelet count 50,000 to 100,000/mm^3, and class 3 as a platelet count more than 100,000/mm^3. Although this classification does appear to correlate to some degree with the prognosis and speed of resolution, it is not widely accepted.

ETIOLOGY AND PATHOPHYSIOLOGY

Like preeclampsia, endothelial dysfunction, with resultant activation of the intravascular coagulation cascade, has been proposed as the central pathogenesis of HELLP syndrome. However, unlike preeclampsia, HELLP syndrome occurs more often in whites, in multipara, and in women older than 35 years. Some investigators regard HELLP syndrome as an entirely distinct disease entity from preeclampsia.

When preeclampsia is complicated by HELLP syndrome, the maternal and perinatal death rates are significantly increased. Reported maternal death rates are 0–24%; death results most often from liver rupture, DIC, acute renal failure, pulmonary edema, carotid thrombosis, and cerebrovascular accident.[51] Perinatal death is related most closely to complications of prematurity, fetal growth restriction, and placental abruption. Reported perinatal death rates are 7.7–60%.[51] Delayed diagnosis and delayed or inappropriate treatment are commonly cited as reasons for the poor overall prognosis associated with HELLP syndrome. Early identification of this syndrome, coupled with prompt and appropriate intervention, can significantly reduce maternal and perinatal death and complication rates. Accordingly, parturients with HELLP syndrome should ideally be managed in a tertiary care facility.

MANAGEMENT

Stabilization of the mother's conditions and assessment of fetal well-being are the first responsibilities of management for parturients with HELLP syndrome. Seizure prophylaxis should be administered in the form of parenteral magnesium sulfate. If the pregnancy is less than 34 weeks, antenatal corticosteroids should be given to enhance fetal

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lung maturation. With few exceptions, immediate delivery is indicated, irrespective of gestational age. The decision of whether to delay delivery for 48 hours to complete a full course of antenatal corticosteroids should be individualized. Immediate delivery does not necessarily mean cesarean delivery. However, if the pregnancy is remote from term (<32 weeks) and the cervix is unfavorable, an elective cesarean delivery is a reasonable option. Because the incidence of hematoma formation after cesarean delivery in women with HELLP syndrome may be as high as 20%,[49] it may be prudent to place one or more subfascial and/or subcutaneous drains at the time of surgery, especially if there is evidence of significant intraoperative oozing or severe thrombocytopenia (<50,000/mm^3). The drains can be removed electively in 24 to 48 hours. If the gestational age is more than 34 weeks, induction of labor can be initiated with or without cervical ripening, if indicated. It is our usual practice to check coagulation test results as well as hepatic and renal function test results every 6 hours until delivery, and then daily until stable.

Several specific therapeutic maneuvers have been proposed in an effort to cure or alleviate HELLP syndrome. These include, among others, plasma volume expansion (using crystalloid or albumin), thrombolytic agents (low-dose aspirin, dipyridamole, heparin, antithrombin III, prostacyclin/thromboxane synthetase inhibitors), immunosuppressive agents (corticosteroids), exchange plasmapheresis, and dialysis. Magann et al[52] reported that antepartum dexamethasone administration to women with HELLP syndrome significantly increased maternal platelet count, decreased serum alanine aminotransferase and LDH, increased maternal urine output, and resulted in a longer entry-to-delivery interval compared with women who did not receive corticosteroids. A subsequent study by the same group from the University of Mississippi Medical Center reported that dexamethasone was more effective than betamethasone in the antepartum "treatment" of HELLP syndrome.[53] Of note, the dose of dexamethasone recommended in these studies for antepartum treatment of HELLP syndrome (12 mg q12h until delivery) is significantly higher than that recommended by the National Institutes of Health[54] or the American College of Obstetricians and Gynecologists (ACOG) for promotion of fetal lung maturity (6 mg q12h for 48 hours[55]). Moreover, corticosteroid administration in these studies was by the intravenous rather than the intramuscular route, as recommended by the National Institutes of Health[54] and ACOG.[55] The effect of large doses of intravenous corticosteroids on fetal adrenal function and fetal development is not known. As such, expectant management and antepartum "treatment" of HELLP syndrome with large doses of corticosteroids is not universally accepted.

In addition to antepartum corticosteroids, Magann et al[56] have also reported on the use of postpartum intravenous corticosteroids (10 mg q12h for two doses followed by 5 mg q12h for two doses) to accelerate the reversal of HELLP syndrome. Although the fetal effect of high-dose corticosteroids is no longer a concern postpartum, larger randomized clinical trials are needed to verify the efficacy of postpartum corticosteroid therapy for HELLP syndrome. With or without corticosteroids, the vast majority of women with HELLP syndrome will recover within 96 hours of delivery.

FUTURE PREGNANCIES

The reported risk of recurrent HELLP syndrome in a subsequent pregnancy ranges from 3%[57] to 27%.[58] Future pregnancies are also at increased risk of other adverse events, including other manifestations of preeclampsia, preterm delivery, fetal growth restriction, placental abruption, and cesarean delivery. The overall risk of such complications is 19–43%.[57,58]

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Liver Rupture

Liver rupture is one of the most severe consequences of severe preeclampsia/HELLP syndrome, with a reported maternal death rate of more than 30%.[59] It occurs most commonly in multiparas of advanced age. Fortunately, it is rare. The precise cause of liver rupture remains unknown. The prevailing theory is that endothelial dysfunction with intravascular fibrin deposits and hepatic sinusoidal obstruction leads to intrahepatic vascular congestion, increased intrahepatic pressure, and distention of Glisson's capsule, and finally to the development of a subcapsular hepatic hematoma and liver rupture.

CLINICAL MANIFESTATIONS AND DIAGNOSIS

A high index of clinical suspicion is the key to prompt and accurate diagnosis. Pain in the right upper quadrant and/or epigastric area and focal tenderness are the most important clinical features, especially if they occur in the setting of preeclampsia/HELLP syndrome. Bilateral shoulder-tip pain is suggestive of intraabdominal hemorrhage. Rarely, an abdominal mass may be palpated. If an abdominal mass is noted, further abdominal examinations should be avoided because such manipulations may cause the hematoma to rupture. Imaging techniques such as ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) may enable early and accurate diagnosis of liver hematoma or rupture.

MANAGEMENT

The management of liver hematoma and rupture requires a multidisciplinary approach in a tertiary care facility, if possible. The first priority is to stabilize the maternal hemodynamic status. Aggressive blood transfusion may be necessary. Immediate consultation with a staff anesthesiologist and a general or vascular surgeon is indicated. If a liver hematoma is diagnosed in the antepartum period without evidence of rupture, an immediate exploratory laparotomy and cesarean delivery should be performed. Unnecessary manipulation of the liver should be avoided because this may precipitate rupture. For the nonexpanding liver hematoma, surgical repair or evacuation is usually not necessary. Expectant management with serial CT or abdominal ultrasound examinations may be all that is needed.

If there is evidence of liver rupture, prompt surgical intervention under general endotracheal anesthesia is mandated. Attention should be focused on the need for invasive hemodynamic monitoring and on blood product replacement and correction of coagulopathy, if indicated. After delivery of the fetus through a vertical skin incision, the upper abdomen should be explored. There are several approaches to the management of liver rupture, and the decision of which approach to take depends on the hemodynamic status of the patient, the extent of the rupture, the magnitude and rate of ongoing hemorrhage, and the experience of the surgeons. Unlike repair of a traumatic liver laceration, simple suturing is rarely effective because the entire liver is edematous and friable and the hepatic parenchyma does not have the tensile strength to retain the sutures.[60] Other surgical options include packing with gauze, topical coagulant agents or collagen fleeces coated with fibrin glue, incorporation of omental pedicles or surgical mesh into the liver, ligation of the hepatic artery, radiologic embolization of the hepatic artery, or hepatic lobectomy. Hepatic artery embolization was recently reported to have the highest maternal survival rate of around 90%[61] and should be attempted if hemorrhage can be controlled and if the patient is hemodynamically stable.

The recurrence rate of liver rupture is undetermined, because only a few cases of pregnancies in such women have been described. However, in all but one reported instance,[62] there was no recurrence.

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Pulmonary Edema

Pulmonary edema refers to an excessive accumulation of fluid in the pulmonary interstitial and alveolar spaces. It complicates around 0.05% of low-risk pregnancies but may develop in up to 2.9% of pregnancies complicated by preeclampsia.[63]

ETIOLOGY AND PATHOPHYSIOLOGY

The causes of pulmonary edema are often multifactorial. According to the Starling equation, any factor that results in a reduction in colloid osmotic pressure (or in the colloid osmotic pressure/pulmonary capillary wedge pressure gradient), an increase in capillary permeability, or an increase in intravascular hydrostatic pressure will lead to extravasation of fluid from the vasculature and predispose to the development of pulmonary edema.[64]

The underlying physiologic changes in the maternal cardiovascular system that accompany pregnancy predispose to the development of pulmonary edema. Such changes include an increase in plasma blood volume, cardiac output, heart rate, and capillary permeability and a decrease in plasma colloid osmotic pressure. These changes are often exaggerated in the setting of preeclampsia, leading to a further increase in the incidence of pulmonary edema. Moreover, in normal pregnancy, plasma colloid osmotic pressure decreases from around 22 mm Hg at term to 16 mm Hg after delivery (and from 18 mm Hg at term to 14 mm Hg postpartum in pregnancies complicated by preeclampsia[65]). The reduction in colloid osmotic pressure after delivery may result from excessive blood loss, fluid shifts secondary to increased capillary permeability (especially in preeclamptic pregnancies), or excessive crystalloid infusion. Such changes help to explain at least in part why 70–80% of cases of pulmonary edema in the setting of preeclampsia develop after delivery.[63,65] Another confounding factor is magnesium sulfate, which is often administered to preeclamptic women for seizure prophylaxis. To address this issue, Yeast et al[66] measured the effect of intravenous magnesium sulfate administered for preterm labor or seizure prophylaxis on colloid osmotic pressure and the risk for pulmonary edema in 294 pregnant women. Only 4 of the 294 women developed pulmonary edema, and all of them had low colloid osmotic pressure in the setting of severe preeclampsia. The authors concluded that magnesium sulfate does not significantly change colloid osmotic pressure and, as such, does not pose a significantly increased risk of pulmonary edema.[66]

Only 30% of cases of pulmonary edema in the setting of preeclampsia occur before delivery.[63] The vast majority (90%) of such patients have underlying chronic hypertension, and they are more likely to be multiparous and of advanced maternal age.[63] In the setting of chronic hypertension with superimposed preeclampsia, systemic vascular resistance and left heart filling pressures are increased. This leads, in turn, to a decrease in cardiac output and an increase in pulmonary vascular hydrostatic pressure, which culminates in the development of pulmonary edema. An additional feature that may predispose to the development of pulmonary edema in the setting of preeclampsia is an increase in capillary leak and capillary fluid extravasation secondary to vascular endothelial damage.[67]

DIAGNOSIS

Pulmonary edema is a clinical diagnosis characterized by worsening dyspnea and orthopnea along with signs of respiratory compromise (tachypnea, auditory crackles and rales, hypoxemia). Arterial blood gas and chest x-ray may assist in the diagnosis. In select patients, electrocardiography, echocardiography, spiral CT imaging, ventilation/perfusion scan, or pulmonary arteriography may be necessary to exclude other causes of cardiopulmonary compromise, such as pulmonary embolism, pneumonia, and cardiomyopathy.

MANAGEMENT

Prompt diagnosis and intervention are mandatory. The goal of management is to stabi-

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lize the mother, expedite resolution of the pulmonary edema, and then make a decision about delivery. Appropriate management of acute pulmonary edema can be summarized by the letters LMNOP:

- Lasix (furosemide) administered intravenously as a single dose of 20 to 40 mg over 2 minutes to promote diuresis. If an adequate response is not seen within 30 to 50 minutes, the dose should be increased to 40 to 60 mg administered by slow intravenous injection to a maximum of 120 mg in 1 hour. Electrolytes (especially potassium) should be supplemented as needed.
- Morphine sulfate should be administered intravenously at a dose of 2 to 5 mg as needed in an attempt to reduce the adrenergic vasoconstrictor stimuli to the pulmonary arteriolar and venous beds.
- Na^+ (sodium) and water restriction, and strict input/output monitoring.
- Oxygen supplementation using a nonrebreather face mask at 8 to 10 L/min, along with continuous monitoring of oxygen saturation using a pulse oximeter.
- Positioning (elevation) of the maternal head and chest to improve ventilation by reducing pulmonary capillary wedge pressure.

In addition to these standard measures, it is appropriate to follow the patient's blood pressure, electrocardiogram, and fetal heart rate tracing. Afterload reduction using a vasodilator (eg, hydralazine, a calcium channel blocker, or an angiotesin-1 converting enzyme inhibitor [which should be used only after delivery]) may be necessary, especially in parturients with chronic hypertension and superimposed preeclampsia. Because most obstetric patients have normal left ventricular systolic function, inotropic support is rarely necessary. According to ACOG, severe preeclampsia with pulmonary edema is one of the indications for invasive pulmonary artery catheterization,[68] although most patients can be managed initially without invasive hemodynamic monitoring. However, if the pulmonary edema is refractory to initial management or if it is accompanied by persistent oliguria, insertion of a pulmonary artery catheter and transfer to an intensive care unit should be considered. In patients with severe pulmonary edema, mechanical ventilatory support may be necessary.

In the setting of congestive heart failure, administration of a β-adrenergic antagonist may be indicated. In the past, β-blockade was considered contraindicated in patients with congestive heart failure. However, more recent studies have shown that such agents can antagonize the deleterious effects of the sympathetic nervous system activation that occurs in congestive heart failure.[69] As such, β-blockade is now considered a key component of the management of acute congestive heart failure. However, the use of such agents in pregnancy and especially in preeclampsia complicated by congestive heart failure remains to be established.

Renal Failure

Acute renal failure is characterized by an abrupt reduction in the maternal glomerular filtration rate, leading to excessive retention of urea and water as well as numerous electrolyte and acid-base abnormalities. Acute renal failure is a rare complication of preeclampsia, but the actual incidence remains undetermined. According to one center's experience, 18% of all cases of acute renal failure were of obstetric origin.[70] Among those patients, 20.9% of cases occurred in the setting of preeclampsia. Other conditions that should be considered include hemolytic uremic syndrome, primary renovascular disease, and placental abruption.

ETIOLOGY AND PATHOGENESIS

The characteristic histologic renal lesion in preeclampsia is glomerular endotheliosis, in which the glomeruli are large and swollen with vacuolated endothelial cells. This histologic feature, coupled with the generalized vasoconstriction that characterizes preeclampsia, leads to a 25–30% decrease in renal plasma flow and glomerular filtration compared with normal pregnancy.[71] How-

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ever, functional impairment of renal function in women with preeclampsia is generally mild and reverses completely after delivery. As such, clinically significant acute renal failure in preeclampsia is rare.

The causes of acute renal failure can be divided into three broad categories: prerenal (which refers to renal hypoperfusion without parenchymal involvement), intrarenal (which suggests intrinsic renal parenchymal damage), and postrenal (which implies obstructive uropathy). Prerenal and intrarenal pathology (acute tubular necrosis) accounts for 83–90% of all cases of acute renal failure in preeclampsia.[72,73] Renal damage secondary to these pathologic changes is seen most commonly in preeclampsia and usually resolves completely after delivery. In contrast, bilateral renal cortical necrosis, which accounts for 10–29% of cases of acute renal failure in pregnancy,[72–74] is a far more serious condition and is associated with significant rates of maternal and perinatal death and complications. It is seen most commonly in women with underlying chronic hypertension and superimposed preeclampsia, known parenchymal renal disease, placental abruption, or DIC.[74]

PROGNOSIS

In 1990, Sibai et al[72] reported on their experience of the short-term pregnancy outcome, subsequent pregnancy outcome, and remote prognosis in 31 patients with preeclampsia complicated by acute renal failure collected over a period of 11 years. The actual incidence of acute renal failure could not be determined because most of their patients were referred from outside institutions. The maternal death rate was 10% (3/31). Overall, 14 of their 31 patients (46.6%) required dialysis, and there was no difference in the percentage of women requiring dialysis for preeclampsia (50%) and chronic hypertension with superimposed preeclampsia (42%). All 18 patients with acute renal failure in the setting of preeclampsia had acute tubular necrosis, with complete resolution of renal function after delivery. In contrast, 3 of the 13 patients with chronic hypertension and superimposed preeclampsia had bilateral cortical necrosis; 9 of 11 (81.8%) surviving patients required long-term dialysis, and 4 had subsequently died of end-stage renal disease before publication. The authors concluded that early identification and appropriate management of acute renal failure in previously healthy parturients with preeclampsia did not result in residual long-term renal damage.

The same investigators from Memphis, Tennessee, subsequently reported their experience with HELLP syndrome and acute renal failure.[75] The overall incidence of acute renal failure in the setting of HELLP syndrome was 7.3% in their cohort, with a maternal death rate of 13% and a perinatal death rate of 34%. The majority of the 32 patients with HELLP syndrome and acute renal failure were postpartum. Further analysis suggested that the presence of underlying chronic hypertension was associated with a less favorable pregnancy outcome and a more guarded long-term prognosis.

MANAGEMENT

The management of acute renal failure in the setting of preeclampsia should focus on excluding other diagnoses, especially conditions that may be reversible (eg, dehydration or obstructive uropathy). Supportive therapy includes blood pressure control, positioning patients so as to improve renal blood flow, correcting fluid and electrolyte imbalance, and maintaining adequate nutrition. If dialysis is required in pregnancy, hemodialysis is preferred over peritoneal dialysis.

Disseminated Intravascular Coagulopathy

DIC is a hematologic disorder characterized by a generalized increase in both fibrin formation and fibrinolysis, leading to excessive consumption of clotting factors, which

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presents clinically as a bleeding diathesis. The most common causes of DIC in pregnancy are excessive blood loss with inadequate blood component replacement, placental abruption, amniotic fluid embolism, and severe preeclampsia/HELLP syndrome.

DIAGNOSIS

Diagnosis requires a high index of suspicion coupled with appropriate blood tests. Thrombocytopenia, which can be documented in about 10% of parturients with severe preeclampsia,[76] is often the first indicator of DIC. Moreover, a normal platelet count effectively excludes the diagnosis. Other hematologic aberrations that can be used to confirm the diagnosis include an increase in circulating fibrin degradation products, D-dimer, platelet factor 4, β-thromboglobulin, thrombomodulin, fibrinopeptide A, thrombin-antithrombin complexes, and a decrease in circulating antithrombin III, fibrinogen, and protein C activity. However, many of these tests are expensive, time-consuming, and not clinically useful. Sibai et al[77] defined DIC as evidence of excessive bleeding with thrombocytopenia (<100,000/mm^3), plasma fibrinogen level less than 300/mg/dL, and fibrin-split products more than 40 μg/mL. Using this strict definition, they reported a 38% incidence of DIC in the setting of HELLP syndrome.[77] However, many pregnancies complicated by severe preeclampsia/HELLP syndrome have evidence of "subclinical" consumptive coagulopathy without evidence of bleeding, suggesting that DIC is a consequence, not a cause, of preeclampsia. Roberts and May,[78] on the other hand, have argued that abnormal laboratory DIC parameters are rarely seen in severe preeclampsia/HELLP syndrome unless there is a concurrent placental abruption. Exactly which laboratory parameters to check is controversial. Metz et al[79] have suggested that the most practical and cost-effective approach to screening for consumptive coagulation in the setting of preeclampsia is a combination of platelet count and activated partial thromboplastin time.

MANAGEMENT

Evidence of DIC in the setting of severe preeclampsia/HELLP syndrome should prompt immediate delivery. The decision of whether to proceed with induction of labor or cesarean delivery depends on such factors as gestational age, parity, cervical Bishop score, motivation of the patient, and the severity of DIC (eg, a rapidly falling platelet count may make cesarean delivery a more appropriate choice). Moderate to severe thrombocytopenia (especially a platelet count <70,000/mm^3) may be a contraindication to regional anesthesia because of the risk of spinal hematoma.[80]

Because DIC is a consumptive coagulopathy and therefore a progressive condition, early diagnosis and prompt and appropriate management are critical to reducing maternal and perinatal death and complication rates. Heparin administration is not generally recommended for the treatment of DIC in parturients with severe preeclampsia/HELLP syndrome.[81] The cornerstones of management include maintenance of intravascular volume and replacement of blood components and/or coagulation factors, as indicated by laboratory parameters. Each unit of packed red blood cells has a volume of 250 mL and contains citrate-phosphate-dextrose as a preservative. Packed red blood cells have a hematocrit of about 70%, and in the absence of continued hemorrhage, each unit should increase the hematocrit by 2–3% and the hemoglobin by about 1 g/dL in a healthy 70-kg (154-lb) woman.[82] Fresh-frozen plasma contains significant amounts of factors II (fibrinogen), V, and VIII as well as providing additional colloid support. Fresh-frozen plasma should be administered when the prothrombin time is at least 1.5-fold normal (ie, when the international normalized ratio [INR] is ≥1.5). The initial dose is usually 2 units. Each unit has a volume of 200 to 250 mL and raises circulating clotting factors by

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about 2–3%.[82] Cryoprecipitate refers to a concentrated extract of fresh-frozen plasma that is enriched with factors II (fibrinogen) and VIII. Each unit has a volume of only 10 to 15 mL. Transfusion of cryoprecipitate should be considered when circulating fibrinogen levels drop below 100 mg/dL in the setting of DIC. When to recommend platelet transfusion, however, is controversial. Some authorities have suggested that platelets be administered routinely if the circulating platelet count is less than 20,000/mm^3 or if the platelet count is less than 50,000/mm^3 if a surgical procedure is planned, if there is active bleeding, or if massive transfusion is anticipated.[82] Other practitioners note that such threshold recommendations are arbitrary and that platelet transfusion can usually be avoided even when platelet counts are below these values.[83] However, in such circumstances, it is usually prudent to have platelets immediately available in the event a platelet transfusion is needed. Platelets are prepared in a volume of 40 mL containing a total of 55×10^9 platelets. One unit of platelet concentrate will usually increase the platelet count by 5,000 to 10,000/mm^3. The usual dosage is 1 unit per 10 kg body weight.[82] Small amounts of erythrocytes are present in platelet concentrates. If ABO and Rh type-specific platelets are not available, an Rh-negative woman can be sensitized by Rh-positive platelets. Anti-D immune globulin (RhoGAM) should be administered, if indicated.

Hypertensive Emergencies

Hypertensive emergencies may complicate preeclampsia as well as chronic hypertension. Although the pathophysiology may be different, the approach to acute evaluation and management is the same, with the principal goal being avoidance of hypertensive encephalopathy and cerebrovascular accident. Less clear is whether aggressive control of blood pressure reduces the risk of eclampsia. Although rare, cerebrovascular accident as a result of acute hypertension is the leading cause of maternal death in preeclampsia.[84]

DIFFERENTIAL DIAGNOSIS

Acute hypertension may be the result of any one of a number of disorders. Although the etiology is usually apparent, consideration should be given to diagnostic possibilities other than preeclampsia if the clinical presentation is atypical. Such alternative diagnoses include pheochromocytoma, renal vein thrombosis, clonidine withdrawal, cocaine ingestion, methamphetamine ingestion, and acute flare of an underlying collagen vascular disease. In most instances, however, the cause of acute hypertension is the result of either worsening of underlying essential hypertension or acute exacerbation of preeclampsia.

PATHOPHYSIOLOGY

Why hypertensive emergencies occur in some patients and not others remains unclear. Some authorities have attempted to define threshold parameters for hypertensive crisis and have suggested that a diastolic blood pressure of more than 115 mm Hg and/or a systolic blood pressure of more than 200 mm Hg should be used to define hypertensive crisis.[85,86] However, clinical experience has shown that cerebrovascular accident can occur in women whose blood pressure has remained consistently below these threshold parameters. Others have proposed that it is the rate of blood pressure change, rather than an absolute measurement, that is responsible for the cerebral injury.[85]

Hypertensive crises can affect numerous organ systems. Retinal detachment and/or hemorrhage, congestive heart failure, myocardial infarction, renal failure, liver failure, placental abruption, and hypertensive encephalopathy may all result from acute and uncontrolled hypertension. Clinical evidence of any of the above end-organ effects should prompt a rapid response, with efforts directed at blood pressure control. Most patients may be managed without using inva-

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sive hemodynamic monitoring, but patients with severe or atypical cases are best managed in a tertiary center with such monitoring under the direction of clinicians skilled in critical care medicine.

MANAGEMENT

Hypertensive emergencies in pregnancy present a significant clinical challenge. The most important first step in the management of hypertensive crisis is to lower blood pressure. Dramatic and rapid lowering of blood pressure should be avoided. Ideally, an initial reduction of blood pressure of about 20%, with systolic and diastolic pressure goals of 140 to 150 mm Hg and 90 to 100 mm Hg, respectively, will provide the most favorable outcome.[87] Hypertension refractory to medical therapy is an indication for urgent termination of the pregnancy, and, in extreme circumstances, perimortem cesarean delivery may be necessary.[85]

In acute hypertension complicated by hypertensive encephalopathy, management must occur in an intensive care facility. Intravenous sodium nitroprusside is the antihypertensive agent of choice in this setting. At doses exceeding 8 μg/kg per minute, concerns about cyanide and thiocyanate accumulation in the fetal compartment have been expressed. As such, close monitoring of cyanide levels in patients receiving high doses of sodium nitroprusside for extended periods is recommended. Other medications that may be used in this setting to acutely lower blood pressure are summarized in Table 3.

The definitive management of hypertensive crisis in the setting of preeclampsia is delivery. Regional analgesia and anesthesia are preferred in this setting, provided there is no evidence of coagulopathy and no other contraindications to regional anesthesia. Avoidance of hypotension is critical in these patients. If general anesthesia is needed, blood pressure control is essential, and premedication may be necessary to avoid the increase in blood pressure that often accompanies induction of general anesthesia.

TABLE 3. Pharmacologic Management of Acute Hypertensive Crisis

Drug	Dosing	Comment
Recommended First-Line Therapy		
Hydralazine	5 mg IV push q 10 min × 2 doses; then 10 mg IV push q 20 min as needed until blood pressure has stabilized at 140–150/90–100 mm Hg	Be aware of hypotension and potential to adversely effect uteroplacental perfusion.
Labetalol	10–20 mg IV push; repeat q 10–20 min with doubling doses (not to exceed 80 mg in any single dose) to a maximum of 300 mg total	Be aware of hypotension and potential to adversely effect uteroplacental perfusion.
Nifedipine	10 mg orally q 30 min × 2 doses; then 10–20 mg orally q 4–6 hourly	Sublingual nifedipine is best avoided.*
Recommended Therapy in Women Refractory to First-Line Agents		
Sodium nitroprusside	0.5–3.0 μg/kg/min IV infusion (not to exceed 800 μg/min)	Should be used only by someone with critical care experience
Nitroglycerin	5 μg/min IV infusion, increase as required every 5 min to maximum dose of 100 μg/min	Relatively contraindicated in the setting of hypertensive encephalopathy as it may increase cerebral blood flow and intracranial pressure*

Adapted from Repke JT. Preeclampsia and hypertension. In: Repke JT, ed. Intrapartum Obstetrics. New York: Churchill Livingstone, 1996:271.

* Grossman E, Messerli FH, Grodzicki T, Kowey P. Should a moratorium be placed on sublingual nifedipine capsules given for hypertensive emergencies and pseudoemergencies? JAMA. 1996; 276:1328–1331.

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Hypertensive Encephalopathy and Cortical Blindness

Cortical blindness is a known complication of severe preeclampsia. Other ophthalmologic manifestations of preeclampsia include retinal detachment, retinal arteriolar vasospasm, and thrombosis of the central retinal arteries.[88,89] The incidence of cortical blindness as a manifestation of hypertensive encephalopathy in severe preeclampsia is 1–15%.[90,91]

PATHOPHYSIOLOGY

The brain is normally protected from extremes of blood pressure by an autoregulatory system that ensures constant perfusion over a wide range of systemic pressures. In response to systemic hypotension, cerebral arterioles dilate to maintain adequate perfusion, whereas vessels constrict in response to high systemic pressures. Above the upper limit of autoregulation, hypertensive encephalopathy may develop.[92] Hypertensive encephalopathy is a subacute neurologic syndrome characterized by headache, seizures, visual aberrations, and other neurologic disturbances (altered mental status, focal neurologic signs) in the setting of elevated blood pressure. Although the syndrome is usually reversible if the hypertension is treated early, it may be fatal if it is unrecognized or if treatment is delayed.[93,94] The clinical findings are nonspecific and the diagnosis may be difficult to establish, particularly in patients who have other illnesses. Various neurologic conditions such as cerebrovascular accident, venous thrombosis, and encephalitis can mimic hypertensive encephalopathy.[95] Radiologic imaging studies may be useful in establishing the diagnosis in the appropriate clinical setting.[96]

The classic autopsy studies of Sheehan and Lynch[97] in the 1960s refuted the prevailing opinion that preeclampsia/eclampsia was frequently associated with widespread cerebral edema. The most common lesions described were multiple petechial hemorrhages in the cortex, subcortical region, white matter, and midbrain. Because petechial hemorrhages were associated with capillary thrombi, the authors concluded that the lesions were caused by a vascular disturbance that produced local ischemia. Severe diffuse cerebral edema is occasionally seen in eclampsia; however, the more typical lesion is localized edema at the gray matter/white matter junction in the occipital lobe. The susceptibility of the posterior circulation to the lesions of hypertensive encephalopathy is a well-known but poorly understood phenomenon.[98,99] One possible explanation involves the regional heterogeneity of the sympathetic vascular innovation. In experimental studies, the sympathetic innervation of the intracranial arterioles has been shown to protect the brain from marked increases in blood pressure.[100] Moreover, ultrastructural studies have shown that the internal carotid system is much better supplied with sympathetic innervation than is the vertebrobasilar system.[101] Acute hypertension would, according to this hypothesis, stimulate the perivascular sympathetic nerves, which would protect the anterior but not the more poorly innervated posterior circulation. This would result in breakthrough of autoregulation with edema mainly in the occipital lobes, and resultant ophthalmologic manifestations.

Two theories have been proposed to account for the clinical and radiologic abnormalities associated with hypertensive encephalopathy and cortical blindness. The first postulates that hypertensive encephalopathy results from spasm of the cerebral vasculature in response to acute hypertension, resulting in ischemic injury, arteriolar necrosis, and cytotoxic edema.[102–105] A more recent alternative hypothesis suggests that the syndrome results from breakthrough of autoregulation with passive overdistention of cerebral arterioles, leading to increased capillary permeability with leakage of fluid and proteins into the surrounding tissues, resulting in vasogenic (hydrostatic) edema.[92,96,106] In both instances, the end re-

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sult is focal cerebral edema. The presence of cerebral edema on head CT or MRI is therefore not helpful in defining the mechanism underlying hypertensive encephalopathy. The availability of improved neuroimaging, including single-photon emission computed tomography (SPECT), which can distinguish between areas of hyper- and hypoperfusion, has enabled a more detailed investigation of the response of the cerebral vasculature to hypertension.

In 1992, Schwartz et al[96] reported on the use of CT, MRI, and SPECT in 14 patients with hypertensive encephalopathy, including 8 with preeclampsia. All patients had hypodense lesions in the occipital lobes on CT, which correlated with lesions of increased signal intensity on T2-weighted MRI. SPECT performed on two patients during hypertensive episodes revealed areas of increased cerebral perfusion, which corresponded with lesions on CT and MRI. These data support the concept that hypertensive encephalopathy results primarily from increased capillary permeability leading to vasogenic edema. If vasospasm and resultant ischemia were important features, decreased cerebral perfusion on SPECT would have been observed with possible infarction. However, infarction is a rare occurrence both clinically[93,96,98,103,104] and experimentally.[107]

MANAGEMENT

Cortical blindness and other manifestations of hypertensive encephalopathy are a contraindication to expectant management of preeclampsia in pregnancy. Delivery of the fetus and placenta remains the only curative treatment. Other responsibilities of management include exclusion of other causes of blindness (eg, occipital hemorrhage and retinal detachment) and aggressive blood pressure control. Cortical blindness will reverse completely after delivery, although resolution may take many weeks.[96,106]

Conclusion

Preeclampsia remains a significant cause of maternal and perinatal death and complications. Once the diagnosis of preeclampsia has been made, treatment options are limited. For this reason, much attention has recently been focused on preeclampsia prevention. Despite an extensive research effort, no single strategy has yet been shown to be beneficial in preventing the development of preeclampsia in either low- or high-risk populations.[36] Preeclampsia is a disorder of placental implantation and is therefore not entirely preventable. Delivery of the fetus and placenta remains the only curative treatment. A healthy respect for this condition, coupled with aggressive and early intervention in the event of preeclampsia complications, may be able to minimize adverse maternal and perinatal events in the setting of severe preeclampsia.

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