CME CREDIT

Medical aspects of pregnancy

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■ **BACKGROUND** Physiologic changes during pregnancy can precipitate or exacerbate potentially serious maternal illnesses that may adversely affect the outcome for both mother and fetus.

■ **OBJECTIVE** To review the common medical conditions that may complicate pregnancy.

■ **SUMMARY** Venous thrombolembolic disease is the most common medical disorder complicating pregnancy; heparin is the safest and most effective treatment and prophylactic agent in high-risk patients. Systemic lupus erythematosus may flare during pregnancy and may require therapy with corticosteroids, which may also be needed to treat immune thrombocytopenic purpura. Hypertension should be monitored closely throughout the pregnancy and puerperium; certain antihypertensive agents control blood pressure without affecting the fetus. Asthma may worsen or improve during pregnancy; therapy is similar to that for nonpregnant women. Diabetes mellitus may antedate pregnancy or become manifest during pregnancy; detection and strict glycemic control are the keys to a successful outcome. Approximately 30% of infants born to mothers with established HIV infection acquire the syndrome of immunodeficiency; testing must continue until 15 months of life. Mothers with epilepsy should use the lowest effective dose of a single antiepileptic agent to prevent congenital birth defects.

■ **CONCLUSIONS** When the internist, obstetrician, anesthesiologist, and perinatologist use a team approach, most patients can expect a successful outcome.

■ INDEX TERMS: PREGNANCY; PREGNANCY COMPLICATIONS; THROMBOSIS; LUPUS ERYTHEMATOUS, SYSTEMIC; PURPURA, THROMBOCYTOPENIC; HYPERTENSION; ECLAMPSIA; HEART DISEASES; HEART DEFECTS, CONGENITAL; ASTHMA; PREGNANCY IN DIABETES; HIV INFECTIONS; EPILEPSY ■ CLEVE CLIN J MED 1994; 61:263–271

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MEDICAL DISEASES during pregnancy place both the mother and fetus at risk for serious complications and even death. Few situations in medicine require cooperation among specialists as does the care of a pregnant patient with medical illness. The knowledgeable internist with interest in the care of pregnant patients with medical illness must work closely with the obstetrician, anesthesiologist, and perinatologist to strive for a successful outcome.

Many medical conditions, if untreated or unrecognized, can lead to maternal death. Of the major causes of maternal death, hemorrhage and eclampsia have decreased in incidence over the last 10 years, while thromboembolism has increased.[1] Maternal diseases affect the health of the fetus in many ways, causing intrauterine growth retardation, macrosomia, congenital heart block, and fetal hemorrhage (*Table 1*).[2]

This review will consider teratogens, thromboembolic disease, systemic lupus erythematosus, immune thrombocytopenic purpura, hypertension, preeclampsia and eclampsia, cardiac disease, asthma, diabetes, human immunodeficiency virus infection, and epilepsy in how they can affect or be affected by pregnancy.

TABLE 1
MATERNAL DISORDERS AND THEIR EFFECTS ON THE FETUS OR NEONATE*

Maternal disorder	Fetal or neonatal effects
Cyanotic heart disease	Intrauterine growth retardation
Diabetes mellitus	Macrosomia, hypoglycemia, hypocalcemia, hyperbilirubinemia
Hypertension	Intrauterine growth retardation, placental abruption
Immune thrombocytopenia purpura	Thrombocytopenia, bleeding
Systemic lupus erythematosus	Congenital heart block, fetal wasting, thrombocytopenia

*From Carlson, reference 4

TABLE 2
TERATOGENS AND THEIR FETAL EFFECTS

Agent	Fetal effects
Alcohol	Fetal alcohol syndrome (intrauterine growth retardation, central nervous system diseases, midline facial defects)
Anticoagulants	Warfarin embryopathy, central nervous system diseases, blindness
Anticonvulsants (phenytoin valproate, trimethadione)	Fetal hydantoin syndrome, coagulopathy, neural tube defects
Antithyroid agents (propylthiouracil, methimazole, iodine 131)	Hypothyroidism, aplasia cutis
Isotretinoin	Facial defects, central nervous system anomalies, cardiovascular defects
Tetracycline	Dental staining, impaired fibular growth
Angiotensin-converting enzyme inhibitors	Oligohydramnios, renal failure

TERATOGENS

Teratogens ingested by the mother can cause serious developmental abnormalities and even fetal death. The list of teratogens is quite extensive, and all agents should be considered teratogenic until reviewed (*Table 2*).[3–5]

THROMBOEMBOLIC DISEASE

Thromboembolic disease is the most common medical complication of pregnancy. Superficial or deep vein thrombophlebitis occurs in one out of every 70 pregnancies, and 1% of all deliveries result in nonfatal pulmonary embolus.[6] Risk factors for thromboembolic disease include previous deep vein thrombosis, cesarean section, increasing age or parity, antepartum bed rest, obstetric complications, obesity, and antithrombin III deficiency.[6]

Many physiologic changes that occur during pregnancy lead to a hypercoagulable state. For example, progesterone decreases venous tone, and the gravid uterus can compress the inferior vena cava. As labor begins, the fetal head engages in the pelvis, resulting in mechanical obstruction to venous flow. There is a marked increase in fibrinogen concentration as pregnancy progresses. In addition, factors XII, X, IX, VIII, VII, and V increase during pregnancy. Platelet counts remain normal, but platelet activity increases in the postpartum period. Plasminogen activator-inhibitors increase dramatically, and the PAI-2 concentration remains elevated for at least 72 hours after delivery. Finally, blood viscosity and circulating blood volume increase. All of these changes promote thrombosis.

Superficial thrombophlebitis, the most common form of thromboembolic disease, can occur at any time during pregnancy, although the greatest frequency is in the puerperium (85% develop within 72 hours after delivery). Deep vein thrombosis and pulmonary embolism are even more difficult to diagnose clinically in pregnant patients than in the nonpregnant population. Leg edema, venous varicosities, leg pain, and physiologic dyspnea are all common findings in normal pregnant patients.

Noninvasive methods of diagnosing deep vein thrombosis include impedance plethysmography and duplex ultrasonography. Invasive methods include leg scanning with iodine-125-labeled fibrinogen, venography with technetium-labeled red blood cells, and contrast venography.

The main concern in diagnosing deep vein thrombosis and pulmonary embolism in this population is radiation exposure to the fetus. In a retrospective analysis, Ginsberg and Hirsh[7] determined that a total exposure of less than 5 rad leads to a slight increase in relative risk of childhood cancer but no increase in birth defects (*Table 3*).

Therefore, one should minimize fetal radiation exposure when diagnosing maternal thromboembolic disease, especially in the first trimester. Negative noninvasive test results are as likely to be valid in excluding proximal deep vein thrombosis in pregnant patients as in nonpregnant patients. Venography remains the most reliable test in the third trimester, but all noninvasive tests can give false-positive results in this period.

Although some have advocated using warfarin to treat thromboembolic disease in the second and third trimesters, the safest therapeutic strategy uses heparin throughout pregnancy. For acute deep vein thrombosis, intravenous heparin in full doses for 5 to 7 days is recommended, followed by subcutaneous heparin injections to prolong the activated partial thromboplastin time (measured 6 hours after injection) to 1.5 times laboratory control. In pregnant patients who have had a previous deep vein thrombosis or pulmonary embolus, 5000 units of heparin should be administered subcutaneously every 12 hours until the middle of the third trimester. At this point, the heparin dose should be adjusted to prolong the 6-hour postinjection activated partial thromboplastin time to 1.5 times laboratory control.[8,9]

Warfarin-induced embryopathy, characterized by nasal hypoplasia and stippled epiphyses of bones, develops when the embryo is exposed to warfarin between the sixth and ninth weeks of development. Other complications of warfarin use in pregnancy include bleeding and neurologic disorders. Neurologic disorders (optic atrophy, agenesis of the corpus callosum, mental retardation) can occur with exposure to warfarin at any time during development. Blindness may occur in up to 50% of exposed fetuses.

Side effects of heparin use include bleeding and osteoporosis. The latter complication generally occurs when more than 15 000 units per day are given for 6 months or more. Other treatment options for thromboembolic disease in pregnancy include pulmonary embolectomy, venous ligation, thrombectomy, vena caval filter, and thrombolysis.[8,9]

TABLE 3
RADIATION EXPOSURE TO THE FETUS IN PROCEDURES USED TO DIAGNOSE VENOUS THROMBOEMBOLIC DISEASE*

Procedure	Estimated radiation dose to fetus, rad
Limited venography	< 0.05
Bilateral venography without abdominal shield	0.628
Pulmonary angiography (brachial)	< 0.05
Ventilation-perfusion lung scan (1 mCi technetium macroaggregates of human albumin or technetium sulphur colloid)	0.007–0.017
Chest roentgenogram	< 0.001

*Adapted from Ginsberg et al, reference 7

TABLE 4
CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS*

Four or more of the following criteria must be present to suggest the diagnosis:
Facial erythema (butterfly rash or malar rash)
Discoid lupus
Photosensitivity
Oral or nasopharyngeal ulceration
Arthritis without deformity (pain on motion, tenderness or effusion or periarticular soft-tissue swelling)
Lupus erythematosus cells, ANA positivity
Chronic false-positive serologic test for syphilis
Profuse proteinuria (>3.5 g/day)
Cellular casts
Pleuritis or pericarditis
Psychosis or convulsions
Hemolytic anemia, leukopenia, or thrombocytopenia

*Summarized from Cohen et al, reference 11

SYSTEMIC LUPUS ERYTHEMATOSUS

Systemic lupus erythematosus (SLE) is the most common collagen vascular disease that complicates pregnancy. The diagnostic criteria for SLE in pregnant patients are the same as in nonpregnant patients (*Table 4*).[10,11] Most cases of SLE are diagnosed before pregnancy. Patients with SLE appear to have normal fertility rates, but patients with severe lupus nephritis have decreased fertility rates. Early spontaneous abortions may occur in as many as 90% of pregnancies in women with SLE, and clinically recognized spontaneous abortions may occur in 25% of pregnancies.[12]

SLE activity before conception is generally accepted as the best predictor of the course of SLE during pregnancy. However, the presence of maternal anti-Sjögren's syndrome antigen A antibodies suggests an increased likelihood of congenital complete heart block.[13]

The presence of circulating lupus anticoagulant or anticardiolipin antibodies has been associated with recurrent spontaneous abortion. These substances, along with the biologic false-positive sero-

TABLE 5
CLASSIFICATION OF HYPERTENSION IN PREGNANCY*

Preeclampsia and eclampsia
Chronic hypertension
Essential
Secondary
Preeclampsia superimposed on chronic hypertension
Transient hypertension

*According to Gifford et al, reference 18

logic test for syphilis, provide laboratory evidence for the antiphospholipid antibody syndrome. However, a recent study found no evidence that lupus anticoagulant or anticardiolipin antibodies were risk factors in women who presented with their first spontaneous abortion.[14]

Many therapies have been suggested, including corticosteroids and aspirin, aspirin alone, and heparin. None have provided definitive results, although a recent study suggested that heparin was better than prednisone in preventing maternal and fetal complications.[15]

Treatment of a "lupus flare" during pregnancy initially requires the use of corticosteroids. If life-threatening complications develop, "pulse" therapy with methylprednisolone in high doses for 3 to 7 days is appropriate. If the patient does not respond to corticosteroids, one can consider adding azathioprine or cyclophosphamide. Disease activity may be determined by a multitude of laboratory tests; however, elevated antidouble-stranded DNA antibody levels or hypocomplementemia may be particularly useful markers.

IMMUNE THROMBOCYTOPENIC PURPURA

This syndrome is believed to result from an immunoglobulin G (IgG) antibody primarily produced in the spleen that is directed toward a platelet-associated antigen.[16] It is first suspected when a routine platelet count is below 150×10^9/L. However, such a count may merely reflect platelet clumping; therefore, a second sample should be obtained in a tube containing sodium citrate. Bone marrow examination reveals an increased number of megakaryocytes. This finding, however, is *not* pathognomonic, and other causes should be sought, including asymptomatic human immunodeficiency virus infection. Splenomegaly, hypertension, elevated hepatic enzymes, and disseminated intravascular coagulopathy must be absent in order to diagnose immune thrombocytopenic purpura, as these findings may suggest the HELLP syndrome (*h*emolysis, *e*levated *l*iver-enzymes, *l*ow *p*latelet count).

In numerous studies, pregnancy did not appear to make immune thrombocytopenic purpura worse, but the disease often causes complications, notably neonatal and postpartum hemorrhage. Fetal and neonatal thrombocytopenia may occur due to transplacental passage of maternal IgG platelet autoantibodies. The frequency of thrombocytopenia in neonates ranges from 12.5% to 48.0% in this condition. The only maternal characteristics that appear to predict neonatal thrombocytopenia are platelet counts of fewer than 50×10^9/L and resistance to corticosteroid therapy.[17]

Oral corticosteroids, the cornerstone of therapy for pregnant patients with immune thrombocytopenic purpura, appear to increase platelet production rather than decrease the activity of the antiplatelet antibody. The dose is generally 1.0 to 1.5 mg/kg/day of prednisone. If a complete response has not occurred by 6 weeks, it is unlikely to develop. Intravenous IgG or splenectomy are second- and third-line modes of therapy. Case reports have identified plasmapheresis and chemotherapeutic agents as alternatives.[16,17]

HYPERTENSION

Hypertension occurs in almost 10% of pregnancies, more often in nulliparous women and in those with multiple fetuses. A working group report from the National High Blood Pressure Education Program[18] defines hypertension in pregnancy as an increase in systolic blood pressure of 30 mm Hg or more or an increase in diastolic blood pressure of 15 mm Hg or more from values obtained in early pregnancy. If values before the 20th week of pregnancy are unknown, blood pressure values of 140/90 mm Hg or greater are considered high (*Table* 5).

Preeclampsia and eclampsia

Preeclampsia associated with preexisting renal disease or chronic hypertension clearly places both the fetus and mother at great risk for complications or death. Preeclampsia occurs late in pregnancy, mainly after week 20, and is characterized by hypertension, edema, proteinuria (≥ 0.3 g/24 hours), and, less commonly, coagulopathy and impaired liver function. *Eclampsia* denotes the presence of general-

ized seizures in addition to these findings.

Signs that predict poor outcome for both the fetus and mother include severe hypertension, the new onset of proteinuria, serum creatinine concentrations greater than 2 mg/dL, thrombocytopenia, abdominal pain, headache or central nervous system signs, pulmonary edema, fetal growth retardation, and papilledema.[19] Often, preeclampsia progresses to eclampsia with some warning signs (hyperreflexia, headaches). However, a subtle rise in blood pressure with small changes in platelet counts can progress to the life-threatening HELLP syndrome. In this setting, termination of pregnancy is recommended. Once the fetus is delivered, preeclampsia promptly resolves. A few women who receive bromocriptine after delivery may acquire late postpartum eclampsia. Therapy of preeclampsia begins with hospitalization and close observation. In certain circumstances (severe persistent hypertension, thrombocytopenia, liver dysfunction, progressive renal insufficiency, premonitory signs of eclampsia, fetal distress), labor should be induced, regardless of gestational age.[19]

The ideal antihypertensive agent in preeclampsia would reduce blood pressure in a controlled and predictable manner, avoiding a compromise in utero-placental blood flow. Many authors advocate using hydralazine, diazoxide, or labetalol in this setting. Calcium-channel blockers may also be effective. However, magnesium sulfate, given to prevent eclampsia, may potentiate the effects of calcium-channel blockers, resulting in hypotension.

Chronic hypertension

Chronic hypertension, existing before pregnancy or diagnosed before the 20th week, is most often idiopathic or "essential." Chronic hypertension in pregnancy can often be easily treated. However, preeclampsia with chronic hypertension results in a high incidence of maternal and fetal complications and death. Agents frequently used to treat chronic hypertension in pregnancy include methyldopa, beta blockers (including labetalol), and hydralazine. Recent reports have implicated angiotensin-converting enzyme inhibitors with complications in the second and third trimesters, and these agents should not be used during pregnancy. Salt-sensitive women who have used diuretics before pregnancy can continue to use them.[18–22]

TABLE 6
RISK OF MATERNAL DEATH WITH SPECIFIC CARDIAC DISEASES*

Low risk (< 1%)	Septal defects
	Patent ductus arteriosus
	Pulmonic or tricuspid lesions
Moderate risk (5%–15%)	Mitral stenosis (New York Heart Association Grade III)
	Aortic stenosis
	Marfan's syndrome (normal aortic root)
	Uncomplicated coarctation of aorta
	History of myocardial infarction
High risk (25%–50%)	Eisenmenger's syndrome
	Pulmonary hypertension
	Marfan's syndrome with aortic root dilation

*From Clark, reference 26, with permission

CARDIAC DISEASE

The prevalence of rheumatic heart disease has fallen dramatically, and marked improvements in surgical correction of congenital heart disease are making it possible for an increasing number of women to undergo pregnancy and delivery who could not have in the past. To predict the risk and natural progression of heart disease during pregnancy, one must appreciate the normal physiologic cardiovascular changes in pregnancy, including increased cardiac output, increased plasma volume, decreased systemic vascular resistance, increased systemic blood volume, and decreased reserve for increased pulmonary blood volume. Once these factors have been accounted for, a patient's risk can be determined, based on the underlying cardiac lesion, the pathophysiologic effects of that lesion, and the development of pregnancy-related complications (*Table 6*).[23–26]

Selected congenital cardiac defects

Atrial septal defect. This is the most common congenital cardiac defect unrecognized until adulthood. The secundum type is most common and is often very well tolerated in pregnancy. The only risk occurs in sudden acute blood loss (increased left-to-right shunting) or in paroxysmal tachycardia. Pulmonary hypertension is uncommon and usually occurs in the fourth or fifth decade of life.

TABLE 7
SEVERITY OF AN ASTHMA ATTACK IN PREGNANCY

Mild	pH elevated PCO_2 low PaO_2 low
Moderate	pH normal PCO_2 normal PaO_2 low
Severe	pH low PCO_2 elevated PaO_2 low

Aortic stenosis. Although uncommon in women, aortic stenosis is potentially serious. An increase in stroke volume causes an increase in left ventricular work without an increase in blood flow. If the heart rate must increase to counteract the lack of increase in stroke volume, coronary blood flow may decrease. Syncope is often the presenting symptom. Bed rest, beta blockers, and nitrates are useful adjuncts in pregnant patients with this lesion, but ideally, patients with aortic stenosis should undergo surgical correction before becoming pregnant.

Mitral stenosis. Often rheumatic in origin, mitral stenosis is potentially life-threatening in pregnancy. The diastolic volume of the left ventricle decreases because of left atrial outflow obstruction, resulting in a fixed cardiac output. Pulmonary edema results, along with atrial fibrillation and thrombus formation. Labor and delivery pose a serious risk for mothers with mitral stenosis. With placental separation, up to 500 mL of blood is "transfused" into the maternal circulation, potentially resulting in acute pulmonary edema.

Coarctation of the aorta. It is rare that a patient will progress to childbearing age without repair of this lesion. In pregnancy, such patients have a risk of aortic dissection, rupture of an intracranial aneurysm, and end-organ complications secondary to hypertension, with a rate as high as 3% to 6%. A bicuspid aortic valve is associated with coarctation, increasing the risk for infective endocarditis.

Tetralogy of Fallot. This is the most common cyanotic congenital right-to-left shunt found in pregnant women. This lesion consists of valvular pulmonic stenosis, right ventricular hypertrophy, overriding aorta, and ventricular septal defect.

Pregnant patients with tetralogy of Fallot are at risk of increased shunting due to the physiologic decrease in systemic vascular resistance. Patients with this entity depend on adequate venous return and right-sided end-diastolic volume. Blood loss during delivery and from postpartum hemorrhage poses considerable danger.

Eisenmenger's syndrome. Patients with high pulmonary vascular resistance due to shunting cannot tolerate pregnancy, and their mortality rate approaches 50% to 70%. They should be counseled against pregnancy, as should patients with pulmonary hypertension, regardless of the cause.

Marfan's syndrome. The main risk posed by pregnancy in Marfan's syndrome is aortic dissection or rupture of a dilated aortic root. In addition, because this condition is an autosomal dominant trait, pregnancy should be avoided if either parent has it.

If the patient's cardiac lesion predisposes her to infective endocarditis, she should begin antibiotic prophylaxis at the time of delivery consisting of ampicillin 2 g intravenously and gentamicin 1.5 mg/kg intravenously. Patients allergic to penicillin should receive vancomycin 1 g intravenously instead of ampicillin. This regimen should be given every 8 hours for three doses.

ASTHMA

Although asthma complicates only 1% of pregnancies, the variable effect of pregnancy on asthma makes this disorder unpredictable. Most pregnant patients experience no change in their "attack" frequency or severity, although Schatz studied 330 women during 366 pregnancies and found that 35% felt asthma worsened during pregnancy, 33% noted no change, and 28% improved.[27] Physiologic dyspnea develops in pregnancy and is initially seen as hyperventilation as early as the first trimester. Compensated respiratory alkalosis then develops. Tidal volume increases by 50% in pregnancy, and the functional residual volume decreases by 20%, mainly in the third trimester.

The severity of an asthmatic attack during pregnancy is assessed using the same criteria as in nonpregnant patients, gleaned from the history, physical examination, and laboratory tests. Arterial blood gas analysis is often used to determine the severity of an attack (*Table 7*). However, home monitoring of peak expiratory flow rates may establish the asthma status earlier and more reliably.

Therapy for exacerbation of asthma is similar in pregnant and nonpregnant patients. Beta-adrenergic agonists, theophylline, and corticosteroids are all effective in pregnancy and are generally safe for both

the mother and fetus. Many believe, however, that epinephrine is the drug of choice. Terbutaline has also been advocated as a safe and effective first-line agent, having been used as a tocolytic agent for years.

The major risk factor for adverse fetal outcomes with asthma in pregnancy is a PaO_2 less than 60 mm Hg. All efforts should be made to maintain adequate ventilation and oxygenation. Once the acute exacerbation has resolved, long-term therapy should commence to prevent recurrent attacks.[28,29]

TABLE 8
CRITERIA FOR INTERPRETING THE 100-GRAM GLUCOSE TOLERANCE TEST TO DIAGNOSE GESTATIONAL DIABETES*

	Glucose concentrations, mg/dL			
	National Diabetes Data Group		Carpenter and Coustan	
	Plasma	Whole blood	Plasma	Whole blood
Fasting	105	90	95	90
1 hour	190	170	180	165
2 hour	165	145	155	143
3 hour	145	125	140	127

*Two or more readings as high or higher than the listed values constitute an abnormal test. Summarized from the National Diabetes Data Group, reference 32, and Coustan and Carpenter, reference 33

DIABETES

Diabetic women can now expect to complete pregnancy successfully, but they must commit themselves to frequent perinatal examinations, strict dietary adherence, aggressive blood glucose monitoring at home, and frequent fetal surveillance.[30] Normal pregnancy is a physiologic "starvation" state, with fasting hypoglycemia and with increased glucose and insulin levels in the postprandial period. A state of relative insulin resistance develops in the second half of pregnancy, and insulin requirements increase during this period in patients with preexisting diabetes.

Gestational diabetes is defined as the development of hyperglycemia in a pregnant woman who has no previous history of diabetes. All women should have their blood glucose measured 1 hour after a nonfasting 50-g glucose challenge between the 24th and 28th week, and those with values of 140 mg/dL or greater should undergo a glucose tolerance test.[31] Recently, the criteria adopted by the National Diabetes Data Group[32] have been challenged by a modified, more strict set of criteria proposed by Carpenter and Coustan (*Table 8*).[33] In a study of over 2000 pregnant women, 50% more cases of gestational diabetes mellitus were diagnosed using the modified criteria than with the standard criteria, and the additional women so identified had similar maternal and fetal complications.[34]

Factors influencing the outcome of pregnancy are glycemic control and the severity of underlying vascular disease. Infants of diabetic mothers are at risk for macrosomia, neonatal metabolic complications, congenital anomalies, and diabetes. In the mother, pregnancy may worsen diabetic nephropathy, retinopathy, and gastroparesis. Many pregnant patients with diabetic nephropathy experience transient worsening of renal function.

Persistent patient education about strict glycemic control is mandatory. In the first trimester, patients should follow a diet that includes 30 kcal per kg of ideal body weight (45% carbohydrate, 20% protein, 35% fat). Insulin should be used to maintain strict glycemic control; oral hypoglycemic agents must be avoided, as they cross the placenta and result in prolonged neonatal hypoglycemia. Patients should continue to monitor their blood glucose concentrations at home in the second trimester. In addition, maternal alpha-fetoprotein levels should be assayed because of the increased frequency of neural tube defects in diabetic mothers. Fetal ultrasonography may also be performed.

In the third trimester, frequent fetal surveillance accompanies insulin therapy, if needed. Near term, assessment of fetal lung maturity should be done via amniocentesis, using the lecithin-sphingomyelin ratio and concentration of phosphatidylcholine.

Approximately 85% of patients with gestational diabetes can be managed with diet therapy alone. Gestational diabetic patients who require insulin should be managed in the same manner as patients with preexisting diabetes.

HUMAN IMMUNODEFICIENCY VIRUS INFECTION

The acquired immunodeficiency syndrome (AIDS) can complicate pregnancy and place the fetus at risk for perinatal transmission of the virus. AIDS in children represents approximately 2% of

TABLE 9
GUIDELINES FOR ANTIEPILEPTIC DRUG THERAPY IN PREGNANCY*

Use first-choice drug for seizure type and epilepsy syndrome
Use single antiepileptic drug at lowest dose and plasma level that protects against tonic-clonic seizures
Avoid valproate and carbamazepine when there is a family history of neural tube defects
Avoid polytherapy
Monitor plasma antiepileptic drug levels regularly, and, if possible, free or unbound plasma antiepileptic drug levels
Continue folate supplementation and ensure normal plasma red blood cell folate levels during the first trimester
Avoid high plasma levels of valproate
If valproate and carbamazepine are used, offer amniocentesis for alpha-fetoprotein at 16 weeks and ultrasonography at 18 to 19 weeks, looking for neural tube defects

*Adapted from Delgado-Escueta and Janz, reference 41

all cases in the United States. The major risk factor for human immunodeficiency virus (HIV) infection in women is intravenous drug abuse, although heterosexual transmission is on the rise. Most children with HIV infection acquire it perinatally from their mother, either in the uterus, during birth, or afterward. The seroprevalence rate of HIV in pregnant women ranges from 0.25% to 0.80%, and the transmission rate from mother to infant is from 25% to 40%.[35–37]

Near delivery, passive transfer of maternal antibody across the placenta occurs. If the mother is HIV-positive, the infant will also be positive. However, this does not indicate infection in the neonate unless the antibody persists after 15 months of age. Infants initially positive for the HIV antibody should be examined every 3 months, and antibody testing should be performed at least every 6 months. If children younger than 15 months develop clinical symptoms with immunologic abnormalities and have persistent HIV antibodies or P-24 antigens, they likely have HIV infection.[37]

Pregnant HIV-infected women should be offered counseling, and the physician should look for other sexually transmitted diseases such as syphilis, gonorrhea, chlamydia, and hepatitis B. Tuberculosis testing should also be routine in HIV-infected pregnant patients.[38] Pregnancy causes an exacerbation in the immunocompromised state, with a fall in CD4 cell counts; CD8 cell counts remain stable. If low CD4 counts are detected during pregnancy, the patient should be offered prophylactic treatment for *Pneumocystis carinii* pneumonia; prophylaxis must also be considered when a patient completes therapy for documented *P carinii* pneumonia.[39]

During delivery, every effort must be made to avoid nosocomial spread of HIV infection. Universal blood and secretion precautions must be followed in every delivery. The method of delivery does not appear to affect the risk of perinatal transmission of HIV infection. However, as there is a small risk of transmission of the HIV virus via breast milk, HIV-infected mothers should consider avoiding breast feeding.[40]

EPILEPSY

Women with epilepsy who contemplate pregnancy should first undergo effective counseling about the inherent risks to infants of epileptic mothers: the risk of developmental abnormalities is two to three times higher in infants of mothers who receive antiepileptic drugs. Other topics of instruction should include the need for good nutrition and health before conception (including high dietary concentrations of folic acid), the importance of strict compliance with antiepileptic drug therapy, and the maintenance of good sleep habits during pregnancy.

Despite voluminous data on the risks of major and minor developmental abnormalities in infants exposed to antiepileptic drugs, no one agent has emerged as safe in pregnancy, and none of the four major antiepileptic drugs (phenytoin, valproate, carbamazepine, and phenobarbital) is safer than the others. This has prompted the establishment of various guidelines for the use of antiepileptic drugs in pregnancy (*Table* 9). One should use single agents at the lowest dose and plasma level that prevent seizures.[41]

Most women with epilepsy have a normal vaginal delivery. A generalized tonic-clonic seizure occurs during labor in 1% to 2% of women with epilepsy, and within 24 hours after delivery in another 1% to 2%. These seizures are best managed with intravenous benzodiazepines. Indications for elective or emergent cesarean section in epileptic mothers are few and include substantial neurologic or cognitive deficits, poor seizure control late in pregnancy, previous seizures during heavy physical or emotional stress, or generalized tonic-clonic seizures during labor.[42]

SUMMARY

Pregnancy and birth are normal processes, but physiologic changes that occur during pregnancy can precipitate certain potentially serious conditions or exacerbate preexisting ones. In addition, preexisting diseases can dangerously complicate pregnancy. These situations pose special problems for physicians; the safety of the fetus is always a consideration. Nevertheless, working closely with specialists from other disciplines, the internist can usually have the satisfaction of helping the patient bring her pregnancy to a successful conclusion.

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