

18. Obstetrics - *William R. Crombleholme, MD*

DIAGNOSIS & DIFFERENTIAL DIAGNOSIS OF PREGNANCY

Introduction

It is advantageous to diagnose pregnancy as promptly as possible when a sexually active woman misses a menstrual period or has symptoms suggestive of pregnancy. In the event of a desired pregnancy, prenatal care can begin early, and potentially harmful medications and activities such as drug and alcohol use, smoking, and occupational chemical exposure can be halted. In the event of an unwanted pregnancy, counseling about adoption or termination of the pregnancy can be provided at an early stage.

Pregnancy Tests

All urine or blood pregnancy tests rely on the detection of hCG produced by the placenta. hCG levels increase shortly after implantation, approximately double every 48 hours, reach a peak at 50-75 days, and fall to lower levels in the second and third trimesters. Laboratory and home pregnancy tests use monoclonal antibodies specific for hCG. These tests are performed on serum or urine and are accurate at the time of the missed period or shortly after it.

Compared with intrauterine pregnancies, ectopic pregnancies may show lower levels of hCG that level off or fall in serial determinations. Quantitative assays of hCG repeated at 48- to 72-hour intervals are used in the diagnosis of ectopic pregnancy as well as in cases of molar pregnancy, threatened abortion, and missed abortion. Comparison of hCG levels between laboratories may be misleading in a given patient because different international standards may produce results that vary by as much as twofold.

Manifestations of Pregnancy

The following symptoms and signs are usually due to pregnancy, but none are diagnostic. A record of the time and frequency of coitus is helpful for diagnosing and dating a pregnancy.

A. Symptoms

Amenorrhea, nausea and vomiting, breast tenderness and tingling, urinary frequency and urgency, "quickening" (perception of first movement noted at about the 18th week), weight gain.

B. Signs (in Weeks From LMP)

Breast changes (enlargement, vascular engorgement, colostrum), abdominal enlargement, cyanosis of vagina and cervical portio (about the seventh week), softening of the cervix (seventh week), softening of the cervicouterine junction (eighth week), generalized enlargement and diffuse softening of the corpus (after eighth week).

The uterine fundus is palpable above the pubic symphysis by 12-15 weeks from the LMP and reaches the umbilicus by 20-22 weeks. Fetal heart tones can be heard by Doppler at 10-12 weeks of gestation and at 20 weeks with an ordinary fetoscope.

Differential Diagnosis

The nonpregnant uterus enlarged by myomas can be confused with the gravid uterus, but it is usually very firm and irregular. An ovarian tumor may be found midline, displacing the nonpregnant uterus to the side or posteriorly. Ultrasonography and a pregnancy test will provide accurate diagnosis in these circumstances.

ESSENTIALS OF PRENATAL CARE

Introduction

The first prenatal visit should occur as early as possible after the diagnosis of pregnancy and should include the following: history, physical examination, laboratory tests, advice to patients, and tests and procedures.

History

Age, ethnic background, occupation. Onset of LMP and its normality, possible conception dates, bleeding after LMP, medical history, all prior pregnancies (duration, outcome, and complications), symptoms of present pregnancy. Use of drugs, alcohol, tobacco, caffeine, nutritional habits ([Table 18-1](#)). Family history of congenital anomalies and heritable diseases. History of childhood varicella. Prior STDs or risk factors for HIV infection.

Physical Examination

Height, weight, blood pressure, general physical examination. Abdominal and pelvic examination: (1) estimate uterine size or measure fundal height; (2) evaluate bony pelvis for symmetry and adequacy; (3) evaluate cervix for structural anatomy, infection, effacement, dilation; (4) detect fetal heart sounds by Doppler device after 10 weeks or fetoscope after 18 weeks.

Laboratory Tests

Urinalysis, culture of a clean-voided midstream urine sample, complete blood count with red cell indices, serologic test for syphilis, rubella antibody titer, blood group, Rh type, atypical antibody screening, and HBsAg evaluation. Human immunodeficiency virus (HIV) screening should be offered to all pregnant women. Cervical cultures are usually obtained for *Neisseria gonorrhoeae* and chlamydia, along with a Papanicolaou smear of the cervix. All black women should have sickle cell screening. Women of African, Asian, or Mediterranean ancestry with anemia or low MCV values should have hemoglobin electrophoresis performed to identify abnormal hemoglobins (Hb S, C, F, α -thalassemia, β -thalassemia). Tuberculosis skin testing is indicated for immigrant and inner city populations. Genetic counseling with the option of chorionic villus sampling or genetic amniocentesis should be offered to all women

who will be 35 years of age or older at delivery and those who have had prior offspring with chromosomal abnormalities. Tay-Sachs blood screening is offered to Jewish women with Jewish partners. Screening for cystic fibrosis is offered to all pregnant women. Hepatitis C antibody screening should be offered only to those pregnant women who are at high risk of infection.

Pregnant women who work in medical-dental health care or the police and fire departments and those who are household contacts of a hepatitis B virus carrier or a hemodialysis patient and are HBsAg-negative at prenatal screening are at high risk of acquiring hepatitis B. They should be vaccinated during pregnancy.

Advice to Patients

A. Prenatal Visits

Prenatal care should begin early and maintain a schedule of regular prenatal visits: 0-28 weeks, every 4 weeks; 28-36 weeks, every 2 weeks; 36 weeks on, weekly.

B. Diet

Eat a balanced diet containing the major food groups.

Take prenatal vitamins with iron and folic acid.

Expect to gain 20-40 lb. Do not diet to lose weight during pregnancy.

Decrease caffeine intake to 0-1 cup of coffee, tea, or caffeinated cola daily.

Avoid eating raw or rare meat, and wash hands after handling raw meat.

Eat fresh fruits and vegetables and wash them before eating.

C. Medications

Do not take medications unless prescribed or authorized by your provider.

D. Alcohol and Other Drugs

Abstain from alcohol, tobacco, and all recreational ("street") drugs. No safe level of alcohol intake has been established for pregnancy. Fetal effects are manifest in the **fetal alcohol syndrome**, which includes growth restriction, facial abnormalities, and serious central nervous system dysfunction. These effects are thought to result from direct toxicity of ethanol itself as well as of its metabolites such as acetaldehyde. Characteristic findings include shortened palpebral fissures, low-set ears, midfacial hypoplasia, a smooth philtrum, a thin upper lip, microcephaly, mental retardation, and attention deficit disorder. Skeletal and cardiac abnormalities may also be seen.

Cigarette smoking results in fetal exposure to carbon monoxide and nicotine, and this is thought to eventuate in a number of adverse pregnancy outcomes. An increased risk of abruptio placentae, placenta previa, and premature rupture of the membranes is documented among women who smoke. Premature delivery occurs 20% more frequently among smoking pregnant women, and the birth weights of their infants are on average 200 g lower than infants of nonsmokers. Women who smoke should quit smoking or at least reduce the number of cigarettes smoked per day to as few as possible. Pregnant women should also avoid exposure to environmental smoke ("passive smoking").

Sometimes compounding the above effects on pregnancy outcome are the independent adverse effects of illicit drugs. Cocaine use in pregnancy is associated with an increased risk of premature rupture of membranes, preterm delivery, placental abruption, intrauterine growth restriction, neurobehavioral deficits, and sudden infant death syndrome. Similar adverse pregnancy effects are associated with amphetamine use, perhaps reflecting the vasoconstrictive potential of both amphetamines and cocaine. Adverse effects associated with opioid use include intrauterine growth restriction, prematurity, and fetal death.

E. X-Rays and Noxious Exposures

Avoid x-rays unless essential and approved by a physician. Inform your dentist and your providers that you are pregnant. Avoid chemical or radiation hazards. Avoid excessive heat in hot tubs or saunas. Avoid handling cat feces or cat litter. Wear gloves when gardening.

F. Rest and Activity

Obtain adequate rest each day. Abstain from strenuous physical work or activities, particularly when heavy lifting or weight bearing is required. Exercise regularly at a mild to moderate level. Avoid exhausting or hazardous exercises or new athletic training programs during pregnancy. Heart rate should be kept below 140 beats/min during exercise.

G. Birth Classes

Enroll with your partner in a childbirth preparation class well before your due date.

Tests & Procedures

A. Each Visit

Weight, blood pressure, fundal height, fetal heart rate, urine specimen for protein and glucose. Review patient's concerns about pregnancy, health, and nutrition.

B. 6-12 Weeks

Confirm uterine size and growth by pelvic examination. Document fetal heart tones (audible at 10-12 weeks of gestation by Doppler). Transvaginal chorionic villus sampling (CVS) between 10 and 12 weeks when indicated or screening for trisomy 18, 21, and cardiac defects using nuchal translucency measurement on sonography, hCG, and pregnancy-associated plasma protein-A (PAPP-A).

C. 12-18 Weeks

Genetic counseling for women age 35 years or older at EDC and those with a family history of congenital anomalies or a previous child with a chromosomal abnormality, metabolic disease, or neural tube defect. Amniocentesis is performed as indicated and requested by the patient.

D. 12-24 Weeks

Fetal ultrasound examination to determine pregnancy dating and evaluate fetal anatomy. An earlier examination provides the most accurate dating, and a later examination demonstrates fetal anatomy in greater detail. The best compromise is at 18-20 weeks of gestation.

E. 16-20 Weeks

Maternal serum a-fetoprotein testing is offered to all women to screen for neural tube defects. In some states, such testing is mandatory. Serum a-fetoprotein is usually combined with measurement of estriol and hCG (triple screen) for the detection of fetal Down's syndrome.

F. 20-24 Weeks

Instruct patient in symptoms and signs of preterm labor and rupture of membranes.

G. 24 Weeks to Delivery

Ultrasound examination is performed as indicated. Typically, fetal size and growth are evaluated when fundal height is 3 cm less than or more than expected for gestational age. In multiple pregnancies, ultrasound should be performed every 4 weeks to evaluate for discordant growth.

H. 26-28 Weeks

Screening for gestational diabetes by a 50-g glucose load (Glucola) and a 1-hour post-Glucola blood glucose determination. Abnormal values should be followed up with a 3-hour glucose tolerance test ([Table 18-3](#)).

I. 28 Weeks

If initial antibody screen is negative, repeat antibody testing for Rh-negative patients, but result is not required before Rh₀(D) immune globulin is administered.

J. 28-32 Weeks

Repeat the complete blood count to evaluate for anemia of pregnancy.

K. 28 Weeks to Delivery

Determination of fetal position and presentation. Question the patient at each visit for symptoms or signs of preterm labor or rupture of membranes. Assess maternal perception of fetal movement at each visit. Antepartum fetal testing is performed as medically indicated.

L. 36 Weeks to Delivery

Repeat syphilis and HIV testing, cervical cultures for *N gonorrhoeae*, and *Chlamydia trachomatis* in at-risk patients. Discuss with the patient the indicators of onset of labor, admission to hospital, management of labor and delivery, and options for analgesia and anesthesia. Weekly cervical examinations are not necessary unless indicated to assess a specific clinical situation. Elective delivery (whether by induction or cesarean section) prior to 39 weeks of gestation requires confirmation of fetal lung maturity.

The CDC has recommended universal prenatal culture-based screening for group B streptococcal colonization in pregnancy. A single standard culture of the distal vagina and anorectum is collected at 35-37 weeks. No prophylaxis is needed if the screening culture is negative. Patients whose cultures are positive receive intrapartum penicillin prophylaxis with labor. Patients with risk factors such as a previous infant with invasive group B streptococcal disease, or group B streptococcal bacteriuria during the pregnancy, or delivery at less than 37 weeks of gestation also receive intrapartum prophylaxis. Patients whose cultures at 35-37 weeks were not done or whose results are not known receive prophylaxis only with the risk factors of intrapartum temperature greater than 38 °C or membrane rupture greater than 18 hours.

The routine recommended regimen for prophylaxis is penicillin G, 5 million units intravenously as a loading dose and then 2.5 million units intravenously every 4 hours until delivery. In penicillin-allergic patients not at high risk for anaphylaxis, one should give cefazolin 2 g intravenously as an initial dose and then 1 g intravenously every 8 hours until delivery. In patients at high risk for anaphylaxis, use vancomycin 1 g intravenously every 12 hours until delivery or, after confirmed susceptibility testing of group B streptococcal isolate, clindamycin 900 mg intravenously every 8 hours or erythromycin 500 mg intravenously every 6 hours until delivery.

M. 41 Weeks and Beyond

Examine the cervix to determine the probability of successful induction of labor. Based on this, induction of labor is undertaken if the cervix is favorable (generally, cervix = 2 cm dilated = 50% effaced, vertex at -1 station, soft cervix, and midposition); if unfavorable, antepartum fetal testing is begun.

Schrag S et al: Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC. MMWR Recomm Rep

2002;51(RR-11):1. [\[PMID: 12211284\]](#)

Vintzileos AM et al: The impact of prenatal care in the United States on preterm births in the presence and absence of antenatal high-risk conditions, Am J Obstet Gynecol, 2002; 187:1254. [\[PMID: 12439515\]](#)

NUTRITION IN PREGNANCY

Nutrition in pregnancy significantly affects maternal health and infant size and well-being. Pregnant women should have nutrition counseling early in prenatal care and access to supplementary food programs if necessary. Counseling should stress abstinence from alcohol, smoking, and recreational drugs. Caffeine and artificial sweeteners should be used only in small amounts. "Empty calories" should be avoided, and the diet should contain the following foods: protein foods of animal and vegetable origin, milk and milk products, whole-grain cereals and breads, and fruits and vegetables — especially green leafy vegetables.

Weight gain in pregnancy should be 20-40 lb, which includes the added weight of the fetus, placenta, and amniotic fluid and of maternal reproductive tissues, fluid, blood, increased fat stores, and increased lean body mass. Maternal fat stores are a caloric reserve for pregnancy and lactation; weight restriction in pregnancy to avoid developing such fat stores may affect the development of other fetal and maternal tissues and is not advisable. Obese women can have normal infants with less weight gain (15-20 lb) but should be encouraged to eat high-quality foods. Normally, a pregnant woman gains 2-5 lb in the first trimester and slightly less than 1 lb/wk thereafter. She needs approximately an extra 200-300 kcal/d (depending on energy output) and 30 g/d of additional protein for a total protein intake of about 75 g/d. Appropriate caloric intake in pregnancy helps prevent the problems associated with low birth weight.

Rigid salt restriction is not necessary. While consumption of highly salted snack foods and prepared foods is not desirable, 2-3 g/d of sodium is permissible. The increased calcium needs of pregnancy (1200 mg/d) can be met with milk, milk products, green vegetables, soybean products, corn tortillas, and calcium carbonate supplements.

The increased need for iron and folic acid should be met from foods as well as vitamin and mineral supplements. (See section on anemia in pregnancy.) Megavitamins should not be taken in pregnancy, as they may result in fetal malformation or disturbed metabolism. However, a balanced prenatal supplement containing 30-60 mg of elemental iron, 0.5-0.8 mg of folate, and the recommended daily allowances of various vitamins and minerals is widely used in the United States and is probably beneficial to many women with marginal diets. There is evidence that periconceptional folic acid supplements can decrease the risk of neural tube defects in the fetus. For this reason, the United States Public Health Service recommends the consumption of 0.4 mg of folic acid per day for all pregnant women (and thus all women capable of becoming pregnant). Women with a prior pregnancy complicated by neural tube defect may require higher supplemental doses as determined by their providers. Lactovegetarians and ovo-lactovegetarians do well in pregnancy; vegetarian women who eat neither eggs nor milk products should have their diets assessed for adequate calories and protein and should take oral vitamin B₁₂ supplements during pregnancy and lactation.

Picciano MF: Pregnancy and lactation: physiological adjustments, nutritional requirements and the role of dietary supplements. J Nutr 2003;133:1997S. [\[PMID: 12771353\]](#)

TRAVEL & IMMUNIZATIONS DURING PREGNANCY

During an otherwise normal low-risk pregnancy, travel can be planned most safely between the 18th and 32nd weeks. Commercial flying in pressurized cabins does not pose a threat to the fetus. An aisle seat will allow frequent walks. Adequate fluids should be taken during the flight.

It is not advisable to travel to endemic areas of yellow fever in Africa or Latin America; similarly, it is inadvisable to travel to areas of Africa or Asia where chloroquine-resistant falciparum malaria is a hazard, since complications of malaria are more common in pregnancy.

Ideally, all immunizations should precede pregnancy. Live virus products are contraindicated (measles, rubella, yellow fever), including smallpox. Inactivated poliovaccine (Salk) can be used instead of the oral vaccine. Vaccines against pneumococcal pneumonia, meningococcal meningitis, and hepatitis A can be used as indicated. Influenza vaccine is indicated in all pregnant women who will be in their second or third trimester during "flu season."

Pooled immune globulin to prevent hepatitis A is safe and does not carry a risk of HIV transmission. Hepatitis A vaccine contains formalin-inactivated virus but can be given in pregnancy when needed. Chloroquine can be used for malaria prophylaxis in pregnancy, and proguanil is also safe.

Water should be purified by boiling, since iodine purification may provide more iodine than is safe during pregnancy.

Do not use prophylactic antibiotics or bismuth subsalicylate during pregnancy to prevent diarrhea. Use oral rehydration fluids, and treat bacterial diarrhea with erythromycin or ampicillin if necessary.

VOMITING OF PREGNANCY (Morning Sickness) & HYPEREMESIS GRAVIDARUM (Pernicious Vomiting of Pregnancy)

Introduction



Essentials of Diagnosis

- Morning or evening nausea and vomiting.
- Persistent vomiting severe enough to result in
- weight loss, dehydration, starvation ketosis, hypochloremic alkalosis, hypokalemia.
- May have transient elevation of liver enzymes.
- Appears related to high or rising serum hCG.
- More common with multiple gestation or hydatidiform mole.

General Considerations

Nausea and vomiting begin soon after the first missed period and cease by the fifth month of gestation. Up to three-fourths of women complain of nausea and vomiting during early pregnancy, with the vast majority noting nausea throughout the day. This problem exerts no adverse effects on the pregnancy and does not presage other complications.

Persistent, severe vomiting during pregnancy — hyperemesis gravidarum — can be disabling and require hospitalization. Thyroid dysfunction can be associated with hyperemesis gravidarum, so it is advisable to determine TSH and free T₄ values in these patients.

Treatment

A. Mild Nausea and Vomiting of Pregnancy

Reassurance and dietary advice are all that is required in most instances. Because of possible teratogenicity, drugs used during the first half of pregnancy should be restricted to those of major importance to life and health. Antiemetics, antihistamines, and antispasmodics are generally unnecessary to treat nausea of pregnancy. Vitamin B₆ (pyridoxine), 50-100 mg/d orally, is nontoxic and may be helpful in some patients.

B. Hyperemesis Gravidarum

Hospitalize the patient in a private room at bed rest. Give nothing by mouth for 48 hours, and maintain hydration and electrolyte balance by giving appropriate parenteral fluids and vitamin supplements as indicated. Rarely, total parenteral nutrition may become necessary. As soon as possible, place the patient on a dry diet consisting of six small feedings daily plus clear liquids 1 hour after eating. Prochlorperazine rectal suppositories may be useful. After in-patient stabilization, the patient can be maintained at home even if she requires intravenous fluids in addition to her oral intake.

Goodwin TM et al: Understanding and treating nausea and vomiting of pregnancy. Sponsored by NICHD. Am J Obstet Gynecol 2002;186(Suppl 5):S181. [\[PMID: 12011884\]](#)

Lacroix R et al: Nausea and vomiting during pregnancy: a prospective study of its frequency, intensity, and patterns of change. Am J Obstet Gynecol 2000;182:931. [\[PMID: 10764476\]](#)

SPONTANEOUS ABORTION

Introduction



Essentials of Diagnosis

- Intrauterine pregnancy at less than 20 weeks.
- Low or falling levels of hCG.
- Bleeding, midline cramping pain.
- Open cervical os.
- Complete or partial expulsion of products of conception.

General Considerations

About three-fourths of spontaneous abortions occur before the 16th week; of these, three-fourths occur before the eighth week. Almost 20% of all clinically recognized pregnancies terminate in spontaneous abortion.

More than 60% of spontaneous abortions result from chromosomal defects due to maternal or paternal factors; about 15% appear to be associated with maternal trauma, infections, dietary deficiencies, diabetes mellitus, hypothyroidism, or anatomic malformations. There is no reliable evidence that abortion may be induced by psychic stimuli such as severe fright, grief, anger, or anxiety. In about one-fourth of cases, the cause of abortion cannot be determined. There is no evidence that video display terminals or associated electromagnetic fields are related to an increased risk of spontaneous abortion.

It is important to distinguish women with a history of incompetent cervix from those with more typical early abortion and those with premature labor or rupture of the membranes. Characteristically, incompetent cervix presents as "silent" cervical dilation (ie, with minimal uterine contractions) between 16 and 28 weeks of gestation. Women with incompetent cervix often present with significant cervical dilation (2 cm or more) and minimal symptoms. When the cervix reaches 4 cm or more, active uterine contractions or rupture of the membranes may occur secondary to the degree of cervical dilation. This does not change the primary diagnosis. Factors that predispose to incompetent cervix are a history of incompetent cervix with a previous pregnancy, cervical conization or surgery, cervical injury, DES exposure, and anatomic abnormalities of the cervix. Prior to pregnancy or during the first trimester, there are no methods for determining whether the cervix will eventually be incompetent. After 14-16 weeks, ultrasound may be used to evaluate the internal anatomy of the lower uterine segment and cervix for the funneling and shortening abnormalities consistent with cervical incompetence.

Clinical Findings

A. Symptoms and Signs

1. Threatened abortion —

Bleeding or cramping occurs, but the pregnancy continues. The cervix is not dilated.

2. Inevitable abortion —

The cervix is dilated and the membranes may be ruptured, but passage of the products of conception has not occurred. Bleeding and cramping persist, and passage of the products of conception is considered inevitable.

3. Complete abortion —

The fetus and placenta are completely expelled. Pain ceases, but spotting may persist.

4. Incomplete abortion —

Some portion of the products of conception (usually placental) remain in the uterus. Only mild cramps are reported, but bleeding is persistent and often excessive.

5. Missed abortion —

The pregnancy has ceased to develop, but the conceptus has not been expelled. Symptoms of pregnancy disappear. There is a brownish vaginal discharge but no free bleeding. Pain does not develop. The cervix is semifirm and slightly patulous; the uterus becomes smaller and irregularly softened; the adnexa are normal.

B. Laboratory Findings

Pregnancy tests show low or falling levels of hCG. A complete blood count should be obtained if bleeding is heavy. Determine Rh type, and give Rh₀(D) immune globulin if the type is Rh-negative. All tissue recovered should be assessed by a pathologist and may be sent for genetic analysis in selected cases.

C. Ultrasonographic Findings

The gestational sac can be identified at 5-6 weeks from the LMP, a fetal pole at 6 weeks, and fetal cardiac activity at 6-7 weeks. Serial observations are often required to evaluate changes in size of the embryo. A small, irregular sac without a fetal pole with accurate dating is diagnostic of an abnormal pregnancy.

Differential Diagnosis

The bleeding that occurs in abortion of a uterine pregnancy must be differentiated from the abnormal bleeding of an ectopic pregnancy and anovular bleeding in a nonpregnant woman. The passage of hydropic villi in the bloody discharge is diagnostic of hydatidiform mole.

Treatment

A. General Measures

1. Threatened abortion —

Place the patient at bed rest for 24-48 hours followed by gradual resumption of usual activities, with abstinence from coitus and douching. Hormonal treatment is contraindicated. Antibiotics should be used only if there are signs of infection.

2. Missed or inevitable abortion —

This calls for counseling regarding the fate of the pregnancy and planning for its elective termination at a time chosen by the patient and physician. Insertion of a laminaria to dilate the cervix followed by aspiration is the method of choice for a missed abortion. Prostaglandin vaginal suppositories are an effective alternative.

B. Surgical Measures

1. Incomplete abortion —

Prompt removal of any products of conception remaining within the uterus is required to stop bleeding and prevent infection. Analgesia and a paracervical block are useful, followed by uterine exploration with ovum forceps or uterine aspiration.

2. Cerclage and restriction of activities —

These are the treatment of choice for incompetent cervix. A variety of suture materials including a 5-mm Mersilene band can be used to create a purse-string type of stitch around the cervix, using either the McDonald or Shirodkar method. Cerclage should be undertaken with caution when there is advanced cervical dilation or when the membranes are prolapsed into the vagina. Rupture of the membranes and infection are specific contraindications to cerclage. Cervical cultures for *N gonorrhoeae*, chlamydia, and group B streptococci should be obtained before or at the time of cerclage.

George L et al: Plasma folate levels and risk of spontaneous abortion. JAMA 2002;288:1867. [\[PMID: 12377085\]](#)

RECURRENT (HABITUAL) ABORTION

Introduction

Recurrent abortion has been defined as the loss of three or more previable (< 500 g) pregnancies in succession. Recurrent abortion occurs in about 0.4-0.8% of all pregnancies. Abnormalities related to recurrent abortion can be identified in approximately half of the couples. If a woman has lost three previous pregnancies without identifiable cause, she still has a 70-80% chance of carrying a fetus to viability. If she has aborted four or five times, the likelihood of a successful pregnancy is 65-70%.

Recurrent abortion is a clinical rather than pathologic diagnosis. The clinical findings are similar to those observed in other types of abortion (see above).

Treatment

A. Preconception Therapy

Preconception therapy is aimed at detection of maternal or paternal defects that may contribute to abortion. A thorough general and gynecologic examination is essential. Polycystic ovaries should be ruled out. A random blood glucose test and thyroid function studies (including thyroid antibodies) should be done. Detection of lupus anticoagulant and other hemostatic abnormalities (proteins S and C and antithrombin III deficiency, hyperhomocysteinemia, anticardiolipin antibody, factor V Leiden mutations) and an antinuclear antibody test may be indicated with second trimester losses. Endometrial tissue should be examined in the postovulation stage of the cycle to determine the adequacy of the response of the endometrium to hormones. The competency of the cervix must be determined and hysteroscopy or hysterothorgraphy used to exclude submucous myomas and congenital anomalies. Chromosomal (karyotype) analysis of both partners rules out balanced translocations (found in 5% of infertile couples).

Studies have focused on the major histocompatibility complex (MHC) of chromosome 6, which carries HLA loci and other genes that may influence reproductive success. Some women demonstrate a lack of maternal antibody response to paternal lymphocytes, which is customarily found in normal women after successful childbearing. However, several randomized controlled trials have found no benefit of IGIV therapy for recurrent spontaneous abortion.

B. Postconception Therapy

Provide early prenatal care and schedule frequent office visits. Complete bed rest is justified only for bleeding or pain. Empiric sex steroid hormone therapy is contraindicated.

Prognosis

The prognosis is excellent if the cause of abortion can be corrected.

Management of recurrent pregnancy loss. ACOG Practice Bulletin No. 24, 2001. Int J Gynaecol Obstet 2002;78:179. [\[PMID: 12360906\]](#)

ECTOPIC PREGNANCY

Introduction



Essentials of Diagnosis

- Amenorrhea or irregular bleeding and spotting.
- Pelvic pain, usually adnexal.
- Adnexal mass by clinical examination or ultrasound.
- Failure of serum level of hCG to double every 48 hours.
- No intrauterine pregnancy on transvaginal ultrasound with serum β -hCG of < 2000 mU/mL.

General Considerations

Ectopic implantation occurs in about one out of 150 live births. About 98% of ectopic pregnancies are tubal. Other sites of ectopic implantation are the peritoneum or abdominal viscera, the ovary, and the cervix. Any condition that prevents or retards migration of the fertilized ovum to the uterus can predispose to an ectopic pregnancy, including a history of infertility, pelvic inflammatory disease, ruptured appendix, and prior tubal surgery. Combined intra- and extrauterine pregnancy (heterotopic) may occur rarely. In the United States, undiagnosed or undetected ectopic pregnancy is currently the most common cause of maternal death during the first trimester.

Clinical Findings

A. Symptoms and Signs

They may be acute or chronic.

1. Acute (40%) —

Severe lower quadrant pain occurs in almost every case. It is sudden in onset, lancinating, intermittent, and does not radiate. Backache is present during attacks. Shock occurs in about 10%, often after pelvic examination. At least two-thirds of patients give a history of abnormal menstruation; many have been infertile.

2. Chronic (60%) —

Blood leaks from the tubal ampulla over a period of days, and considerable blood may accumulate in the peritoneum. Slight but persistent vaginal spotting is reported, and a pelvic mass can be palpated. Abdominal distention and mild paralytic ileus are often present.

B. Laboratory Findings

Blood studies may show anemia and slight leukocytosis. Quantitative serum pregnancy tests will show levels generally lower than expected for normal pregnancies of the same duration. If pregnancy tests are followed over a few days, there may be a slow rise or a plateau rather than the near doubling every 2 days associated with normal early intrauterine pregnancy or the falling levels that occur with spontaneous abortion.

C. Imaging

Ultrasonography can reliably demonstrate a gestational sac 6 weeks from the LMP and a fetal pole at 7 weeks if located in the

uterus. An empty uterine cavity raises a strong suspicion of extrauterine pregnancy, which can occasionally be revealed by endovaginal ultrasound. Specified levels of serum hCG have been reliably correlated with ultrasound findings of an intrauterine pregnancy. For example, an hCG level of 6500 mU/mL with an empty uterine cavity by transabdominal ultrasound is virtually diagnostic of an ectopic pregnancy. Similarly, an hCG value of 2000 mU/mL or more can be indicative of an ectopic pregnancy if no products of conception are detected within the uterine cavity by transvaginal ultrasound.

D. Special Examinations

With the advent of high-resolution transvaginal ultrasound, culdocentesis is rarely used in evaluation of possible ectopic pregnancy. Laparoscopy is the surgical procedure of choice both to confirm an ectopic pregnancy and in most cases to permit pelviscopic removal of the ectopic pregnancy without the need for exploratory laparotomy.

Differential Diagnosis

Clinical and laboratory findings suggestive or diagnostic of pregnancy will distinguish ectopic pregnancy from many acute abdominal illnesses such as acute appendicitis, acute pelvic inflammatory disease, ruptured corpus luteum cyst or ovarian follicle, and urinary calculi. Uterine enlargement with clinical findings similar to those found in ectopic pregnancy is also characteristic of an aborting uterine pregnancy or hydatidiform mole. Ectopic pregnancy should be suspected when postabortal tissue examination fails to reveal placenta. Steps must be taken for immediate diagnosis, including prompt microscopic tissue examination, ultrasonography, and serial hCG titers every 48 hours. Patients must be warned of possible ectopic pregnancy problems and followed very closely.

Treatment

When a patient with an ectopic pregnancy is unstable or when surgical therapy is planned, the patient is hospitalized. Blood is typed and cross-matched. Ideally, diagnosis and operative treatment should precede frank rupture of the tube and intra-abdominal hemorrhage.

Surgical treatment is definitive. In a stable patient, diagnostic laparoscopy is the initial surgical procedure performed. Depending on the size of the ectopic pregnancy and whether or not it has ruptured, salpingostomy with removal of the ectopic or a partial or complete salpingectomy can usually be performed pelviscopically. Clinical conditions permitting, patency of the contralateral tube can be established by injection of indigo carmine into the uterine cavity and flow through the contralateral tube confirmed visually by the surgeon.

In a stable patient, methotrexate (50 mg/m^2) — given systemically as single or multiple doses — is acceptable medical therapy for early ectopic pregnancy. Favorable criteria are that the pregnancy should be less than 3.5 cm in largest dimension and unruptured, with no active bleeding.

Iron therapy for anemia may be necessary during convalescence. Give Rh₀(D) immune globulin (300 ug) to Rh-negative patients.

Prognosis

Repeat tubal pregnancy occurs in about 12% of cases. This should not be regarded as a contraindication to future pregnancy, but the patient requires careful observation and early ultrasound confirmation of an intrauterine pregnancy.

Hajenius PJ et al: Interventions for tubal ectopic pregnancy. Cochrane Database Syst Rev 2000;(2):CD000324. [\[PMID: 10796710\]](#)

Lipscomb GH et al: Oral methotrexate for treatment of ectopic pregnancy. Am J Obstet Gynecol 2002;186:1192. [\[PMID: 12066097\]](#)

PREECLAMPSIA-ECLAMPSIA

Introduction



Essentials of Diagnosis

Preeclampsia

- Blood pressure of ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic after 20 weeks of gestation.
- Proteinuria of ≥ 0.3 g in 24 hours.

Severe Preeclampsia

- Blood pressure of ≥ 160 mm Hg systolic or ≥ 110 mm Hg diastolic.
- Proteinuria ≥ 5 g in 24 hours or 4+ on dipstick.
- Oliguria of < 500 mL in 24 hours.
- Thrombocytopenia.
- Hemolysis, elevated liver enzymes, low platelets (HELLP).
- Pulmonary edema.
- Fetal growth restriction.

General Considerations

Preeclampsia is defined as the presence of elevated blood pressure and proteinuria during pregnancy. Eclampsia occurs with the addition of seizures. Classically, the presence of three elements was required for the diagnosis of preeclampsia-eclampsia: hypertension, proteinuria, and edema. Edema was difficult to objectively quantify and is no longer a required element.

Preeclampsia-eclampsia can occur any time after 20 weeks of gestation and up to 6 weeks postpartum. It is a disease unique to pregnancy, with the only cure being delivery of the fetus and placenta. Approximately 7% of pregnant women in the United States develop preeclampsia-eclampsia. Primiparas are most frequently affected; however, the incidence of preeclampsia-eclampsia is

increased with multiple pregnancies, chronic hypertension, diabetes, renal disease, collagen-vascular and autoimmune disorders, and gestational trophoblastic disease. Five percent of women with preeclampsia progress to eclampsia. Uncontrolled eclampsia is a significant cause of maternal death.

The basic cause of preeclampsia-eclampsia is not known. Epidemiologic studies suggest an immunologic cause for preeclampsia, since it occurs predominantly in women who have had minimal exposure to sperm (having used barrier methods of contraception) or have new consorts, in primigravidas, and in women both of whose parents have similar HLA antigens. Preeclampsia is an endothelial disorder resulting from poor placental perfusion, which releases a factor that injures the endothelium, causing activation of coagulation and an increased sensitivity to pressors. Before the syndrome becomes clinically manifest in the second half of pregnancy, there has been vasospasm in various small vessel beds, accounting for the pathologic changes in maternal organs and the placenta with consequent adverse effects on the fetus.

The use of diuretics, dietary restriction or enhancement, sodium restriction, aspirin, and vitamin-mineral supplements such as calcium or vitamin C and E have not yet been shown to be useful in clinical studies. The only cure is termination of the pregnancy at a time as favorable as possible for fetal survival.

Clinical Findings

Clinically, the severity of preeclampsia-eclampsia can be measured with reference to the six major sites in which it exerts its effects: the central nervous system, the kidneys, the liver, the hematologic and vascular systems, and the fetal-placental unit. By evaluating each of these areas for the presence of mild to moderate versus severe preeclampsia-eclampsia, the degree of involvement can be assessed, and an appropriate management plan can be formulated that is integrated with gestational age assessment ([Table 18-2](#)).

A. Preeclampsia

1. Mild to moderate —

Precise differentiation between mild and moderate preeclampsia is difficult because the abnormalities that define the disease are quite variable and fail to accurately predict progression to more severe disease. Symptoms are generally minimal or mild. With mild preeclampsia, patients usually have few complaints, and the diastolic blood pressure is less than 90-100 mm Hg. Edema is usually more pronounced with moderate disease, and diastolic blood pressures are in the range of 90-110 mm Hg. The platelet count is over 100,000/uL, antepartum fetal testing is reassuring, central nervous system irritability is minimal, epigastric pain is not present, and liver enzymes are not elevated.

2. Severe —

Symptoms are more dramatic and persistent. The blood pressure is often quite high, with readings over 160/110 mm Hg. Thrombocytopenia (platelet counts < 100,000/uL) may be present and progress to disseminated intravascular coagulation. Severe epigastric pain may be present from hepatic subcapsular hemorrhage with significant stretch or rupture of the liver capsule. The HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) is a form of severe preeclampsia.

B. Eclampsia

The occurrence of seizures defines eclampsia. It is a manifestation of severe central nervous system involvement. The other abnormal findings of severe preeclampsia are also observed with eclampsia.

Differential Diagnosis

Preeclampsia-eclampsia can mimic and be confused with many other diseases, including chronic hypertension, chronic renal disease, primary seizure disorders, gallbladder and pancreatic disease, immune or thrombotic thrombocytopenic purpura, and hemolytic uremic syndrome. It must always be considered a possibility in any pregnant woman beyond 20 weeks of gestation. It is particularly difficult to diagnose when preexisting disease such as hypertension is present. Uric acid values can be quite helpful in such situations, since hyperuricemia is uncommon in pregnancy except with gout, renal failure, or preeclampsia-eclampsia.

Treatment

A. Preeclampsia

Early recognition is the key to treatment. This requires careful attention to the details of prenatal care — especially subtle changes in blood pressure and weight. The objectives are to prolong pregnancy if possible, to allow fetal lung maturity while preventing progression to severe disease and eclampsia. The critical factors are the gestational age of the fetus, fetal pulmonary maturity status, and the severity of maternal disease. Preeclampsia-eclampsia at 36 weeks or more of gestation is managed by delivery regardless of how mild the disease is judged to be. Prior to 36 weeks, severe preeclampsia-eclampsia requires delivery except in unusual circumstances associated with extreme fetal prematurity, in which case prolongation of pregnancy may be attempted. Epigastric pain, thrombocytopenia, and visual disturbances are strong indications for delivery of the fetus. For mild to moderate preeclampsia-eclampsia, bed rest is the cornerstone of therapy. This increases central blood flow to the kidneys, heart, brain, liver, and placenta and may stabilize or even improve the degree of preeclampsia-eclampsia for a period of time.

Bed rest may be attempted at home or in the hospital. Prior to making this decision, the provider should evaluate the six sites of involvement listed in [Table 18-2](#) and make an assessment about the severity of disease.

1. Home management —

Home management with bed rest may be attempted for patients with mild preeclampsia and a stable home situation. This requires homemaking assistance, rapid access to the hospital, a reliable patient, and the ability to obtain frequent blood pressure readings. A home health nurse can often provide frequent home visits and assessment.

2. Hospital care —

Hospitalization is required for women with moderate or severe preeclampsia or those with unreliable home situations. Regular

assessment of blood pressure, reflexes, urine protein, and fetal heart tones and activity are required. A complete blood count, platelet count, and electrolyte panel including liver enzymes should be checked every 1 or 2 days. A 24-hour urine collection for creatinine clearance and total protein should be obtained on admission and repeated as indicated. Sedatives and opioids should be avoided because the fetal central nervous system depressant effects interfere with fetal testing. Magnesium sulfate is not used until the diagnosis of severe preeclampsia-eclampsia is made or until labor occurs.

Fetal evaluation should be obtained as part of the workup. If the patient is being admitted to the hospital, fetal testing must be performed on the same day to make certain that the fetus is safe. This may be done by fetal heart rate testing with nonstress or stress testing or by biophysical profile. A regular schedule of fetal surveillance must then be followed. Daily fetal kick counts can be recorded by the patient herself. Consideration should be given to amniocentesis to evaluate fetal lung maturity status if hospitalization occurs at 30-37 weeks of gestation. If immaturity is present, steroids (betamethasone 12 mg or dexamethasone 16 mg, two doses intramuscularly 12-24 hours apart) can be administered to the mother. Fetuses between 26 and 30 weeks of gestation can be presumed to be immature, and steroids should be given.

The method of delivery is determined by the maternal and fetal status. Cesarean section is reserved for the usual fetal indications.

B. Eclampsia

1. Emergency care —

If the patient is convulsing, she is turned on her side to prevent aspiration and to improve blood flow to the placenta. Fluid or food is aspirated from the glottis or trachea. The seizure may be stopped by giving an intravenous bolus of either magnesium sulfate, 4 g, or diazepam, 5-10 mg, over 4 minutes or until the seizure stops. A continuous intravenous infusion of magnesium sulfate is then started at a rate of 2-3 g/h unless the patient is known to have significantly reduced renal function. Magnesium blood levels are then checked every 4-6 hours and the infusion rate adjusted to maintain a therapeutic blood level (4-6 meq/L). Urinary output is checked hourly and the patient assessed for signs of possible magnesium toxicity such as loss of deep tendon reflexes or decrease in respiratory rate and depth, which can be reversed with calcium gluconate.

2. General care —

The occurrence of eclampsia necessitates delivery once the patient is stabilized. It is important, however, that assessment of the status of the patient and fetus take place first. Continuous fetal monitoring must be performed and blood typed and cross-matched quickly. A urinary catheter is inserted to monitor urinary output, and blood is sent for complete blood count, platelets, liver enzymes, uric acid, creatinine or urea nitrogen, and electrolytes. If hypertension is present with diastolic values over 110 mm Hg, antihypertensive medications should be administered to reduce the diastolic blood pressure to 90-100 mm Hg. Lower blood pressures than this may induce placental insufficiency through reduced perfusion. Hydralazine given in 5- to 10-mg increments intravenously every 20 minutes is frequently used to lower blood pressure. Nifedipine, 10 mg sublingually or orally, or labetalol, 10-20 mg intravenously, both every 20 minutes, can also be used.

3. Delivery —

Except in unusual circumstances, delivery is mandated once eclampsia has occurred. Vaginal delivery may be attempted if the patient has already been in active labor or the cervix is quite favorable *and* the patient is clinically stable. The rapidity with which delivery must be achieved depends on the fetal and maternal status following the seizure and the availability of laboratory data on the patient. Oxytocin may be used to induce or augment labor. Regional analgesia or anesthesia is acceptable. Cesarean section is used for the usual obstetric indications or when rapid delivery is necessary for maternal or fetal indications.

4. Postpartum —

Magnesium sulfate infusion (2-3 g/h) should be continued until preeclampsia-eclampsia has begun to resolve postpartum, but in any case for at least 24 hours. This may take 1-7 days. The most reliable indicator of this resolution is the onset of diuresis with urinary output of over 100-200 mL/h. When this occurs, magnesium sulfate can be discontinued. Late-onset preeclampsia-eclampsia can occur during the postpartum period. It is usually manifested by either hypertension or seizures. Treatment is the same as prior to delivery — ie, with magnesium sulfate — though other antiseizure medications can be used since the fetus is no longer present.

Diagnosis and management of pre-eclampsia and eclampsia. ACOG Practice Bulletin No. 33, 2002. Int J Gynaecol Obstet 2002;77:67. [\[PMID: 12094777\]](#)

Lain KY et al: Contemporary concepts of the pathogenesis and management of preeclampsia. JAMA 2002;287:3183. [\[PMID: 12076198\]](#)

GESTATIONAL TROPHOBLASTIC DISEASE (Hydatidiform Mole & Choriocarcinoma)

Introduction



Essentials of Diagnosis

Hydatidiform Mole

- Amenorrhea.
- Irregular uterine bleeding.
- Serum hCG β -subunit < 40,000 mU/mL.
- Passage of grape-like clusters of enlarged edematous villi per vagina.
- Ultrasound of uterus with characteristic "snowstorm" image and no fetus or placenta.
- Cytogenetic composition is 46,XX (85%), completely of paternal origin.

General Considerations

Gestational trophoblastic disease is a spectrum of disorders that includes hydatidiform mole, invasive mole, and choriocarcinoma. Partial moles generally show evidence of an embryo or gestational sac; are polyploid, slower-growing, and less symptomatic; and often present clinically as a missed abortion. Partial moles tend to follow a benign course, while complete moles have a greater tendency to become choriocarcinomas.

The highest rates of gestational trophoblastic disease occur in some developing countries, with rates of 1:125 pregnancies in certain areas of Asia. In the United States, the frequency is 1:1500 pregnancies. Risk factors include low socioeconomic status, a history of mole, and age below 18 or above 40. Approximately 10% of women require further treatment after evacuation of the mole; 5% develop choriocarcinoma.

Clinical Findings

A. Symptoms and Signs

Excessive nausea and vomiting occur in over one-third of patients with hydatidiform mole. Uterine bleeding, beginning at 6-8 weeks, is observed in virtually all instances. In about one-fifth of cases, the uterus is larger than would be expected in a normal pregnancy of the same duration. Bilaterally enlarged cystic ovaries are sometimes palpable. They are the result of ovarian hyperstimulation due to excess of hCG.

Preeclampsia-eclampsia, frequently of the fulminating type, may develop during the second trimester of pregnancy, but this is unusual.

Choriocarcinoma may be manifested by continued or recurrent uterine bleeding after evacuation of a mole or following delivery, abortion, or ectopic pregnancy. The presence of an ulcerative vaginal tumor, pelvic mass, or evidence of distant metastatic tumor may be the presenting observation. The diagnosis is established by pathologic examination of curettings or by biopsy.

B. Laboratory Findings

A serum hCG β -subunit value above 40,000 mU/mL or a urinary hCG value in excess of 100,000 units/24 h increases the likelihood of hydatidiform mole.

C. Imaging

Ultrasound has virtually replaced all other means of preoperative diagnosis of hydatidiform mole. A preoperative chest film is indicated to rule out pulmonary metastases of trophoblast.

Treatment

A. Specific (Surgical) Measures

The uterus should be emptied as soon as the diagnosis of hydatidiform mole is established, preferably by suction. Ovarian cysts should not be resected nor ovaries removed; spontaneous regression of theca lutein cysts will occur with elimination of the mole.

If malignant tissue is discovered at surgery or during the follow-up examination, chemotherapy is indicated.

Thyrotoxicosis indistinguishable clinically from that of thyroid origin may occur. While hCG usually has minimal TSH-like activity, the very high hCG levels associated with moles result in the release of T_3 and T_4 and cause hyperthyroidism. Patients thyrotoxic on this basis should be stabilized with β -blockers prior to induction of anesthesia for their surgical evacuation. Surgical removal of the mole promptly corrects the thyroid overactivity.

B. Follow-Up Measures

Effective contraception (preferably birth control pills) should be prescribed. Weekly quantitative hCG level measurements are initially required. Following successful surgical evacuation, moles show a progressive decline in hCG. After two negative weekly tests (< 5 mU/mL), the interval may be increased to monthly for 6 months and then to every 2 months for a total of 1 year. If levels plateau or begin to rise, the patient should be evaluated by repeat chest film and D&C before the initiation of chemotherapy.

C. Antitumor Chemotherapy

For low-risk patients with a good prognosis, methotrexate, 0.4 mg/kg intramuscularly over a 5-day period, or dactinomycin, 10-12 μ g/kg/d intravenously over a 5-day period, is used (see [Table 40-3](#)). Patients with a poor prognosis should be referred to a cancer center, where multiple-agent chemotherapy probably will be given. The side effects — anorexia, nausea and vomiting, stomatitis, rash, diarrhea, and bone marrow depression — usually are reversible in about 3 weeks and can be ameliorated by the administration of leucovorin (0.1 mg/kg). Repeated courses of methotrexate 2 weeks apart generally are required to destroy the trophoblast and maintain a zero chorionic gonadotropin titer, as indicated by β -hCG determination.

D. Supportive Measures

Oral contraceptives (if acceptable) or another reliable birth control method should be prescribed to avoid the hazard and confusion of elevated hCG from a new pregnancy. The hCG levels should be negative for a year before pregnancy is again attempted. In the pregnancy following a mole, the hCG level should be checked 6 weeks postpartum.

Prognosis

Five years survival after courses of chemotherapy, even when metastases have been demonstrated, can be expected in at least 85% of cases of choriocarcinoma.

Seckl MJ et al: Choriocarcinoma and partial hydatidiform moles. *Lancet* 2000;356:36. [\[PMID: 10892763\]](#)

Shapter AP et al: Gestational trophoblastic disease. *Obstet Gynecol Clin North Am* 2001;28:805. [\[PMID: 11766153\]](#)

THIRD-TRIMESTER BLEEDING

Five to 10 percent of women have vaginal bleeding in late pregnancy. The clinician must distinguish between placental causes (placenta previa, placental abruption, vasa previa) and nonplacental causes (infection, disorders of the lower genital tract, systemic disease). The approach to bleeding in late pregnancy should be conservative and expectant unless fetal distress or risk of maternal hemorrhage occurs.

The patient should be hospitalized and placed at bed rest with continuous fetal monitoring. A complete blood count (including platelets) should be obtained and two to four units of blood typed and cross-matched. Coagulation studies should be ordered as clinically indicated. Ultrasound examination should be performed to determine placental location. Speculum and digital pelvic examinations are done only after ultrasound study has ruled out placenta previa. Continuous electronic fetal monitoring is required to exclude fetal distress. While uterine contractions, pain, or tenderness often indicate associated abruptio placentae, an ultrasound negative for retroplacental clot does not exclude it.

If the patient is at less than 36 weeks of gestation, continued hospitalization and bed rest may be necessary, especially with placenta previa during the initial 7-10 days following vaginal bleeding. If the patient has close proximity to the hospital and immediate access, can be on strict bed rest, and has complete resolution of bleeding and uterine contractions, home management may be considered. She must be well instructed and counseled regarding the risks. Patients with vaginal bleeding at less than 36 weeks of gestation should also be considered for amniocentesis to test for fetal lung maturity. Steroid therapy (betamethasone 12 mg intramuscularly, two doses 12-24 hours apart) is indicated if fetal lung immaturity is present.

Hadlky K et al: Placental abruption. *Obstet Gynecol Surv* 2002; 57:299. [\[PMID: 11997676\]](#)

MEDICAL CONDITIONS COMPLICATING PREGNANCY

Anemia

Plasma volume increases 50% during pregnancy, while red cell volume increases 25%, causing lower hemoglobin and hematocrit values, which are maximally changed around the 24th to 28th weeks. Anemia in pregnancy is often defined as a hemoglobin measurement below 10 g/dL or hematocrit below 30%. Anemia is very common in pregnancy, causing fatigue, anorexia, dyspnea, and edema. Prevention through optimal nutrition and iron and folic acid supplementation is desirable.

A. Iron Deficiency Anemia

Many women enter pregnancy with low iron stores resulting from heavy menstrual periods, previous pregnancies, breast feeding, or poor nutrition. It is difficult to meet the increased requirement for iron through diet, and anemia often develops unless iron supplements are given. Red cells may not become hypochromic and microcytic until the hematocrit has fallen significantly. When this occurs, a serum iron level below 40 ug/dL and a transferrin saturation less than 10% suggest iron deficiency anemia (see [Chapter 13](#)). Treatment consists of a diet containing iron-rich foods and 60 mg of elemental iron (eg, 300 mg of ferrous sulfate) three times a day with meals. Iron is best absorbed if taken with a source of vitamin C (raw fruits and vegetables, lightly cooked greens). All pregnant women should take daily iron supplements.

B. Folic Acid Deficiency Anemia

Folic acid deficiency anemia is the main cause of macrocytic anemia in pregnancy, since vitamin B₁₂ deficiency anemia is rare in the childbearing years. The daily requirement of folic acid doubles from 0.4 mg to 0.8 mg in pregnancy. Twin pregnancies, infections, malabsorption, and use of anticonvulsant drugs such as phenytoin can precipitate folic acid deficiency. The anemia may first be seen in the puerperium owing to the increased need for folate during lactation.

The diagnosis is made by finding macrocytic red cells and hypersegmented neutrophils in a blood smear (see [Chapter 13](#)). However, blood smears in pregnancy may be difficult to interpret, since they frequently show iron deficiency changes as well. Because the deficiency is hard to diagnose and folate intake is inadequate in some socioeconomic groups, 0.8-1 mg of folic acid is given as a supplement in pregnancy; the dose in established deficiency is 1-5 mg/d.

Good sources of folate in food are leafy green vegetables, orange juice, peanuts, and beans. Cooking and storage of food destroy folic acid. Strict vegetarians who eat no eggs or milk products should take vitamin B₁₂ supplements during pregnancy and lactation.

C. Sickle Cell Anemia

Women with sickle cell anemia are subject to serious complications in pregnancy. The anemia becomes more severe, and crises may occur more frequently. Complications include infections, bone pain, pulmonary infarction, congestive heart failure, and preeclampsia. There is an increased rate of spontaneous abortion and higher maternal and perinatal mortality rates. Intensive medical treatment may improve the outcome for mother and fetus. Frequent indicated transfusions of packed cells or leukocyte-poor washed red cells lower the level of hemoglobin S and elevate the level of hemoglobin A; this minimizes the severity of anemia and the risk of sickle cell crises.

Genetic counseling should be offered to patients with sickle cell disease or sickle trait. They may wish to undergo first-trimester chorionic villus biopsy or second-trimester amniocentesis to determine whether the abnormality has been passed on to the fetus. IUDs and oral contraceptives are relatively contraindicated, but progestin-only contraceptives may be used. Women with sickle cell trait alone usually have an uncomplicated gestation except for an increased risk of urinary tract infection. Sickle cell-hemoglobin C disease in pregnancy is similar to sickle cell anemia and is treated similarly.

Allen LH: Anemia and iron deficiency: effects on pregnancy outcome. *Am J Clin Nutr* 2000;71(5 Suppl):1280S. [\[PMID: 10799402\]](#)

Lupus Anticoagulant-Anticardiolipin-Antiphospholipid Antibody Syndrome

The presence of antibodies to phospholipids and a variety of clinical symptoms, including vascular thromboses, thrombocytopenia, and recurrent pregnancy loss, characterize the lupus anticoagulant-anticardiolipin-antiphospholipid antibody syndrome. Many of these patients have SLE-like symptoms but do not meet specific diagnostic criteria for that disease. The lupus anticoagulant and

anticardiolipin antibody may occur in these patients, and both may cause arterial and venous thromboses. Detection of these antiphospholipid antibodies may require a combination of laboratory tests. The lupus anticoagulant will prolong both the partial thromboplastin time (PTT) and the Russell viper venom time. The latter is a more sensitive predictor of disease. Such patients should also be screened for the presence of the factor V Leiden mutation. Anticardiolipin antibody may be detected with ELISA testing. Either antibody may cause false-positive serologic tests for syphilis.

This syndrome may require treatment with anticoagulant medications. In a small number of patients with recurrent pregnancy loss and a diagnosis of lupus anticoagulant syndrome, improved outcomes have been reported following treatment with heparin anticoagulation (8000-20,000 units in two or three doses daily) or low-molecular-weight heparin (1 mg/kg twice daily) and low-dose aspirin begun before or early in pregnancy and continued until the postpartum period. The addition of monthly infusions of IGIV to this regimen did not improve outcomes in such patients.

Levine JS et al: The antiphospholipid syndrome. *N Engl J Med* 2002;346:752. [\[PMID: 11882732\]](#)

Tincani A et al: Treatment of pregnant patients with antiphospholipid syndrome. *Lupus* 2003;12:524. [\[PMID: 12892392\]](#)

Asthma

The effect of pregnancy on asthma is unpredictable. About 50% of patients have no change, 25% improve, and 25% get worse. Management of acute and chronic asthma during pregnancy does not differ significantly from that of nonpregnant women. The goal is to maintain maternal PO₂ < 80 mm Hg to sustain normal fetal oxygenation (see [Chapter 9](#)).

The use of newer asthma and allergy medications during pregnancy. ACOG and ACAAI. *Ann Allergy Asthma Immunol* 2000;84:475. [\[PMID: 10830999\]](#)

AIDS During Pregnancy

Heterosexual acquisition (51%) and injecting drug use (45%) are the principal modes of HIV infection in women. In 15%, no risk factor is reported or identified. Asymptomatic infection is associated with a normal pregnancy rate and no increased risk of adverse pregnancy outcomes. There is no evidence that pregnancy causes AIDS progression.

Although some fetuses appear to acquire HIV infection antenatally by transplacental transmission, approximately two-thirds are infected close to or during the time of delivery. Zidovudine (500 mg/d orally) given to the mother antenatally starting at 14 weeks of gestation and during labor (1 mg/kg/h intravenously) and then to the infant (2 mg/kg orally four times daily) for the first 6 weeks of life reduces the transmission rate from 25% to 8%. Pregnancy does not preclude the use of combinations of highly active antiretroviral therapy (HAART). HIV-positive pregnant women should be assessed by CD4 count, plasma RNA levels, and prior or current antiretroviral use. In general, pregnant HIV-positive women should receive at least zidovudine but also HAART as appropriate for their HIV disease status after counseling regarding the potential impact of therapy on the fetus and infant after delivery. The use of prophylactic elective cesarean section before the onset of labor or rupture of the membranes to prevent vertical transmission of HIV infection from mother to fetus has been shown to reduce the transmission rate to 2% in infants of mothers taking zidovudine. There is limited information on the impact of elective cesarean section on transmission rates in infants of mothers on HAART or with viral loads less than 1000 copies/mL. However, with HAART therapy and undetectable viral loads (< 50 copies/mL), there may be no additional benefit of cesarean delivery since the calculated upper 95% confidence interval for transmission risk for vaginal delivery in such patients is < 2%. HIV-infected women should be advised not to breast-feed their infants.

ACOG committee opinion. Scheduled cesarean delivery and the prevention of vertical transmission of HIV infection. Number 234, May 2000. Committee on Obstetric Practice, Compendium of selected publications, American College of Obstetricians and Gynecologists, 2004.

Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States. <http://www.hivatis.org/Watts> DH: Management of human immunodeficiency virus in pregnancy. *N Engl J Med* 2002;346:1879. [\[PMID: 12063373\]](#)

Diabetes Mellitus

Pregnancy is associated with increased tissue resistance to insulin, resulting in increased levels of blood insulin as well as glucose and triglycerides. These changes are due to placental lactogen and elevated circulating estrogens and progesterone. Although pregnancy does not appear to alter the long-term consequences of diabetes, retinopathy and nephropathy may first appear or become worse during pregnancy. Debate continues over whether gestational diabetes are women whose glucose intolerance is solely a function of their pregnant compared with their nonpregnant state. Alternatively, pregnancy may merely serve to unmask an underlying propensity for glucose intolerance, which will be evident even in the nonpregnant state at some time in the future if not in the immediate postpartum period. However, goals for glycemic control during pregnancy are the same whether the diagnosis is made before or during the pregnancy.

Prepregnancy counseling and evaluation of diabetic women should include a complete chemistry panel, HbA_{1c} determination, 24-hour urine collection for total protein and creatinine clearance, funduscopic examination, and an ECG. Any medical problems should be addressed, and HbA_{1c} levels of less than 8% should be achieved before pregnancy. Euglycemia should be established before conception and maintained during pregnancy with daily home glucose monitoring by the patient. A well-planned dietary program is a key component, with an intake of 1800-2200 kcal/d divided into three meals and three snacks. Insulin is given subcutaneously in a split-dose regimen with frequent dosage adjustments. Patients taking oral agents prior to pregnancy should be switched to insulin. However, limited information suggests that agents such as glyburide may be safe and effective in pregnancy. The use of continuous insulin pump therapy has been found to be very useful during pregnancy in women with type 1 diabetes mellitus.

Congenital anomalies result from hyperglycemia during the first 4-8 weeks of pregnancy. They occur in 4-10% of diabetic pregnancies (two to three times the rate in nondiabetic pregnancies). Euglycemia in the early weeks of pregnancy, when organogenesis is occurring, reduces the rate of anomalies to near-normal levels. Even so, because few women with diabetes begin a rigorous program to achieve euglycemia until well after they have become pregnant, congenital anomalies are the principal cause of perinatal fetal deaths in diabetic pregnancies. All women with diabetes should receive counseling about pregnancy and, when the decision has been made to start a family, should receive prepregnancy management by physicians experienced in diabetic pregnancies.

Fasting and preprandial glucose values are lower during pregnancy in both diabetic and nondiabetic women. Euglycemia is considered to be 60-80 mg/dL while fasting and 30-45 minutes before meals and < 120 mg/dL 2 hours after meals. This is the target for good diabetic control during pregnancy. Glycated hemoglobin levels help determine the quality of glucose control both before and during pregnancy.

While perinatal problems for mother and baby are decreased by fastidious diabetic control, the incidence of hydramnios, preeclampsia-eclampsia, infections, and prematurity is increased even in carefully managed diabetic pregnancies. Diabetes is an inherently unstable disease characterized by fluctuations of blood glucose levels, particularly late in pregnancy. The risk of fetal demise in the third trimester (stillbirth) and neonatal death increases with the level of hyperglycemia. Consequently, pregnant women with diabetes must receive regular antepartum fetal testing (nonstress testing, contraction stress testing, biophysical profile) during the third trimester. The timing of delivery is dictated by the quality of diabetic control, the presence or absence of medical complications, and fetal status. The goal is to reach 39 weeks (38 completed weeks) and then proceed with delivery. Confirmation of lung maturity is necessary only for delivery prior to 39 weeks. Cesarean sections are performed for obstetric indications.

Because 15% of patients with gestational diabetes require insulin during pregnancy and because the infants of gestational diabetics have some risks similar to those of infants of diabetic mothers (particularly macrosomia), screening of women for glucose intolerance has been recommended between the 24th and 28th weeks of pregnancy (Table 18-3). Patients with gestational diabetes should be evaluated 6-8 weeks postpartum by a 2-hour oral glucose tolerance test (75 g glucose load).

ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 30, September 2001. Gestational diabetes. *Obstet Gynecol* 2001;98:525. [PMID: 11547793]

Gabbe SG et al: Benefits, risks, costs and patient satisfaction associated with insulin pump therapy for the pregnancy complicated by type 1 diabetes mellitus. *Am J Obstet Gynecol* 2000;182:1283. [PMID: 10871440]

Langer O et al: A comparison of glyburide and insulin in women with gestational diabetes mellitus. *N Engl J Med* 2000; 343:1134. [PMID: 11036118]

Temple R et al: Association between outcome of pregnancy and glycaemic control in early pregnancy in type I diabetics: population based study. *BMJ* 2002;325:1275. [PMID: 12458245]

Heart Disease

Overall, 5% of maternal deaths are due to heart disease. Most heart disease complicating pregnancy in the United States is congenital heart disease. Normal pregnancy causes a faster pulse, an increase of cardiac output of more than 30%, and a rise in plasma volume greater than red cell mass with relative hemodilution. Vital capacity and oxygen consumption rise only slightly.

For practical purposes, the functional capacity of the heart is the best single measurement of cardiopulmonary status.

FUNCTIONAL CARDIAC ASSESSMENT

- Class I Ordinary physical activity causes no discomfort (perinatal mortality rate about 5%).
- Class II Ordinary activity causes discomfort and slight disability (perinatal mortality rate 10-15%).
- Class III Less than ordinary activity causes discomfort or disability; patient is barely compensated (perinatal mortality rate about 35%).
- Class IV Patient decompensated; any physical activity causes acute distress (perinatal mortality rate over 50%).

In general, patients with class I or class II functional disability (80% of pregnant women with heart disease) do well obstetrically, with four-fifths of maternal deaths due to heart disease occurring in women with class III or class IV disability. Congestive failure is the usual cause of death. Most deaths occur in the early puerperium. Pregnancy is contraindicated in Eisenmenger's complex, in primary pulmonary hypertension, in severe mitral stenosis with secondary pulmonary hypertension, and in Marfan's syndrome, in which the aorta is prone to dissection and rupture. In addition, pregnancy is poorly tolerated in patients with aortic stenosis, aortic coarctation, tetralogy of Fallot, and active rheumatic carditis.

Therapeutic abortion and elective sterilization should be offered to patients with significant cardiac disease. Cesarean section should be performed only for obstetric indications. Women with valvular heart disease, mitral valve prolapse associated with mitral insufficiency, or idiopathic hypertrophic cardiomyopathy should receive appropriate antibiotic prophylaxis against infective endocarditis during labor and delivery or termination of pregnancy.

Lupton M et al: Cardiac disease in pregnancy. *Curr Opin Obstet Gynecol* 2002;14:137. [PMID: 11914690]

Sadler L et al: Pregnancy outcomes and cardiac complications in women with mechanical bioprosthetic and homograft valves. *Br J Obstet Gynaecol* 2000;107:245. [PMID: 10688509]

Peripartum Cardiomyopathy

Cardiac failure that develops during pregnancy or during the first 6 months postpartum in a woman without a history of heart disease and with no cause for heart failure other than pregnancy is termed peripartum cardiomyopathy. The incidence varies from 1:4000 to 1:1000. It is higher in Africa. It occurs more often in older women, those with twins, and in patients with pregnancy-induced

hypertension. The cause of peripartum cardiomyopathy is unknown. In patients who continue to have symptoms and signs of disease for more than 6 months postpartum, the mortality rate is high, and subsequent pregnancy is especially dangerous.

Symptoms of peripartum cardiomyopathy are those of congestive heart failure. An ECG may reveal tachycardia and atrial or ventricular arrhythmias. Death may occur as a result of arrhythmia or embolism. Autopsy usually reveals an enlarged, dilated heart, and mural thrombi (the source of pulmonary and systemic emboli) are often found.

The treatment of peripartum cardiomyopathy is that of congestive cardiomyopathy (see [Chapter 10](#)). Patients with persistent cardiomegaly or mural thrombi shown by echocardiography require anticoagulant therapy. The long-term prognosis in these patients depends on whether cardiomegaly resolves within 6 months after the onset of symptoms. If it does not resolve, the 5-year mortality rate is 6%. If cardiomegaly does not resolve and another pregnancy intervenes, cardiomyopathy recurs in 50% of cases, with a 19% mortality rate.

Pearson GD et al: Peripartum cardiomyopathy: National Heart Lung and Blood Institute and Office of Rare Disease (National Institutes of Health) workshop recommendations and review. JAMA 2000;283:1183. [\[PMID: 10703781\]](#)

Herpes Genitalis (See also [Chapter 6](#))

Infection of the lower genital tract by herpes simplex virus type 2 (HSV-2) is a common sexually transmitted disease of potential seriousness to pregnant women and their newborn infants. Although up to 20% of women in an obstetric practice may have antibodies to HSV-2, a history of the infection is unreliable and the incidence of neonatal infection is low (1:20,000-1:3000 live births). Most infected neonates are born to women with no symptoms, signs, or history of infection.

Women who have had *primary* herpes infection late in pregnancy are at high risk of shedding virus at delivery. Some authors suggest use of prophylactic acyclovir, 400 mg orally twice daily, to decrease the likelihood of active lesions at the time of labor and delivery.

Women with a history of *recurrent* genital herpes have a neonatal attack rate of 5% and should be followed by clinical observation and culture of any suspicious lesions. Since asymptomatic viral shedding is not predictable by antepartum cultures, current recommendations do not include routine cultures in individuals with a history of herpes without active disease. However, when labor begins, vulvar and cervical inspection and cultures should be performed, with prompt treatment of a newborn after a positive culture.

For treatment, see [Chapter 32](#). The use of acyclovir in pregnancy is acceptable when there is significant fetal or neonatal risk.

Cesarean section is indicated at the time of labor if there are prodromal symptoms, active genital lesions, or a positive cervical culture obtained within the preceding week.

ACOG Practice Bulletin. Management of herpes in pregnancy. Number 8 October 1999. Clinical management guidelines for obstetrician-gynecologists. Int J Gynaecol Obstet 2000; 68:165. [\[PMID: 10717827\]](#)

Sheffield JS et al: Acyclovir prophylaxis to prevent herpes simplex virus recurrence at delivery: a systematic review. Obstet Gynecol 2003;102:1396. [\[PMID: 14662233\]](#)

Hypertensive Disease

Hypertensive disease in women of childbearing age is usually essential hypertension, but secondary causes should be considered: coarctation of the aorta, pheochromocytoma, hyperaldosteronism, and renovascular and renal hypertension.

Preeclampsia is superimposed on 20% of pregnancies in hypertensive women and appears earlier, is more severe, and is more often associated with intrauterine growth retardation. It may be difficult to determine whether or not hypertension in a pregnant woman precedes or derives from the pregnancy if she is not examined until after the 20th week. Serum uric acid can help differentiate, since it is elevated with preeclampsia and generally normal in chronic hypertension unless the patient is receiving diuretics. If hypertension persists for 6-8 weeks postpartum, essential hypertension is likely.

Pregnant women with chronic hypertension require medication only if the diastolic pressure is sustained at or above 100 mm Hg. For initiation of treatment, methyldopa has the longest record of safety in a dosage of 250 mg orally twice daily, increasing in divided doses as needed to as much as 3 g daily. The goal is to keep the diastolic pressure between 80 mm Hg and 100 mm Hg.

If a hypertensive woman is being managed successfully by medical treatment when she registers for antenatal care, one may generally continue the antihypertensive medication. Diuretics may be continued in pregnancy. ACE inhibitors should be replaced with a drug of another class because of reports of fetal and neonatal renal failure with these compounds.

Use of antihypertensive medications in preeclampsia remains controversial. This should be attempted only with significant fetal prematurity, absence of fetal compromise, and close supervision of the patient.

Therapeutic abortion may be indicated in cases of severe hypertension during pregnancy. If pregnancy is allowed to continue, the risk to the fetus must be assessed periodically in anticipation of early delivery. An early second-trimester ultrasound examination will confirm the duration of pregnancy, and follow-up examinations after 28 weeks will evaluate intrauterine growth retardation.

Barrilleaux PS et al: Hypertension therapy during pregnancy. Clin Obstet Gynecol 2002;45:22. [\[PMID: 11862056\]](#)

Maternal Hepatitis B & C Carrier State

There are an estimated 200 million chronic carriers of hepatitis B virus worldwide. Among these people there is an increased incidence of chronic active hepatitis, cirrhosis, and hepatocellular carcinoma. The frequency of the hepatitis B carrier state varies from 1% in the United States and Western Europe to 35% in parts of Africa and Asia. All pregnant women should be screened for hepatitis B surface antigen (HBsAg). Transmission of the virus to the baby after delivery is likely if both surface antigen and e antigen are positive. Vertical transmission can be blocked by the immediate postdelivery administration to the newborn of 0.5 mL of hepatitis B immunoglobulin and hepatitis B vaccine intramuscularly. The vaccine dose is repeated at 1 and 6 months of age.

Hepatitis C virus infection is the most common chronic blood-borne infection in the United States. Risk factors for transmission

include blood transfusion, injecting drug use, employment in patient care or clinical laboratory work, exposure to a sex partner or household member who has had a history of hepatitis, exposure to multiple sex partners, and low socioeconomic level. The average rate of HCV infection among infants born to HCV-positive, HIV-negative women is 5-6%. However, the average infection rate increases to 14% when mothers are coinfecting with HCV and HIV. The principal factor associated with transmission is the presence of HCV RNA in the mother at the time of birth.

Roberts EA: Maternal-infant transmission of hepatitis C virus infection. *Hepatology* 2002;36(5 Suppl 1):S106. [\[PMID: 12407583\]](#)

Acute Fatty Liver of Pregnancy

Acute fatty liver of pregnancy is a disorder limited to the gravid state. It occurs in the third trimester of pregnancy and involves acute hepatic failure. With improved recognition and immediate delivery, the mortality range is now 20-30%. The disorder is usually seen after the 35th week of gestation and is more common in primigravidas and those with twins. The incidence is about 1:14,000 deliveries.

The cause of acute fatty liver of pregnancy is not known. Pathologic findings are unique to the disorder, with fatty engorgement of hepatocytes. Clinical onset is gradual, with flu-like symptoms that progress to the development of abdominal pain, jaundice, encephalopathy, disseminated intravascular coagulation, and death. On examination, the patient shows signs of hepatic failure.

Laboratory findings show marked elevation of alkaline phosphatase but only moderate elevations of ALT and AST. Prothrombin time and bilirubin are also elevated. The white blood cell count is elevated, and the platelet count is depressed. Hypoglycemia may be extreme.

The differential diagnosis is that of fulminant hepatitis. However, liver aminotransferases for fulminant hepatitis are higher (< 1000 units/mL) than those for acute fatty liver of pregnancy (usually < 500 units/mL). It is also important to review the appropriate history and perform the appropriate tests for toxins that cause liver failure. Preeclampsia may involve the liver but typically does not cause jaundice. The elevations in liver function tests in patients with preeclampsia usually do not reach the levels seen in patients with acute fatty liver of pregnancy.

Diagnosis of acute fatty liver of pregnancy mandates immediate delivery. Supportive care during labor includes administration of glucose, platelets, and fresh frozen plasma as needed. Vaginal delivery is preferred. Resolution of encephalopathy occurs over days, and supportive care with a low-protein diet is needed.

Recurrence rates for this liver disorder are unclear. Most authorities advise against subsequent pregnancy, but there have been reported cases of successful outcomes in later pregnancies.

Treem WR: Mitochondrial fatty acid oxidation and acute fatty liver of pregnancy. *Semin Gastrointest Dis* 2002;13:55. [\[PMID: 11944635\]](#)

Seizure Disorders

Epileptic women contemplating pregnancy who have not had a seizure for 5 years should consider a prepregnancy trial of withdrawal from treatment. Those with recurrent epilepsy should use a single drug with blood level monitoring. Trimethadione and valproate are contraindicated during pregnancy; phenytoin and carbamazepine may be teratogenic in the first trimester and should not be used unless absolutely necessary. There is limited information available on the safety of newer antiepilepsy drugs (eg, lamotrigine), and they should generally be avoided.

Phenobarbital is considered the drug of choice. Serum levels should be measured in each trimester and dosage adjustments made to keep serum levels in the low normal therapeutic range. Pregnant women taking phenobarbital and phenytoin should receive vitamin supplements, including folic acid and vitamin D, throughout pregnancy. Vitamin K, 10-20 mg/d, is administered during the last month to help prevent bleeding problems in the newborn, who is at risk of bleeding tendencies due to decreased levels of clotting factors. Such infants should receive an injection of vitamin K₁, 1 mg subcutaneously immediately after delivery, and should have clotting studies 2-4 hours later. Breast feeding is not contraindicated for infants of mothers taking antiseizure medications.

Syphilis, Gonorrhea, & *Chlamydia trachomatis* Infection (See also Chapters 33 and 34.)

These sexually transmitted diseases have significant consequences for mother and child. Untreated syphilis in pregnancy will cause late abortion, stillbirth, transplacental infection, and congenital syphilis. Gonorrhea will produce large-joint arthritis by hematogenous spread as well as ophthalmia neonatorum. Maternal chlamydial infections are largely asymptomatic but are manifested in the newborn by inclusion conjunctivitis and, at age 2-4 months, by pneumonia. The diagnosis of each can be reliably made by appropriate laboratory tests, which should be included in all prenatal care. The sexual partners of women with sexually transmitted diseases should be identified and treated also if that can be done.

Gene M et al: Syphilis in pregnancy. *Sex Transm Infect* 2000; 76:73. [\[PMID: 10858706\]](#)

Group B Streptococcal Infection

Group B streptococci frequently colonize the lower female genital tract, with an asymptomatic carriage rate in pregnancy of 5-30%. This rate depends on maternal age, gravidity, and geographic variation. Vaginal carriage is asymptomatic and intermittent, with spontaneous clearing in approximately 30% and recolonization in about 10% of women. Adverse perinatal outcomes associated with group B streptococcal colonization include urinary tract infection, intrauterine infection, premature rupture of membranes, preterm delivery, and postpartum endometritis.

Women with postpartum endometritis due to infection with group B streptococci, especially after cesarean section, develop fever, tachycardia, and abdominal distention, usually within 24 hours after delivery. Approximately 35% of these women are bacteremic.

Group B streptococcal infection is a common cause of neonatal sepsis. Transmission rates are high, yet the rate of neonatal sepsis is surprisingly low at less than 4:1000 live births. Unfortunately, the mortality rate associated with early-onset disease can be as high as 50% in premature infants and approaches 25% even in those at term. Moreover, these infections can contribute markedly to chronic morbidity, including mental retardation and neurologic disabilities. Late-onset disease develops through contact with hospital

nursery personnel. Up to 45% of these health care workers can carry the bacteria on their skin and transmit the infection to newborns.

CDC recommendations for screening for and prophylaxis of group B streptococcal colonization are set forth in this chapter in the section on tests and procedures.

Brozanski BS et al: Effect of a screening-based prevention policy on prevalence of early-onset group B streptococcal sepsis. *Obstet Gynecol* 2000;95:496. [\[PMID: 10725479\]](#)

Shrag SJ et al: A population-based comparison of strategies to prevent early-onset group B streptococcal disease in neonates. *N Engl J Med* 2002;347:233. [\[PMID: 12140298\]](#)

Varicella

Commonly known as chickenpox, varicella-zoster virus (VZV) infection has a fairly benign course when incurred during childhood but may result in serious illness in adults, particularly during pregnancy. Infection results in lifelong immunity. Approximately 95% of women born in the United States have VZV antibodies by the time they reach reproductive age. The incidence of VZV infection during pregnancy has been reported as up to 7:10,000.

The incubation period for this infection is 10-20 days. A primary infection follows and is characterized by a flu-like syndrome with malaise, fever, and development of a pruritic maculopapular rash on the trunk which becomes vesicular and then crusts. Pregnant women are prone to the development of VZV pneumonia, often a fulminant infection sometimes requiring respiratory support. After primary infection, the virus becomes latent, ascending to dorsal root ganglia. Subsequent reactivation can occur as zoster, often under circumstances of immunocompromise, though this is rare during pregnancy.

Two types of fetal infection have been documented. The first is congenital VZV syndrome, which typically occurs in 0.4-2% of fetuses exposed to primary VZV infection during the first trimester. Anomalies include limb and digit abnormalities, microphthalmos, and microcephaly.

Infection during the second and third trimesters is less threatening. Maternal IgG crosses the placenta, protecting the fetus. The only infants at risk for severe infection are those born after maternal viremia but before development of maternal protective antibody. Maternal infection manifesting 5 days before or after delivery is the time period arbitrarily determined to be most hazardous for transmission to the fetus.

Diagnosis is commonly made on clinical grounds. Laboratory verification of recent infection is made most often by antibody detection techniques, including ELISA, fluorescent antibody, and hemagglutination inhibition. Serum obtained by cordocentesis may be tested for VZV IgM to document fetal infection.

Varicella-zoster immune globulin (VZIG) has been shown to prevent or modify the symptoms of infection in some women. Treatment success depends on identification of susceptible women at or just following exposure. Women with a questionable or negative history of chickenpox should be checked for antibody, since the overwhelming majority will have been exposed previously. If the antibody is negative, VZIG (625 units intramuscularly) should be given within 96 hours after exposure. There are no known adverse effects of VZIG administration during pregnancy. Infants born within 5 days after onset of maternal infection should also receive VZIG (125 units).

Infected pregnant women should be closely observed and hospitalized at the earliest signs of pulmonary involvement. Intravenous acyclovir (10-15 mg/kg every 8 hours for 7-10 days) is recommended in the treatment of VZV pneumonia.

Harger JH et al: Frequency of congenital varicella syndrome in a prospective cohort of 347 pregnant women. *Obstet Gynecol* 2002;100:260. [\[PMID: 12151147\]](#)

Thyroid Disease

Thyrotoxicosis during pregnancy may result in fetal anomalies, late abortion, or preterm labor and fetal hyperthyroidism with goiter. Thyroid storm in late pregnancy or labor is a life-threatening emergency.

Radioactive isotope therapy must never be given during pregnancy. The thyroid inhibitor of choice is propylthiouracil, which acts to prevent further thyroxine formation by blocking iodination of tyrosine. There is a 2- to 3-week delay before the pretreatment hormone level begins to fall. The initial dose of propylthiouracil is 100-150 mg three times a day; the dose is lowered as the euthyroid state is approached. It is desirable to keep free T_4 in the high normal range during pregnancy. A maintenance dose of 100 mg/d minimizes the chance of fetal hypothyroidism and goiter.

Recurrent postpartum thyroiditis occurs 3-6 months after delivery. A hyperthyroid state of 1-3 months' duration is followed by hypothyroidism, sometimes misdiagnosed as depression. Thyroperoxidase antibodies and thyroglobulin antibodies are present. Recovery is spontaneous in over 90% of cases after 3-6 months.

Maternal hypothyroidism — even subclinical hypothyroidism manifested only by elevated levels of thyroid-stimulating hormone (TSH) — may adversely affect subsequent neuropsychologic development of the child. Mothers with known or suspected hypothyroidism should have the TSH level measured at the first prenatal visit. Replacement therapy with levothyroxine should be adjusted to maintain levels of TSH in the normal range.

Lazarus JH et al: Thyroid disease in relation to pregnancy: a decade of change. *Clin Endocrinol* 2000;53:265. [\[PMID: 10971442\]](#)

Tuberculosis

The diagnosis of tuberculosis in pregnancy is made by history taking, physical examination, and skin testing, with special attention to women from ethnic groups with a high prevalence of the disease (such as women from southeast Asia). Chest films should not be obtained as a routine screening measure in pregnancy but should be used only in patients with a skin test conversion or with suggestive findings in the history and physical examination. Abdominal shielding must be used if a chest film is obtained.

If adequately treated, tuberculosis in pregnancy has an excellent prognosis. There is no increase in spontaneous abortion, fetal problems, or congenital anomalies.

Treatment is with isoniazid and ethambutol or isoniazid and rifampin (see Chapters 9 and 33). Because isoniazid therapy may result in vitamin B₆ deficiency, a supplement of 50 mg/d of vitamin B₆ should be given simultaneously. Streptomycin, ethionamide, and most other antituberculous drugs should be avoided in pregnancy.

Urinary Tract Infection

The urinary tract is especially vulnerable to infections during pregnancy because the altered secretions of steroid sex hormones and the pressure exerted by the gravid uterus upon the ureters and bladder cause hypotonia and congestion and predispose to urinary stasis. Labor and delivery and urinary retention postpartum also may initiate or aggravate infection. *Escherichia coli* is the offending organism in over two-thirds of cases.

From 2% to 8% of pregnant women have asymptomatic bacteriuria, which some believe to be associated with an increased risk of prematurity. It is estimated that 20-40% of these women will develop pyelonephritis during pregnancy if untreated.

A first-trimester urine culture is indicated in women with a history of recurrent or recent episodes of urinary tract infection. If the culture is positive, treatment should be initiated as a prophylactic measure. Nitrofurantoin (100 mg twice daily), ampicillin (500 mg four times daily), and cephalexin (500 mg four times daily) are acceptable medications for 3-7 days. Sulfonamides should not be given in the third trimester because they interfere with bilirubin binding and thus impose a risk of neonatal hyperbilirubinemia and kernicterus. Fluoroquinolones are also contraindicated because of their potential teratogenic effects on fetal cartilage and bone. If bacteriuria returns, suppressive medication (one daily dose of an appropriate antibiotic) for the remainder of the pregnancy is indicated. Acute pyelonephritis requires hospitalization for intravenous administration of antibiotics until the patient is afebrile; this is followed by a full course of oral antibiotics.

Delzell JE Jr et al: Urinary tract infections during pregnancy. Am Fam Physician 2000;61:713. [\[PMID: 10695584\]](#)

SURGICAL COMPLICATIONS DURING PREGNANCY

Introduction

Elective major surgery should be avoided during pregnancy. Normal uncomplicated pregnancy does not alter operative risk except as it may interfere with the diagnosis of abdominal disorders and increase the technical problems of intra-abdominal surgery. Abortion is not a serious hazard after operation unless peritoneal sepsis or other significant complications occur. During the first trimester, congenital anomalies may be induced in the developing fetus by hypoxia. Thus, the second trimester is usually the optimal time for operative procedures.

Appendicitis

Appendicitis occurs in about one of 1500 pregnancies. Diagnosis may be difficult, since the appendix is carried high and to the right, away from McBurney's point, as the uterus enlarges, and localization of pain does not always occur. Nausea, vomiting, fever, and leukocytosis occur regularly. Any right-sided abdominal pain associated with these symptoms should arouse suspicion. In at least 20% of obstetric patients, the diagnosis of appendicitis is not made until rupture occurs and peritonitis has become established. Such a delay may lead to premature labor or abortion. With early diagnosis and appendectomy, the prognosis is good for mother and baby.

Mourad J et al: Appendicitis in pregnancy: new information that contradicts long-held clinical beliefs. Am J Obstet Gynecol 2000;182:1027. [\[PMID: 10819817\]](#)

Sharp HT: The acute abdomen during pregnancy. Clin Obstet Gynecol 2002;45:405. [\[PMID: 12048399\]](#)

Carcinoma of the Breast

Cancer of the breast (see also [Chapter 16](#)) is diagnosed approximately once in 3500 pregnancies. Pregnancy may accelerate the growth of cancer of the breast, and delay in diagnosis affects the outcome of treatment. Inflammatory carcinoma is an extremely virulent type of breast cancer that occurs most commonly during lactation. Prepregnancy mammography should be encouraged for women over age 35 who are anticipating a pregnancy.

Breast enlargement during pregnancy obscures parenchymal masses, and breast tissue hyperplasia decreases the accuracy of mammography. Any discrete mass should be evaluated by aspiration to verify its cystic structure, with fine-needle biopsy if it is solid. A definitive diagnosis may require excisional biopsy under local anesthesia. If breast biopsy confirms the diagnosis of cancer, surgery should be done regardless of the stage of the pregnancy. If spread to the regional glands has occurred, irradiation or chemotherapy should be considered. Under these circumstances, the alternatives are termination of an early pregnancy or delay of therapy for fetal maturation.

Cholelithiasis, Cholecystitis, & Idiopathic Cholestasis of Pregnancy

Severe cholelithiasis and cholecystitis are not uncommon during pregnancy. When they do occur, it is usually in late pregnancy or in the puerperium. About 90% of patients with cholecystitis have gallstones; 90% of stones will be visualized by ultrasonography. Symptomatic relief may be all that is required.

Conventional gallbladder surgery in pregnant women should be attempted only in complicated cases (eg, obstruction), because it may increase the perinatal mortality rate to about 15%. Cholecystostomy and lithotomy may be all that is feasible during advanced pregnancy, cholecystectomy being deferred until after delivery. On the other hand, withholding surgery may result in necrosis and perforation of the gallbladder and peritonitis. Cholangitis due to impacted common duct stone requires surgical removal of gallstones and establishment of biliary drainage. Endoscopic retrograde cholangiopancreatography and endoscopic retrograde sphincterotomy can be performed safely in pregnant women if precautions are taken to minimize exposure to radiation. In the early to mid second trimester, laparoscopic cholecystectomy can be performed with minimal maternal morbidity and no fetal mortality.

Idiopathic cholestasis of pregnancy is due to a hereditary metabolic (hepatic) deficiency aggravated by the high estrogen levels of pregnancy. It causes intrahepatic biliary obstruction of varying degrees. The rise in bile acids is sufficient in the third trimester to cause severe, intractable, generalized itching and sometimes clinical jaundice. There may be mild elevations in blood bilirubin and alkaline phosphatase levels. The fetus is also threatened by this condition. An increased incidence of preterm delivery has been reported as well as unexplained intrauterine fetal demise. For this reason, antenatal surveillance of the fetus is mandatory in patients with this diagnosis. Resins such as cholestyramine (4 g three times a day) absorb bile acids in the large bowel and relieve pruritus but are difficult to take and may cause constipation. Their use requires vitamin K supplementation. Limited but very encouraging experience has been reported with ursodeoxycholic acid, 16 mg/kg/d orally for 3 weeks, or dexamethasone, 12 mg/d orally for 7 days. The disorder is relieved once the infant has been delivered, but it recurs in subsequent pregnancies and sometimes with the use of oral contraceptives.

Ovarian Tumors

The most common adnexal mass in early pregnancy is the corpus luteum, which may become cystic and enlarge to 6 cm in diameter. Any persistent mass over 6 cm should be evaluated by ultrasound examination; unilocular cysts are likely to be corpus luteum cysts, whereas septated or semisolid tumors are likely to be neoplasms. The incidence of malignancy in ovarian masses over 6 cm in diameter is 2.5%. Ovarian tumors may undergo torsion and cause abdominal pain and nausea and vomiting and must be differentiated from appendicitis, other bowel disease, and ectopic pregnancy. Patients with suspected ovarian cancer should be referred to a tertiary perinatal center to determine whether the pregnancy can progress to fetal viability or whether treatment should be instituted without delay.

PREVENTION OF HEMOLYTIC DISEASE OF THE NEWBORN (Erythroblastosis Fetalis)

The antibody anti-Rh₀(D) is responsible for most severe instances of hemolytic disease of the newborn (erythroblastosis fetalis). About 15% of whites and much lower proportions of blacks and Asians are Rh₀(D)-negative. If an Rh₀(D)-negative woman carries an Rh₀(D)-positive fetus, she may develop antibodies against Rh₀(D) when fetal red cells enter her circulation during small fetomaternal bleeding episodes in the early third trimester or during delivery, abortion, ectopic pregnancy, abruptio placentae, or other antepartum bleeding problems. This antibody, once produced, remains in the woman's circulation and poses the threat of hemolytic disease for subsequent Rh-positive fetuses.

Passive immunization against hemolytic disease of the newborn is achieved with Rh₀(D) immune globulin, a purified concentrate of antibodies against Rh₀(D) antigen. The Rh₀(D) immune globulin (one vial of 300 ug intramuscularly) is given to the mother within 72 hours after delivery (or spontaneous or induced abortion or ectopic pregnancy). The antibodies in the immune globulin destroy fetal Rh-positive cells so that the mother will not produce anti-Rh₀(D). During her next Rh-positive gestation, erythroblastosis will be prevented. An additional safety measure is the administration of the immune globulin at the 28th week of pregnancy. The passive antibody titer that results is too low to significantly affect an Rh-positive fetus. The maternal clearance of the globulin is slow enough that protection will continue for 12 weeks.

Hemolytic disease of varying degrees, from mild to serious, continues to occur in association with Rh subgroups (C, c, or E) or Kell, Kidd, and other factors. Therefore, the presence of atypical antibodies should be checked in the third trimester of all pregnancies.

Moise KJ Jr: Management of rhesus alloimmunization in pregnancy. *Obstet Gynecol* 2002;100:600. [\[PMID: 12220785\]](#)

Prevention of Rh D alloimmunization. Clinical management guidelines for obstetrician-gynecologists. ACOG Practice Bulletin No. 4, 1999. *Int J Gynaecol Obstet* 1999;66:63. [\[PMID: 10458556\]](#)

PREVENTION OF PRETERM (PREMATURE) LABOR

Preterm (premature) labor is labor that begins before the 37th week of pregnancy; it is responsible for 85% of neonatal illnesses and deaths. The onset of labor is a result of a complex sequence of biologic events involving regulatory factors that are still poorly understood. Significant risk factors for the onset of preterm labor are a past history of preterm delivery, premature rupture of the membranes, urinary tract infection, exposure to diethylstilbestrol, multiple gestation, and abdominal or cervical surgery. In high-risk women (prior preterm birth), ultrasound measurement of cervical length (< 25 mm) in the second trimester may also identify a significant risk.

Low rates of preterm delivery are associated with success in educating patients to identify regular, frequent uterine contractions and in alerting medical and nursing staff to evaluate these patients early and initiate treatment if cervical changes can be identified. Distinguishing true from false labor in patients with a history of previous preterm births can be facilitated by the use of fetal fibronectin measurement in cervicovaginal specimens. This ubiquitous protein can be released by several different stimuli. Its absence (< 50 ng/mL) in the face of uterine contractions in a patient with a previous preterm birth has a negative predictive value of 93-97% for delivery within 7-14 days. Despite initial promising findings, several prospective randomized controlled trials have failed to demonstrate a benefit of home uterine activity monitoring in preventing preterm birth. On the other hand, a recent study has suggested that weekly injections of 17a-hydroxyprogesterone caproate from 16 to 36 weeks of gestation in women with a history of preterm delivery can substantially reduce the rate of recurrent preterm birth.

In more acute situations, intravenous magnesium sulfate is effective, as are intravenous β -adrenergic drugs. Magnesium sulfate is given as a 4- or 6-g bolus followed by a continuous infusion of 2-3 g/h. The rate may be increased by 1 g/h every 30 minutes to 2 hours until contractions cease or a blood magnesium concentration of 6-8 mg/dL is reached. Magnesium levels are determined every 4-6 hours to monitor the therapeutic blood level. After contractions have ceased for 12-24 hours, magnesium can be stopped and the situation reassessed.

Uterine smooth muscle is largely under sympathetic nervous system control, and stimulation of β_2 -adrenergic receptors relaxes the myometrium. Consequently, inhibition of uterine contractility often can be accomplished by the administration of β -adrenergic drugs such as ritodrine or terbutaline. Alternatively, use of an oxytocin receptor antagonist might also be expected to inhibit uterine contractility. However, trials of one such antagonist, atosiban, have shown only minimal efficacy.

Ritodrine is no longer manufactured. Terbutaline can be given as an intravenous infusion starting at 2.5 ug/min and increased by 2.5 ug/min every 20 minutes until contractions cease or to a maximum dose of 20 ug/min. Terbutaline can also be administered as subcutaneous injections of 250 ug every 3 hours. Oral terbutaline therapy following parenteral treatment is often elected and consists

of giving 2.5-5 mg every 2-4 hours. With terbutaline, a dose-related elevation of heart rate of 20-40 beats/min may occur. An increase of systolic blood pressure up to 10 mm Hg is likely, and the diastolic pressure may fall 10-15 mm Hg during the infusion. Nifedipine has also been used in doses of 10-20 mg orally every 4-6 hours. Blood pressure may fall with nifedipine, but cardiac output increases considerably. Transient elevation of blood glucose, insulin, and fatty acids together with slight reduction of serum potassium have been reported with β -adrenergic drugs. Fetal tachycardia may be slight or absent. No drug-related perinatal deaths have been reported with β -agonists. Maternal side effects requiring dose limitation are tachycardia ($\approx$ 120 beats/min), palpitations, and nervousness. Fluids should be limited to 2500 mL/24 h. Serious side effects (pulmonary edema, chest pain with or without electrocardiographic changes) are often idiosyncratic, not dose-related, and warrant termination of therapy.

One must identify cases in which untimely delivery is the sole threat to the life or health of the infant. An effort should be made to eliminate (1) maternal conditions that compromise the intrauterine environment and make premature birth the lesser risk, eg, preeclampsia-eclampsia; (2) fetal conditions that either are helped by early delivery or render attempts to stop premature labor meaningless, eg, severe erythroblastosis fetalis; and (3) clinical situations in which it is likely that an attempt to stop labor will be futile, eg, ruptured membranes with chorioamnionitis, cervix fully effaced and dilated more than 3 cm, or strong labor in progress.

In pregnancies of less than 34 weeks' duration, betamethasone, 12 mg intramuscularly, or dexamethasone, 16 mg intramuscularly, repeated in 12-24 hours, is administered to hasten fetal lung maturation and permit delivery 48 hours after initial treatment when further prolongation of pregnancy is contraindicated.

ACOG practice bulletin. Assessment of risk factors for preterm birth. Clinical management guidelines for obstetrician-gynecologists. Number 31, October 2001. *Obstet Gynecol* 2001;98:709. [\[PMID: 11592272\]](#)

Goldenberg RL: The management of preterm labor. *Obstet Gynecol* 2002;100(5 Part 1):1020. [\[PMID: 12423870\]](#)

Meis PJ et al: Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. *N Engl J Med* 2003; 348:2379. [\[PMID: 12802023\]](#)

LACTATION

Introduction

Breast feeding should be encouraged by education throughout pregnancy and the puerperium. Mothers should be told the benefits of breast feeding — it is emotionally satisfying, promotes mother-infant bonding, is economical, and gives significant immunity to the infant. The period of amenorrhea associated with frequent and consistent breast feeding provides some (though not completely reliable) birth control until menstruation begins at 6-12 months postpartum or the intensity of breast feeding diminishes. If the mother must return to work, even a brief period of nursing is beneficial. Transfer of immunoglobulins in colostrum and breast milk protects the infant against many systemic and enteric infections. Macrophages and lymphocytes transferred to the infant from breast milk play an immunoprotective role. The intestinal flora of breast-fed infants inhibits the growth of pathogens. Breast-fed infants have fewer bacterial and viral infections, less severe diarrhea, and fewer allergy problems than bottle-fed infants and are less apt to be obese as children and in adult life.

Frequent breast feeding on an infant-demand schedule enhances milk flow and successful breast feeding. Mothers breast feeding for the first time need help and encouragement from providers, nurses, and other nursing mothers. Milk supply can be increased by increased suckling and increased rest.

Nursing mothers should have a fluid intake of over 2 L/d. The United States RDA calls for 21 g of extra protein (over the 44 g/d baseline for an adult woman) and 550 extra kcal/d in the first 6 months of nursing. Calcium intake should be 1200 mg/d. Continuation of a prenatal vitamin and mineral supplement is wise. Strict vegetarians who eschew both milk and eggs should always take vitamin B₁₂ supplements during pregnancy and lactation.

Effects of Drugs in a Nursing Mother

Drugs taken by a nursing mother may accumulate in milk and be transmitted to the infant ([Table 18-4](#)). The amount of drug entering the milk depends on the drug's lipid solubility, mechanism of transport, and degree of ionization.

Suppression of Lactation

A. Mechanical Suppression

The simplest and safest method of suppressing lactation after it has started is to gradually transfer the baby to a bottle or a cup over a 3-week period. Milk supply will decrease with decreased demand, and minimal discomfort ensues. If nursing must be stopped abruptly, the mother should avoid nipple stimulation, refrain from expressing milk, and use a snug brassiere. Ice packs and analgesics can be helpful. If suppression is desired before nursing has begun, use this same technique. Engorgement will gradually recede over a 2- to 3-day period.

B. Hormonal Suppression

Oral and long-acting injections of hormonal preparations were used at one time to suppress lactation. Because of their questionable efficacy and particularly because of associated side effects such as thromboembolic episodes and hair growth, their use for this purpose has been abandoned. Similarly, lactation suppression with bromocriptine is to be avoided because of reports of severe hypertension, seizures, strokes, and myocardial infarctions associated with its use.

Itto S: Drug therapy for breast-feeding women. *N Engl J Med* 2000;343:118. [\[PMID: 10891521\]](#)

Zembo CT: Breastfeeding. *Obstet Gynecol Clin North Am* 2002; 29:51. [\[PMID: 11892874\]](#)

PUERPERAL MASTITIS (See also [Chapter 16](#))

Postpartum mastitis occurs sporadically in nursing mothers shortly after they return home, or it may occur in epidemic form in the hospital. *Staphylococcus aureus* is usually the causative agent. Inflammation is generally unilateral, and women nursing for the first

time are more often affected. Rarely, inflammatory carcinoma of the breast can be mistaken for puerperal mastitis.

Mastitis frequently begins within 3 months after delivery and may start with a sore or fissured nipple. There is obvious cellulitis in an area of breast tissue, with redness, tenderness, local warmth, and fever. Treatment consists of antibiotics effective against penicillin-resistant staphylococci (dicloxacillin or a cephalosporin, 500 mg orally every 6 hours for 5-7 days) and regular emptying of the breast by nursing followed by expression of any remaining milk by hand or with a mechanical suction device.

If the mother begins antibiotic therapy before suppuration begins, infection can usually be controlled in 24 hours. If delay is permitted, breast abscess can result. Incision and drainage are required for abscess formation. Despite puerperal mastitis, the baby usually thrives without prophylactic antimicrobial therapy.

- **Location In Book:**

- CURRENT MEDICAL DIAGNOSIS & TREATMENT - 44th Ed. (2005)
18. Obstetrics - *William R. Crombleholme, MD*
DIAGNOSIS & DIFFERENTIAL DIAGNOSIS OF PREGNANCY

Table 18-1. Common drugs that are teratogenic or fetotoxic.¹

ACE² inhibitors
Alcohol
Amantadine
Aminopterin
Androgens
Anticonvulsants
Aminoglutethimide
Carbamazepine
Ethotoin
Phenytoin
Valproic acid
Aspirin and other salicylates (third trimester)
Benzodiazepines
Carbarsone (amebicide)
Chloramphenicol (third trimester)
Thalidomide
Cyclophosphamide
Diazoxide
Diethylstilbestrol
Disulfiram
Ergotamine
Estrogens
Griseofulvin
Hypoglycemics, oral
Isotretinoin
Lithium
Methotrexate
Misoprostol
NSAIDs³ (third trimester)
Opioids (prolonged use)
Progestins
Radioiodine (antithyroid)
Reserpine
Ribavirin
Sulfonamides (third trimester)
Tetracycline (third trimester)
Tobacco smoking
Trimethoprim (third trimester)
Warfarin and other coumarin anticoagulants

¹Many other drugs are also contraindicated during pregnancy. Evaluate any drug for its need versus its potential adverse effects. Further information can be obtained from the manufacturer or from any of several teratogenic registries around the country.

²ACE = angiotensin-converting enzyme.

³NSAIDs = nonsteroidal anti-inflammatory drugs.

• **Location In Book:**

- CURRENT MEDICAL DIAGNOSIS & TREATMENT - 44th Ed. (2005)
18. Obstetrics - *William R. Crombleholme, MD*
TABLES
Table 18-1. Common drugs that are teratogenic or fetotoxic.

Table 18-2. Indicators of mild to moderate versus severe preeclampsia-eclampsia.

Site	Indicator	Mild to Moderate	Severe
Central nervous system	Symptoms and signs	Hyperreflexia Headache	Seizures Blurred vision Scotomas Headache Clonus Irritability
Kidney	Proteinuria	0.3-5 g/24 h	> 5 g/24 h or catheterized urine with 4+ protein
	Urinary output	> 20-30 mL/h	< 20-30 mL/h
Liver	AST, ALT, LDH	Normal	Elevated LFTs Epigastric pain Ruptured liver
Hematologic	Platelets	> 100,000/uL	< 100,000/uL
	Hemoglobin	Normal range	Elevated
Vascular	Blood pressure	< 160/110 mm Hg	>160/110 mm Hg
	Retina	Arteriolar spasm	Retinal hemorrhages
Fetal- placental unit	Growth retardation	Absent	Present
	Oligohydramnios	May be present	Present
	Fetal distress	Absent	Present

Key: AST = aspartate aminotransferase; ALT = alanine aminotransferase; LDH = lactate dehydrogenase; LFTs = liver function tests.

- **Location In Book:**

- CURRENT MEDICAL DIAGNOSIS & TREATMENT - 44th Ed. (2005)

18. Obstetrics - *William R. Crombleholme, MD*

TABLES

Table 18-2. Indicators of mild to moderate versus severe preeclampsia-eclampsia.

Table 18-3. Screening and diagnostic criteria for gestational diabetes mellitus.

Screening for gestational diabetes mellitus

1. 50-g oral glucose load, administered between the 24th and 28th weeks, without regard to time of day or time of last meal. Universal blood glucose screening is indicated for patients who are of Hispanic, African, Native American, South or East Asian, Pacific Island, or Indigenous Australian ancestry. Other patients who have no known diabetes in first-degree relatives, are under 25 years of age, have normal weight before pregnancy, and have no history of abnormal glucose metabolism or poor obstetric outcome do not require routine screening.
2. Venous plasma glucose measure 1 hour later.
3. Value of 130 mg/dL (7.2 mmol/L) or above in venous plasma indicates the need for a full diagnostic glucose tolerance test.

Diagnosis of gestational diabetes mellitus

1. 100-g oral glucose load, administered in the morning after overnight fast lasting at least 8 hours but not more than 14 hours, and following at least 3 days of unrestricted diet (< 150 g carbohydrate) and physical activity.
2. Venous plasma glucose is measured fasting and at 1, 2, and 3 hours. Subject should remain seated and should not smoke throughout the test.
3. Two or more of the following venous plasma concentrations must be equaled or exceeded for a diagnosis of gestational diabetes: fasting, 95 mg/dL (5.3 mmol/L); 1 hour, 180 mg/dL (10 mmol/L); 2 hours, 155 mg/dL (8.6 mmol/L); 3 hours, 140 mg/dL (7.8 mmol/L).

• **Location In Book:**

- CURRENT MEDICAL DIAGNOSIS & TREATMENT - 44th Ed. (2005)
 - 18. Obstetrics - *William R. Crombleholme, MD*
 - TABLES
 - Table 18-3. Screening and diagnostic criteria for gestational diabetes mellitus.

Table 18-4. Drugs and substances that require a careful assessment of risk before they are prescribed for breast-feeding women.¹

Category	Specific Drugs or Compounds	Management Plan and Rationale
Analgesic drugs	Meperidine, oxycodone	Use alternatives to meperidine and oxycodone. Breast-fed infants whose mothers were receiving meperidine had a higher risk of neurobehavioral depression than breast-fed infants whose mothers were receiving morphine. In breast-fed infants, the level of exposure to oxycodone may reach 10% of the therapeutic dose. For potent analgesia, morphine may be given cautiously. Acetaminophen and nonsteroidal anti-inflammatory drugs are safe.
Antiarthritis drugs	Gold salts, methotrexate, high-dose aspirin	Consider alternatives to gold therapy. Although the bioavailability of elemental gold is unknown, a small amount is excreted in breast milk for a prolonged period. Therefore, the total amount of elemental gold that an infant could ingest may be substantial. No toxicity has been reported. Consider alternatives to methotrexate therapy, although low-dose methotrexate therapy for breast-feeding women with rheumatic diseases had lower risks of adverse effects in their infants than did anticancer chemotherapy. High-dose aspirin should be used with caution, since there is a case report of metabolic acidosis in a breast-fed infant whose mother was receiving high-dose therapy. Although the risk seems small, the infant's condition should be monitored clinically if the mother is receiving long-term therapy with high-dose aspirin.
Anticoagulant drugs	Phenindione ²	Use alternatives to phenindione. Currently available vitamin K antagonists such as warfarin and acenocoumarol are considered safe, as is heparin.
Antidepressant drugs and lithium	Fluoxetine, doxepin, lithium ²	Use fluoxetine, doxepin, and lithium with caution. Although the concentrations of these drugs in breast milk are low, colic (with fluoxetine) and sedation (with doxepin) have been reported in exposed infants. Near-therapeutic plasma concentrations of lithium were reported in an infant exposed to the drug in utero and through breast-feeding. The incidence of these adverse events is unknown.
Antiepileptic drugs	Phenobarbital, ethosuximide, primidone	In breast-fed infants, the level of exposure to phenobarbital, ethosuximide, and primidone may exceed 10% of the weight-adjusted therapeutic dose. Consider alternatives such as carbamazepine, phenytoin, and valproic acid.
Antimicrobial drugs	Chloramphenicol, tetracycline	Use alternatives to chloramphenicol and tetracycline. Idiosyncratic aplastic anemia is a possibility among breast-fed infants whose mothers are receiving chloramphenicol. Although tetracycline-induced discoloration of the teeth of breast-fed infants has not been reported, the potential risk of this event needs to be clearly communicated to lactating women.
Anticancer drugs	All (eg, cyclophosphamide, ² methotrexate, ² doxorubicin ²)	Because of their potent pharmacologic effects, cytotoxic drugs should not be given to breast-feeding women.
Anxiolytic drugs	Diazepam, alprazolam	Avoid long-term use of diazepam and alprazolam in breast-feeding women. Intermittent use poses little risk to their infants, but regular use may result in the accumulation of the drug and its metabolites in the infants. Lethargy and poor weight gain have been reported in an infant exposed to diazepam in breast milk, and the withdrawal syndrome was reported in a breast-fed infant after the mother discontinued alprazolam.
Cardiovascular and antihypertensive drugs	Acebutolol, amiodarone, atenolol, nadolol, sotalol	The use of acebutolol, amiodarone, atenolol, nadolol, and sotalol by breast-feeding women may cause relatively high levels of exposure among their infants, and these agents should therefore be used with caution. The two β -adrenergic antagonists propranolol and labetalol are considered safe.
Endocrine drugs and hormones	Estrogens, bromocriptine ²	Estrogens and bromocriptine may suppress milk production. Oral contraceptives containing little or no estrogen have smaller risk than formulations with higher concentrations of estrogen. Nevertheless, caution should be exercised in their use.
Immunosuppressive drugs	Cyclosporine, ² azathioprine	Maternal plasma concentrations of cyclosporine and azathioprine should be monitored. In nine reported cases in breast-fed infants who were exposed to azathioprine in breast milk, no obvious adverse effects were noted.
Respiratory drugs	Theophylline	Theophylline should be used with caution. When the mother's doses are high, the levels of exposure in the infant may be substantial (ie, 20% of the therapeutic dose).
Radioactive compounds	All	Breast feeding should be stopped until the level of radioactivity in milk has returned to the background level.

Drugs of abuse	All	The use of drugs of abuse precludes breast feeding; cocaine-induced toxicity has been reported among breast-fed infants whose mothers abused cocaine. Methadone, used for the treatment of addiction, is safe for infants of breast-feeding women, at doses of up to 80 mg per day. Buprenorphine may be a safer alternative to methadone.
Nonmedicinal substances	Ethanol, caffeine, nicotine	In order to avoid exposure of the infant to ethanol, the mother should not consume alcohol or should consume no more than one drink 2 to 3 hours before breast feeding. The ingestion of moderate amounts of caffeine should be safe. Because of the effects of second-hand smoke and the fact that nicotine is excreted in breast milk, smoking is contraindicated in breast-feeding women.
Miscellaneous compounds	Iodides and iodine, ergotamine, ² ergonovine	Use alternatives to iodine-containing antiseptic agents. Ergotamine and ergonovine may suppress prolactin secretion in breast-feeding women. However, the use of methylergonovine to stimulate uterine involution is considered safe in breast-feeding women.

¹Data modified from Ito S: Drug therapy for breast-feeding women. N Engl J Med 2000;343:120. Drugs for which there is no information are not included, though a careful risk assessment is necessary before such drugs are prescribed.

²The use of this drug or these drugs by breast-feeding women is contraindicated according to the American Academy of Pediatrics.

- **Location In Book:**

- CURRENT MEDICAL DIAGNOSIS & TREATMENT - 44th Ed. (2005)

18. Obstetrics - *William R. Crombleholme, MD*

TABLES

Table 18-4. Drugs and substances that require a careful assessment of risk before they are prescribed for breast-feeding women.